Efficiency in Lung Transplant Allocation Strategies

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ABSTRACT

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Currently in the United States, lungs are allocated to transplant candidates based on the Lung Allocation Score (LAS). The LAS is an empirically derived score aimed at increasing total life span pre- and post-transplantation, for patients on lung transplant waiting lists. The goal here is to develop efficient allocation strategies in the context of lung transplantation.

In this study, patient and organ arrivals to the waiting list are modeled as independent homogeneous Poisson processes. Patients' health status prior to allocations are modeled as evolving according to independent and identically distributed finite-state inhomogeneous Markov processes, in which death is treated as an absorbing state. The expected post-transplantation residual life is modeled as depending on time on the waiting list and on current health status. For allocation strategies satisfying certain minimal fairness requirements, the long-term limit of expected average total life exists, and is used as the standard for comparing allocation strategies.

Via the Hamilton-Jacobi-Bellman equations, upper bounds as a function of the ratio of organ arrival rate to the patient arrival rate for the long-term expected average total life are derived, and corresponding to each upper bound is an allocable set of (state, time) pairs at which patients would be optimally transplanted. As availability of organs increases, the allocable set expands monotonically, and ranking members of the waiting list according to the availability at which they enter the allocable set provides an allocation strategy that

leads to long-term expected average total life close to the upper bound.

Simulation studies are conducted with model parameters estimated from national lung transplantation data from United Network for Organ Sharing (UNOS). Results suggest that compared to the LAS, the proposed allocation strategy could provide a 7% increase in average total life.

Table of Contents

List of Figures	iii
List of Tables	iv
1 Introduction	1
1.1 Waiting Lists for Organ Transplantation	1
1.2 Standards for Comparing Allocation Rules	2
1.3 Previous Studies on Optimal Organ Allocation	4
1.4 Modeling Issues for Lung Transplantation Waiting Lists	6
1.5 Current Lung Allocation Strategies	7
1.6 Proposed Model and Overview of Results	8
2 Notation	11
2.1 Modeling the Waiting List	11
2.2 Fair Allocation Rules	15
2.3 Long-term Average Total Life as the Standard	16
3 The Optimization Problem	20
3.1 Long-term Average Occupancy	21
3.2 Limiting Transplantation Rate	28
3.3 Long-term Average Life	34
3.4 Constraints on the Transplantation Rate	35

4	Solution to the Optimization Problem	38
4.1	The Primal and the Dual Problems	39
4.2	Optimal Transplantation Rate	41
4.3	Optimal Transplantation Rate in Discrete Time	49
5	The Proposed Allocation Strategy	56
5.1	Priority Ranking for Transplantation	57
5.2	Proof of the Monotonicities	58
6	Comparison of Allocation Strategies	64
7	Discussion	70
	Bibliography	73
	Appendices	79
A	Tables and Graphs	80
B	Properties of the Waiting List Process	86
C	List of Symbols	99

List of Figures

6.1	Proposed strategy (left) vs. LAS (right) in 90-day periods	67
6.2	Refined LAS (left) vs. LAS (right) in 90-day periods	68
6.3	Simulation Results	69
A.1	The Proposed Strategy	85
A.2	The LAS	85
A.3	The Refined LAS	85

List of Tables

6.1	Comparison of Allocation Strategies	69
A.1	Coefficient Estimates for Time-on-Waiting-List Hazard for Death	80
A.2	Coefficient Estimates for Post-Transplantation Hazard for Death	83
A.3	Definition of Patients' Health States in Terms of (S_{wl}, S_{μ})	85

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*To Prof. Daniel Rabinowitz,
who is ~~never~~ happy with this dissertation.
always*

Chapter 1

Introduction

Lung transplantation is the preferred treatment, and sometimes the only possible treatment, in severe lung disease. There are not enough organs available to meet the need for transplantation, however, so patients with lung diseases are placed on waiting lists. Allocation rules are used to determine which patient on a waiting list receives a transplantation when a lung becomes available. Given a standard for comparing different allocation rules, and given a model for the waiting list process, a question arises: what allocation rule is optimal?

1.1 Waiting Lists for Organ Transplantation

This section provides an overview of issues that arise in the modeling of waiting lists in organ transplantation generally. In subsequent sections, the exposition will focus more narrowly on lung transplantation waiting lists and the particular family of models that is the focus here.

A waiting list for organ transplantation consists of patients added at random calendar times. Patients arrive with different characteristics such as diagnosis, demographic characteristics, and health status indicators. Patients' characteristics may change during their sojourn on the waiting list, and their hazards for death and expected residual life after transplantation may depend on their health characteristics, and thus may also change during their sojourns.

Organs, either from deceased or living donors, also become available at random calendar

times. Whenever an organ becomes available, a patient in the waiting list is selected for transplantation. The selected patient can refuse, in which case another patient in turn is selected for transplantation, and so on, until a patient accepts an offer. Due to the short time between when an organ from a deceased donor becomes available and when the organ is no longer viable for transplantation, available organs from deceased donors are transplanted almost instantly. An organ recipient's health characteristics at the time of transplantation and the recipient's compatibility with the organ influence the expected post-transplantation residual life (UNOS [2011]). Candidates who are not transplanted will remain in the waiting list for future transplantation opportunities. Except in rare circumstances, patients leave the waiting list only in case of transplantation or death.

In living-donor transplantation, there is also a possibility for organ exchange. Patient-donor pairs exchange organs in a chain so that patients and donors can receive and donate compatible organs.

Allocation rules are used to determine which patient in the current waiting list is selected for transplantation when an organ is available. Allocation rules may make use of any information about the current state or history of the patients in the waiting list.

1.2 Standards for Comparing Allocation Rules

Some standards for comparing allocation rules that have been considered may be characterized in terms of expectations. Examples include patients' total life expectancy (in-waiting-list life expectancy plus post-transplantation life expectancy among patients receiving a transplantation), the in-waiting-list or the post-transplantation life expectancy alone, quality-adjusted life expectancy (Zenios et al. [2000], Su and Zenios [2006], Alagoz et al. [2004], Alagoz et al. [2004, 2007a,b], Akan et al. [2012]), patients' probability of in-waiting-list deaths (Akan et al. [2012]), expected graft survival rate (Ahn and Hornberger [1996], Hornberger and Ahn [1997], Su and Zenios [2004, 2005]), the expected number of discarded organs and average number of matches (Su and Zenios [2004, 2005], Roth et al. [2004, 2005], Ashlagi et al. [2011, 2012]). Equity standards, which in some cases cannot be expressed in terms of expectations, have also been considered (Zenios et al. [2000]). An example of an

allocation rule chosen to serve an equity standard is the first-come-first-serve rule.

There are ethical issues to be considered. Allocation rules that are not consistent over time or that are affected by factors other than waiting times and relevant health characteristics of patients might be viewed as inequitable. Relevant health characteristics are those that predict factors relevant to the standard by which allocation rules are compared, factors such as the current and future hazards for death and/or post-transplantation survival. Fair allocations should depend on waiting times and health characteristics of the patients in the waiting list at the time of organ arrivals and possible independent randomizations. An example of a fair allocation rule is the first-come-first-served rule. A class of fair allocation rules is obtained by defining an index as a function of a patient's waiting time and relevant characteristics and allocating to the patient in the list with the highest index value (or randomly among patients tied for the highest value).

Defining a standard for comparing allocation rules in terms of an expectation, for example, defining a standard in terms of expected total life, does not unambiguously define an optimization problem. Such a definition begs the question of which patients' expectations are to be maximized. Fortunately, as will be seen, with rather minimal assumptions on the nature of patient and organ arrivals, with allocation rules satisfying a fairness requirement, waiting list distributions converge, and thus it is natural to take the standard to be the limit, as the time of operation of the waiting list increases, of the average life for patients entering the waiting list.

Thus, in order to compare allocation rules, the limiting distribution of the waiting list needs to be understood. The limiting distribution depends on the following: the probabilistic properties of patients' arrivals and initial conditions and organs' arrivals, the probabilistic properties of patients' health characteristics trajectories, the relationship between health characteristics and the risk of death and expected post-transplantation survival, recipient-donor compatibility, the probabilistic behavior of patients' choices of whether to accept organs when offered, and the difference between living-donor and cadaveric organ transplantation in organ exchanges.

1.3 Previous Studies on Optimal Organ Allocation

Relevant early studies focused on modeling general resource allocation problems and solving for optimal allocation rules under given standards. Derman et al. [1971], Albright and Derman [1972], Derman et al. [1975], developed optimal solutions to a sequential assignment problem, in which candidates received resources that arrived sequentially at regular intervals. Ruth et al. [1985] constructed a simulation model to assess the impact of changes in the number of available cadaveric kidneys on the number of candidates in the waiting list. Righter [1989] solved a continuous-time resource allocation problem in which finite number of independent activities following independent Markov processes were to be allocated to resources that arrived at random times. David and Yechiali [1985, 1990, 1995] and David [1995] found optimal solutions to maximize total rewards in several sequential matching problems, in which a finite amount of offers with random rewards arrived in continuous-time and were to be assigned to a finite number of candidates characterized by different attributes. Ahn and Hornberger [1996] and Hornberger and Ahn [1997] designed procedures for deciding individual patient's eligibility for living-donor kidney transplantation and evaluated whether incorporating patient preferences could improve patients' life expectancy.

In recent studies, researchers have modeled the organ transplantation problem with increased complexity in order to reflect aspects of the problem such as those discussed in the previous section. Moreover, with increased availability of clinical data, simulation studies have been conducted with parameters estimated from real transplantation data to compare life outcomes with different allocation rules. Zenios [1999], Zenios et al. [1999] and Zenios et al. [2000] modeled the waiting list for kidney transplantation with a deterministic continuous-time fluid model, in which patients and organ donors were categorized based on their demographic, immunological, and physiological characteristics. An optimal allocation rule was derived under the standard of a linear combination of quality-adjusted life expectancy and two measures of inequity: the likelihood of transplantation of various types of patients and the difference in mean waiting time across patient types. Su and Zenios [2004, 2005, 2006] studied the effect of patient choice on kidney transplantation with a sequential assignment model, where a finite number of patients were to be allocated a finite number of kidneys that arrived sequentially in discrete time. Alagoz et al. [2004] modeled

the health status of individual patients waiting for living-donor liver transplantation as a discrete time Markov chain with ordered states and stationary transition probabilities, and found optimal decisions of whether to accept a transplantation offer from a single patient's perspective under discounted rewards. Under similar model settings, Alagoz et al. [2007a,b] studied optimal patient strategies for accepting or rejecting offers of cadaveric and living-donor livers. Akan et al. [2012] modeled the candidate waiting list for donated livers with a multi-class fluid model with possible improvements or deteriorations in patient health status, and derived optimal allocation strategies under a standard combining expected total number of in-waiting-list deaths and expected total quality-adjusted years of life.

Other aspects of the organ transplantation problem have also been studied. Roth et al. [2004, 2005], Ashlagi et al. [2011, 2012] studied the efficiency and benefit of kidney exchange programs by examining theoretical properties of exchange chains under different assumptions. Cechlárová and Lacko [2012] evaluated the computational difficulty in finding donors in exchange chains. Bertsimas et al. [2013] developed a data-driven method for designing national policies for the allocation of deceased-donor kidneys based on weighted score components, such as waiting time, specific patient health characteristics, and tissue matching, to approximately maximize life-year gains subject to any set of standards and fairness constraints chosen by the policy maker.

In one of the few studies on lung transplantation, Vock et al. [2013] evaluated the survival benefit of lung transplantation with the LAS rule from a causal inference perspective. They modeled candidates for lung transplantation with changing health states as independent subjects, and represented the effect of lung transplantation on patients' residual life by the difference between distributions of patients' counterfactual residual life, with or without transplantation. The benefit of lung transplantation under the LAS was estimated with a G-estimator, in which each subject's probability of receiving a transplantation when an organ was available was modeled. The G-estimator was selected to reflect that the allocation assignment was not independent across patients as a result of the competitions among patients for limited organs.

1.4 Modeling Issues for Lung Transplantation Waiting Lists

Relative to the richness of the literature on kidney and liver transplantation, few attempts have been made to model the waiting list for lung transplantation. Several characteristics distinguish lung transplantation from the transplantation of other organs, however, and models for waiting lists for kidney and liver transplantation cannot be appropriated wholesale in the service of designing allocation rules for lung transplantation. In this section, the discussion focuses more narrowly on issues specific to lung transplantation.

In contrast to the case of kidney and liver transplantation, living donor transplantation is extremely rare in lung transplantation: according to UNOS [2011], 8,674 patients were in the waiting list from year 2009 to 2011, 5,172 received deceased-donor transplant and only two received living donor transplant (reasons for the rare occurrences of living-donor transplantations include concerns about donor complications, lack of functional or survival advantage comparing to cadaveric transplantation, and the shortened waiting time for sicker patients provided by the new lung allocation system (Kotloff and Thabut [2012])). Reflecting the almost total absence of living donors for lung transplantation, the focus here is on deceased-donor transplantations only.

Statistics in UNOS [2011] also show that from 2009 to 2011 only twenty patients refused when offered a transplant, indicating patient choice is practically negligible in modeling lung transplantation. Therefore, in modeling lung transplantation here we ignore the possibility of organ refusal.

Candidates aged sixty-five years or older have been added to the waiting list faster than candidates in other age groups (UNOS [2011]), as it has become more accepted that functional age is more important than chronological age in predicting potential outcomes (Kotloff and Thabut [2012]). Because of the importance of recording changes in patients' functional age during their time on the lung transplantation waiting list, recorded health characteristics are updated over time for patients in the waiting list (UNOS [2011]).

Lung transplantations may take one of several forms. Single lung transplantation and bilateral lung transplantation currently make up the majority of all procedures. Heart-lung transplantation is also an option for patients with certain diagnoses. Underlying diseases and other health related characteristics of patients are the main factors in choosing between

procedures (Kotloff and Thabut [2012]). Consequently, the difference in the benefit of the various procedures as a function of patients' health characteristics must also be taken into account in modeling lung transplantation.

1.5 Current Lung Allocation Strategies

Currently in the United States, lungs are allocated to transplant candidates primarily on the basis of age, geography, blood type (ABO) compatibility, and the Lung Allocation Score (LAS). Since the implementation of LAS in 2005, candidates waiting for lungs receive priority for deceased donor lung offers based on their LAS if they are at least twelve years of age. Candidates less than twelve years of age receive deceased donor lung offers based on medical urgency (UNOS [2015]). The difference between allocation rules for children and for adults is due to the difficulty in developing accurate models of outcomes for young pediatric patients. The difficulty stems from the diversity in diagnoses and the small numbers of pediatric patients (Sweet [2009]).

The LAS is computed from two measures: the Waitlist Urgency Measure and the Post-transplant Survival Measure. The measures are, respectively, estimates of the expected number of days a candidate will live without a transplant during an additional year on the waiting list, and the expected number of days a candidate will live during the first year post-transplant.

Proportional hazard regressions with time-varying covariates are fitted by UNOS to compute the Waitlist Urgency Measure and the Post-transplant Survival Measure of patients. Predictors in the model include age, lung function measurements, pulmonary diagnoses, and interactions of these variables. Predictors are required to be updated for each patient at least once in every six months (UNOS [2015]). Potential future changes in the values of the predictors while patients are waiting for transplants and the resulting changes in the hazards, however, are not reflected in the LAS: at each update of the LAS, expected survivals are computed as if patients' health characteristics would remain constant in the future.

The LAS is the difference between the Post-transplant Survival Measure and twice the Waitlist Urgency Measure, normalized to a scale ranging from zero to one hundred. When

an organ is available, patients in the waiting list are ranked according to their LAS values (estimated from most recently recorded predictor values). The candidate with the highest LAS has priority for transplantation (UNOS [2015]).

Prioritizing via the LAS was an ad-hoc approach originally implemented to minimize wait-list mortality while considering the probability of post-transplant survival. Allocating lungs using the LAS also had the effect of de-emphasizing time on the waiting list, reducing incentive for early listing (UNOS [2011]). However, recent studies have demonstrated that LAS might have the effect of increasing post-transplant morbidity and mortality as well as increasing the risk of post-transplant complications (Liu et al. [2010], Russo et al. [2010, 2011]). To address these and other concerns, and to seek possible modifications and refinements, the LAS is under regular review, with new factors that are predictive to life outcomes and reflect medical urgency under consideration for inclusion in the proportional hazard regressions (Kotloff and Thabut [2012]).

1.6 Proposed Model and Overview of Results

We propose a model for the lung transplantation waiting list based on common characteristics shared by different organ types and on characteristics unique to lungs. Patient and organ arrivals are modeled as independent homogeneous Poisson processes. Counterfactual patient health status trajectories, that is, trajectories that would be observed were there no transplantations, are modeled as independent and identically distributed Markov processes.

It is shown that with these assumptions, with any allocation rule satisfying certain fairness criteria, the waiting list has a unique limiting distribution as calendar time increases. And on average, patients entering the waiting list are transplanted according to a unique allocation-rule-specific limiting transplantation rate, which is a function of waiting time and health state. The long-term average of patients' total life (in-waiting-list life plus post-transplantation life) and the long-term average of patients' life gain from transplantation, represented as functionals of the limiting transplantation rate, are used as the standards for comparing fair allocation rules.

It is also shown that the expected proportion of transplanted patients is bounded by the

ratio of the intensity of organ arrivals to that of patient arrivals, and that the transplantation rate satisfies boundedness constraints related to the counterfactual transition rate. We frame the problem of solving for the optimal fair allocation rule as the search for the limiting waiting time and health state specific transplantation rate that optimizes the long-term average life subject to the boundedness constraints.

The Hamilton-Jacobi-Bellman equations are used to characterize the form of the optimal limiting transplantation rate. As will be seen, the optimal rate is nonzero at waiting time and health state where the difference between the expected residual life with an immediate transplantation and the expected residual life without an immediate transplantation but with the possibility of future transplantation opportunities, is greater than one minus the probability of future transplantations, scaled by a penalty parameter associated with the ratio of organ arrival rate to patient arrival rate.

Not every transplantation rate satisfying the constraints is a limiting rate for some allocation strategies. And in particular, the rate corresponding to the solution of the optimization problem is not achievable. When an organ is available, patients in the waiting list that are alive and not transplanted do not necessarily include those at waiting times and states where the optimal rate is non-zero.

Here we propose an allocation strategy that is designed so that the corresponding waiting time and health state specific transplantation rate is close to the rate corresponding to the solution of the optimization problem. The specific form of the proposed allocation strategy is based on the observation that as the rate of organ arrivals increases, the set of waiting time and health state combinations for which the transplantation rates corresponding to the optimal solution are non-zero increases monotonically: the proposed strategy is to allocate according to the index defined by the order in which combinations enter the allocable set.

Finally, simulation studies are conducted with model parameters estimated from national lung transplantation data from United Network for Organ Sharing (UNOS). Results of simulations show that the proposed allocation strategy can provide a non-trivial gain in expected total life of patients over that of the current LAS system.

In what follows, the second chapter presents notation for the model for lung transplantation. The third chapter characterizes the comparison of allocation rules in terms of a

constrained optimization problem. The fourth chapter provides the solution of the constrained optimization problem. The fifth chapter presents a practical allocation strategy in the form of an allocation index based on the solution. The sixth chapter compares average total life of patients with the proposed allocation strategy and the LAS by simulation studies, in which the data are generated with parameters estimated from the UNOS data. The final chapter describes where the current research might be expanded.

Chapter 2

Notation

In this chapter, we introduce notation for patient and organ arrivals, trajectories of patients' health characteristics, and patients' life outcomes. Then the notation is used to characterize fair allocation rules and to define the standards for comparing allocation rules (the long-term average total life and the long-term average life gain from transplantation). The waiting list is modeled in terms of time of waiting and observed transitions of individual patients while they remain on the list. Allocation rules are modeled in terms of the indices of transplanted patients. Only fair allocation rules are considered in the comparison, and the fairness requirement is characterized in terms of how the waiting list evolves when organs are available for transplantation and allocation decisions are made. Patients' limiting average total life, including both in-waiting-list life and post-transplantation life, and the limiting average life gain from transplantation, are represented in terms of the life outcomes and actual transitions, and are used as the standards in comparing fair allocation rules.

2.1 Modeling the Waiting List

Let $\tau < \infty$ denote the intensity of the Poisson process of patient arrivals to the waiting list, and let $0 < T_1 < T_2 < \dots$ denote the patients' arrival times. For convenience, let N_I denote the number of patient arrivals in calendar time interval $I \subset [0, \infty)$. Let $\rho < \infty$ denote the intensity of the Poisson process of organ arrivals, and let $0 < S_1 < S_2 < \dots$ denote the arrival times of organs. Let O_I denote the number of organ arrivals in calendar time interval

$I \subset [0, \infty)$. Assume organ arrivals are independent of patient arrivals. We are interested in settings when $\rho < \tau$, as otherwise the supply of organs would generally meet the demand, and there would be no need for an allocation rule.

Let $\mathcal{X} = \{0, 1, \dots, n\}$ denote the finite set of possible patient states, where, without loss of generality, 0 denotes the absorbing state corresponding to death. Let $\{X(s) : s \geq 0\}$ denote a generic health status trajectory indexed by waiting time and let $R(s)$ denote a generic counterfactual post-transplant residual life if transplantation occurs at waiting time $s \geq 0$. Assume that the characterization of patient health states is sufficiently informative such that for any $s \geq 0$, $R(s)$ and $\sigma(\{X(u) : u < s\})$ are conditionally independent given $\sigma(X(s))$. Assume further that $\sup_{s \geq 0, i \in \mathcal{X}} E(|R(s)| \mid X(s) = i) < \infty$. Denote $\mu_i(s) = E(R(s) \mid X(s) = i)$ for any $i \in \mathcal{X}$ and $s \geq 0$ and let $\boldsymbol{\mu}_s = (\mu_1(s), \dots, \mu_n(s))$.

Let T be the upper bound of a patient's waiting time (waiting times are limited by reasonable bounds on the human life-span). That is, let $P(X(s) = 0) = 1$ for all $s \geq T$. Let the vector $\mathbf{p} = (p_1, \dots, p_n)$ denote the distribution of patients' initial states upon arrival, where $p_i = P(X(0) = i)$ for each $i \in \mathcal{X}$. As patients must enter the waiting list alive, $\mathbf{1}_n \cdot \mathbf{p} = 1$, where $\mathbf{1}_n$ is the vector of length n with all elements being 1.

Assume $\{X(s) : s \geq 0\}$ is a càdlàg Markov process with transition kernel $p_{s,t}(i, j)$ and infinitesimal generator $q_{ij}(s) = \lim_{t \downarrow s} (p_{s,t}(i, j) - I(i = j)) / (t - s)$, where $I(\cdot)$ is the indicator function. Suppose the total transition rate $-q_{ii}(s) = \sum_{j \neq i} q_{ij}(s) < \infty$. In addition, suppose the expected number of transitions in any finite waiting time interval is finite, for which a sufficient condition is $\int_0^T q_{ij}(s) ds < \infty$ for any $i, j \in \mathcal{X}$.

Let $\{(X^{(k)}(s), R^{(k)}(s)) : s \geq 0\}$ denote the health status trajectories and counterfactual post-transplant residual life processes of the k th patient. Assume $\{(X^{(k)}(s), R^{(k)}(s)) : s \geq 0, k \in \mathbb{N}\}$ are independent and identically distributed according to the generic pair $\{(X(s), R(s)) : s \geq 0\}$ and are independent of $\{T_k, S_j : i, j \in \mathbb{N}\}$.

An allocation sequence $J_1, J_2, \dots$ is a random sequence of indices of patients who receive transplantation, such that for each $i \in \mathbb{N}$, $T_{J_i} \leq S_i$, $X^{(J_i)}(S_i - T_{J_i}) \neq 0$, and $J_i \neq J_k$ if $i \neq k$. This definition reflects that patients who receive transplantation must have entered the waiting list and still be alive at the time of allocation, and that no patient receives more than one organ.

Let $T_T^{(k)}$ denote time waited until transplantation for the k th patient, that is, $T_T^{(k)} = S_i - T_k$ if $J_i = k$ and $T_T^{(k)} = \infty$ if $k \notin \{J_i : i \in \mathbb{N}\}$. Let $(n+1)$ denote the post-transplantation state and let $\mathcal{X}_0 = \mathcal{X} \cup \{n+1\}$ denote the augmented patient state space. The k th patient's actual trajectory $\{\tilde{X}^{(k)}(s) : s \geq 0\}$ is defined on $\mathcal{X}_0$ as

$$\tilde{X}^{(k)}(s) = X^{(k)}(s) \cdot I(s < T_T^{(k)}) + (n+1) \cdot I(s \geq T_T^{(k)})$$

for any $s \geq 0$.

Remark. $\tilde{X}^{(k)}(s)$ is a càdlàg process since both $X^{(k)}(s)$ and the organ arrival process are càdlàg.

The following filtrations are generated by events including patient and organ arrivals, patients' counterfactual health state transitions and allocation decisions.

Definition 2.1.1. (Filtrations)

For calendar time $t \geq 0$, let

$$\mathcal{F}_t := \sigma\left(T_k, S_i, J_i, \{X^{(k)}(s) : s \in [0, t - T_k]\} : T_k, S_i \in [0, t]\right),$$

so that $\{\mathcal{F}_t : t \geq 0\}$ is the filtration generated by all patient and organ arrivals, counterfactual transitions and allocations up to calendar time t . Also define the filtration

$$\mathcal{G}_t := \sigma\left(T_k, S_i, \{X^{(k)}(s) : s \in [0, t - T_k]\} : T_k, S_i \in [0, t]\right) \vee \sigma(J_i : S_i < t),$$

which excludes the allocation decision at t .

At any time, the currently observed waiting list consists of patients who have arrived and have not died or received transplantation. To simplify the expression, we first introduce the following index set of available patients:

Definition 2.1.2. (Index Set of Patients Available for Transplantation)

For any allocation sequence $\mathcal{J} = \{J_1, J_2, \dots\}$, define the random patient index set at each calendar time $t \geq 0$ (for simplicity, the index $\mathcal{J}$ is omitted in the notation)

$$\mathcal{I}_t := \{k \in \mathbb{N} : T_k \leq t, \tilde{X}^{(k)}(t - T_k) \notin \{0, n+1\}\}$$

of patients who have arrived before (including) t and are alive and have not been transplanted at t . Let $|\mathcal{I}_t|$ denote the number of elements in $\mathcal{I}_t$.

Remark. Since for each k ,

$$\begin{aligned} I(k \in \mathcal{I}_t) &= I(T_k \leq t, \tilde{X}^{(k)}(t - T_k) \notin \{0, n + 1\}) \\ &= I(T_k \leq t, X^{(k)}(t - T_k) \neq 0, k \notin \{J_i : S_i \leq t\}), \end{aligned}$$

$\mathcal{I}_t$ is adapted to $\{\mathcal{F}_t\}$. Moreover, since $I(T_k \leq t)$ and $I(\tilde{X}^{(k)}(t - T_k) \notin \{0, n + 1\})$ are càdlàg processes, $\bigcap_{n=1}^{\infty} \mathcal{I}_{t+1/n} = \mathcal{I}_t$, and

$$\mathcal{I}_{t-} = \bigcup_{n=1}^{\infty} \mathcal{I}_{t-1/n} = \{k \in \mathbb{N} : T_k < t, \tilde{X}^{(k)}((t - T_k)-) \notin \{0, n + 1\}\},$$

which is the index set of patients in the current list who are alive and have not been transplanted before time t . Let $|\mathcal{I}_{t-}|$ denote the number of elements in $\mathcal{I}_{t-}$.

If an organ becomes available at time t , a patient in $\mathcal{I}_t$ will be selected for transplantation. Here we allow the allocation to happen right after a change in the patient's health state at t , that is, suppose the k th patient is selected, it is possible that $X^{(k)}((t - T_k)-) \neq X^{(k)}(t - T_k)$ while $\tilde{X}^{(k)}(t - T_k) = n + 1$, though such events have zero probability.

In what follows, the waiting list process is characterized in terms of the state and waiting time pairs of patients who are alive and not transplanted at t .

Definition 2.1.3. (The Waiting List Process)

On the state space $W = \bigcup_{d=1}^{\infty} ([0, T] \times \mathcal{X})^d \cup \{w_0\}$ and its Borel σ -algebra $\mathcal{B}(W)$, where w_0 denotes the empty state corresponding to $|\mathcal{I}_t| = 0$, define the waiting list process:

$$W_t := \{(t - T_k, \tilde{X}^{(k)}(t - T_k)) : k \in \mathcal{I}_t\}. \quad (2.1)$$

Remark. Since $\mathcal{I}_t$ is adapted to the filtration $\{\mathcal{F}_t : t \geq 0\}$ and (2.1) is equal to $\{(t - T_k, X^{(k)}(t - T_k)) : k \in \mathcal{I}_t\}$, $\{W_t : t \geq 0\}$ is also adapted to $\{\mathcal{F}_t\}$. As potential discontinuities of $\{W_t : t \geq 0\}$ can only be results of arrivals of patients and organs, or of transitions in

$\tilde{X}^{(k)}$, which are càdlàg, W_t is càdlàg. By the definition of W_t ,

$$W_{t-} = \{(t - T_k, \tilde{X}^{(k)}((t - T_k)-)) : k \in \mathcal{I}_{t-}\}.$$

For convenience, also introduce the following notation for the waiting list right before potential allocations.

Definition 2.1.4. (Waiting List Before Allocation)

Denote the waiting list before potential allocation at calendar time t by

$$W'_t := \{(t - T_k, X^{(k)}(t - T_k)) : T_k \leq t, k \notin \{J_i : S_i < t\}, X^{(k)}(t - T_k) \neq 0\}. \quad (2.2)$$

Remark. $\{W'_t : t \geq 0\}$ is adapted to the filtration $\{\mathcal{G}_t : t \geq 0\}$ as $I(k \notin \{J_i : S_i < t\}) \in \mathcal{G}_t$. Moreover, W'_t is progressively measurable as each component in (2.2) is either right or left continuous and thus progressively measurable.

2.2 Fair Allocation Rules

Allocation rules should satisfy fairness requirements. Our definition of fairness of an allocation sequence are as follows: given the information of the waiting list up to the time of allocation, fair allocation decisions should only depend on the waiting times and states of patients who are currently alive and not transplanted, along with a possible randomization that is conditionally independent of the history of the waiting list given the current state of the waiting list. In addition, only realistic allocation rules that are non-informative of patients' post-transplant residual life are considered.

Note that by the definition of the filtration $\{\mathcal{G}_t : t \geq 0\}$, for any $j \in \mathbb{N}$, S_j is a $\{\mathcal{G}_t\}$ -stopping time. Let

$$\mathcal{G}_{S_j} := \{A : A \cap \{S_j \leq t\} \in \mathcal{G}_t, \forall t \geq 0\}$$

denote the σ -algebra generated by information in $\{\mathcal{G}_t\}$ up to the arrival time of the j th organ. Note W'_{S_j} is measurable with respect to $\mathcal{G}_{S_j}$ as W'_s is progressively measurable. Then the fairness requirement is formally characterized in terms of the behavior of the jump of

the waiting list due to allocations when organs are available.

Definition 2.2.1. (Fair Allocation Rules)

An allocation sequence $\mathcal{J} = \{J_1, J_2, \dots\}$ is termed fair, if for any $j \in \mathbb{N}$ and $A \in \mathcal{B}(W)$,

$$P(W_{S_j} \in A \mid \mathcal{G}_{S_j}) = \gamma^{\mathcal{J}}(A; W'_{S_j}), \quad (2.3)$$

where $\gamma^{\mathcal{J}}$ is a transition kernel: for any $A \in \mathcal{B}(W)$, $\gamma^{\mathcal{J}}(A; \cdot)$ is a measurable function on $(W, \mathcal{B}(W))$, and for any fixed $w \in W$, $\gamma^{\mathcal{J}}(\cdot; w)$ is a probability measure on $(W, \mathcal{B}(W))$.

In addition to the fairness requirement, assume that $\mathcal{J} = \{J_1, J_2, \dots\}$ are such that for any $j \in \mathbb{N}$ and $A \in \mathcal{B}(W)$,

$$P(W_{S_j} \in A \mid W'_{S_j}, \{S_i, T_k : i, k \in \mathbb{N}\}) = \gamma^{\mathcal{J}}(A; W'_{S_j}), \quad (2.4)$$

$$P(W_{S_j} \in A \mid W'_{S_j}, \{X^{(k)}(s), R^{(k)}(s) : s \geq 0, k \in \mathbb{N}\}) = \gamma^{\mathcal{J}}(A; W'_{S_j}), \quad (2.5)$$

as given the current waiting list, allocation decisions should be conditionally independent of arrivals, counterfactual transitions and residual life, including those would happen in the future.

2.3 Long-term Average Total Life as the Standard

The limiting long-term average of patients' total life (in-waiting-list life plus post-transplant life) as the calendar time increases is used as the standard for comparing fair allocation rules. The following counting process notation for each patient's counterfactual and actual transitions will facilitate the representation of the limiting average total life:

Definition 2.3.1. (Counting Processes and At-risk Indicators)

For the k th patient, define the càdlàg counting process for actual transitions, including transplantation:

$$d\tilde{N}_{ij}^{(k)}(s) := I(\tilde{X}^{(k)}(s-) = i, \tilde{X}^{(k)}(s) = j),$$

so that $\tilde{N}_{ij}^{(k)}(s, t] := \int_{(s, t]} d\tilde{N}_{ij}^{(k)}(u)$ is the number of actual transitions from state i to j in waiting time interval $(s, t]$. Similarly, for the counterfactual transitions, let $N_{ij}^{(k)}(s, t] :=$

$\int_{(s,t]} dN_{ij}^{(k)}(u)$, where

$$dN_{ij}^{(k)}(s) := I(X^{(k)}(s-) = i, X^{(k)}(s) = j).$$

Also define at-risk indicators for the k th patient's actual transitions. For $i \in \mathcal{X}_0$ and $s \geq 0$, let

$$\tilde{Y}_i^{(k)}(s) := I(\tilde{X}^{(k)}(s) = i)$$

and

$$\tilde{Y}_i^{(k)}(s-) := I(\tilde{X}^{(k)}(s-) = i).$$

Similarly, for counterfactual transitions, let

$$Y_i^{(k)}(s) := I(X^{(k)}(s) = i)$$

and

$$Y_i^{(k)}(s-) := I(X^{(k)}(s-) = i).$$

The k th patient's time of waiting until exit from the list due to death or transplantation is $\inf_{t \geq 0} \{X^{(k)}(t) = 0\} \wedge T_T^{(k)}$, and thus the total life, including life in-waiting list and post-transplantation, can be represented with the counting process notation as

$$\inf_{t \geq 0} \{X^{(k)}(t) = 0\} \wedge T_T^{(k)} + \int_0^T R^{(k)}(s) d\tilde{N}_{i,n+1}^{(k)}(s).$$

The limiting long-term average of total life of all patients ever enter the list, including in-waiting-list life and post-transplantation life, if exists, can be written as

$$\lim_{l \rightarrow \infty} \frac{1}{N_{[0,l]}} \sum_{k=1}^{N_{[0,l]}} \left[\inf_{t \geq 0} \{X^{(k)}(t) = 0\} \wedge T_T^{(k)} + \sum_{i \in \mathcal{X}} \int_0^T R_i^{(k)}(s) d\tilde{N}_{i,n+1}^{(k)}(s) \right]. \quad (2.6)$$

It is also of interest to know the life gain from transplantation, that is, the difference between the potential residual life if the patient is currently at a certain waiting time and state and is transplanted immediately and the potential residual life if the patient is never transplanted.

Definition 2.3.2. (Residual Life Gain from Transplantation)

Let

$$\tilde{R}^{(k)}(s) = R^{(k)}(s) - \left(\inf_{t \geq 0} \{X^{(k)}(t) = 0\} - s \right) \quad (2.7)$$

be the difference between the k th patient's counterfactual post-transplantation residual life if transplanted at waiting time s and the counterfactual residual life if never transplanted. Let $\tilde{\boldsymbol{\mu}}_s = (\tilde{\mu}_1(s), \dots, \tilde{\mu}_n(s))$, where $\tilde{\mu}_i(s) := E(\tilde{R}^{(k)}(s) \mid X^{(k)}(s) = i)$ is the expected life gain for patients transplanted at waiting time $s \geq 0$ and state $i \in \mathcal{X}$.

The limiting average life gain from transplantation, if exists, can be represented with the counting process notation as

$$\lim_{l \rightarrow \infty} \frac{1}{N_{[0,l]}} \sum_{k=1}^{N_{[0,l]}} \sum_{i \in \mathcal{X}} \int_0^T \tilde{R}^{(k)}(s) d\tilde{N}_{i,n+1}^{(k)}(s). \quad (2.8)$$

Remark. By the definition (2.7), for any $k \in \mathbb{N}$,

$$\begin{aligned} & \inf_{t \geq 0} \{X^{(k)}(t) = 0\} \wedge T_T^{(k)} + \sum_{i=1}^n \int_0^T R^{(k)}(s) d\tilde{N}_{i,n+1}^{(k)} \\ &= \inf_{t \geq 0} \{X^{(k)}(t) = 0\} \wedge T_T^{(k)} + \sum_{i=1}^n \int_0^T \left(\inf_{t \geq 0} \{X^{(k)}(t) = 0\} - s \right) d\tilde{N}_{i,n+1}^{(k)}(s) \\ & \quad + \sum_{i=1}^n \int_0^T \left(R^{(k)}(s) - \left(\inf_{t \geq 0} \{X^{(k)}(t) = 0\} - s \right) \right) d\tilde{N}_{i,n+1}^{(k)}(s) \\ &= \inf_{t \geq 0} \{X^{(k)}(t) = 0\} \wedge T_T^{(k)} + \sum_{i=1}^n \int_0^T \left(\inf_{t \geq 0} \{X^{(k)}(t) = 0\} - s \right) d\tilde{N}_{i,n+1}^{(k)}(s) \\ & \quad + \sum_{i=1}^n \int_0^T \tilde{R}^{(k)}(s) d\tilde{N}_{i,n+1}^{(k)}(s). \end{aligned}$$

Since $d\tilde{N}_{i,n+1}^{(k)}(s) = 1$ only at $s = T_T^{(k)}$ if $T_T^{(k)} < \infty$ and $d\tilde{N}_{i,n+1}^{(k)}(s) = 0$ for all $i \in \mathcal{X}$ and $s \geq 0$ if $T_T^{(k)} = \infty$, in either case,

$$\inf_{t \geq 0} \{X^{(k)}(t) = 0\} \wedge T_T^{(k)} + \sum_{i=1}^n \int_0^T \left(\inf_{t \geq 0} \{X^{(k)}(t) = 0\} - s \right) d\tilde{N}_{i,n+1}^{(k)}(s) = \inf_{t \geq 0} \{X^{(k)}(t) = 0\},$$

which is the counterfactual total life of the k th patient if never transplanted. Therefore,

(2.6) and (2.8) are only different by a constant that is invariant to the choice of allocation rules, and using (2.6) and (2.8) as standards in comparing fair allocation rules are equivalent. In chapters 3 and for the continuous-time model in chapter 4 and 5, we will focus on the long-term average residual life gain (2.8) for simplicity of expressions. For the discrete-time model in chapter 4 and 5 and the simulation studies in chapter 6, results are presented in the form of the average total life (2.6) for easiness of interpretations.

Chapter 3

The Optimization Problem

In the previous chapter, the problem of comparing allocation rules is formulated as the comparison of limiting average total life, or equivalently, limiting average life gain from transplantation, among waiting lists under fair allocation rules. Two questions arise naturally. First, it is unknown whether the limits (2.6) and (2.8) exist. Second, if the limits exist, given a fair allocation rule, how to calculate (2.6) and (2.8).

This chapter address the above questions by showing that with any fair allocation rule, there exists a limiting transplantation rate for any pair of waiting time and health state, such that on average patients in the waiting list are allocated according to the transplantation rate. The limiting average total life (2.6) and the limiting average life gain from transplantation (2.8) are then shown to be well defined and are represented in terms of the transplantation rate.

It is also shown the transplantation rate should satisfy certain constraints. In particular, the limiting proportion of transplanted patients, which is a functional of the transplantation rate, is bounded by the ratio of the organ arrival rate to the patient arrival rate. Also, the transplantation rate should satisfy certain boundedness constraints related to the counterfactual transition rate.

With the representation of the long-term average life in terms of the transplantation rate and the constraints, fair allocation rules can be compared through their corresponding transplantation rates. A constrained optimization problem is formulated with the derived objective function and constraints, and we hope the solution of the optimal transplantation

rate can give hints to the development of efficient allocation strategies.

3.1 Long-term Average Occupancy

To define the transplantation rate, we first show the waiting list with any fair allocation rule is strong Markov and positive recurrent, so that the average occupancy $\sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s)/N_{[0,t]}$ of any state $i \in \mathcal{X}$ at any waiting time $s \geq 0$ converges almost surely as calendar time t increases. An alternative treatment of the results based on the fact that the waiting list is a Piecewise Deterministic Markov Process (PDMP) is given in Section B in the appendix.

In the next section, the transplantation rate is characterized in terms of the difference between the limiting average occupancy and the counterfactual occupancy absent transplantation.

Theorem 3.1.1. (*The Strong Markov Property*)

With any fair allocation sequence $\mathcal{J} = \{J_1, J_2, \dots\}$ that satisfies conditions (2.3), (2.4) and (2.5), the process combining the waiting list and the arrivals of patients and organs

$$\{(W_t, N_{[0,t]}, O_{[0,t]}) : t \geq 0\}$$

is strong Markov with respect to its natural filtration $\tilde{\mathcal{F}}_t = \sigma\{(W_s, N_{[0,s]}, O_{[0,s]}) : s \leq t\}$.

Proof. It suffices to show $\{(W_t, N_{[0,t]}, O_{[0,t]}) : t \geq 0\}$ is strong Markov with respect to any stopping time of $\sigma\{(W_s, N_{[0,s]}, O_{[0,s]}) : s \leq t\}$. Let the increasing sequence $\tilde{T}_1 < \tilde{T}_2 < \dots$ denote the jumping times of $(W_t, N_{[0,t]}, O_{[0,t]})$, that is,

$$\begin{aligned} \{\tilde{T}_i : i \in \mathbb{N}\} &= \{T_k : k \in \mathbb{N}\} \cup \{S_j : j \in \mathbb{N}\} \cup \{t > 0 : W_t \neq W_{t-}\} \\ &= \{T_k : k \in \mathbb{N}\} \cup \{S_j : j \in \mathbb{N}\} \\ &\quad \cup \{t > 0 : \exists k \in \mathcal{I}_{t-}, \text{ s.t. } X^{(k)}(t - T_k) \neq X^{(k)}((t - T_k)-)\}. \end{aligned} \quad (3.1)$$

Since $(W_t, N_{[0,t]}, O_{[0,t]})$ is deterministic between the jumps with the only changing components being patients' waiting times, by results in Section 4 of Davis [1984], for any stopping

time t_0 of $\{\tilde{\mathcal{F}}_t\}$, there exist functions τ_i of

$$(W_0, \tilde{T}_1, (W_{\tilde{T}_1}, N_{[0, \tilde{T}_1]}, O_{[0, \tilde{T}_1]}), \dots, \tilde{T}_{i-1}, (W_{\tilde{T}_{i-1}}, N_{[0, \tilde{T}_{i-1}]}, O_{[0, \tilde{T}_{i-1}]})$$

such that for any $i \in \mathbb{N}$,

$$t_0 \cdot I(t_0 \in (\tilde{T}_{i-1}, \tilde{T}_i]) = (\tilde{T}_i \wedge \tau_i) \cdot I(t_0 \in (\tilde{T}_{i-1}, \tilde{T}_i]),$$

which indicates that for any stopping time t_0 , t_0 is either 0, $\tilde{T}_i$ for some $i \in \mathbb{N}$, or $\tilde{T}_{i-1} + \tau_i$ for some $i \in \mathbb{N}$ on $\{t_0 < \infty\}$. Let $t_1 = \inf \{t > t_0 : (W_t, N_{[0, t]}, O_{[0, t]}) \neq (W_t, N_{[0, t-]}, O_{[0, t-]})\}$, then in any of the above cases, by (3.1),

$$P(\{t_1 > t_0 + s\} \cap \{t_0 < \infty\} \mid \tilde{\mathcal{F}}_{t_0}) = F(s, W_{t_0}) \cdot I(t_0 < \infty), \quad (3.2)$$

where $F(s, x)$ is the survival function of inter-jump times from state x of the waiting list, by the Markov properties of patient and organ arrivals and patients' counterfactual transitions.

Given that the allocations satisfy the fairness requirement (2.3), the post-jump state, including the post-transplantation state, is independent of $\{\tilde{\mathcal{F}}_s : s < t_0\}$ given $(W_{t_0}, N_{[0, t_0]}, O_{[0, t_0]})$, as for any $B \in \mathcal{B}(W)$ and $n, o \in \mathbb{N}$,

$$\begin{aligned} & P(\{W_{t_1} \in B, N_{[0, t_1]} = n, O_{[0, t_1]} = o\} \cap \{t_0 < \infty\} \mid \tilde{\mathcal{F}}_{t_0}) \\ &= E[E(I(W_{t_1} \in B, N_{[0, t_1]} = n, O_{[0, t_1]} = o) \mid \mathcal{G}_{t_1}) \mid \tilde{\mathcal{F}}_{t_0}] \cdot I(t_0 < \infty), \end{aligned} \quad (3.3)$$

in which

$$\begin{aligned} E(I(W_{t_1} \in B, N_{[0, t_1]} = n, O_{[0, t_1]} = o) \mid \mathcal{G}_{t_1}) &= P(W_{t_1} \in B \mid \mathcal{G}_{t_1}) \cdot I(N_{[0, t_1]} = n, O_{[0, t_1]} = o) \\ &= P(W_{t_1} \in B \mid W'_{t_1}) \cdot I(N_{[0, t_1]} = n, O_{[0, t_1]} = o) \end{aligned}$$

by the fairness requirement (2.3), and

$$\begin{aligned} & E[P(W_{t_1} \in B \mid W'_{t_1}) \cdot I(N_{[0,t_1]} = n, O_{[0,t_1]} = o) \mid \tilde{\mathcal{F}}_{t_0}] \\ &= E[P(W_{t_1} \in B \mid W'_{t_1}) \cdot I(N_{[0,t_1]} = n, O_{[0,t_1]} = o) \mid \sigma(W_{t_0}, N_{[0,t_0]}, O_{[0,t_0]})] \end{aligned} \quad (3.4)$$

by discussing the type of t_1 in (3.1) and using the independence between the counterfactual transitions and patient and organ arrivals and the Markov property of the arrivals and counterfactual transitions. Combining (3.3) and (3.4) with (3.2) and applying the above argument recursively lead to the desired strong Markov property. $\square$

Essentially, the waiting list process $\{W_t : t \geq 0\}$ and the arrivals of patients and organs are piecewise deterministic Markov processes (PDMP) and the strong Markov property can be shown as in Davis [1993]. For a detailed study of the waiting list process as a PDMP, including its constructions and transition kernel, see the optional chapter in Appendix B.

The next result shows that the waiting list with any fair allocation rule is positive recurrent to the empty state w_0 . Note here w_0 is selected as the recurrent state for the simplicity of the proof, and the positive recurrence of the waiting list can also be shown with other states that may take much shorter time for the waiting list to return to.

Proposition 3.1.2. *Let $\tau_{w_0} := \inf\{t \geq 0 : W_t = w_0\}$ be the first time the waiting list becomes empty. Then $\forall w \in W$,*

$$E_w[\tau_{w_0}] < \infty, \quad (3.5)$$

where E_w is the expectation under the probability P_w of the waiting list process given the waiting list starts at state w .

Proof.

$$\begin{aligned}
E_w(\tau_{w_0}) &= \int_0^\infty P_w(\tau_{w_0} > s) ds \\
&= \int_0^\infty (1 - P_w(\tau_{w_0} \leq s)) ds \\
&= \int_0^T (1 - P_w(\tau_{w_0} \leq s)) ds + \int_T^\infty (1 - P_w(\tau_{w_0} \leq s)) ds \\
&\leq T + \int_T^\infty (1 - P_w(\exists i \in \{1, \dots, \lceil s/T \rceil\} : N_{[(i-1)T, iT]} = 0)) ds \\
&= T + \int_T^\infty (1 - e^{-T\tau})^{\lceil s/T \rceil} ds \\
&\leq T + \int_T^\infty (1 - e^{-T\tau})^{s/T} ds \\
&= T - \frac{T(1 - e^{-T\tau})}{\log(1 - e^{-T\tau})} < \infty.
\end{aligned}$$

The first inequality is a result of

$$\{\exists i \in \{1, \dots, \lceil s/T \rceil\} : N_{[(i-1)T, iT]} = 0\} \subset \{\tau_{w_0} \leq s\},$$

which describes that if at least one of the intervals $[(i-1)T, iT]$ has no patient arrival, then all existing patients in the waiting list will die before a new patient arrives, and the waiting list must return to the empty state at least once before s . The equation

$$P_w(\exists i \in \{1, \dots, \lceil s/T \rceil\} : N_{[(i-1)T, iT]} = 0) = 1 - (1 - e^{-T\tau})^{\lceil s/T \rceil}$$

is shown by the property of independent increments of Poisson process. $\square$

As a result of the positive recurrence, one can define the infinite sequence of return times $\{M_i : i = 0, 1, 2, \dots\}$, where $M_0 = 0$ and

$$M_i := \inf\{t > M_{i-1} : W_t = w_0\}$$

for all $i \geq 1$. The next result states the waiting list can be partitioned into independent and identically distributed epochs using the recurrence times.

Proposition 3.1.3. $\forall i \in \mathbb{N}$ and any measurable set $B \in \mathcal{B}(W)$,

$$P(W_{t+M_i} \in B \mid \tilde{\mathcal{F}}_{M_i}) = P_{w_0}(W_t \in B).$$

Moreover, $\{M_i - M_{i-1}, i = 1, 2, \dots\}$ are independent and identically distributed with finite expectations.

Proof. We first show by induction that $M_i, i = 0, 1, \dots$ are stopping times with respect to the filtration $\{\tilde{\mathcal{F}}_t : t \geq 0\}$. $M_0 = 0$ is a stopping time of $\{\tilde{\mathcal{F}}_t\}$. Assume M_{i-1} is a stopping time of $\{\tilde{\mathcal{F}}_t\}$, then $\{M_{i-1} \leq t\} \in \tilde{\mathcal{F}}_t$ for all $t \geq 0$. Since

$$\begin{aligned} \{M_i \leq t\} &= \{M_{i-1} \leq t\} \cap \\ &\quad \bigcap_{k \in \mathbb{N}} \{ \{T_k > t\} \cup \{T_k \leq M_{i-1}\} \} \\ &\quad \cup \{ \{T_k \in (M_{i-1}, t]\} \cap \{\tilde{X}^{(k)}(t) \in \{0, n+1\}\} \}, \end{aligned}$$

and each set on the right side is in $\tilde{\mathcal{F}}_t$ by the definition of the filtration, M_i is also a stopping time of $\{\tilde{\mathcal{F}}_t\}$.

As shown previously, the waiting list process W_t is a strong Markov process with respect to the filtration $\tilde{\mathcal{F}}_t$. For any $i \in \mathbb{N}$, since $E(M_i) < \infty$, $P(M_i < \infty) = 1$. Therefore $\forall B \in \mathcal{B}(W)$,

$$P(W_{t+M_i} \in B \mid \tilde{\mathcal{F}}_{M_i}) = P_{(w_0, N_{[0, M_i]}, O_{[0, M_i]})}(W_t \in B) = P_{w_0}(W_t \in B),$$

by the independent increment of arrivals and the independence between counterfactual transitions and the arrivals.

As a corollary, $M_i - M_{i-1}, i = 1, 2, \dots$ are independent and identically distributed, and $E(M_i - M_{i-1}) = E(M_1) < \infty$ by the positive recurrence. $\square$

Now we are ready to show the main result of this section that the average of patients' occupancy of any state $i \in \mathcal{X}$ at waiting time $s \in [0, T]$ converges as calendar time increases.

Theorem 3.1.4. *(Existence and Definition of $\pi_i(s)$ and $\pi_i(s-)$)*

For any $i \in \mathcal{X}$ and $s \geq 0$,

$$\pi_i(s) := \lim_{t \rightarrow \infty} \frac{\sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s)}{N_{[0,t]}} \quad (3.6)$$

exists almost surely, and for all $s > 0$,

$$\pi_i(s-) := \lim_{t \rightarrow \infty} \frac{\sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s-)}{N_{[0,t]}}$$

exist almost surely. Moreover, $\pi_i(s)$ is of finite variation and càdlàg with left limits $\pi_i(s-)$. Denote vectors $\boldsymbol{\pi}_s = (\pi_1(s), \dots, \pi_n(s))$ and $\boldsymbol{\pi}_{s-} = (\pi_1(s-), \dots, \pi_n(s-))$. Let $\boldsymbol{\pi}_{0-} = \mathbf{p}$, which is the distribution of patients' initial states upon arrival.

Proof. With the return times $\{M_j\}$ and $L_t := \max\{k \in \mathbb{N} : M_k \leq t\}$,

$$\sum_{j=1}^{L_t} \sum_{k=N_{[0,M_{j-1}]}+1}^{N_{[0,M_j]}} \tilde{Y}_i^{(k)}(s) \leq \sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s) \leq \sum_{j=1}^{L_t+1} \sum_{k=N_{[0,M_{j-1}]}+1}^{N_{[0,M_j]}} \tilde{Y}_i^{(k)}(s). \quad (3.7)$$

For each $j \in 1, \dots, L_t$,

$$\sum_{k=N_{[0,M_{j-1}]}+1}^{N_{[0,M_j]}} \tilde{Y}_i^{(k)}(s) = \lim_{\text{mesh} \downarrow 0} \sum_{k=1}^{n-1} I(W_{t_k} \in B_{(s,i)}),$$

where $M_{j-1} = t_1 < \dots < t_n = M_j$ is a partition of $[M_{j-1}, M_j]$, and $B_{(s,i)} = \bigcup_{d=1}^{\infty} \bigcup_{k=1}^d ([0, T] \times \mathcal{X})^{k-1} \times (s, i) \times ([0, T] \times \mathcal{X})^{d-k} \in \mathcal{B}(W)$. Therefore by Proposition 3.1.3 and the property of independent increments of $\{M_j\}$,

$$\left\{ \sum_{k=N_{[0,M_{j-1}]}+1}^{N_{[0,M_j]}} \tilde{Y}_i^{(k)}(s) : j \in 1, \dots, L_t + 1 \right\}$$

are independent and identically distributed, and

$$E \left[\sum_{k=N_{[0,M_{j-1}]}+1}^{N_{[0,M_j]}} \tilde{Y}_i^{(k)}(s) \right] = E_{w_0} \left[\sum_{k=1}^{N_{[0,M_1]}} \tilde{Y}_i^{(k)}(s) \right],$$

which is bounded by $E_{w_0}(N_{[0,M_1]})$. For convenience, we omit w_0 in E_{w_0} as the waiting list starts from the empty state. Note $N([0, t]) - \tau t$ is a $\{\tilde{\mathcal{F}}_t\}$ -martingale, by the optional sampling theorem, for any $t > 0$, $E(N_{[0,M_1 \wedge t]}) = \tau E(M_1 \wedge t)$. Letting $t \rightarrow \infty$, by the Monotone and Dominated Convergence theorem, $E(N_{[0,M_1]}) = \tau E(M_1) < \infty$ by the positive recurrence. By the elementary renewal theorem, $E(t^{-1}L_t) \rightarrow E(M_1)^{-1}$. Therefore by the Strong Law of Large Numbers and the inequalities in (3.7),

$$t^{-1} \sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s) \rightarrow E(M_1)^{-1} E \left[\sum_{k=1}^{N_{[0,M_1]}} \tilde{Y}_i^{(k)}(s) \right]$$

almost surely. Since $t^{-1}N_{[0,t]} \rightarrow \tau$ almost surely,

$$\pi_i(s) = \lim_{t \rightarrow \infty} t^{-1} \sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s) / (t^{-1}N_{[0,t]}) = (\tau E(M_1))^{-1} E \left[\sum_{k=1}^{N_{[0,M_1]}} \tilde{Y}_i^{(k)}(s) \right] \quad (3.8)$$

is well defined. The almost surely convergence of $\pi_i(s-) = \lim_{t \rightarrow \infty} N_{[0,t]}^{-1} \sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s-)$ is shown along the same lines.

Since

$$\sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s) = \sum_{k=1}^{N_{[0,t]}} \left[\tilde{Y}_i^{(k)}(0) + \sum_{j \neq i} (\tilde{N}_{ij}^{(k)}(0, s) - \tilde{N}_{ji}^{(k)}(0, s)) \right],$$

in which both $\sum_{j \neq i} \tilde{N}_{ij}^{(k)}(0, s]$ and $\sum_{j \neq i} \tilde{N}_{ji}^{(k)}(0, s]$ are non-decreasing with respect to s , $\pi_i(s)$ is of finite variation.

For any $t \geq 0$ and $n \in \mathbb{N}$, as $\epsilon \rightarrow 0$,

$$\sum_{k=1}^n \tilde{Y}_i^{(k)}(s - \epsilon) \rightarrow \sum_{k=1}^n \tilde{Y}_i^{(k)}(s-),$$

except on a measure zero set. Therefore as $\epsilon \rightarrow 0$,

$$\sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s - \epsilon) \rightarrow \sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s-)$$

almost surely, for the probability of the convergence does not hold is bounded by a countable sum of zeros when intersecting with $\{N_{[0,t]} = k\}$ for $k \in \mathbb{N}$. Then by (3.8),

$$\pi_i(s - \epsilon) - \pi_i(s-) = (\tau E(M_1))^{-1} E \left[\sum_{k=1}^{N_{[0,M_1]}} \tilde{Y}_i^{(k)}(s - \epsilon) - \sum_{k=1}^{N_{[0,M_1]}} \tilde{Y}_i^{(k)}(s-) \right].$$

As $\epsilon \rightarrow 0$, the right side converges to zero by the Dominated Convergence Theorem. The right continuity of π_i is shown similarly. $\square$

Without organ allocations, the average occupancy of state i at waiting time s would converge to the counterfactual probability of a patient being in state i at waiting time s . Therefore, the difference between the actual and the counterfactual limiting average occupancy reveals the allocation rate to patients in a state at a given waiting time. In what follows, we define the limiting transplantation rate in terms of the difference between the actual and counterfactual limiting average occupancies, and show that the defined transplantation rate is indeed the limiting average rate at which patients are transplanted.

3.2 Limiting Transplantation Rate

To start with, we define the following matrix $\mathbf{Q}$ of measures induced by patients' counterfactual transitions.

Definition 3.2.1. Let $\mathbf{Q}$ be the measure matrix such that for any $i, j \in \mathcal{X}$ and Borel set $A \in \mathcal{B}([0, T])$,

$$Q_{ij}(A) = \int_A q_{ij}(s) ds,$$

where $\mathbf{q}$ is the matrix of counterfactual transition rates.

For any waiting time $s \in [0, T]$, $\pi_{s-} d\mathbf{Q}_s$ is the potential change in the average occupancy if there is no transplantation, while $d\pi$ is the actual change in the average occupancy. The

transplantation rate is defined as the difference between the counterfactual and the actual change in the long-term average occupancy:

Definition 3.2.2. (Limiting Transplantation Rate)

For any waiting time $s \in [0, T]$, let $\Psi_s := (\Psi_1(s), \dots, \Psi_n(s))$ denote the vector of cumulative transplantation rate, where

$$d\Psi_s = \pi_{s-} d\mathbf{Q}_s - d\pi_s. \quad (3.9)$$

Whenever $\pi_i(s-) \neq 0$, define the diagonal matrix $d\Lambda$, in which the i th diagonal element

$$d\Lambda_i(s) = d\Psi_i(s) / \pi_i(s-).$$

If $\pi_i(s-) = 0$, it is shown later in Proposition 3.4.2 that $d\Psi_i(s) \in [0, \{\pi_{s-} d\mathbf{Q}_s\}_i]$, where $\{\cdot\}_i$ denotes the i th element of the vector. In this case, let

$$\Lambda_i(\{s\}) = d\Psi_i(s) / \{\pi_{s-} d\mathbf{Q}_s\}_i.$$

As calendar time increases, the limiting average rate of transplantation to patients in state i at waiting time s is indeed $d\Psi_i(s)$. With a little abuse of notation, essentially, as $l \rightarrow \infty$,

$$\frac{1}{N_{[0,l]}} \sum_{k=1}^{N_{[0,l]}} d\tilde{N}_{i,n+1}^{(k)}(s) \rightarrow d\Psi_i(s). \quad (3.10)$$

In what follows, we present the main result of this section, in which (3.10) is formulated and proved with probability rigor.

Theorem 3.2.3. *Suppose $\{(H^{(k)}(s), X^{(k)}(s)) : s \geq 0\}$ are independent copies of a generic process $\{(H(s), X(s)) : s \geq 0\}$ and are independent of $\{T_k, S_j : k, j \in \mathbb{N}\}$. Assume that for all $j, k \in \mathbb{N}$, $s \geq 0$ and $A \in \mathcal{B}(W)$,*

$$H^{(k)}(s) \perp\!\!\!\perp \sigma(\{X^{(k)}(u) : u \leq s\}) \mid X^{(k)}(s) \quad (3.11)$$

and

$$P(W_{S_j} \in A \mid W'_{S_j}, \{H^{(k)}(s) : s \geq 0\}) = P(W_{S_j} \in A \mid W'_{S_j}). \quad (3.12)$$

In addition, assume that

$$\sup_{s \geq 0, i \in \mathcal{X}} E[|H(s)| \mid X(s) = i] < \infty. \quad (3.13)$$

Then for any $t \geq 0$ and $i \in \mathcal{X}$,

$$\lim_{l \rightarrow \infty} \int_0^t \frac{1}{N_{[0,l]}} \sum_{k=1}^{N_{[0,l]}} H_i^{(k)}(s) d\tilde{N}_{i,n+1}^{(k)}(s) = \int_0^t E[H(s) \mid X(s) = i] d\Psi_i(s) \quad (3.14)$$

almost surely.

Remark. Note that condition (3.12) is the same as condition (2.5), implying the result can be applied to the residual life $R^{(k)}(s)$. Moreover, a special case of Theorem 3.2.3 is when $\{H(s) : s \geq 0\}$ are bounded deterministic functions. In particular, when $H^{(k)}(s) \equiv 1$, it holds almost surely that

$$\lim_{l \rightarrow \infty} \int_0^t \frac{1}{N_{[0,l]}} \sum_{k=1}^{N_{[0,l]}} d\tilde{N}_{i,n+1}^{(k)}(s) = \int_0^t d\Psi_i(s). \quad (3.15)$$

This special case is useful later in showing the constraint Ψ should satisfy as a result of the scarcity of organs.

Proof. First, similar to (3.7), for all $t, l \in [0, T]$,

$$\begin{aligned} \sum_{j=1}^{L_l} \sum_{k=N_{[0,M_{j-1}]}+1}^{N_{[0,M_j]}} \int_0^t H^{(k)}(s) d\tilde{N}_{i,n+1}^{(k)}(s) &\leq \sum_{k=1}^{N_{[0,l]}} \int_0^t H^{(k)}(s) d\tilde{N}_{i,n+1}^{(k)}(s) \\ &\leq \sum_{j=1}^{L_l+1} \sum_{k=N_{[0,M_{j-1}]}+1}^{N_{[0,M_j]}} \int_0^t H^{(k)}(s) d\tilde{N}_{i,n+1}^{(k)}(s), \end{aligned}$$

where $L_l := \sup\{k \in \mathbb{N} : M_k \leq l\}$ is the number of recurrences to the empty state w_0 up to calendar time l .

First we show $\{\sum_{k=N_{[0,M_{j-1}]}+1}^{N_{[0,M_j]}} \int_0^t H^{(k)}(s) d\tilde{N}_{i,n+1}^{(k)}(s) : j = 1, 2, \dots\}$ are independent and

identically distributed, so that a Strong Law of Large Numbers argument as in Theorem 3.1.4 can be applied. For any $A_1, A_2 \in \mathcal{B}(\mathbb{R})$, let $B_1 = \left\{ \sum_{k=1}^{N_{[0, M_{j-1})}} \int_0^t H^{(k)}(s) d\tilde{N}_{i, n+1}^{(k)}(s) \in A_1 \right\}$, $B_2 = \left\{ \sum_{k=N_{[0, M_{j-1})}+1}^{N_{[0, M_j]}} \int_0^t H^{(k)}(s) d\tilde{N}_{i, n+1}^{(k)}(s) \in A_2 \right\}$, then $P(B_1 \cap B_2)$ can be decomposed into

$$\sum_{n_1, n_2, o_1, o_2 \in \mathbb{N}} P\left(B_1 \cap B_2 \cap \{N_{[0, M_{j-1})} = n_1\} \cap \{O_{[0, M_{j-1})} = o_1\} \cap \{N_{[M_{j-1}, M_j]} = n_2\} \cap \{O_{[M_{j-1}, M_j]} = o_2\}\right). \quad (3.16)$$

Since for all $n_1, n_2, o_1, o_2 \in \mathbb{N}$, on $\{N_{[0, M_{j-1})} = n_1\} \cap \{O_{[0, M_{j-1})} = o_1\} \cap \{N_{[M_{j-1}, M_j]} = n_2\} \cap \{O_{[M_{j-1}, M_j]} = o_2\}$,

$$B_1 = \left\{ \sum_{k=1}^{n_1} \sum_{i=1}^{o_1} H^{(k)}(S_i - T_k) \cdot I(S_i - T_{J_i} = S_i - T_k) \in A_1 \right\}$$

and

$$B_2 = \left\{ \sum_{k=n_1+1}^{n_2} \sum_{i=o_1+1}^{o_2} H^{(k)}(S_i - T_k) \cdot I(S_i - T_{J_i} = S_i - T_k) \in A_2 \right\},$$

where $\{S_i - T_k : i \leq o_1, k \leq n_1\}$ are independent of $\{S_i - T_k : i > o_1, k > n_1\}$, and $S_i - T_{J_i} \in \sigma\{W_{S_i}, W_{S_i-}\}$. By the strong Markov property of $\{(W_t, N_{[0, t]}, O_{[0, t]}) : t \geq 0\}$, the independence among $\{(H^{(k)}, X^{(k)}) : k \in \mathbb{N}\}$, the independence between $\{(H^{(k)}, X^{(k)}) : k \in \mathbb{N}\}$ and $\{T_k, S_j : k, j \in \mathbb{N}\}$, and condition (3.12), $\{\{H^{(k)}(s) : s \geq 0\}, S_i - T_k, S_i - T_{J_i} : i \leq o_1, k \leq n_1\}$ and $(N_{[0, M_{j-1})}, O_{[0, M_{j-1})})$ are independent of $\{\{H^{(k)}(s) : s \geq 0\}, S_i - T_k, S_i - T_{J_i} : i > o_1, k > n_1\}$ and $(N_{[M_{j-1}, M_j]}, O_{[M_{j-1}, M_j]})$, and thus (3.16) is equal to

$$\sum_{n_1, n_2, o_1, o_2 \in \mathbb{N}} P\left(B_1 \cap \{N([0, M_{j-1})) = n_1\} \cap \{O([0, M_{j-1})) = o_1\}\right) \cdot P\left(B_2 \cap \{N_{[0, M_j]} = n_2\} \cap \{O([M_{j-1}, M_j + u)) = o_2\}\right) = P(B_1) \cdot P(B_2).$$

By Fubini-Tonelli,

$$\begin{aligned} E \left[\left| \sum_{k=N_{[0, M_{j-1}]}+1}^{N_{[0, M_j]}} \int_0^t H^{(k)}(s) d\tilde{N}_{i, n+1}^{(k)}(s) \right| \right] &= E \left[\left| \sum_{k=1}^{N_{[0, M_1]}} \int_0^t H^{(k)}(s) d\tilde{N}_{i, n+1}^{(k)}(s) \right| \right] \\ &\leq E \left[\sum_{k=1}^{\infty} \int_0^t I(T_k < M_1) |H^{(k)}(s)| d\tilde{N}_{i, n+1}^{(k)}(s) \right] = \sum_{k=1}^{\infty} \int_0^t E \left[I(T_k < M_1) |H^{(k)}(s)| d\tilde{N}_{i, n+1}^{(k)}(s) \right]. \end{aligned} \quad (3.17)$$

For each k , it follows from

$$d\tilde{N}_{i, n+1}^{(k)}(s) \in \sigma \left(T_k, X^{(k)}(s), X^{(k)}(s-), J_j, S_j : S_j \in [0, T_k + s] \right) \in \mathcal{F}_{T_k+s}$$

and $\{T_k < M_1\} \in \mathcal{F}_{T_k \wedge M_1} \subset \mathcal{F}_{T_k} \subset \mathcal{F}_{T_k+s}$ that

$$\begin{aligned} &E \left[I(T_k < M_1) |H^{(k)}(s)| d\tilde{N}_{i, n+1}^{(k)}(s) \right] \\ &= E \left[E \left(I(T_k < M_1) |H^{(k)}(s)| d\tilde{N}_{i, n+1}^{(k)}(s) \mid \mathcal{F}_{T_k+s} \right) \right] \\ &= E \left[I(T_k < M_1) E(|H^{(k)}(s)| \mid \mathcal{F}_{T_k+s}) d\tilde{N}_{i, n+1}^{(k)}(s) \right], \end{aligned} \quad (3.18)$$

in which by (3.11), (3.12) and the independence between $H^{(k)}$ and $\{T_k, S_j : i, j \in \mathbb{N}\}$,

$$\begin{aligned} &E(|H^{(k)}(s)| \mid \mathcal{F}_{s+T_k}) \\ &= E(|H^{(k)}(s)| \mid T_i, S_j, J_j, \{X^{(i)}(u) : u \in [0, s + T_k - T_i]\} : T_i, S_j \in [0, s + T_k]) \\ &= E(|H^{(k)}(s)| \mid X^{(k)}(s)). \end{aligned}$$

Therefore (3.17) equals to

$$\begin{aligned} &E \left[\sum_{k=1}^{N_{[0, M_1]}} \int_0^t E(|H^{(k)}(s)| \mid X^{(k)}(s) = i) d\tilde{N}_{i, n+1}^{(k)}(s) \right] \\ &\leq \sup_{s \geq 0, i \in \mathcal{X}} E[|H(s)| \mid X(s) = i] E(N_{[0, M_1]}) < \infty, \end{aligned}$$

given (3.13) and the fact that $E(N_{[0, M_1]}) = \tau E(M_1) < \infty$.

By the Strong Law of Large Numbers and a similar calculation of the expectation by

conditioning on $\mathcal{F}_{s+T_k}$, $\int_0^t \sum_{k=1}^{N_{[0,l]}} H_i^{(k)}(s) d\tilde{N}_{i,n+1}^{(k)}(s) / N_{[0,l]}$ converges almost surely to

$$(\tau E(M_1))^{-1} E \left[\sum_{k=1}^{N_{[0,M_1]}} \int_0^t E[H(s) \mid X(s) = i] d\tilde{N}_{i,n+1}^{(k)}(s) \right] \quad (3.19)$$

as $l \rightarrow \infty$.

To show (3.19) is indeed $\int_0^t E[H(s) \mid X(s) = i] d\Psi_i(s)$, note that for all $s > 0$,

$$\begin{aligned} d\pi_i(s) &= (\tau E(M_1))^{-1} E \left[\sum_{k=1}^{N_{[0,M_1]}} \sum_{j \in \mathcal{X}_0 \setminus \{i\}} \left(d\tilde{N}_{ji}^{(k)}(s) - d\tilde{N}_{ij}^{(k)}(s) \right) \right] \\ &= (\tau E(M_1))^{-1} E \left[\sum_{k=1}^{N_{[0,M_1]}} \sum_{j \in \mathcal{X} \setminus \{i\}} \left(dN_{ji}^{(k)}(s) \cdot \tilde{Y}_j^{(k)}(s-) - dN_{ji}^{(k)}(s) \Delta \tilde{N}_{j,n+1}^{(k)}(s) \right. \right. \\ &\quad \left. \left. - \left(dN_{ij}^{(k)}(s) \cdot \tilde{Y}_i^{(k)}(s-) - dN_{ij}^{(k)}(s) \Delta \tilde{N}_{i,n+1}^{(k)}(s) + d\tilde{N}_{i,n+1}^{(k)}(s) \right) \right) \right] \\ &= (\tau E(M_1))^{-1} E \left[\sum_{k=1}^{\infty} I(T_k < M_1) \sum_{j \in \mathcal{X} \setminus \{i\}} \left(dN_{ji}^{(k)}(s) \cdot \tilde{Y}_j^{(k)}(s-) \right. \right. \\ &\quad \left. \left. - dN_{ij}^{(k)}(s) \cdot \tilde{Y}_i^{(k)}(s-) - d\tilde{N}_{i,n+1}^{(k)}(s) \right) \right], \end{aligned} \quad (3.20)$$

as $dN_{ji}^{(k)}(s) \Delta \tilde{N}_{j,n+1}^{(k)}(s)$ and $dN_{ij}^{(k)}(s) \Delta \tilde{N}_{i,n+1}^{(k)}(s)$ are zero almost surely. Since for all k ,

$$\begin{aligned} &E \left[\sum_{j \in \mathcal{X} \setminus \{i\}} I(T_k < M_1) (dN_{ji}^{(k)}(s) \cdot \tilde{Y}_j^{(k)}(s-) - dN_{ij}^{(k)}(s) \cdot \tilde{Y}_i^{(k)}(s-)) \right] \\ &= E \left[\sum_{j \in \mathcal{X} \setminus \{i\}} E \left(I(T_k < M_1) (dN_{ji}^{(k)}(s) \cdot \tilde{Y}_j^{(k)}(s-) - dN_{ij}^{(k)}(s) \cdot \tilde{Y}_i^{(k)}(s-)) \mid \mathcal{F}_{T_k+s-} \right) \right] \\ &= E \left[\sum_{j \in \mathcal{X} \setminus \{i\}} I(T_k < M_1) (dQ_{ji}(s) \cdot \tilde{Y}_j^{(k)}(s-) - dQ_{ij}(s) \cdot \tilde{Y}_i^{(k)}(s-)) \right], \end{aligned}$$

(3.20) leads to

$$d\pi_i(s) = \{\pi_{s-d\mathbf{Q}}\}_i - (\tau E(M_1))^{-1} E \left[\sum_{k=1}^{N_{[0,M_1]}} d\tilde{N}_{i,n+1}^{(k)}(s) \right]. \quad (3.21)$$

Therefore by Fubini-Tonelli, (3.19) is

$$\int_0^t E[H(s) \mid X(s) = i](\{\pi_s d\mathbf{Q}\}_i - d\pi_i(s)),$$

which gives the desired result. $\square$

3.3 Long-term Average Life

Recall the limiting average total life (2.6) and the limiting average life gain from transplantation (2.8) are averages of integrals of life quantities on $d\tilde{N}_{i,n+1}^{(k)}(s)$ in the limit. In what follows, we use Theorem 3.2.3 to show the existence of (2.6) and (2.8) by representing them as integrals with respect to $d\Psi$. As shown previously, each fair allocation rule has a corresponding limiting transplantation rate Ψ . Therefore in addition to delineating the practical meaning of Ψ , Theorem 3.2.3 also provides a means to showing the existence of the objective used in comparing allocations rules and explicitly characterizing the effect of any fair allocation rule on the objective.

Theorem 3.3.1. (*Calculation of Average Total Life*)

The average total life of all patients ever enter the waiting list converges to

$$\int_{[0,T]} \pi_s \mathbf{1}_n ds + \int_{[0,T]} d\Psi_s \mu_s \quad (3.22)$$

almost surely.

Proof. The limiting average total life (2.6) is the sum of limiting average in-waiting-list life and limiting average post-transplantation life

$$\lim_{l \rightarrow \infty} \frac{1}{N_{[0,l]}} \sum_{k=1}^{N_{[0,l]}} \left[\inf_{t \geq 0} \{X^{(k)}(t) = 0\} \wedge T_T^{(k)} + \sum_{i \in \mathcal{X}} \int_0^T R^{(k)}(s) d\tilde{N}_{i,n+1}^{(k)}(s) \right]. \quad (3.23)$$

Since each patient's in-waiting-list life is bounded by T , by Fubini-Tonelli and the Dominated

Convergence Theorem, the limiting average in-waiting-list life is almost surely

$$\begin{aligned}
& \lim_{l \rightarrow \infty} \frac{1}{N_{[0,l]}} \sum_{k=1}^{N_{[0,l]}} \inf_{t \geq 0} \{X^{(k)}(t) = 0\} \wedge T_T^{(k)} \\
&= \lim_{t \rightarrow \infty} \frac{1}{N_{[0,l]}} \sum_{k=1}^{N_{[0,l]}} \int_{[0,T]} I(\tilde{Y}_0^{(k)}(s) \neq 1, \tilde{Y}_{n+1}^{(k)}(s) \neq 1) ds \\
&= \int_{[0,T]} \sum_{i=1}^n \lim_{t \rightarrow \infty} \frac{1}{N_{[0,l]}} \sum_{k=1}^{N_{[0,l]}} \tilde{Y}_i^{(k)}(s) ds = \int_{[0,T]} \boldsymbol{\pi}_s \mathbf{1}_n ds.
\end{aligned}$$

For the post-transplantation residual life part, by Theorem 3.2.3 and condition (2.5), it holds almost surely

$$\lim_{l \rightarrow \infty} \frac{1}{N_{[0,l]}} \sum_{k=1}^{N_{[0,l]}} \int_0^T \sum_{i \in \mathcal{X}} R^{(k)}(s) d\tilde{N}_{i,n+1}(s) = \int_0^T d\boldsymbol{\Psi}_s \boldsymbol{\mu}_s.$$

□

The following representation of the limiting long-term average life gain from transplantation in terms of $\tilde{\boldsymbol{\mu}}$ and $\boldsymbol{\Psi}$ can be shown similarly.

Theorem 3.3.2. (Long-term Average Life Gain)

The limiting average life gain from to transplantation of all patients ever entered the waiting list

$$\lim_{l \rightarrow \infty} \frac{1}{N_{[0,l]}} \sum_{k=1}^{N_{[0,l]}} \sum_{i \in \mathcal{X}} \int_0^T \tilde{R}^{(k)}(s) d\tilde{N}_{i,n+1}^{(k)}(s) = \int_{[0,T]} d\boldsymbol{\Psi}_s \cdot \tilde{\boldsymbol{\mu}}_s \quad (3.24)$$

almost surely.

Proof. The desired result comes directly from condition (2.5) and Theorem 3.2.3. □

3.4 Constraints on the Transplantation Rate

With standards of limiting average life represented in terms of $\boldsymbol{\Psi}$ as in (3.22) and (3.24), fair allocation rules can be compared through their corresponding transplantation rates. To search for the optimal fair allocation rule that maximizes the limiting average life, a natural method is to solve for the optimal transplantation rate, and then find fair allocation rules that lead to the targeted transplantation rate.

However, not every Ψ has a corresponding fair allocation rule. Admissible Ψ should also satisfy certain constraints, which are discussed in this section.

First, the proportion of transplanted patients in all patients ever enter the waiting list, in the limit as calendar time tends to infinity, is bounded by the ratio of organ arrival rate to patient arrival rate, which leads to the following constraint on Ψ :

Proposition 3.4.1. Ψ satisfies

$$\int_{[0,T]} d\Psi_s \mathbf{1}_n \leq \frac{\rho}{\tau}. \quad (3.25)$$

Proof. The limiting proportion of patients who ever receive transplantation is

$$\begin{aligned} & \lim_{l \rightarrow \infty} \frac{\#\{\text{of transplanted patients who arrive in } [0, l]\}}{N_{[0,l]}} \\ &= \lim_{l \rightarrow \infty} \frac{1}{N_{[0,l]}} \sum_{k=1}^{N_{[0,l]}} \int_{[0,T]} \sum_{i \in \mathcal{X}} d\tilde{N}_{i,n+1}^{(k)}(s). \end{aligned}$$

Let $H(s) = 1$ for all $s \leq 0$, then as noted before, $\{H(s)\}$ satisfies conditions in Theorem 3.2.3, and thus almost surely,

$$\lim_{l \rightarrow \infty} \frac{1}{N_{[0,l]}} \sum_{k=1}^{N_{[0,l]}} \int_{[0,T]} \sum_{i \in \mathcal{X}} d\tilde{N}_{i,n+1}^{(k)}(s) = \int_{[0,T]} d\Psi_s \mathbf{1}_n,$$

which is bounded by ρ/τ since the ratio of the number of organ arrivals to the number of patient arrivals converges to the ratio ρ/τ of arrival rates almost surely. $\square$

In addition to (3.22), definitions of π and Ψ imply the following boundedness constraints. Essentially, since the change in the limiting occupancy of any state at any moment is the difference between the inflow of transitions from other states and the outflow of transitions to other states and of transplantations at that moment, the transplantation rate is bounded by the maximal allowance of the occupancy that can be used to flow out for transplantation.

Proposition 3.4.2. For all $s \geq 0$ and $i \in \mathcal{X}$,

1. $\pi_i(s) \in [0, \pi_i(s-)]$, $d\pi_i(s) \in (-\infty, \{\pi_{s-} d\mathbf{Q}_s\}_i]$,
2. $\Psi_i(\{s\}) \in [0, \pi_i(s-)]$, $d\Psi_i(s) \in [0, \infty)$,

3. If $\pi_i(s-) = 0$, then $d\pi_i(s) \in [0, \{\pi_{s-d\mathbf{Q}_s}\}_i]$ and $d\Psi_i(s) \in [0, \{\pi_{s-d\mathbf{Q}_s}\}_i]$.

Proof. Recall that in definition (3.6), $\pi_i(s) = \lim_{t \rightarrow \infty} \sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s)/N_{[0,t]}$. Since for any $t, s_1, s_2 \geq 0$ such that $s_1 < s_2$,

$$\begin{aligned} & \sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s_2) - \sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s_1) = \sum_{k=1}^{N_{[0,t]}} \sum_{j \in \mathcal{X}_0 \setminus \{i\}} \left(\tilde{N}_{ji}^{(k)}(s_1, s_2) - \tilde{N}_{ij}^{(k)}(s_1, s_2) \right) \\ &= \sum_{k=1}^{N_{[0,t]}} \sum_{j \in \mathcal{X} \setminus \{i\}} \left[\int_{(s_1, s_2]} dN_{ji}^{(k)}(u) (\tilde{Y}_j^{(k)}(u-) - \Delta \tilde{N}_{j,n+1}^{(k)}(u)) - \right. \\ & \quad \left. dN_{ij}^{(k)}(u) (\tilde{Y}_i^{(k)}(u-) - \Delta \tilde{N}_{i,n+1}^{(k)}(u)) - d\tilde{N}_{i,n+1}^{(k)}(u) \right]. \end{aligned} \quad (3.26)$$

Since $\Delta \tilde{N}_{i,n+1}^{(k)}(u) \in [0, \tilde{Y}_i^{(k)}(u-)]$, $(\sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s_2) - \sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s_1))/N_{[0,t]}$ is bounded from above by

$$\frac{1}{N_{[0,t]}} \sum_{k=1}^{N_{[0,t]}} \sum_{j \in \mathcal{X} \setminus \{i\}} \int_{(s_1, s_2]} \left(dN_{ji}^{(k)}(u) \tilde{Y}_j^{(k)}(u-) - dN_{ij}^{(k)}(u) \tilde{Y}_i^{(k)}(u-) \right),$$

which converges to $\int_{(s_1, s_2]} \{\pi_{s-d\mathbf{Q}_s}\}_i$ almost surely, as shown in the proof of Theorem 3.2.3.

Letting $s_2 = s$ and $s_1 \uparrow s_2$ gives

$$\lim_{t \rightarrow \infty} \frac{1}{N_{[0,t]}} \left[\sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s) - \sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s-) \right] \leq \int_{\{s\}} \{\pi_{u-d\mathbf{Q}_u}\}_i = 0,$$

which concludes the proof of the first statement. The second statement is a corollary of the first and the definition of Ψ .

The third statement is a consequence of applying the following inequalities to (3.26):

$$\begin{aligned} \sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s-) &\geq \sum_{k=1}^{N_{[0,t]}} \int_{\{s\}} d\tilde{N}_{i,n+1}^{(k)}(u), \\ \sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s-) &\geq \sum_{k=1}^{N_{[0,t]}} \int_{\{s\}} dN_{ij}^{(k)}(u) (\tilde{Y}_i^{(k)}(u-) - \Delta \tilde{N}_{i,n+1}^{(k)}(u)). \end{aligned}$$

If $\pi_i(s-) = 0$, letting $s_2 = s$ and $s_1 \uparrow s_2$ in (3.26) leads to $d\pi_i(s) \geq 0$. $\square$

Chapter 4

Solution to the Optimization Problem

Results in the previous chapter provide an approach to comparing fair allocation rules and searching for the optimal fair allocation rule. With the objective (3.22) (or equivalently, (3.24)) and constraints in (3.25) and Proposition 3.4.2, represented in terms of the limiting transplantation rate Ψ , the comparison of fair allocation rules can be formulated as the comparison of transplantation rates, and, one hopes, the optimal fair allocation rule can be obtained by first solving for the optimal transplantation rate and then finding the corresponding fair allocation rule.

This chapter addresses the problem of characterizing the optimal transplantation rate that maximizes the objective while satisfying the constraints. There are two challenges in the problem: the first is that the constraints in the primal problem add difficulties to the search for the optimal Ψ ; the second is that the problem has a recursive nature, as the transplantation rate at waiting time s affects patients' actual transitions after s , which in turn affects allocation decisions after s . In what follows, we use the primal-dual problem framework to convert the constrained problem to an unconstrained problem, in which a penalty parameter c is used to represent the constraint on the limiting proportion of transplanted patients. Then we apply the Hamilton-Jacobi-Bellman equations to the unconstrained problem and recursively solve for the optimal transplantation rate given any value of the penalty parameter c . For the objective and constraints derived in the previous chapter, we show the solution to the primal problem is the same as the solution to the dual problem, in which the penalty c is solved such that the penalized objective is minimal.

When it is difficult to fully specify the infinite dimensional model parameters such as the expected residual life μ and the counterfactual transition kernel Q , a model in which waiting time is discretized to epochs may be a reasonable approximation to the continuous-time model. At the end of this chapter, we introduce notation relevant to the discrete-time model and provide the optimal transplantation rate in the discrete scenario.

4.1 The Primal and the Dual Problems

The search of the limiting optimal transplantation rate Ψ is formulated as the following primal problem. Find Ψ in the admissible control set

$$\begin{aligned} C := \{ & \Psi : \forall s \geq 0, d\Psi_s = \pi_{s-}dQ_s - d\pi_s, \pi_{0-} = p, \\ & \Psi_i(\{s\}) \in [0, \pi_i(s-)], d\Psi_i(s) \in [0, \infty) \text{ if } \pi_i(s-) \neq 0, \\ & d\Psi_i(s) \in [0, \{\pi_{s-}dQ_s\}_i] \text{ if } \pi_i(s-) = 0 \} \end{aligned}$$

such that the upper bound of the objective

$$\int_{[0,T]} d\Psi_s \tilde{\mu}_s \tag{4.1}$$

is achieved, subject to the constraint

$$\int_{[0,T]} d\Psi_s \cdot \mathbf{1}_n \leq \frac{\rho}{\tau}. \tag{4.2}$$

Note here we are using the limiting average life gain from transplantation (2.8) as the objective. As discussed previously, it is equivalent to using the limiting average total life (2.6) without affecting the form of the optimal solution.

Solving the above constrained problem directly is difficult. We extend the above problem to a general problem, where the objective remains the same, while the constraint is replaced by

$$\int_{[0,T]} d\Psi_s \cdot \mathbf{1}_n \leq u, \tag{4.3}$$

with u being any positive real number. Define

$$F(\Psi, u) = \begin{cases} -\int_{[0,T]} d\Psi_s \cdot \tilde{\mu}_s & \text{if } \Psi \in C \text{ and } \int_{[0,T]} d\Psi_s \cdot \mathbf{1}_n \leq u, \\ \infty & \text{otherwise.} \end{cases}$$

Also define the Lagrangian, which is the conjugate function of F ,

$$L(\Psi, c) = \inf_u \{F(\Psi, u) + \langle u, c \rangle\}.$$

Note that for any $c \geq 0$ and $\Psi \in C$,

$$L(\Psi, c) = -\int_{[0,T]} d\Psi_s \cdot \tilde{\mu}_s + c \cdot \int_{[0,T]} d\Psi_s \cdot \mathbf{1}_n.$$

Solving the general problem with a given value of u requires calculating

$$\varphi(u) := \inf_{\Psi} \{F(\Psi, u)\}.$$

Note

$$\begin{aligned} \inf_{\Psi} L(\Psi, c) &= \inf_{\Psi} \inf_u \{F(\Psi, u) + \langle u, c \rangle\} \\ &= \inf_u \inf_{\Psi} \{F(\Psi, u) + \langle u, c \rangle\} \\ &= \inf_u \{\varphi(u) + \langle u, c \rangle\}, \end{aligned}$$

which is the conjugate of $-\varphi(u)$. By Rockafellar [1974], the conjugates of both sides are

$$-(\inf_{\Psi} L(\Psi, c))^* = \sup_{c \in [0, \infty)} \{\inf_{\Psi} L(\Psi, c) - \langle u, c \rangle\} = \text{cocl}(\varphi(u)),$$

where $(\inf_{\Psi} L(\Psi, c))^*$ is the conjugate of $\inf_{\Psi} L(\Psi, c)$ and $\text{cocl}(\varphi(u))$ is the closure of the convex hull of φ .

The following result shows that given the form of the objective and constraints in our problem, for any $u \in (0, \infty)$, the convex closure of φ at u is $\varphi(u)$ itself. Consequently, $\varphi(u)$

can be obtained by first solving for the Ψ^c that maximizes the unconstrained objective

$$\int_{[0,T]} d\Psi_s \cdot \tilde{\mu}_s - c \cdot \int_{[0,T]} d\Psi_s \cdot \mathbf{1}_n \quad (4.4)$$

for each c over all Ψ in the admissible control set C , and then solving the corresponding c for the given u that maximizes

$$\inf_{\Psi} L(\Psi, c) - \langle u, c \rangle = - \int_{[0,T]} d\Psi_s^c \cdot \tilde{\mu}_s + c \cdot \int_{[0,T]} d\Psi_s^c \cdot \mathbf{1}_n - c \cdot u, \quad (4.5)$$

in particular, for the upper bound $u = \rho/\tau$ in constraint (4.2).

Proposition 4.1.1. *φ is convex and continuous on any $u \in (0, \infty)$.*

Proof. First we show C is convex. Suppose $\Psi^1, \Psi^2 \in C$ and $d\Psi_s^i = \pi_{s-}^i dQ_s - d\pi_s^i$ for $i = 1, 2$, then for all $a \in [0, 1]$, $d(a\Psi_s^1 + (1-a)\Psi_s^2) = \pi_{s-}' dQ_s - d\pi_s'$, where $\pi_s' = a\pi_s^1 + (1-a)\pi_s^2$ and $\pi_{0-}' = p$. It is easy to check the inequalities in the definition of C are satisfied for $a\Psi_s^1 + (1-a)\Psi_s^2$ and π_s' and hence the convexity.

Both the objective (4.1) and the constraint (4.3) are linear functionals of Ψ and hence are convex and continuous on C . Therefore $F(\Psi, u)$ is convex and closed in (Ψ, u) , which leads to the convexity of $\varphi(u) := \inf_{\Psi} \{F(\Psi, u)\}$.

Define the effective domain of φ as $\text{dom } \varphi = \{u : \varphi(u) > -\infty\}$, then any $u \in (0, \infty)$ is in the interior of the effective domain of φ ($\text{int dom } \varphi$), as for any $\Psi \in C$, $-\int_{[0,T]} d\Psi_s \cdot \tilde{\mu}_s \geq -\int_{[0,T]} d\Psi_s \cdot \sup_{\{s \geq 0\}} \{\tilde{\mu}_s\} = -\sup_{\{s \geq 0\}} \{\tilde{\mu}_s\} \cdot (\int_{[0,T]} \pi_{s-} dQ_s - d\pi_s)$, which is bounded from below by $-\sup_{\{s \geq 0\}} \{\tilde{\mu}_s\} \cdot (|\sup_{\{i \in \mathcal{X}\}} \int_0^T q_i(s) ds| \cdot \mathbf{1}_n + \mathbf{1}_n) > -\infty$. By Theorem 8 of Rockafellar [1974], φ is continuous on $\text{int dom } \varphi$, which contains $(0, \infty)$. $\square$

4.2 Optimal Transplantation Rate

As shown in the previous section, solving the constrained primal problem is equivalent to optimizing the penalized objective (4.4) in which c maximizes $\inf_{\Psi} L(\Psi, c) - \langle \rho/\tau, c \rangle$ and then find the appropriate c . We are interested in the case where the inequality constraint is active such that the optimal c ensures $\int_{[0,T]} d\Psi_s^c \cdot \mathbf{1}_n = \rho/\tau$, as otherwise it is implied that transplantation harms instead of benefits patients' life.

The purpose of this section is to characterize the optimal Ψ that maximizes (4.4) given any value of c . Here we approach the problem by starting from the end of waiting time T : the optimal Ψ at each $s \in [0, T]$ is solved recursively as a function of the optimal transplantation rates at waiting times greater than s .

As a preparation for the characterization of the optimal transplantation rate Ψ , or equivalently, the optimal Λ , we solve the ordinary differential equation (3.9) in the definitions of Ψ and Λ to explicitly represent π in terms of a product integral of the counterfactual transition measure $\mathbf{Q}$ and the allocation matrix Λ . The product integral is defined as follows (Gill and Johansen [1990]):

Definition 4.2.1. (Product Integral $\mathcal{P}()$)

Suppose real matrix-valued measure $\mathbf{Q}$ defined on $\mathcal{B}([0, T])$ is of finite variation, that is, for all $0 \leq s < t \leq T$,

$$\sup_{\mathcal{T}} \sum_{i=1}^n |\mathbf{Q}((t_{i-1}, t_i])| < \infty,$$

where $\mathcal{T} = \{t_i : s = t_0 < \dots < t_n = t\}$ is a partition of the interval $(s, t]$ and the norm $|\mathbf{Q}| = \max_i \sum_j |\mathbf{Q}_{ij}|$. Let $\mathcal{P}$ denote the product integral:

$$\mathcal{P}_{(s,t]}(\mathbf{I} + d\mathbf{Q}) := \lim_{\max |t_i - t_{i-1}| \rightarrow 0} \prod_i (\mathbf{I} + \mathbf{Q}((t_{i-1}, t_i])), \quad (4.6)$$

where $\mathbf{I}$ is the identity matrix, $s = t_0 < \dots < t_n = t$ is a partition of the interval $(s, t]$, and $\mathbf{Q}((t_{i-1}, t_i]) = \int_{(t_{i-1}, t_i]} d\mathbf{Q}$. Theorem 1 in Gill and Johansen [1990] shows the existence of the limit in (4.6) and the multiplicative property of the product integral.

Theorem 3 in Gill and Johansen [1990] shows the duality between the integral $\int$ and the product integral $\mathcal{P}$.

Theorem 4.2.2. (Gill and Johansen [1990])

If α is additive and of finite variation, and μ is defined by

$$\mu((s, t]) = \mathcal{P}_{(s,t]}(\mathbf{I} + d\alpha), \quad (4.7)$$

then

$$\alpha((s, t]) = \int_{(s, t]} d(\boldsymbol{\mu} - \mathbf{I}). \quad (4.8)$$

Similarly, if $\boldsymbol{\mu}$ is multiplicative and $\boldsymbol{\mu} - \mathbf{I}$ of finite variation, and if α is defined by (4.8), then (4.7) holds.

Theorem 4 of Gill and Johansen [1990] provides an equivalent representation of (4.7).

Theorem 4.2.3. (*Gill and Johansen [1990]*)

$$\prod_{(s, t]} (I + d\alpha) = I + \sum_{n=1}^{\infty} \int_{u_1 < \dots < u_n; u_i \in (s, t]} \alpha(du_1) \dots \alpha(du_n).$$

Applying the above results to the definition of Ψ and Λ provides a product integral representation of π in terms of Λ and Q :

Proposition 4.2.4. *For any $0 \leq s < t \leq T$,*

$$\pi_t = \pi_s \cdot \prod_{(s, t]} (I + dQ)(I - d\Lambda). \quad (4.9)$$

Proof. Note that the definition of Λ implies that for any $s \geq 0$, $\pi_{s-}(I + dQ_s)d\Lambda_s = d\Psi_s$. Since $d\Psi_s = \pi_{s-}dQ_s - d\pi_s$, $d\pi_s = \pi_{s-}(dQ_s - d\Lambda_s - dQ_s d\Lambda_s)$. As shown in Theorem 3.1.4, π is of finite variation, and thus

$$\begin{aligned} \pi_t &= \pi_s + \int_{(s, t]} \pi_{u_1-} \cdot (dQ_{u_1} - d\Lambda_{u_1} - dQ_{u_1} d\Lambda_{u_1}) \\ &= \pi_s + \int_{(s, t]} \left(\pi_{s-} + \int_{(s, u_1)} \pi_{u_2-} \cdot (dQ_{u_2} - d\Lambda_{u_2} - dQ_{u_2} d\Lambda_{u_2}) \right) \\ &\quad \cdot (dQ_{u_1} - d\Lambda_{u_1} - dQ_{u_1} d\Lambda_{u_1}) \\ &= \dots = \pi_s \cdot \left(I + \sum_{n=1}^{\infty} \int_{u_1 < \dots < u_n; u_i \in (s, t]} \alpha(du_1) \dots \alpha(du_n) \right), \end{aligned}$$

where $d\alpha(s) = dQ_s - d\Lambda_s - dQ_s d\Lambda_s$. Applying Theorem 4.2.3 finishes the proof of (4.9). $\square$

Some properties of π that are useful later in solving for the optimal Ψ are given by multiplicative properties of the product integral:

Proposition 4.2.5. *For all s and t such that $0 \leq s < t \leq T$,*

$$\begin{aligned}
\pi_{t-} &= \pi_s \cdot \prod_{(s,t)} (I + dQ)(I - d\Lambda), \\
\pi_{t-} &= \pi_{s-} \cdot \prod_{[s,t)} (I + dQ)(I - d\Lambda), \\
\pi_t &= \pi_{s-} \cdot \prod_{[s,t]} (I + dQ)(I - d\Lambda), \\
\pi_t &= \pi_{t-} \cdot \prod_{\{t\}} (I + dQ)(I - d\Lambda) = \pi_{t-} \cdot (I - \Lambda(\{t\})).
\end{aligned} \tag{4.10}$$

Proof. (4.10) results from the fact

$$\prod_{\{t\}} (I + dQ)(I - d\Lambda) = (I + Q(\{t\}))(I - \Lambda(\{t\})) = I - \Lambda(\{t\}),$$

as the measure Q is absolutely continuous to the Lebesgue measure. All other equations can be shown by the multiplicative property of the product integral and (4.10). $\square$

Proposition 4.2.6. $\prod_{[0,t]} (I - d\Lambda)$ can be written as the product of its atomic part and continuous part

$$\prod_{[0,t]} (I - d\Lambda) = \prod_{s \in [0,t]} (I - \Lambda(\{s\})) \cdot \prod_{s \in [0,t], \Lambda(\{s\})=0} (I - d\Lambda).$$

Proof. Since $d\Lambda_s$ is diagonal, $\prod_{[0,t]} (I - d\Lambda_s)$ is commutative in multiplication. When $d\Lambda$ is atomic at s such that for some i , $\Lambda_i(\{s\}) \neq 0$, by the definition (4.6), the product integral over such atomic points is just the product $\prod_{s \in [0,t]} (I - \Lambda(\{s\}))$. $\square$

With the preparations above, the main result of this section gives the form of the optimal transplantation rate:

Theorem 4.2.7. (Optimal Solution)

Under any fixed penalty parameter $c \geq 0$, the optimal Ψ^c and Λ^c that maximizes (4.4) satisfy

$$\Psi_i^c(\{s\}) = \Lambda_i^c(\{s\}) \cdot \pi_i(s-) := I(\varphi_i^c(s) > c) \cdot \pi_i(s-) \tag{4.11}$$

if $\pi_i(s-) > 0$, and

$$\frac{d\Psi_i^c(s)}{ds} = \Lambda_i^c(\{s\}) \cdot \sum_{x \in \mathcal{X}} \pi_x(s-) q_{x,i}(s) = I(\varphi_i^c(s) > c) \cdot \sum_{x \in \mathcal{X}} \pi_x(s-) q_{x,i}(s) \quad (4.12)$$

if $\pi_i(s-) = 0$, for all $s \in [0, T]$ and $x \in \mathcal{X}$. Here

$$\varphi_i^c(s) = \frac{\tilde{\mu}_i(s) - \gamma_i^c(s+) \eta_i^c(s+)}{1 - \gamma_i^c(s+)}, \quad (4.13)$$

in which the vector

$$\gamma^c(s+) \boldsymbol{\eta}^c(s+) = \int_{(s,T]} \prod_{(s,t)} (I + d\mathbf{Q})(I - d\mathbf{\Lambda}^c) \cdot d\mathbf{\Lambda}_t^c \cdot \tilde{\boldsymbol{\mu}}_t, \quad (4.14)$$

whose i th element is the expected life gain from transplantation after waiting time s if the occupancy is concentrated in state i at $s-$ and none is transplanted at s , while the vector

$$\gamma^c(s+) = \int_{(s,T]} \prod_{(s,t)} (I + d\mathbf{Q})(I - d\mathbf{\Lambda}^c) \cdot d\mathbf{\Lambda}_t^c \cdot \mathbf{1}_n, \quad (4.15)$$

whose i th element is the cumulative rate of transplantation after waiting time s if the occupancy is concentrated in state i at $s-$ and none is transplanted at s .

Proof. Since $\int_{[0,T]} d\Psi_s \cdot \mathbf{1}_n$ is bounded and non-negative, for each $i \in \mathcal{X}$, Ψ_i is a finite measure on $([0, T], \mathcal{B}([0, T]))$. By Lebesgue decomposition theorem (c.f. for example Halmos [1974]),

$$\Psi_i = \Psi_i^{ac} + \Psi_i^s,$$

where Ψ_i^{ac} is a finite non-negative measure that is absolutely continuous with respect to the Lebesgue measure and Ψ_i^s is a finite non-negative measure that is singular to the Lebesgue measure. By Radon-Nikodym theorem, there exists a unique (up to Lebesgue measure) measurable derivative $\psi_i : [0, T] \rightarrow [0, \infty)$ such that for any $A \in \mathcal{B}([0, T])$

$$\int_A d\Psi_i^{ac}(s) = \int_A \psi_i(s) ds.$$

By the definition of singular measures, there exists $B \in \mathcal{B}([0, T])$ such that its Lebesgue measure $\int_B ds = 0$ and

$$\int_B d\Psi_i^s = \int_{[0, T]} d\Psi_i^s.$$

Define the value function $V_{s-}(\boldsymbol{\pi})$ as the supremum of the penalized objective function (4.4) if the occupancy is $\boldsymbol{\pi}$ at time $s-$:

$$V_{s-}(\boldsymbol{\pi}) = \sup_{\{\boldsymbol{\Psi}_t: s \leq t \leq T\}} \left\{ \int_{[s, T]} d\boldsymbol{\Psi}_t \cdot (\tilde{\boldsymbol{\mu}}_t - c \cdot \mathbf{1}_n) \right\} \quad (4.16)$$

Where $d\boldsymbol{\Psi}_t = \boldsymbol{\pi}_{t-} d\mathbf{Q}_t - d\boldsymbol{\pi}_t$, $\boldsymbol{\pi}_{s-} = \boldsymbol{\pi}$ and $\boldsymbol{\pi}_t = \boldsymbol{\pi} \cdot \prod_{[s, t]} (\mathbf{I} + d\mathbf{Q})(\mathbf{I} - d\boldsymbol{\Lambda})$ for any $t \in [s, T]$.

By the dynamic programming principle (see, for example, Fleming and Soner [2006]), for all $s \in [0, T]$ and $\Delta s > 0$,

$$V_{s-}(\boldsymbol{\pi}) = \sup_{\{\boldsymbol{\Psi}_t: s \leq t < s + \Delta s\}} \left\{ V_{(s+\Delta s)-}(\boldsymbol{\pi}_{(s+\Delta s)-}) + \int_{[s, s+\Delta s]} (d\boldsymbol{\Psi}^{ac}(t) + d\boldsymbol{\Psi}^s(t)) \cdot (\tilde{\boldsymbol{\mu}}_t - c \cdot \mathbf{1}_n) \right\}$$

which leads to

$$\sup_{\{\boldsymbol{\Psi}_t: s \leq t < s + \Delta s\}} \left\{ \frac{V_{(s+\Delta s)-}(\boldsymbol{\pi}_{(s+\Delta s)-}) - V_{s-}(\boldsymbol{\pi}_{s-})}{\Delta s} + \frac{1}{\Delta s} \int_{[s, s+\Delta s]} (d\boldsymbol{\Psi}^{ac}(t) + d\boldsymbol{\Psi}^s(t)) \cdot (\tilde{\boldsymbol{\mu}}_t - c \cdot \mathbf{1}_n) \right\} = 0.$$

If $s \notin B$, $\int_{\{s\}} d\Psi_i^s(u) = 0$ for all $i \in \mathcal{X}$, and the Radon-Nikodym derivative ψ_i exists at s , in which case the value function is a solution to the Hamilton-Jacobi-Bellman equations

$$\frac{\partial V}{\partial s} + \sup_{\{\boldsymbol{\Psi}_t: s \leq t < s + \Delta s\}} \left\{ \boldsymbol{\psi}_s \tilde{\boldsymbol{\mu}}_s - c \cdot \boldsymbol{\psi}_s \mathbf{1}_n + \frac{\partial V}{\partial \boldsymbol{\pi}} \cdot \frac{d\boldsymbol{\pi}}{ds} \right\} = 0, \quad (4.17)$$

where

$$\frac{\partial V}{\partial \boldsymbol{\pi}} = \int_{(s, T]} \prod_{(s, t)} (\mathbf{I} + d\mathbf{Q})(\mathbf{I} - d\boldsymbol{\Lambda}) \cdot d\boldsymbol{\Lambda}_t \cdot (\tilde{\boldsymbol{\mu}}_t - c \mathbf{1}_n),$$

as $\boldsymbol{\pi}_{t-}(\mathbf{I} + d\mathbf{Q}_t)d\boldsymbol{\Lambda}_t = d\boldsymbol{\Psi}_t$ and $\boldsymbol{\pi}_{t-} = \boldsymbol{\pi} \cdot \prod_{[s, t]} (\mathbf{I} + d\mathbf{Q})(\mathbf{I} - d\boldsymbol{\Lambda})$ by the multiplicative

property of π in Proposition 4.2.5, and

$$\frac{d\pi}{ds} = \pi_{s-} \cdot \mathbf{q}_s - \psi_s.$$

If s is an atomic point of Ψ_i , then $\pi_i(s-) > 0$, and letting $\Delta s \rightarrow 0$ leads to the Hamilton-Jacobi-Bellman equations

$$\begin{aligned} V_{s-}(\pi) &= \sup_{\Lambda(\{s\})} \{V_s(\pi(I - \Lambda(\{s\}))) + \pi\Lambda(\{s\})(\tilde{\mu}_s - c \cdot \mathbf{1}_n)\} \\ &= \sup_{\Lambda(\{s\})} \left\{ \pi\Lambda(\{s\}) \cdot (\tilde{\mu}_s - c \cdot \mathbf{1}_n) \right. \\ &\quad \left. + \int_{(s,T]} \pi \cdot \prod_{[s,t)} (I + d\mathbf{Q})(I - d\Lambda) \cdot d\Lambda_t \cdot (\tilde{\mu}_t - c \cdot \mathbf{1}_n) \right\}, \end{aligned} \quad (4.18)$$

where $\Lambda(\{s\})$ satisfies

$$0 \leq \pi\Lambda(\{s\}) \leq \pi.$$

We claim that if a function V satisfies (4.17) and (4.18), depending on whether Ψ is absolutely continuous or singular to Lebesgue measure at s , then V is the value function as defined in (4.16) for all waiting time $s \in [0, T]$ and distribution $\pi = (\pi_1, \dots, \pi_n)$ of initial states. To show this, we first prove V is an upper bound of the value function. Since

$$\begin{aligned} V_{(s+\Delta s)-}(\pi_{(s+\Delta s)-}) &= V(s-, \pi_{s-}) \\ &\quad + \int_{[s, s+\Delta s) \cap B^c} \left(\frac{\partial V}{\partial s} + \frac{\partial V}{\partial \pi} \cdot \frac{d\pi}{ds} \right) ds \\ &\quad + \sum_{u \in [s, s+\Delta s) \cap B} (V(u, \pi_u) - V(u-, \pi_{u-})), \end{aligned}$$

with (4.17) and (4.18), the left side of the above equation is no greater than

$$V(s-, \pi_{s-}) - \int_{[s, s+\Delta s)} (d\Psi_t^{ac} + d\Psi_t^s) \cdot (\tilde{\mu}_t - c \cdot \mathbf{1}_n)$$

with any Ψ . Letting $s + \Delta s = T$ leads to

$$V(s-, \pi_{s-}) \geq \int_{[s, T)} (d\Psi^{ac}(t) + d\Psi^s(t)) \cdot (\tilde{\mu}_t - c \cdot \mathbf{1}_n), \quad (4.19)$$

which verifies that V is an upper bound of the value function.

Now we show the equality can be achieved in (4.19) by providing the solution form of Ψ leading to V that satisfies (4.17) and (4.18), and conclude that V is indeed the value function.

From the Hamilton-Jacobi-Bellman equations (4.17),

$$\begin{aligned} -\frac{\partial V}{\partial s} = & \sup_{\{\Psi_t: s \leq t < s + \Delta s\}} \{(\tilde{\mu}_s - \gamma^c(s+) \boldsymbol{\eta}^c(s+) - c(\mathbf{1}_n - \gamma^c(s+)) \cdot \boldsymbol{\psi}_s \\ & + (\gamma^c(s+) \boldsymbol{\eta}^c(s+) - c \gamma^c(s+)) \cdot \boldsymbol{\pi}(s-) \cdot \mathbf{q}(s)\}, \end{aligned}$$

and the supremum on the right side is obtained by taking

$$\psi_i^c(s) = \begin{cases} \infty, & \text{if } \frac{\tilde{\mu}_i(s) - \gamma_i^c(s+) \eta_i^c(s+)}{1 - \gamma_i^c(s+)} > c \text{ and } \pi_x(s-) > 0, \\ \sum_{x \in \mathcal{X}} \pi_x(s-) q_{x,i}(s), & \text{if } \frac{\tilde{\mu}_i(s) - \gamma_i^c(s+) \eta_i^c(s+)}{1 - \gamma_i^c(s+)} > c \text{ and } \pi_x(s-) = 0, \\ 0, & \text{if } \frac{\tilde{\mu}_i(s) - \gamma_i^c(s+) \eta_i^c(s+)}{1 - \gamma_i^c(s+)} \leq c. \end{cases} \quad (4.20)$$

Note the function in the supremum of (4.18) is a linear functional of $\mathbf{\Lambda}$ with coefficient

$$\tilde{\mu}_s - \gamma^c(s+) \boldsymbol{\eta}^c(s+) - c(\mathbf{1}_n - \gamma^c(s+)),$$

indicating the optimal $\mathbf{\Lambda}^c$ at any $s \in [0, T]$ should satisfy

$$\mathbf{\Lambda}^c(\{s\}) = I(\varphi^c(s) > c). \quad (4.21)$$

Combining the absolutely continuous and singular solutions (4.20) and (4.21) proves the desired solution form.

Finally, we show $\{\gamma^c(s+) \boldsymbol{\eta}^c(s+)\}_i$ is indeed the expected life gain after waiting time s if the occupancy is concentrated in state i at $s-$ and none is transplanted at s . Let $\mathbf{e}_i$ denote

the n -dimensional vector with the i th element being 1 and all other elements being 0, then

$$\{\gamma^c(s+)\eta^c(s+)\}_i = \mathbf{e}_i \cdot \int_{(s,T]} \prod_{(s,t)} (\mathbf{I} + d\mathbf{Q})(\mathbf{I} - d\mathbf{\Lambda}^c) \cdot d\mathbf{\Lambda}_t^c \cdot \tilde{\boldsymbol{\mu}}_t.$$

Since for any $t \in (s, T]$, $\mathbf{e}_i \cdot \prod_{(s,t)} (\mathbf{I} + d\mathbf{Q})(\mathbf{I} - d\mathbf{\Lambda}^c)$ is the limiting average occupancy at waiting time $t-$ if started from full occupancy of state i at $s-$ and if none is transplanted at s , we have the desired result. The result for $\{\gamma^c(s+)\}_i$ can be shown similarly. $\square$

4.3 Optimal Transplantation Rate in Discrete Time

The form of the optimal transplantation rate characterized in the previous section relies on the assumption that model parameters such as the expected residual life $\boldsymbol{\mu}_s$ and the counterfactual transition kernel $d\mathbf{Q}_s$ are fully specified for all $s \in [0, T]$. While it is a valid assumption in the model, estimations of the parameters in practice depend on the quality of the data. For example, when the data is relatively sparse, it may be difficult to obtain accurate estimations of $\boldsymbol{\mu}$ and $\mathbf{Q}$ due to their infinite dimensions. Under such circumstances, it might be reasonable to consider an approximate model in which waiting time is discretized to reduce the dimension of unknown parameters.

In this section, we characterize the form of the optimal $\mathbf{\Lambda}$ for a discrete waiting time model. Here we assume waiting time is discretized into epochs $\{0, 1, \dots, T\}$ and transitions and transplantations can only occur at the end of each epoch. In discrete time, the model depends on the order of transitions and transplantations. As a first approximation, assume transplantations are always ahead of transitions at the end of each epoch. The form of the solution for the transplantation-after-transition case can be readily solved along the same lines. Let $\mathbf{B}_t$ denote the counterfactual transition matrix from epoch t to $t+1$, then the counterparts of the limiting average occupancy $\boldsymbol{\pi}$ and limiting transplantation rate $\mathbf{\Lambda}$ in the discrete model satisfy

$$\boldsymbol{\pi}_{t+1} = \boldsymbol{\pi}_t (\mathbf{I} - \mathbf{\Lambda}_t) \mathbf{B}_t. \quad (4.22)$$

For convenience, define

$$A_{ij}(t) := (1 - \Lambda_i(t)) \cdot B_{ij}(t),$$

then $\pi_{t+1} = \pi_t \mathbf{A}_t$ for all $t \in \{0, 1, \dots, T-1\}$.

As the counterpart of (3.22), the objective of limiting average total life is

$$\sum_{t=0}^T (\pi_t \mathbf{1}_n + \pi_t \mathbf{\Lambda}_t \boldsymbol{\mu}_t), \quad (4.23)$$

and the counterpart of the constraint (3.25) is

$$\sum_{t=0}^T \pi_t \mathbf{\Lambda}_t \mathbf{1}_n \leq \frac{\rho}{\tau}. \quad (4.24)$$

Use the Lagrange multiplier $c \geq 0$ to represent the penalty if $\sum \pi_t \mathbf{\Lambda}_t \mathbf{1}_n > \rho/\tau$, define the penalized objective function as

$$\sum_{t=0}^T (\pi_t \mathbf{1}_n + \pi_t \mathbf{\Lambda}_t \boldsymbol{\mu}_t - \pi_t \mathbf{\Lambda}_t c \cdot \mathbf{1}_n) + \frac{c \cdot \rho}{\tau}. \quad (4.25)$$

Define the value function as the supremum of the objective if the system starts at time t and state π :

$$V_t(\pi) = \sup_{\{\mathbf{\Lambda}_s: s \geq t\}} \left\{ \sum_{s=t}^T (\pi_s \mathbf{1}_n + \pi_s \mathbf{\Lambda}_s \boldsymbol{\mu}_s - c \pi_s \mathbf{\Lambda}_s \mathbf{1}_n) \right\} + c \cdot \frac{\rho}{\tau}.$$

Proposition 4.3.1. (*Discrete Time Hamilton-Jacobi-Bellman Equations*)

$$V_t(\pi) = \sup_{\mathbf{\Lambda}_t} (V_{t+1}(\pi \cdot (\mathbf{I} - \mathbf{\Lambda}_t) \mathbf{B}_t) + f_t(\pi, \mathbf{\Lambda}_t)), \quad (4.26)$$

where

$$f_t(\pi, \mathbf{\Lambda}_t) = \mathbf{1}_n \pi_t + \pi_t \mathbf{\Lambda}_t \boldsymbol{\mu}_t - c \pi_t \mathbf{\Lambda}_t \mathbf{1}_n$$

is the one-step pay-off function given the current state π and allocation policy $\mathbf{\Lambda}_t$.

Proof. The equation follows from the definition of the value function and the dynamic programming principle that the optimal allocation rule at time t is such that the sum of one step reward and the optimal objective function starting from $t+1$ and state $\pi \cdot (\mathbf{I} - \mathbf{\Lambda}_t) \mathbf{B}_t$ after the one-step transition or allocation is optimal. $\square$

(4.26) can be represented explicitly using the product integral representation (in the discrete time case, it is just the usual product of matrices), and the form of the solution is the similar to that of the continuous time model. For the simplicity of expressions, from now on we will denote

$$\prod_{t+1}^{s-1} := \prod_{u=t+1}^{s-1} (I - \Lambda_u) B_u,$$

and for any $t \geq 0$

$$\prod_t^{t-1} := I.$$

Proposition 4.3.2. (Optimal Solution in Discrete Time)

Then for each waiting time t , the optimal solution vector Λ_t satisfies

$$\begin{aligned} \Lambda_t &= I(\mu_t - \sum_{s=t+1}^T (B_t \cdot (\mathbf{1}_n + \prod_{t+1}^{s-1} \Lambda_s (\mu_s - c \cdot \mathbf{1}_n))) > c \cdot \mathbf{1}_n) \\ &= I(\mu_t - \mathbf{l}_t > c \cdot (\mathbf{1}_n - \mathbf{p}_t)), \end{aligned} \quad (4.27)$$

where the i th element of the vector

$$\mathbf{l}_t = \sum_{s=t+1}^T B_t \cdot \prod_{t+1}^{s-1} \cdot (\mathbf{1}_n + \Lambda_s \mu_s)$$

is the expected residual life if the limiting average occupancy is concentrated in state i at waiting time t and not transplanted at t , and the i th element of the vector

$$\mathbf{p}_t = \sum_{s=t+1}^T B_t \cdot \prod_{t+1}^{s-1} \cdot \Lambda_s \mathbf{1}_n$$

is the probability of being transplanted after t , if the limiting average occupancy is concentrated in state i at waiting time t and not transplanted at t .

Proof. Rewrite (4.22) with the product integral representation (without ambiguity, let the dimension of each vector/matrix be adaptive to the formulae):

$$\pi_t = \pi_0 \prod_{u=0}^{t-1} (I - \Lambda_u) B_u.$$

Substituting into (4.23) gives the objective function (recall that $\prod_0^{t-1}$ denotes $\prod_0^{t-1}(\mathbf{I} - \mathbf{\Lambda}_u)\mathbf{B}_u$ and $\prod_t^{t-1}$ is equal to the identity matrix)

$$\sum_{t=0}^T \pi_0 \cdot \prod_0^{t-1} \cdot (\mathbf{1}_n + \mathbf{\Lambda}_t(\boldsymbol{\mu}_t - c \cdot \mathbf{1}_n)).$$

For an arbitrary waiting time t^* , the derivative of this function with respect to $\boldsymbol{\pi}_{t^*}\mathbf{\Lambda}_{t^*} = \pi_0 \prod_0^{t^*-1} \mathbf{\Lambda}_{t^*}$ is

$$\sum_{t=t^*+1}^T (-\mathbf{B}_{t^*} \prod_{t^*+1}^{t-1}) \cdot (\mathbf{1}_n + \mathbf{\Lambda}_t(\boldsymbol{\mu}_t - c \cdot \mathbf{1}_n)) + (\boldsymbol{\mu}_{t^*} - c \cdot \mathbf{1}_n),$$

which indicates the objective function is linear with respect to $\boldsymbol{\Lambda}_{t^*}\boldsymbol{\pi}_{t^*}$ and $\mathbf{\Lambda}_{t^*}$, and to optimize it, let $\Lambda_i(t^*) = 1$, so that $\pi_i(t^*)\Lambda_i(t^*) = \pi_i(t^*)$ if the i th element of the above vector is positive, and let $\Lambda_i(t^*) = 0$ otherwise, which gives (4.27).

To see $l_i(t^*)$ is indeed the expected residual life after t^* if the limiting average occupancy is concentrated in state i at waiting time t^* and not transplanted at t^* , as in the continuous-time model, let $\mathbf{e}_i$ denote the n -dimensional vector with the i th element 1 and all others 0, then

$$\begin{aligned} l_i(t^*) &= \mathbf{e}_i \sum_{s=t^*+1}^T (\mathbf{B}_{t^*} \prod_{t^*+1}^{s-1} (\mathbf{1}_n + \mathbf{\Lambda}_s \boldsymbol{\mu}_s)) \\ &= \sum_{s=t^*+1}^T (\mathbf{e}_i \mathbf{B}_{t^*} \prod_{t^*+1}^{s-1} (\mathbf{1}_n + \mathbf{\Lambda}_s \boldsymbol{\mu}_s)) \\ &= \sum_{s=t^*+1}^T \pi_s (\mathbf{1}_n + \mathbf{\Lambda}_s \boldsymbol{\mu}_s), \end{aligned}$$

where $\boldsymbol{\pi}_s$ is the state of the system at s if the limiting average occupancy is concentrated in state i at time t^* . Similarly,

$$p_i(t^*) = \sum_{s=t+1}^T \pi_s \mathbf{\Lambda}_s \mathbf{1}_n.$$

Checking the form of objective function (4.23) and the constraint (4.24) leads to the desired result for $l_i(t)$ and $p_i(t)$. $\square$

An alternative method to show the solution form is to use the Kuhn-Tucker Conditions:

Proposition 4.3.3. *The optimal solution that optimizes (4.23) with constraint (4.24) is*

$$\Lambda_i(t) = I(\mu_i(t) - \{\mathbf{B}_t \boldsymbol{\lambda}_{t+1}\}_i > c), \quad (4.28)$$

where $\boldsymbol{\lambda}_t = \partial H^{(t)}(\boldsymbol{\pi}_t, \boldsymbol{\Lambda}_t, \boldsymbol{\lambda}_{t+1}, c) / \partial \boldsymbol{\pi}$ is the partial derivative of the Hamiltonian at $\boldsymbol{\pi} = \boldsymbol{\pi}_t$, $\boldsymbol{\Lambda} = \boldsymbol{\Lambda}_t$, $\boldsymbol{\lambda} = \boldsymbol{\lambda}_{t+1}$ and c

$$H^{(t)}(\boldsymbol{\pi}, \boldsymbol{\Lambda}, \boldsymbol{\lambda}, c) = \boldsymbol{\pi} \mathbf{1}_n + \boldsymbol{\pi} \boldsymbol{\Lambda} (\boldsymbol{\mu}_t - c \cdot \mathbf{1}_n) + (\boldsymbol{\pi} (\mathbf{I} - \boldsymbol{\Lambda}) \mathbf{B}_t) \boldsymbol{\lambda}. \quad (4.29)$$

Proof. (4.22) can be taken as sharp constraints. Since there are T constraints in total, insert T Lagrange multiplier vectors $\boldsymbol{\lambda}_1, \dots, \boldsymbol{\lambda}_T$, the Lagrangian is

$$L := \sum_{t=0}^T (\boldsymbol{\pi}_t \mathbf{1}_n + \boldsymbol{\pi}_t \boldsymbol{\Lambda}_t \boldsymbol{\mu}_t - \boldsymbol{\pi}_t \boldsymbol{\Lambda}_t c \cdot \mathbf{1}_n) + \frac{c \cdot \rho}{\tau} + \sum_{t=0}^{T-1} (\boldsymbol{\pi}_t (\mathbf{I} - \boldsymbol{\Lambda}_t) \mathbf{B}_t - \boldsymbol{\pi}_{t+1}) \boldsymbol{\lambda}_{t+1}. \quad (4.30)$$

Define dummy variables $\boldsymbol{\lambda}_0$ and $\boldsymbol{\lambda}_{T+1} = 0$ for the simplicity of expressions, the Lagrangian equals to

$$\begin{aligned} L &= \sum_{t=0}^{T-1} H^{(t)}(\boldsymbol{\pi}_t, \boldsymbol{\Lambda}_t, \boldsymbol{\lambda}_{t+1}, c) - \sum_{t=1}^T \boldsymbol{\pi}_t \boldsymbol{\lambda}_t + (\boldsymbol{\pi}_T \mathbf{1}_n + \boldsymbol{\pi}_T \boldsymbol{\Lambda}_T \boldsymbol{\mu}_T - \boldsymbol{\pi}_T \boldsymbol{\Lambda}_T c \cdot \mathbf{1}_n) + \frac{c \cdot \rho}{\tau} \\ &= \sum_{t=0}^T (H^{(t)}(\boldsymbol{\pi}_t, \boldsymbol{\Lambda}_t, \boldsymbol{\lambda}_{t+1}, c) - \boldsymbol{\pi}_t \boldsymbol{\lambda}_t) + \boldsymbol{\pi}_0 \boldsymbol{\lambda}_0 + \frac{c \cdot \rho}{\tau} \end{aligned}$$

since

$$dL = \sum_{t=0}^T (d\boldsymbol{\pi}_t \cdot (\frac{\partial}{\partial \boldsymbol{\pi}} H^{(t)} - \boldsymbol{\lambda}_t) + d\boldsymbol{\Lambda}_t \cdot \frac{\partial}{\partial \boldsymbol{\Lambda}} H^{(t)}) + d\boldsymbol{\pi}_0 \boldsymbol{\lambda}_0$$

the maximum principle is

$$\begin{aligned}
\pi_{t+1} &= \pi_t(I - \Lambda_t)B_t \\
\frac{\rho}{\tau} &= \sum_{t=0}^T \pi_t \Lambda_t \mathbf{1}_n \\
\lambda_t &= \frac{\partial}{\partial \pi} H^{(t)}(\pi_t, \Lambda_t, \lambda_{t+1}, c) \\
\Lambda_t &= \operatorname{argmax} H^{(t)}(\pi_t, \Lambda_t, \lambda_{t+1}, c).
\end{aligned} \tag{4.31}$$

Solving the last equation of (4.31), since letting $\Psi_t = \pi_t \Lambda_t$ gives

$$H^{(t)}(\pi_t, \Lambda_t, \lambda_{t+1}, c) = \pi_t(\mathbf{1}_n + B_t \lambda_{t+1}) + \Psi_t(\mu_t - c \mathbf{1}_n - B_t \lambda_{t+1}),$$

to maximize $H^{(t)}$, it suffices to let $\Psi_i(t) = \pi_i(t)$ if $\mu_i(t) - \{B_t \lambda_{t+1}\}_i > c$ and let $\Psi_i(t) = 0$ otherwise, which proves the desired solution. $\square$

A natural question is whether the solution from product integral representation and the solution obtained by using Kuhn-Tucker conditions are equivalent. The equivalence is shown in the following result, moreover, we explain practical meanings of the Lagrange multipliers λ_t .

Proposition 4.3.4. *Solutions (4.27) and (4.28) are equivalent, and*

$$\{B_t \lambda_{t+1}\}_i = l_i(t) - c \cdot p_i(t).$$

Proof. By (4.31), it suffices to prove

$$B_t \lambda_{t+1} = B_t \cdot \frac{\partial}{\partial \pi} H^{(t+1)}(\pi_{t+1}, \Lambda_{t+1}, \lambda_{t+2}, c) = l_t - c \cdot p_t.$$

Since

$$\begin{aligned}
\lambda_{t+1} &= \frac{\partial}{\partial \pi} H^{(t+1)}(\pi_{t+1}, \Lambda_{t+1}, \lambda_{t+2}, c) \\
&= (\mathbf{1}_n + \Lambda_{t+1} \mu_{t+1} - c \cdot \Lambda_{t+1}) + (I - \Lambda_{t+1}) B_{t+1} \cdot \lambda_{t+2}
\end{aligned}$$

and $\lambda_{T+1} = 0$, we have

$$\lambda_{t+1} = \sum_{s=t+1}^T \prod_{u=t+1}^{s-1} (I - \Lambda_u) B_u \cdot (\mathbf{1}_n + \Lambda_s(\mu_s - c \cdot \mathbf{1}_n)).$$

Therefore

$$B_t \lambda_{t+1} = \sum_{s=t+1}^T B_t \prod_{u=t+1}^{s-1} (\mathbf{1}_n + \Lambda_s \mu_s) - \sum_{s=t+1}^T B_t \prod_{u=t+1}^{s-1} c \cdot \mathbf{1}_n,$$

which is the desired result. □

Chapter 5

The Proposed Allocation Strategy

Results in the previous section delineate the form of the optimal transplantation rate Ψ . If we can find a fair allocation rule such that the corresponding limiting transplantation rate has the desired form, then allocating organs to patients in the waiting list according to the allocation rule will indeed lead to the maximal long-term average total life (or long-term average life gain) as calendar time increases.

To find such a fair allocation rule, recall that Theorem 3.2.3 essentially shows

$$\frac{1}{N_{[0,l]}} \sum_{k=1}^{N_{[0,l]}} d\tilde{N}_{i,n+1}^{(k)}(s) \rightarrow d\Psi_i(s).$$

Therefore, given the optimal transplantation rate Ψ , the goal (with slight abuse of notation) is to find a fair allocation rule such that $\sum_{k=1}^{N_{[0,l]}} d\tilde{N}_{i,n+1}^{(k)}(s)/N_{[0,l]}$ approaches $d\Psi_i(s)$ as calendar time increases.

However, it is not guaranteed such allocation rules exist. The reason is that even if the form of $d\Psi_i(s)$ indicates all of the patients in state i at waiting time s should be transplanted, when an organ is available for transplantation, such patients may not exist in the waiting list. Since the organ can only be preserved for a limited time before losing its functionality, the transplantation cannot be delayed for patients in the optimal state and waiting time to appear. One of the patients available in the waiting list, though in suboptimal states and waiting times, must receive the transplantation. Essentially, not all practical constraints on the transplantation rate are characterized by constraint (3.25) and Proposition 3.4.2. As a

consequence, the value of the objective corresponding to the optimal Ψ , though is indeed an upper bound of the limiting average life, may not be achievable by any fair allocation rules in practice.

In this chapter, we propose a fair allocation strategy motivated by the form of the optimal transplantation rate. The idea is to use the penalty parameter c in the unconstrained problem at which the solved transplantation rates at waiting time and state combinations are non-zero to prioritize patients' states and waiting times. In what follows, we will describe the proposed allocation strategy and certain monotonicity properties on which its validity relies, then show the monotonicity properties hold.

5.1 Priority Ranking for Transplantation

Since the penalty parameter $c \geq 0$ is associated with the constraint (3.25) on the limiting average proportion of transplanted patients

$$\int_{[0,T]} d\Psi_s \mathbf{1}_n = \lim_{l \rightarrow \infty} \frac{1}{N_{[0,l]}} \sum_{k=1}^{N_{[0,l]}} \int_{[0,T]} \sum_{i \in \mathcal{X}} d\tilde{N}_{i,n+1}^{(k)}(s),$$

it can be interpreted as the penalty for over-using the available resource of organs. As c decreases, the penalty becomes more lenient. A natural property would be as c decreases, the average proportion of transplanted patients increases, as more allocations are allowed. Moreover, as c decreases, the limiting average total life (or life gain) should increase, as more organs are provided to prolong life.

For each value of $c \geq 0$, define corresponding feasible set

$$\mathcal{S}_c := \{(i, s) : i \in \mathcal{X}, s \in [0, T], \Lambda_i^c(s) > 0\}, \quad (5.1)$$

of pairs of states and waiting times that are assigned non-zero transplantation rate in the optimal solution under c , where Λ^c is characterized in Theorem 4.2.7 (or Proposition 4.3.2 and 4.3.3 in the discrete-time model). If the feasible set is also monotone with respect to c , that is,

$$\mathcal{S}_{c_1} \subset \mathcal{S}_{c_2} \quad \text{if } c_1 > c_2, \quad (5.2)$$

which is equivalent to for any $s \in [0, T]$

$$d\mathbf{\Lambda}_s^{c_1} \leq d\mathbf{\Lambda}_s^{c_2} \quad \text{if } c_1 > c_2,$$

then starting from a large positive number c_0 such that $\mathcal{S}_{c_0} = \emptyset$, by decreasing c , a full order ranking of pairs of states and waiting times can be obtained by comparing the order of each pair entering the feasible set $\mathcal{S}_c$, or equivalently, by comparing the maximal c such that the pair is in $\mathcal{S}_c$.

Once the rank of state and waiting time pairs is determined, whenever an organ is retrieved, the patient with the highest rank among all patients in the current waiting list is selected for transplantation. The resulting limiting average total life is expected to be close to the upper bound, as in effect patients are ranked according to their potential contributions to the limiting average life considering the limited availability of organs. This allocation strategy satisfies the fairness requirement, as the allocation decisions are fully determined given states and waiting times of patients in the current list, and are invariant to calendar time and patient index.

5.2 Proof of the Monotonicities

To show the proposed allocation strategy is valid, we prove the conjectured monotonicity properties hold. First, we show the monotonicities for the limiting proportion of transplanted patients and for the limiting average total life, started from the discrete-time scenario:

Proposition 5.2.1. $\sum_{t=0}^T \pi_t^c \mathbf{\Lambda}_t^c \mathbf{1}_n$ is non-decreasing when c decreases.

Proof. Consider a new Lagrangian

$$\begin{aligned} \tilde{L}_c &= \sum_{t=0}^T (\pi_t \mathbf{1}_n + \pi_t \mathbf{\Lambda}_t \boldsymbol{\mu}_t) - c \cdot \sum_{t=0}^T \pi_t \mathbf{\Lambda}_t \mathbf{1}_n + \sum_{t=0}^{T-1} (\pi_t (\mathbf{I} - \mathbf{\Lambda}_t) \mathbf{B}_t - \pi_{t+1}) \boldsymbol{\lambda}_{t+1} \\ &= \sum_{t=0}^T (H^{(t)}(\pi_t, \mathbf{\Lambda}_t, \boldsymbol{\lambda}_{t+1}, c) - \pi_t \boldsymbol{\lambda}_t) + \pi_0 \boldsymbol{\lambda}_0, \end{aligned} \tag{5.3}$$

where $H^{(t)}$ is the Hamiltonian defined in (4.29). Note that comparing to (4.30) there is no term ρ/τ in (5.3). Also, note here c is fixed constant, instead of a parameter to be optimized

over, and $\tilde{L}_c$ is a function of c . To optimize $\tilde{L}$, all partial derivatives of $\tilde{L}$ with respect to $\boldsymbol{\pi}_t$, $\boldsymbol{\Lambda}_t$ and $\boldsymbol{\lambda}_t$ must be zero, which leads to principles:

$$\begin{aligned}\boldsymbol{\pi}_{t+1} &= \boldsymbol{\pi}_t(I - \boldsymbol{\Lambda}_t)\mathbf{B}_t, \\ \boldsymbol{\lambda}_t &= \frac{\partial}{\partial \boldsymbol{\pi}} H^{(t)}(\boldsymbol{\pi}_t, \boldsymbol{\Lambda}_t, \boldsymbol{\lambda}_{t+1}, c), \\ \boldsymbol{\Lambda}_t &= \operatorname{argmax} H^{(t)}(\boldsymbol{\pi}_t, \boldsymbol{\Lambda}_t, \boldsymbol{\lambda}_{t+1}, c).\end{aligned}\tag{5.4}$$

Note (5.4) is just (4.31) without the constraint $\sum_{t=0}^T \boldsymbol{\pi}_t \boldsymbol{\Lambda}_t \mathbf{1}_n = \rho/\tau$.

We need to show that solutions $(\boldsymbol{\pi}_t^1, \boldsymbol{\Lambda}_t^1)$ and $(\boldsymbol{\pi}_t^2, \boldsymbol{\Lambda}_t^2)$ (5.4) under $c = c_1$ and $c = c_2$ satisfy

$$\sum_{t=0}^T \boldsymbol{\pi}_t^2 \boldsymbol{\Lambda}_t^2 \mathbf{1}_n \geq \sum_{t=0}^T \boldsymbol{\pi}_t^1 \boldsymbol{\Lambda}_t^1 \mathbf{1}_n \quad \text{if } c_1 > c_2.\tag{5.5}$$

Since $(\boldsymbol{\pi}_t^j, \boldsymbol{\Lambda}_t^j)$ maximizes $\tilde{L}_{c_j}(\boldsymbol{\pi}_t, \boldsymbol{\Lambda}_t)$, we have the following inequalities

$$\begin{aligned}\tilde{L}_{c_1}(\boldsymbol{\pi}_t^2, \boldsymbol{\Lambda}_t^2) &\leq \tilde{L}_{c_1}(\boldsymbol{\pi}_t^1, \boldsymbol{\Lambda}_t^1) \\ \tilde{L}_{c_2}(\boldsymbol{\pi}_t^1, \boldsymbol{\Lambda}_t^1) &\leq \tilde{L}_{c_2}(\boldsymbol{\pi}_t^2, \boldsymbol{\Lambda}_t^2),\end{aligned}$$

and therefore

$$\begin{aligned}\tilde{L}_{c_1}(\boldsymbol{\pi}_t^2, \boldsymbol{\Lambda}_t^2) + (c_1 - c_2) \sum_{t=0}^T \boldsymbol{\pi}_t^1 \boldsymbol{\Lambda}_t^1 \mathbf{1}_n &\leq \tilde{L}_{c_1}(\boldsymbol{\pi}_t^1, \boldsymbol{\Lambda}_t^1) + (c_1 - c_2) \sum_{t=0}^T \boldsymbol{\pi}_t^1 \boldsymbol{\Lambda}_t^1 \mathbf{1}_n \\ &= \tilde{L}_{c_2}(\boldsymbol{\pi}_t^1, \boldsymbol{\Lambda}_t^1) \leq \tilde{L}_{c_2}(\boldsymbol{\pi}_t^2, \boldsymbol{\Lambda}_t^2).\end{aligned}$$

With the fact

$$\tilde{L}_{c_2}(\boldsymbol{\pi}_t^2, \boldsymbol{\Lambda}_t^2) - \tilde{L}_{c_1}(\boldsymbol{\pi}_t^2, \boldsymbol{\Lambda}_t^2) = (c_1 - c_2) \sum_{t=0}^T \boldsymbol{\pi}_t^2 \boldsymbol{\Lambda}_t^2 \mathbf{1}_n,$$

we have

$$(c_1 - c_2) \sum_{t=0}^T \boldsymbol{\pi}_t^1 \boldsymbol{\Lambda}_t^1 \mathbf{1}_n \leq (c_1 - c_2) \sum_{t=0}^T \boldsymbol{\pi}_t^2 \boldsymbol{\Lambda}_t^2 \mathbf{1}_n.$$

and hence desired monotonicity (5.5) as $c_1 > c_2$. $\square$

Proposition 5.2.2. *The expected total life $\sum_{t=0}^T (\pi_t^c \mathbf{1}_n + \pi_t^c \Lambda_t^c \mu_t)$ is non-decreasing as c decreases.*

Proof. Still assume $c_1 > c_2 \geq 0$. Since (π_t^i, Λ_t^i) satisfies $\pi_{t+1}^i = \pi_t^i (I - \Lambda_t^i) B_t$,

$$\tilde{L}_c = \sum_{t=0}^T (\pi_t \mathbf{1}_n + \pi_t \Lambda_t \mu_t) - c \cdot \sum_{t=0}^T \pi_t \Lambda_t \mathbf{1}_n.$$

By the fact $\tilde{L}_{c_2}(\pi_t^1, \Lambda_t^1) \leq \tilde{L}_{c_2}(\pi_t^2, \Lambda_t^2)$ and $\sum_{t=0}^T \pi_t^2 \Lambda_t^2 \mathbf{1}_n \geq \sum_{t=0}^T \pi_t^1 \Lambda_t^1 \mathbf{1}_n$ from the previous monotonicity result,

$$\sum_{t=0}^T (\pi_t^2 \mathbf{1}_n + \pi_t^2 \Lambda_t^2 \mu_t) - \sum_{t=0}^T (\pi_t^1 \mathbf{1}_n + \pi_t^1 \Lambda_t^1 \mu_t) \geq c_2 \left(\sum_{t=0}^T \pi_t^2 \Lambda_t^2 \mathbf{1}_n - \sum_{t=0}^T \pi_t^1 \Lambda_t^1 \mathbf{1}_n \right) \geq 0.$$

□

We state the following results for the continuous-time model without proofs, as the results can be shown with methods similar to those used in the discrete-time case.

Proposition 5.2.3. $\int_{[0,T]} \pi_{s-}^c d\Lambda_s^c \mathbf{1}_n$ is non-decreasing as c decreases.

Proposition 5.2.4. $\int_{[0,T]} \pi_s^c \mathbf{1}_n ds + \int_{[0,T]} \pi_{s-}^c d\Lambda_s^c \mu_s$ is non-decreasing as c decreases.

Now we show the monotonicity (5.2) of the allocable set. First, for the continuous-time model:

Theorem 5.2.5. (Monotonicity of the Allocation Rule)

Suppose φ^{c_j} satisfy the characterization (4.13) of the optimal transplantation rate under $\{c_j : j = 1, 2\}$, then for all $s \in [0, T]$ and $i \in \mathcal{X}$,

$$I(\varphi_i^{c_1}(s) > c_1) \leq I(\varphi_i^{c_2}(s) > c_2), \quad \text{if } c_1 > c_2. \quad (5.6)$$

Proof. By (4.13), it suffices to show that for all $s \in [0, T]$ and $i \in \mathcal{X}$,

$$\{\tilde{\mu}_s - c_1 \mathbf{1}_n\}_i > \{\gamma^{c_1}(s+) \eta^{c_1}(s+) - c_1 \gamma^{c_1}(s+)\}_i$$

is a sufficient condition for

$$\{\tilde{\boldsymbol{\mu}}_s - c_2 \mathbf{1}_n\}_i > \{\boldsymbol{\gamma}^{c_2}(s+) \boldsymbol{\eta}^{c_2}(s+) - c_2 \boldsymbol{\gamma}^{c_2}(s+)\}_i,$$

where $\{\cdot\}_i$ indicates the i th element of the vector, and $\boldsymbol{\gamma}^{c_1}(s+)$ and $\boldsymbol{\eta}^{c_1}(s+)$ are defined as in (4.14) and (4.15). Note for $j = 1, 2$,

$$\begin{aligned} & \{\boldsymbol{\gamma}^{c_j}(s+) \boldsymbol{\eta}^{c_j}(s+) - c_j \boldsymbol{\gamma}^{c_j}(s+)\}_i \\ &= \mathbf{e}_i \cdot \int_{(s,T]} \prod_{(s,t)} (\mathbf{I} + d\mathbf{Q})(\mathbf{I} - d\boldsymbol{\Lambda}^{c_j}) \cdot d\boldsymbol{\Lambda}^{c_j}(t) \cdot (\tilde{\boldsymbol{\mu}}_t - c_j \cdot \mathbf{1}_n), \end{aligned}$$

where $\{\boldsymbol{\Lambda}^{c_j}(t) : t \in (s, T]\}$ are characterized in (4.11) and (4.12).

A key observation is that for any $s \in [0, T]$, the form of $\{\boldsymbol{\Lambda}^{c_j}(t) : t \in (s, T]\}$ is independent of the initial condition $\boldsymbol{\pi}_s$. Therefore for any $i \in \mathcal{X}$ and $s \in [0, T]$, $\{\boldsymbol{\Lambda}^{c_j}(t) : t \in (s, T]\}$ also maximizes the objective under penalty parameter c_j as if only waiting time greater than s is considered, and all of the occupancy is concentrated at state i at initial time s :

$$\mathbf{e}_i \cdot \int_{(s,T]} \prod_{(s,t)} (\mathbf{I} + d\mathbf{Q})(\mathbf{I} - d\boldsymbol{\Lambda}^{c_j}) \cdot d\boldsymbol{\Lambda}^{c_j}(t) \cdot (\tilde{\boldsymbol{\mu}}_t - c_j \cdot \mathbf{1}_n),$$

which gives

$$\begin{aligned} & \{\boldsymbol{\gamma}^{c_1}(s+) \boldsymbol{\eta}^{c_1}(s+) - c_1 \boldsymbol{\gamma}^{c_1}(s+)\}_i \\ & \geq \mathbf{e}_i \cdot \int_{(s,T]} \prod_{(s,t)} (\mathbf{I} + d\mathbf{Q})(\mathbf{I} - d\boldsymbol{\Lambda}^{c_2}) \cdot d\boldsymbol{\Lambda}^{c_2}(t) \cdot (\tilde{\boldsymbol{\mu}}_t - c_1 \cdot \mathbf{1}_n). \end{aligned}$$

Subtracting $\{\boldsymbol{\gamma}^{c_2}(s+) \boldsymbol{\eta}^{c_2}(s+) - c_2 \boldsymbol{\gamma}^{c_2}(s+)\}_i$ from both sides gives

$$\begin{aligned} & \{\boldsymbol{\gamma}^{c_1}(s+) \boldsymbol{\eta}^{c_1}(s+) - c_1 \boldsymbol{\gamma}^{c_1}(s+)\}_i - \{\boldsymbol{\gamma}^{c_2}(s+) \boldsymbol{\eta}^{c_2}(s+) - c_2 \boldsymbol{\gamma}^{c_2}(s+)\}_i \\ & \geq \mathbf{e}_i \cdot \int_{(s,T]} \prod_{(s,t)} (\mathbf{I} + d\mathbf{Q})(\mathbf{I} - d\boldsymbol{\Lambda}^{c_2}) \cdot d\boldsymbol{\Lambda}^{c_2}(t) \cdot (c_2 \cdot \mathbf{1}_n - c_1 \cdot \mathbf{1}_n). \end{aligned}$$

The term on the right side is no less than $c_2 - c_1$ as the probability of future transplantation

$$\mathbf{e}_i \cdot \int_{(s,T]} \prod_{(s,t)} (\mathbf{I} + d\mathbf{Q})(\mathbf{I} - d\mathbf{\Lambda}^{c_2}) \cdot d\mathbf{\Lambda}^{c_2}(t) \cdot \mathbf{1}_n \leq 1,$$

therefore

$$\gamma^{c_1}(s+) \boldsymbol{\eta}^{c_1}(s+) + c_1(\mathbf{1}_n - \gamma^{c_1}(s+)) \geq \gamma^{c_2}(s+) \boldsymbol{\eta}^{c_2}(s+) + c_2(\mathbf{1}_n - \gamma^{c_2}(s+)), \quad (5.7)$$

and hence whenever

$$\{\tilde{\boldsymbol{\mu}}_s - c_1 \mathbf{1}_n\}_i > \{\gamma^{c_1}(s+) \boldsymbol{\eta}^{c_1}(s+) - c_1 \gamma^{c_1}(s+)\}_i,$$

we must have

$$\{\tilde{\boldsymbol{\mu}}_s - c_2 \mathbf{1}_n\}_i > \{\gamma^{c_2}(s+) \boldsymbol{\eta}^{c_2}(s+) - c_2 \gamma^{c_2}(s+)\}_i.$$

□

Then the proof of the monotonicity of the allocable set in the discrete-time model:

Proposition 5.2.6.

$$\mathbf{\Lambda}_t^{c_1} \leq \mathbf{\Lambda}_t^{c_2} \quad \text{if } c_1 > c_2 \quad (5.8)$$

where $\{\mathbf{\Lambda}_t^{c_i} : t = 0, \dots, T\}$ are characterized in (4.27) and (4.28).

Proof. We prove (5.8) with induction. Since $\mathbf{\Lambda}_T^{c_i} = I(\boldsymbol{\mu}_T > c_i \mathbf{1}_n)$, (5.8) is true for $t = T$. Now assume the monotonicity is true for waiting time t , by the form of optimal solution (4.28),

$$\boldsymbol{\mu}_t - c_1 \mathbf{1}_n > \mathbf{l}_t^{c_1} - c_1 \mathbf{p}_t^{c_1} \Rightarrow \boldsymbol{\mu}_t - c_2 \mathbf{1}_n > \mathbf{l}_t^{c_2} - c_2 \mathbf{p}_t^{c_2},$$

where

$$\mathbf{l}_t^{c_j} = \sum_{s=t+1}^T (\mathbf{1}_n + \mathbf{\Lambda}_s^{c_j} \boldsymbol{\mu}_s) \prod_{t+1}^{s-1} \cdot \mathbf{B}_t^T$$

and

$$\mathbf{p}_t^{c_j} = \sum_{s=t+1}^T c_j \cdot \mathbf{1}_n \prod_{t+1}^{s-1} \cdot \mathbf{B}_t^T.$$

Now we want to prove for waiting time $t - 1$,

$$\mathbf{\Lambda}_{t-1}^{c_1} \leq \mathbf{\Lambda}_{t-1}^{c_2} \quad \text{if } c_1 > c_2,$$

which is true if for any $i \in \mathcal{X}$,

$$\mu_{t-1,i} - c_1 > \{l_{t-1}^{c_1} - c_1 p_{t-1}^{c_1}\}_i \Rightarrow \mu_{t-1,i} - c_2 > \{l_{t-1}^{c_2} - c_2 p_{t-1}^{c_2}\}_i.$$

Suppose

$$\mu_{t-1,i} - c_1 > \{l_{t-1}^{c_1} - c_1 p_{t-1}^{c_1}\}_i,$$

we need to show that

$$\mu_{t-1,i} - c_2 > \{l_{t-1}^{c_2} - c_2 p_{t-1}^{c_2}\}_i.$$

By (4.31),

$$\boldsymbol{\lambda}_t^{c_j} = \frac{\partial}{\partial \boldsymbol{\pi}} H^{(t)}(\boldsymbol{\pi}_t, \mathbf{\Lambda}_t, \boldsymbol{\lambda}_{t+1}, c_j) = \mathbf{1}_n + \mathbf{B}_t \boldsymbol{\lambda}_{t+1}^{c_j} + (\boldsymbol{\mu}_t - \mathbf{B}_t \boldsymbol{\lambda}_{t+1}^{c_j} - c_j) \cdot I(\boldsymbol{\mu}_t - \mathbf{B}_t \boldsymbol{\lambda}_{t+1}^{c_j} > c_j),$$

which is equivalent to the Hamilton-Jacobi-Bellman equations

$$\{l_{t-1}^{c_j} - c_j p_{t-1}^{c_j}\}_i = \mathbf{e}_i B_{t-1} \mathbf{1}_n + \mathbf{e}_i B_{t-1} \cdot [(l_t^{c_j} - c_j \mathbf{p}_t^{c_j}) \vee (\boldsymbol{\mu}_t - c_j \mathbf{1}_n)].$$

Since the first part on the right side is free of the penalty parameter c_j , to show $\mu_{t-1,i} - c_2 > \{l_{t-1}^{c_2} - c_2 p_{t-1}^{c_2}\}_i$, it suffices to show

$$\mathbf{e}_i B_{t-1} \cdot [(l_t^{c_1} - c_1 \mathbf{p}_t^{c_1}) \vee (\boldsymbol{\mu}_t - c_1 \mathbf{1}_n)] + c_1 \geq \mathbf{e}_i B_{t-1} \cdot [(l_t^{c_2} - c_2 \mathbf{p}_t^{c_2}) \vee (\boldsymbol{\mu}_t - c_2 \mathbf{1}_n)] + c_2,$$

which is condition (5.7) proved in the continuous-time model. The rest of the proof follows the proof of Theorem 5.2.5. $\square$

Chapter 6

Comparison of Allocation Strategies

In this chapter, we consider the application of the proposed allocation strategy in the context of realistic lung transplant waiting lists, and evaluate the proposed strategy and the Lung Allocation Score (LAS) system currently used by United Network for Organ Sharing (UNOS) with results of simulation studies.

The data used are the waiting list, transplant and follow-up UNOS Standard Transplant Analysis and Research files for heart, lung, and simultaneous heart-lung registrations and transplants that were listed or performed in the United States and reported to the Organ Procurement and Transplantation Network (OPTN) from October 1, 1987 to December 31, 2012. Only patients waiting for lungs and were at least 12 years of age are considered, as before June 11, 2013, only patients at least 12 years of age received priority for deceased donor lung offers based on the LAS. There were 16,049 such patients registered in the time period, with 129,881 medical records containing medical measurements updated sporadically at different times for different patients during their tenure on the waiting list. Among the 16,049 candidates, 64.6% received transplantation, 18.4% died while waiting in the list, and the remaining were still waiting at the end of the study period or censored by loss of follow-up. Among patients who received transplantation, 37.8% died and 62.2% were still alive at the end of the study period or were censored due to loss of follow-up.

Parameters estimated from the data include the intensity of the patient arrival process τ , the intensity of the organ arrival process ρ , the health states $\mathcal{X}$, the counterfactual transition kernel $\mathbf{Q}$, the distribution $\{P(X(0) = x_i) : i = 1, \dots, n\}$ of the initial state upon arrival, the

in-waiting list and post-transplant waiting time and health state specific hazards for death, and the expected post-transplantation residual life $\mu_s(x)$ given the state x and waiting time s at the point of transplantation. In order to reduce computation time in the simulations and to obtain enough patient history records for the estimation of the transition probabilities, time is discretized into periods of 90 days.

A multi-stage strategy was used to estimate the parameters. First, a time-dependent covariates proportional hazard regression is fitted to estimate the time-on-waiting-list specific hazard for death. Covariates in the proportional hazard regression are those used in the in-waiting-list survival calculation in the LAS system by UNOS, whenever they are available in the data. Conditioning on the covariates, the potential hazard for death while waiting is invariant to the allocation decisions, and thus the censoring due to organ allocations can be treated as censoring at random. Moreover, using the same covariates as in the LAS calculation for the proposed allocation strategy prevents potential advantage gained from better covariate selections in estimating the hazard, so that the LAS and the proposed strategy can be compared fairly. See Table A.1 in the appendix for the list of covariates and coefficient estimates.

The linear combination of predictors $\sum_j \beta_j Z_j$ in the proportional hazard regression is transformed double-exponentially

$$\exp(-\exp(\sum_j \beta_j Z_j))$$

to reflect the survival function and the expected residual life in the waiting list. Then the transformed linear combination is discretized into a three-level state variable S_{wl} .

Second, a proportional hazard regression is used to estimate the hazard for post-transplant death. Covariates in the proportional hazard regression are those used in the post-transplant survival calculation in the LAS system, whenever available in the data. See Table A.2 in the appendix for the list of covariates and coefficient estimates.

The linear combination of predictors of each patient in the proportional hazard regression is also transformed double-exponentially to reflect the expected post-transplantation life given the time-of-transplant specific characteristics of patients, and discretized into a three-

level state variable S_μ .

Third, patients' health states are characterized in terms of the pair (S_{wl}, S_μ) , that is, the pair of states related to the in-waiting-list and post-transplantation survivals. See Figure A.3 in the appendix for the reference table of health states defined as interactions of S_{wl} and S_μ .

In estimating the transition probabilities of patients' health states, due to the sparsity of available patient records, we use the following logistic model

$$\log \frac{P_{s,s+1}(i, j)}{P_{s,s+1}(i, i)} = a_{ij} + d_j \cdot s$$

to estimate the transition probabilities of S_{wl} and S_μ separately, where s is the time period and i is the state selected to be the baseline. The counterfactual transition probabilities of the pair (S_{wl}, S_μ) are calculated as products of the transition probabilities of the components.

Fourth, the distribution of initial states $\{P(X(0) = i) : i = 1, \dots, n\}$ is estimated with the proportion of patients arrived in each state.

Fifth, proportional hazard regressions are used to estimate the hazard for in-waiting-list death and the matrix $\boldsymbol{\mu}$ of post-transplantation life expectancy corresponding to each combination of waiting time and state.

In the data, the first transplantation date was May 5, 2005, although the first patient arrival date was Jan 22, 1993. To estimate the organ arrival rate ρ and the patient arrival rate τ more precisely, we use mean numbers of patient arrivals and organ arrivals per 45-day period after year 2006 as our estimates $\hat{\rho} = 156$, $\hat{\tau} = 259$.

Given parameters estimated using methods described above, for a fixed value of the penalty parameter c , whether a combination of waiting time and state is allocable is calculated as in (4.27) and (4.28). Based on the monotonicity of the proposed allocation rule, a full order ranking of transplant priorities for combinations of waiting times and states is obtained using the order of their appearances in the allocable set as c decreases.

Two LAS-type allocation systems are considered. First, the LAS currently used by the UNOS is $\text{LAS} = 100 \cdot (\text{PTAUC} - 2 \cdot \text{WLAUC} + 730)/1095$, where WLAUC is the estimated in-waiting list life expectancy during an additional year and PTAUC is the estimated post-

transplant life expectancy during the first year, given the patient's current state. Patients with higher LAS have higher priorities of transplantation.

Observing from the data that patients' in-waiting-list and post-transplantation life are usually much longer than one year, we provide a refined LAS, which is the difference between two times of the estimated post-transplant life expectancy and the estimated in-waiting list life expectancy without the one year constraint. Rankings of transplantation priorities for all combinations of waiting times and states are calculated for both LAS systems. See Figures 6.1 and 6.2 below for a comparison between rankings with the proposed allocation strategy and the LAS systems, where blue indicates higher priority for transplantation, while red indicates lower priority.

Figure 6.1: Proposed strategy (left) vs. LAS (right) in 90-day periods
 x : states defined by in-waiting-list residual life; y : states by post-transplant residual life
 (higher index indicates longer estimated life)

Figure 6.2: Refined LAS (left) vs. LAS (right) in 90-day periods
 x : states defined by in-waiting-list residual life; y : states by post-transplant residual life
 (higher index indicates longer estimated life)

Patient arrivals according to a homogeneous Poisson process with the estimated intensity $\hat{\tau}$ and organ arrivals according to a homogeneous Poisson process with the estimated intensity $\hat{\rho}$ are simulated independently. At the end of each waiting time period, counterfactual transitions in patients' health states are simulated with the estimated transition probabilities. Using priority rankings of the proposed allocation strategy and the two LAS systems, organs, whenever available, are allocated to patients with the highest ranked pairs of waiting times and states in the current waiting list. Patients who are not selected for transplants remain on the waiting list and are open to future counterfactual transitions and potential allocations. At the end of the simulation, the average total life for patients under each of the allocation strategies is recorded in days.

See Table 6.1 and Figure 6.3 for the means and standard deviations of results of ten independent simulations, in which we compare the outcomes under the proposed allocation strategy and the LAS systems. In addition, we compare them with outcomes under a purely random allocation strategy in which patients are chosen for transplantation randomly, and outcomes under the presumably worst strategy whose ranking of priority is the opposite

of the proposed allocation strategy. Outcomes of all strategies are compared to the upper bound of average patient total life in the model.

	Average Total Life (SD)	Average Life in Wait-ing List (SD)	Average Life Post-Transplant (SD)
Upper Bound	1,853	NA	NA
Optimal	1,820 (22.3)	150 (7.8)	1,670 (32.4)
LAS	1,705 (19.0)	206 (7.4)	1,499 (25.5)
Refined LAS	1,707 (19.4)	203 (7.2)	1,503 (25.6)
Random Strategy	1,573 (60.2)	167 (22.3)	1,407 (71.3)
Worst Strategy	1,416 (19.4)	162 (9.9)	1,255 (28.4)

Table 6.1: Comparison of Allocation Strategies

Figure 6.3: Simulation Results

Chapter 7

Discussion

We have presented an approach to modeling the lung transplantation waiting list and comparing allocation rules. Here patient and organ arrivals are modeled as independent homogeneous Poisson processes, and counterfactual patient health status trajectories absent transplantation are modeled as independent and identically distributed inhomogeneous Markov processes. Patients' expected post-transplantation residual life depends on both the health state at the time of transplantation and the time waited for transplantation. The model setting here is capable of capturing the randomness in patient and organ arrivals and complex dynamics of patients' health characteristics and their effect on life outcomes. In practice, the researchers and/or policy makers can always expand the state space of patient health status so that trajectories of the transitions of health states are indeed Markov. For example, previous medical records of patients can be included if they are believed to contain important information for predicting future transitions.

Allocation rules are modeled as index sequences of transplanted patients. Only fair allocation rules are considered in the comparison. Under fair allocation rules, the choice of patients for transplantations are decided by patients' health states and waiting times at the time of organ arrival and a random variable that is conditionally independent of patients' past and future states and survivals. Allocation probabilities are also required to be invariant to patient index and calendar time. This definition of fairness has two implications: first, unrealistic rules that can predict patients' future states and survivals are not considered; second, given patients' health states and waiting times, the allocation

decisions are independent of other factors. Therefore the definition of fairness here implicitly addresses the equity issue in organ allocations.

It is shown each fair allocation rule has a corresponding limiting transplantation rate. Under a fair allocation rule, the average rate of transplantation to patients in any state and waiting time converges to the corresponding transplantation rate as calendar time increases. The limiting transplantation rate satisfies certain constraints to reflect the scarcity of organs. The main constraint is that the average proportion of transplanted patients in the limit is bounded by the ratio of organ arrivals to that of patient arrivals. The limiting average total life (or equivalently, the limiting average life gain from transplantation), represented in terms of the transplantation rate, is used as the standard in comparing fair allocation rules.

The optimal transplantation rate subject to the constraints is characterized recursively with the Hamilton-Jacobi-Bellman equations. Then a fair allocation strategy is developed based on the form and monotonicity properties of the optimal transplantation rate. The allocation strategy is to use the penalty parameter c associated with the constraint on the average proportion of transplanted patients as an index to prioritize patients' states and waiting times. The index c is related to the Gittins Index (Bertsimas and Niño-Mora [2000]). Allocating resources using Gittins index leads to optimal or asymptotically optimal objectives in problems where subjects remain static if not selected for allocations (Weber [1992], Whittle [1980], Whittle [1988]) and in settings where the rates of patient and organ arrivals tend to infinity. In restless bandits problems in which all subjects are constantly in transitions, including the problem studied here, though there are sufficient conditions for Gittins Index to be optimal (Bertsimas and Niño-Mora [1996], Niño-Mora [2001]), the optimality is not guaranteed in general.

Simulation studies show it may be possible to improve the Lung Allocation Score (LAS) currently used by UNOS and increase the average total life by as much as 7%. Results provided here are provisional, a deeper understanding of the lung allocation procedure and the optimal allocation strategy requires further effort. As discussed previously, there may be a gap between the objective using the proposed strategy and the practical upper bound of the objective. The gap may be a result of the lack of patients in optimal states and waiting times when organs are available, which may stem from the fact the constraints in

the optimization problem do not cover all practical confinements on the allocations. Issues related to donor-recipient matching, cross-region transplantation, or other practical aspects in lung transplantation may also require further constraints to be imposed in formulating the optimal transplantation rate and developing allocation strategies.

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Appendices

Appendix A

Tables and Graphs

Table A.1: Coefficient Estimates for Time-on-Waiting-List Hazard for Death

Covariate	Coefficient	p -value
Initial Age	0.026	2.62×10^{-9} (***)
Body mass index (BMI; kg/m^2)	$0.119 \times (20 - \text{BMI})$ for BMI less than $20 kg/m^2$	0.001 (**)
Ventilation status if candidate is hospitalized	0.895 if continuous mechanical ventilation needed	0.0001 (***)
Creatinine (serum, mg/dL)	0.438 if at least 18 years of age	2.11×10^{-6} (***)
Diagnosis Group A	0	NA
Diagnosis Group B	1.500	9.44×10^{-6} (***)
Diagnosis Group C	0.958	3.51×10^{-5} (***)
Diagnosis Group D	0.997	5.93×10^{-10} (***)
Eisenmenger's syndrome	-0.485	0.510
Lymphangioleiomyomatosis	-1.367	0.174
Obliterative bronchiolitis	-1.548	0.123

Pulmonary fibrosis, not idiopathic	0.012	0.947
Sarcoidosis with PA mean pressure greater than 30 mm Hg	-0.412	0.087 (.)
Sarcoidosis with PA mean pressure of 30 mm Hg or less	0.403	0.178
Forced vital capacity (FVC)	-0.225	0.0004 (***)
Functional Status	-0.480 if no assistance needed with activities of daily living	0.021 (*)
Oxygen needed to maintain adequate oxygen saturation (80% or greater) at rest (L/min)	0.085 for Group B, 0.100 for Groups A, C, and D	0.014 (*) < 2×10^{-16} (***)
PCO ₂ (mm Hg): current	0.007 if PCO ₂ is at least 40 mm Hg	0.0001 (***)
Pulmonary artery (PA) systolic pressure (10 mm Hg) at rest, prior to any exercise	0.008 for Group A if the PA systolic pressure is greater than 40 mm Hg, -0.002 for Groups B, C, and D	0.001 (**) 0.604

Six minute walk distance (feet) obtained while the candidate is receiving supplemental oxygen required to maintain an oxygen saturation of 88% or greater at rest. Increase in supplemental oxygen during this test is at the discretion of the center performing the test.	-0.001	$< 2 \times 10^{-16}$ (***)
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Table A.2: Coefficient Estimates for Post-Transplantation Hazard for Death

Covariate	Coefficient	p -value
Initial Age	$0.005 \times (\text{age} - 45)$ if greater than 45 years of age	9.57×10^{-7} (***)
Body mass index (BMI; kg/m^2)	$0.052 \times (20 - \text{BMI})$ for BMI less than $20 kg/m^2$	0.0006 (***)
Ventilation status if candidate is hospitalized	-0.10 if continuous mechanical ventilation needed	0.476
Creatinine (serum, mg/dL)	0.243 if at least 18 years of age	3.97×10^{-5} (***)
Diagnosis Group A	0	NA
Diagnosis Group B	0.318	0.070 (.)
Diagnosis Group C	0.167	0.049 (*)
Diagnosis Group D	0.119	0.005 (**)
Bronchiectasis	-0.113	0.910
Eisenmenger's syndrome	0.788	0.271
Lymphangioleiomyomatosis	-0.605	0.058 (.)
Obliterative bronchiolitis	0.071	0.731
Pulmonary fibrosis, not idiopathic	-0.135	0.107
Sarcoidosis with PA mean pressure greater than 30 mm Hg	-0.259	0.048 (*)
Sarcoidosis with PA mean pressure of 30 mm Hg or less	-0.046	0.795

Functional Status	-0.140 if no assistance needed with activities of daily living	0.314
Oxygen needed to maintain adequate oxygen saturation (80% or greater) at rest (L/min)	-0.010 for Group B 0.009 for Groups A, C, and D	0.734, 0.122
Six minute walk distance (feet) obtained while the candidate is receiving supplemental oxygen required to maintain an oxygen saturation of 88% or greater at rest. Increase in supplemental oxygen during this test is at the discretion of the center performing the test.	$3.287 \times 10^{-4} * (1200 - \text{Six minute walk distance})$, 0 if six-minute-distance-walked is at least 1200 feet	$2.05 \times 10^{-11} (***)$

Table A.3: Definition of Patients' Health States in Terms of (S_{wl}, S_{μ})

State	S_{wl}	S_{μ}	State	S_{wl}	S_{μ}	State	S_{wl}	S_{μ}
1	1	1	4	2	1	7	3	1
2	1	2	5	2	2	8	3	2
3	1	3	6	2	3	9	3	3

(Higher index in S_{wl} and S_{μ} corresponds to longer estimated in-waiting-list and post-transplantation life, respectively.)

Figure A.1: The Proposed Strategy

Figure A.2: The LAS

Figure A.3: The Refined LAS

Blue: high priority
 Red: low priority
 Y-axis: health states
 X-axis: waiting time periods

Appendix B

Properties of the Waiting List Process

The following section is optional and provides an alternative proof of the convergence of the limiting average occupancy π . The proof is based on the fact that the waiting list process is a positive Harris recurrent piecewise deterministic Markov processes, so that the time average of a functional of the process converges to its expected value with respect to the invariant measure.

To proceed, we first define two extended versions of the waiting list process:

Definition B.0.7. (The Extended Waiting List Processes)

For any pair of waiting time $s \in [0, T]$ and state $i \in \mathcal{X} \setminus \{0\}$, define

$$W_t^{(s,i)} := \{(t - T_k, \tilde{X}^{(k)}(t - T_k), I(t - T_k \geq s, \tilde{X}^{(k)}(s) = i)) : t - T_k \in [0, T)\} \quad (\text{B.1})$$

and

$$W_t^{(s-,i)} := \{(t - T_k, \tilde{X}^{(k)}(t - T_k), I(t - T_k \geq s, \tilde{X}^{(k)}(s-) = i)) : t - T_k \in [0, T)\}. \quad (\text{B.2})$$

Without loss of generality, also denote the empty state of both processes by w_0 .

Remark. Both $\{W_t^{(s,i)} : t \geq 0\}$ and $\{W_t^{(s-,i)} : t \geq 0\}$ are càdlàg given the càdlàg nature of the indicator functions in the definition.

In what follows, we prove that the extended waiting list processes $W_t^{(s,i)}$ and $W_t^{(s-,i)}$ are piecewise deterministic Markov processes (PDMP). The definition of PDMP are as follows

(Davis [1984], Dempster and Ye [1992, 1995]). Essentially, such processes are characterized by random Markov jumps and deterministic trajectories between jumps.

Definition B.0.8. (Piecewise Deterministic Markov Process)

A piecewise deterministic process $\{x_t = (\nu_t, \zeta_t) : t \geq 0\}$ defined on the state space $(E, \mathcal{E})$ is characterized by the following definitions:

Let K be a countable set and $d : K \rightarrow \mathbb{N}$ be a given function, for each $\nu \in K$, M_ν is an open subset of $\mathbb{R}^{d(\nu)}$. Then

$$E = \cup_{\nu \in K} M_\nu = \{(\nu, \zeta) : \nu \in K, \zeta \in M_\nu\}.$$

Let $\mathcal{E}$ denote the following class of measurable sets in E :

$$\mathcal{E} = \{\cup_{\nu \in K} A_\nu : A_\nu \in \mathcal{M}_\nu\},$$

where $\mathcal{M}_\nu$ denotes the Borel sets of M_ν . Then $(\mathcal{E}, E)$ is a Borel space.

The probability law of $\{x_t\}$ is determined by the following objects:

1. Vector fields $\{\mathcal{X}_\nu : \nu \in K\}$,
2. A measurable jump rate $\lambda : E \rightarrow \mathbb{R}^+$,
3. A transition measure $Q : \mathcal{E} \times (E \cup \Gamma^*) \rightarrow [0, 1]$ (Γ^* is defined below).

The vector fields $\mathcal{X}_\nu$ are supposed to be such that for each $z \in M_\nu$, there is a unique integral curve $\phi_\nu(t, z)$, such that for $\mathcal{X} = \mathcal{X}_\nu$ and $\zeta(t, z) := \phi_\nu(t, z)$, the following differential equation is satisfied

$$\frac{\partial}{\partial t} f(\zeta(t, z)) = \mathcal{X}f(\zeta(t, z))$$

for all smooth f and $t \geq 0$, under the initial condition

$$\zeta(0, z) = z.$$

Further, it is supposed that the $\mathcal{X}_\nu$ are conservative, i.e., the integral curves are defined for all $t > 0$ (no explosions).

We denote by ∂M_ν the boundary of M_ν and by $\partial^* M_\nu$ those boundary points at which integral curves of M_ν exit from M_ν , i.e.

$$\partial^* M_\nu = \{z \in \partial M_\nu : \phi_\nu(t, \zeta) = z \text{ for some } (t, \zeta) \in \mathbb{R}^+ \times M_\nu\},$$

and

$$\Gamma^* = \cup_{\nu \in K} \partial^* M_\nu.$$

With the convention $\inf\{\emptyset\} = \infty$, define the boundary hitting time for $x = (\nu, \zeta)$:

$$t^*(x) = \inf\{t > 0 : \phi_\nu(t, \zeta) \in \partial^* M_\nu\}.$$

As regards the jump rate λ , suppose that for each $x = (\nu, \zeta) \in E$, there exists $\epsilon > 0$ such that the function $s \rightarrow \lambda(\nu, \phi_\nu(s, \zeta))$ is integrable for $s \in [0, \epsilon)$.

The transition measure $Q(A; x)$ is a measurable function of x for each fixed $A \in \mathcal{E}$ and $x \in E \cup \Gamma^*$ and is a probability measure on $(E, \mathcal{E})$ for each $x \in E$.

The process $\{x_t = (\nu_t, \zeta_t) : t \geq 0\}$ is constructed from any initial state $x = (n, z) \in E$ in the following way:

Define a survival function S by

$$S(t) = \begin{cases} \exp(-\int_0^t \lambda(n, \phi_n(s, z)) ds), & t < t^*(x), \\ 0, & t \geq t^*(x). \end{cases}$$

Select the first jumping time as a random variable Θ_1 such that $P(\Theta_1 > t) = S(t)$. Now select, independently, an E -valued random variable (N, Z) having distribution $Q(\cdot; (n, \phi_n(\Theta_1, z)))$.

The trajectory of x_t for $t \leq \Theta_1$ is given by

$$x_t = (\nu_t, \zeta_t) = \begin{cases} (n, \phi_n(t, z)), & t < \Theta_1 \\ (N, Z), & t = \Theta_1. \end{cases}$$

In particular, $x_{\Theta_1-} = (n, \phi_n(t, z))$ and the state of the process at Θ_1 is decided in the same way as in the construction of a continuous Markov process from a Markov chain with

transition matrix $\mathbf{Q}$. Starting from x_{Θ_1} , we use above steps for the next jumping time Θ_2 by defining the distribution of $\Theta_2 - \Theta_1$ with the jump rate λ , and the distribution of the state x_{Θ_2} with the transition measure $\mathbf{Q}$. By iterating this procedure we have a well defined piecewise deterministic trajectory $\{x_t : t \geq 0\}$ with jumping times $\Theta_1, \Theta_2, \dots$. Under the stated condition on λ , $\Theta_1 > 0$ and $\Theta_i - \Theta_{i-1} > 0$ for each i with probability one.

Finally, a non-explosion condition for the piecewise deterministic process is needed. Let

$$N_t := \sum_i I(t \geq \Theta_i)$$

be the number of jumps in $[0, t]$, then for all $t \geq 0$,

$$E(N_t) < \infty.$$

which also implies that $\Theta_i \rightarrow \infty$ as $i \rightarrow \infty$ with probability one.

Proposition B.0.9. *A piecewise deterministic process $\{x_t = (\nu_t, \zeta_t) : t \geq 0\}$ is strong Markov.*

Proof. See Davis [1984]. □

Now we show that with any fair allocation rule, the extended waiting list processes are indeed PDMP and are therefore strong Markov. The main idea of the proof is to find elements $\mathcal{X}_\nu$, λ , $\mathbf{Q}$, etc. such that $W_t^{(s,i)}$ and $W_t^{(s-,i)}$ can be represented with these elements as in the constructing of a PDMP in its definition.

Theorem B.0.10. (*Extended Waiting List Processes as PDMP*)

With any fair allocation sequence $\mathcal{J} = \{J_1, J_2, \dots\}$, the corresponding extended waiting list processes $\{W_t^{(s,i)}, t \geq 0\}$ and $\{W_t^{(s-,i)}, t \geq 0\}$ defined on the filtration $\{\mathcal{F}_t : t \geq 0\}$ are càdlàg piecewise deterministic Markov processes (PDMP).

Proof. First, note that the state space of both $\{W_t^{(s,i)}, t \geq 0\}$ and $\{W_t^{(s-,i)}, t \geq 0\}$ can be represented as

$$W_0 := \{(\nu, \zeta) : \nu \in K, \zeta \in M_\nu\}, \tag{B.3}$$

where $K = \cup_{d=0}^{\infty} (\mathcal{X}_0 \times \{0, 1\})^d$ is the countable space containing all finite dimensional vectors of possible values of

$$\nu_t = \{(\tilde{X}^{(k)}(t - T_k), I(t - T_k \geq s, \tilde{X}^{(k)}(s) = i)) : t - T_k \in [0, T)\}$$

for $W_t^{(s,i)}$, or

$$\nu_t = \{(\tilde{X}^{(k)}(t - T_k), I(t - T_k \geq s, \tilde{X}^{(k)}(s-) = i)) : t - T_k \in [0, T)\}$$

for $W_t^{(s-,i)}$, including the zero-dimensional empty state w_0 , and $M_\nu = [0, T)^{d(\nu)}$ is the space of corresponding waiting times of patients in the waiting list

$$\zeta_t = \{t - T_k : t - T_k \in [0, T)\},$$

where $d(\nu)$ is the dimension of ν .

Second, in both processes $\{W_t^{(s,i)}, t \geq 0\}$ and $\{W_t^{(s-,i)}, t \geq 0\}$, jumps occur if and only if a new patient arrives, or, if the waiting list is not empty, there is any transition in an existing patient's state, or a patient is transplanted, or if the waiting time of a patient hits $\{s, T\}$ and the condition of the indicator function is satisfied such that the value of the indicator function changes from zero to one. In between these jumping times, the waiting time component ζ_t of both processes increase linearly with the calendar time. Let

$$\phi_\nu(t, z) = z + t \cdot \mathbf{1}_{d(\nu)}, \quad (\text{B.4})$$

where $\mathbf{1}_{d(\nu)}$ is the vector of length $d(\nu)$ with all elements being 1, then in between jumping times we have $\zeta_t = \phi_\nu(t, z)$ with the initial condition $\zeta(0, z) = z$. Let $\mathcal{X}_\nu$ denote the first order differential operator

$$\mathcal{X}_\nu f(z) = \frac{df(z)}{dt} = \sum_{i=1}^{d(\nu)} \left\{ \frac{d\zeta(t, z)}{dt} \right\}_i \frac{\partial f}{\partial x_i}(z) = \begin{cases} \sum_{i=1}^{d(\nu)} \frac{\partial f}{\partial x_i}(z), & \nu \neq w_0, \\ 0, & \nu = w_0. \end{cases} \quad (\text{B.5})$$

By the chain rule of differentiation,

$$\frac{\partial}{\partial t} f(\zeta(t, z)) = \mathcal{X} f(\zeta(t, z))$$

for all smooth f and $t \geq 0$.

Third, for each $\nu \in K$, the boundary ∂M_ν of M_ν is the set of $d(\nu)$ dimensional vectors in which one element is in $\{s, T\}$ and the rest is in $[0, s) \cup (s, T)$, and it is equal to the achievable boundary

$$\partial^* M_\nu = \{z \in \partial M_\nu : \phi_\nu(t, \zeta) = z \text{ for some } (t, \zeta) \in \mathbb{R}^+ \times M_\nu\},$$

given the form of $\phi_\nu(t, \zeta)$ in (B.4). Denote

$$\Gamma^* = \cup_{\nu \in K} \partial^* M_\nu.$$

The boundary hitting time for $(\nu, \zeta) \in W$ is

$$t^*(x) = \inf\{t > 0 : \phi_\nu(t, \zeta) \in \partial^* M_\nu\} = \min_i \{(T - \zeta_i) \wedge (s - \zeta_i)\},$$

where ζ_i is the i th element of the waiting time component ζ .

Fourth, given $W_t^{(s,i)} = w$ (or $W_t^{(s-,i)} = w$), probabilities of a jump occurs in calendar time $[t, t+dt)$ due to patient arrivals, transplantations or transitions are τdt , $\rho dt \cdot I(w \neq w_0)$ and $\sum_{j:(k_j, z_j) \in w} q_{k_j}(z_j) dt$, respectively, where k_j is the state component $\tilde{X}(z_j)$ of the j th element in w and $q_{k_j}(z_j) = \sum_{l \neq k_j} q_{k_j, l}(z_j)$ is a patient's total transition rate from state k_j at waiting time at z_j . By the independence between organ arrivals, patient arrivals and patient transitions, the jump rate of $W_t^{(s,i)}$ and $W_t^{(s-,i)}$ at w is

$$\lambda(w) = \tau + \rho \cdot I(w \neq w_0) + \sum_{j:(k_j, z_j) \in w} q_{k_j}(z_j).$$

Fifth, given $W^{(s,i)}$ jumps at calendar time t and $W_{t-}^{(s,i)} = w$, suppose there are d patients in w before the jump, and their states and waiting times at $t-$ are $\{(k_j, z_j) : j = 1, \dots, d\}$ where $k_j \in \mathcal{X}_0 \times \{0, 1\}$ and $z_j \in [0, T)$, then $W_t^{(s,i)}$ follows a multinomial distribution on

possible outcomes after a transition or a transplantation, or a patient arrival, or one of the current patients' waiting times hits the boundary $\{s, T\}$. The probability of the jump is due to patient transition is

$$\frac{q_{k_j}(z_j)}{\lambda(w)} \cdot \prod_{j:(k_j, z_j) \in w} I(z_j \notin \{s, T\}),$$

the probability of the jump due to transplantation is

$$\frac{\rho}{\lambda(w)} \cdot \prod_{j:(k_j, z_j) \in w} I(z_j \notin \{s, T\}),$$

the probability of the jump due to a patient arrival is

$$\frac{\tau}{\lambda(w)} \cdot \prod_{j:(k_j, z_j) \in w} I(z_j \notin \{s, T\}),$$

and the probability of the jump due to a patient's waiting time hits the boundary $\{s, T\}$ is

$$\sum_{j:(k_j, z_j) \in w} \left[I(z_j = s) \cdot \frac{q_{k_j, i}(z_j)}{q_{k_j}(z_j)} + I(z_j = T) \right].$$

Given the jump is due to a patient arrival, the conditional probability of newly arrived patient is in state i is p_i , which is independent of the jumping time. Given the jump is due to an organ allocation, by the definition of the fair allocation sequence, the conditional distribution of $W_t^{(s, i)}$ given $\mathcal{F}_t$ is decided by $\gamma^{\mathcal{J}}(\cdot; w)$. Similar calculations can be done for $W_t^{(s-, i)}$.

Therefore, there exists a transition kernel $Q(\cdot; \cdot)$ such that $\{W_t^{(s, i)}, t \geq 0\}$ and $\{W_t^{(s-, i)}, t \geq 0\}$ can be represented by the following construction of process x_t : from any initial state (n, z) : the first jumping time Θ_1 has the survival function $P(\Theta_1 > t) = S(t)$ where

$$S(t) = \begin{cases} \exp(-\int_0^t \lambda(n, \phi_n(s, z)) ds), & t < t^*(x) \\ 0, & t \geq t^*(x) \end{cases}$$

The trajectory of x_t for $t \leq \Theta_1$ is given by

$$x_t = (\nu_t, \zeta_t) = \begin{cases} (n, \phi_n(t, z)), & t < \Theta_1 \\ (N, Z), & t = \Theta_1 \end{cases}$$

where random variable (N, Z) has distribution $Q(\cdot; (n, \phi_n(\Theta_1, z)))$ and is independent of Θ_1 .

$\Theta_2, \Theta_3, \dots$ and $\{x_t : t > \Theta_1\}$ are constructed by repeating these steps as in the definition of piecewise deterministic Markov processes.

The no-explosion condition is satisfied since the patient and organ arrivals have finite intensity and patient transitions have finite total transition rate. Therefore with any fair allocation rule, $\{W_t, t \geq 0\}$ is a càdlàg piecewise deterministic Markov process. $\square$

Next we show the existence of finite invariant measures of the extended waiting list processes. The usual recurrence condition is not applicable since the state space of both processes is uncountable. Here we use convergence results for Harris recurrent general space Markov processes. The following definitions and theorems are from Meyn and Tweedie [1993b,a], Dai [1995] and Kaspi and Mandelbaum [1994]:

Definition B.0.11. (Harris Recurrence)

Let $\{X_t : t \geq 0\}$ be a strong Markov process on state space $(X, \mathcal{B}(X))$ with transition semi-group P^t . Let $\{P_x : x \in X\}$ be the probability measure induced by the process with initial condition $X(0) = x$. For any $A \in \mathcal{B}(X)$, let $\tau_A = \inf\{t \geq 0 : X_t \in A\}$. The process $\{X_t : t \geq 0\}$ is **Harris recurrent** if there exists some σ -finite measure ψ on $(X, \mathcal{B}(X))$, such that whenever $\psi(A) > 0$, $P_x(\tau_A < \infty) = 1$, $\forall x \in X$.

Proposition B.0.12. (Existence of Finite Invariant Measure)

If a càdlàg piecewise deterministic Markov process $\{X_t : t \geq 0\}$ is Harris recurrent, then it has a unique (up to constant multiples) invariant measure π .

Proof. See Gettoor [1980], Azema et al. [1967] and Kaspi and Mandelbaum [1994]. $\square$

If the invariant measure π is finite, it can be normalized to be a probability measure. In this case $\{W_t, t \geq 0\}$ is called **positive Harris recurrent**.

A sufficient condition for positive Harris recurrence involves the definition of small sets (c.f. Dai and Meyn [1995]).

Definition B.0.13. A set $C \in \mathcal{B}(X)$ is called small or petite if there exists $t > 0$, a probability measure ν on $\mathcal{B}(X)$ and $\delta > 0$ such that

$$P^t(x, A) \geq \delta \nu(A),$$

for any $x \in C$ and $A \in \mathcal{B}(X)$, where $P^t(x, A) = P_x(X(t) \in A)$.

The following sufficient condition for positive Harris recurrence is from Dai [1995], Meyn and Tweedie [1993b,a]:

Proposition B.0.14. Let $C \in \mathcal{B}(X)$ be a small set, suppose $P_x(\tau_C < \infty) = 1$ and for some $\delta > 0$,

$$\sup_{x \in C} E_x[\tau_C(\delta)] < \infty, \tag{B.6}$$

where $\tau_C(\delta) = \inf\{t \geq \delta : X(t) \in C\}$, then $\{X_t : t \geq 0\}$ is positive Harris recurrent.

Theorem B.0.15. The extended waiting list process $\{W_t^{(s,i)} : t \geq 0\}$ and $\{W_t^{(s-,i)} : t \geq 0\}$ are positive Harris recurrent.

Proof. Define Dirac measure ψ on the state space $(W_0, \mathcal{B}(W_0))$ of both $\{W_t^{(s,i)} : t \geq 0\}$ and $\{W_t^{(s-,i)} : t \geq 0\}$, such that for $\forall A \in \mathcal{B}(W_0)$, $\psi(A) = I(w_0 \in A)$, where w_0 is the empty state of the waiting list. It is obvious that ψ defined above is a finite measure, and $\psi(A) > 0 \Leftrightarrow w_0 \in A$. For both of the extended waiting list processes, if the process starts at $w \in W_0$, $\psi(A) > 0$ indicates $\tau_A \leq \tau_{w_0}$.

To show positive Harris recurrence, first note that it is shown in (3.1.2) that $\forall w \in W_0$,

$$E_w(\tau_{w_0}) < \infty. \tag{B.7}$$

Next we show that $\{w_0\}$ is a small set. Let ν be the Dirac measure on $(W_0, \mathcal{B}(W_0))$ such that $\nu(A) = I(w_0 \in A)$. Suppose there does not exist any $t > 0$ and $\delta > 0$ such that

$$P^t(w_0, A) \geq \delta \nu(A),$$

then for any $A \in \mathcal{B}(W_0)$, we must have $P^t(w_0, A) = 0$ for all $t > 0$, which indicates $P_{w_0}(\tau_A) = \infty$, a.s.. However this conflicts with the result $E_w(\tau_{w_0}) < \infty$ for all $w \in W_0$ which is proved earlier.

Finally we show that the sufficient condition for positive Harris recurrence (B.6) is satisfied. Note that with the small set $C = \{w_0\}$, $\sup_{x \in C} E_x[\tau_C(\delta)] < \infty$ is equivalent to

$$E_{w_0}[\tau_{\{w_0\}}(\delta)] < \infty,$$

where $\tau_{\{w_0\}}(\delta) = \inf\{t \geq \delta : X(t) = w_0\}$ and $X(t)$ is either $W_t^{(s,i)}$ or $W_t^{(s-,i)}$. For any fixed $\delta > 0$, by the Markov property,

$$E_{w_0}[\tau_{\{w_0\}}(\delta)] = \delta + \int_{W_0} E_w(\tau_{w_0}) P^\delta(w_0, dw).$$

Since we have shown $E_w(\tau_{w_0}) < \infty$ for all $w \in W_0$, $E_{w_0}[\tau_{\{w_0\}}(\delta)]$ must also be finite, and hence the positive Harris recurrence for both extended waiting list processes. $\square$

A natural corollary is the following result:

Proposition B.0.16. *There exists a finite invariant measure for each of the extended waiting list processes $\{W_t^{(s,i)} : t \geq 0\}$ and $\{W_t^{(s-,i)} : t \geq 0\}$.*

Positive Harris recurrent processes have the following ergodicity property:

Proposition B.0.17. (Ergodic Theorem)

For any positive Harris recurrent process $\{W_t, t \geq 0\}$ on $(W, \mathcal{B}(W))$, let π be the finite invariant measure of the process, and denote

$$\pi(f) = \int_W f(x) \pi(dx)$$

for any measurable function f . If $\pi(|f|) < \infty$, then

$$\lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t f(W_s) ds = \pi(f),$$

P_w -a.s. for any $w \in W$.

Proof. See, e.g., Dai [1995], Meyn and Tweedie [2009] and Kaspi and Mandelbaum [1994] $\square$

Note that the above ergodic theorem connects the time average of a measurable function of the process with its average under the invariant measure. This result is crucial in proving the existence of the average occupancy of state $i \in \mathcal{X}$ at waiting time $s \in [0, T)$ as the calendar time goes to infinity. To proceed with the proof, we first define the following counting process and at-risk indicators:

We use the same notation for the counting processes and at-risk indicators defined in the previous section. As a reminder:

Definition B.0.18. (Counting Processes and At-risk Indicators)

For the k th patient, define the càdlàg counting process for actual transitions (including organ allocations)

$$d\tilde{N}_{ij}^{(k)}(s) := I(\tilde{X}^{(k)}(s-) = i, \tilde{X}^{(k)}(s) = j),$$

so that $\tilde{N}_{ij}^{(k)}(s, t] := \int_{(s, t]} d\tilde{N}_{ij}^{(k)}(u)$ is the number of actual transitions from state i to j in $(s, t]$. Similarly, define the càdlàg counting process for counterfactual transitions

$$dN_{ij}^{(k)}(s) := I(X^{(k)}(s-) = i, X^{(k)}(s) = j)$$

and $N_{ij}^{(k)}(s, t] := \int_{(s, t]} dN_{ij}^{(k)}(u)$.

Also define at-risk indicators for the k th patient's actual transitions:

$$\tilde{Y}_i^{(k)}(s) := I(\tilde{X}^{(k)}(s) = i)$$

and

$$\tilde{Y}_i^{(k)}(s-) := I(\tilde{X}^{(k)}(s-) = i),$$

and for counterfactual transitions,

$$Y_i^{(k)}(s) := I(X^{(k)}(s) = i)$$

and

$$Y_i^{(k)}(s-) := I(X^{(k)}(s-) = i),$$

for $i, j \in \mathcal{X}_0$ and $s, t \in [0, T)$.

Next we represent the average occupancy of a state at a waiting time in the form of a time average of a measurable of the extended waiting list processes, therefore the limit exists as a result of the ergodic theorem.

Theorem B.0.19. (*Existence and Definition of $\pi_i(s)$ and $\pi_i(s-)$*)

For any $i \in \mathcal{X}$ and $s \in [0, T)$, let $N_{[0,t]}$ denote number of patient arrivals in calendar time interval $[0, t]$, then $\boldsymbol{\pi}(s) = (\pi_1(s), \dots, \pi_n(s))$ and $\boldsymbol{\pi}(s-) = (\pi_1(s-), \dots, \pi_n(s-))$ exist almost surely, where

$$\pi_i(s) := \lim_{t \rightarrow \infty} \frac{1}{N_{[0,t]}} \sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s) \quad (\text{B.8})$$

and

$$\pi_i(s-) := \lim_{t \rightarrow \infty} \frac{1}{N_{[0,t]}} \sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s-)$$

Moreover, $\pi_i(s), \pi_i(s-) \in [0, 1]$.

Proof. Let $\pi^{(s,i)}$ and $\pi^{(s-,i)}$ denote the finite invariant measures of the processes $W_t^{(s,i)}$ and $W_t^{(s-,i)}$.

First define measurable functions

$$f_{s,i}(w) := \sum_{j:(k_j, z_j) \in w} I(k_{j,2} = 1)(w).$$

By the ergodic theorem,

$$\lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t f_{s,i}(W_u^{(s,i)}) du = \pi^{(s,i)}(f_{s,i})$$

and

$$\lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t f_{s,i}(W_u^{(s-,i)}) du = \pi^{(s-,i)}(f_{s,i})$$

exists P_w -a.s. for any initial state $w \in W_0$.

Since for $W_t^{(s,i)}$, $k_{j,2}$ is the indicator component $I(t - T_k \geq s, \tilde{X}^{(k)}(s) = i)$, while for

$W_t^{(s-,i)}$, $k_{j,2}$ is the indicator $I(t - T_k \geq s, \tilde{X}^{(k)}(s-) = i)$, we have

$$\int_0^t f_{s,i}(W_u^{(s,i)})du = \sum_{k=1}^{N_{[0,t-s]}} \tilde{Y}_i^{(k)}(s) \cdot (t - T_k - s) \cdot I(t - T_k \in [s, T))$$

and

$$\int_0^t f_{s,i}(W_u^{(s-,i)})du = \sum_{k=1}^{N_{[0,t-s]}} \tilde{Y}_i^{(k)}(s-) \cdot (t - T_k - s) \cdot I(t - T_k \in [s, T)).$$

By the Strong Law of Large Numbers of renewal processes,

$$\lim_{t \rightarrow \infty} \frac{t}{N_{[0,t]}} = \frac{1}{\tau}.$$

Therefore

$$\begin{aligned} \pi_i(s) &= \lim_{t \rightarrow \infty} \frac{1}{N_{[0,t]}} \sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s) \\ &= \lim_{t \rightarrow \infty} \frac{t}{N_{[0,t]}} \frac{t+s}{t} \cdot \frac{1}{t+s} \cdot \frac{1}{T-s} \int_0^{t+s} f_{s,i}(W_u^{(s,i)})du \\ &= \frac{1}{\tau} \cdot \frac{1}{T-s} \pi^{(s,i)}(f_{s,i}) \end{aligned}$$

P_w -a.s. for any $w \in W_0$. Similarly,

$$\pi_i(s-) = \lim_{t \rightarrow \infty} \frac{1}{N_{[0,t]}} \sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s-) = \frac{1}{\tau} \cdot \frac{1}{T-s} \pi^{(s-,i)}(f_{s,i})$$

P_w -a.s. for any $w \in W_0$.

Since $\forall t \geq 0$, $\sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s)/N_{[0,t]} \in [0, 1]$, we have $\pi_i(s) \in [0, 1]$. The same conclusion applies to $\pi_i(s-) = \lim_{t \rightarrow \infty} \sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s-)/N_{[0,t]}$. $\square$

Appendix C

List of Symbols

$\perp$	Independent
$\lceil \cdot \rceil$	Ceiling of a number
$\mathbf{1}_n$	Vector of length n with all elements being 1
$I(\cdot)$	Indicator function
$\{\cdot\}_i$	The i th element of the vector
$\mathbf{I}$	Identity matrix
$\mathbf{e}_i$	Vector with the i th element being 1 and all other elements being 0
τ	Intensity of Patient Arrivals
ρ	Intensity of Organ Arrivals
T_k	Time of arrival of the k th patient
S_j	Time of arrival of the j th organ
N_I	Number of patient arrivals in calendar time interval I
O_I	Number of organ arrivals in calendar time interval I
$\mathcal{X}$	$\{0, 1, \dots, n\}$, state space of patients' health states, in which 0 denotes death
$X(s)$	Generic counterfactual transitions

$X^{(k)}(s)$	The k th patient's counterfactual transitions
$R(s)$	Generic counterfactual post-transplant residual life if transplanted at s
$R^{(k)}(s)$	The k th patient's counterfactual post-transplant residual life if transplanted at s
μ_s	$\mu_i(s) = E(R(s) \mid X(s) = i)$, expected post-transplantation residual life given state i at time of transplantation s
$\tilde{R}^{(k)}(s)$	$R^{(k)}(s) - (\inf_{t \geq 0} \{X^{(k)}(t) = 0\} - s)$, gain in residual life from transplantation
$\tilde{\mu}_s$	$\tilde{\mu}_i(s) := E(\tilde{R}^{(k)}(s) \mid X^{(k)}(s) = i)$, expected gain in residual life
T	Upper bound of a patient's waiting time
p	$p_i = P(X(0) = i)$ distribution of patients' initial states upon arrival
$q_{ij}(s)$	Infinitesimal generator of the counterfactual transitions
Q	$Q_{ij}(\cdot) = \int q_{ij}(s) ds$, measure matrix for counterfactual transitions
$\mathcal{J} = \{J_1, J_2, \dots\}$	Allocation sequence of indices of transplanted patients
$T_T^{(k)}$	Time waited until transplantation for the k th patient
$(n+1)$	Post-transplantation state
$\mathcal{X}_0$	$\mathcal{X} \cup \{n+1\}$, augmented patient state space
$\tilde{X}^{(k)}(s)$	The k th patient's actual transitions
$d\tilde{N}_{ij}^{(k)}(s)$	$I(\tilde{X}^{(k)}(s-) = i, \tilde{X}^{(k)}(s) = j)$, counting process of actual transitions
$\tilde{Y}_i^{(k)}(s)$	$I(\tilde{X}^{(k)}(s) = i)$, at-risk indicators of actual transitions
$dN_{ij}^{(k)}(s)$	$I(X^{(k)}(s-) = i, X^{(k)}(s) = j)$, counting process of counterfactual transitions
$Y_i^{(k)}(s)$	$I(X^{(k)}(s) = i)$, at-risk indicators of counterfactual transitions
$\mathcal{F}_t$	$\sigma(T_k, S_i, J_i, \{X^{(k)}(s) : s \in [0, t - T_k]\} : T_k, S_i \in [0, t])$
$\mathcal{G}_t$	$\sigma(T_k, S_i, \{X^{(k)}(s) : s \in [0, t - T_k]\} : T_k, S_i \in [0, t]) \vee \sigma(J_i : S_i < t)$

$\tilde{\mathcal{F}}_t$	Natural filtration induced by the waiting list and arrivals of patients and organs
$\mathcal{I}_t$	Index set of patients arrived before (including) t and are alive and have not been transplanted at t
W_t	Waiting list at calendar time t
w_0	Empty state of the waiting list
W	$\cup_{d=1}^{\infty}([0, T] \times \mathcal{X})^d \cup \{w_0\}$, state space of the waiting list
$\mathcal{B}(W)$	Borel σ -algebra of W
W'_t	Waiting list right before potential allocation at t
M_i	Time of the i th recurrence to the empty state of the waiting list
π	$\pi_i(s) = \lim_{t \rightarrow \infty} \sum_{k=1}^{N_{[0,t]}} \tilde{Y}_i^{(k)}(s) / N_{[0,t]}$, patients' limiting average occupancy
Ψ	$d\Psi_s = \pi_{s-} d\mathbf{Q}_s - d\pi_s$, limiting transplantation rate
Λ	$d\Lambda_i(s) = d\Psi_i(s) / \pi_i(s-) \text{ if } \pi_i(s-) \neq 0 \text{ and } \Lambda_i(\{s\}) = d\Psi_i(s) / \{\pi_{s-} d\mathbf{Q}_s\}_i \text{ if otherwise}$
C	Admissible control set of transplantation rates
c	Penalty associated with the constraint $\int_{[0,T]} d\Psi_s \cdot \mathbf{1}_n \leq \rho / \tau$
Ψ^c, Λ^c	Optimal transplantation rate under penalty c
$\mathcal{S}_c$	$\{(i, s) : i \in \mathcal{X}, s \in [0, T], \Lambda_i^c(s) > 0\}$, allocable set under penalty c
$\prod$	The product integral
$\mathbf{B}_t$	Counterfactual transition matrix from epoch t to $t + 1$ in discrete time
S_{wl}	Discrete state variable corresponding to expected in-waiting-list survival
S_{μ}	Discrete state variable corresponding to expected post-transplant survival