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Applications of Operations Research in Solid Organ Transplantation and Random Utility Choice Models

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ABSTRACT

This work is a collection of articles featuring applications of operations research primarily on solid organ transplantation. At the time of writing, 111,434 Americans were waiting for a liver or kidney transplant. Only 26,901 transplants were performed last year – a consequence of the scarcity of organ donors and the lack of technologies that confer the same survival and quality of life as transplantation. 5,541 individuals died waiting for a transplant and 6,059 became too sick to receive one; and perhaps the most unfair hardship borne by many is that they must wait years more for a transplant than an equally sick patient somewhere else.

The national organ procurement and transplantation network is the complex logistical system responsible for allocating organs obtained from deceased donors to potential recipients. Surprising to me also is that this system discarded 4,372 of the organs obtained last year. Most of these organs were of lesser quality but would have otherwise provided lifesaving benefits to patients.

The first two chapters propose restructuring the national system for liver allocation with the aims of reducing geographic disparity in access to liver transplantation and annual mortality. The structures are based on principles from manufacturing and systems engineering and have graph-theoretical and topological motivations. Using heuristics or stochastic, non-convex integer optimization, we obtain several new designs and test their performances with large-scale discrete-event simulations of the entire system. The appendices include additional technical information. These designs significantly reduced geographic disparity, total mortality, and sometimes average transportation cost.

The next two chapters investigate the decision-making of kidney transplant candidates. The first of these develops a multi-state Semi-Markov process model of the patient's overall experience as a candidate for transplantation. The model calculates the average survival time for a newly listed patient that can then be used for delivering prognoses and benchmarking performance. The following chapter responds to the discards of lesser quality organs by conducting individualized decision analyses that determine when it would be beneficial for a patient to accept such organs for transplantation. A comprehensive and realistic computation engine based on decision trees is constructed and demonstrated.

The last chapter is unrelated to the others and presents a method based on robust optimization for dealing with well-known nuisance parameters in the conditional logit discrete-choice model used in applied microeconomics and marketing.

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To labor and to wait

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Improving Liver Allocation Using Optimized Neighborhoods

Liver transplantation is the only restorative therapy for irreversible and progressive liver failure[1,2]. The longevity and quality of life of the thousands of Americans listed with end-stage liver disease (ESLD) are significantly influenced by the performance of the national organ procurement and transplantation system. For the 14,637 patients waitlisted in the United States (US) in 2014, the vast majority of organs for transplantation were obtained from deceased donors (6,449 of 6,729 transplants [96%])[3-5]. Liver transplantation is thus marred by the shortage of available livers that are donated with 1,767 patients dying while waiting for a transplant in 2013 and an additional 1,223 patients removed from the waitlist because they become too sick while waiting[4]. Regrettably, the current structure of the liver allocation system allows geographic disparities in access to a transplant to exist among those with similar medical urgency[6-8].

The United Network for Organ Sharing (UNOS) is responsible for overseeing the national network for organ procurement and organ allocation, and for promoting organ donation. Within UNOS, the Liver and Intestinal Committee[9] is actively seeking to resolve the disparity issue. The current proposal being put to public comment in August 2016 entails redistricting the nation into 8 districts in order to promote fairer distribution of transplanted organs[10-14]. Mehrotra et al. affirmed the significance of the redistricting plan and its methodology but also argued for further independent testing and exploration of alternatives[15,16]. This article responds to invitations to provide such an alternative[17].

Current Liver Allocation:

Liver allocation in the US is overseen through two separate congressionally mandated contracts: the Organ Procurement and Transplantation Network (OPTN) currently held by UNOS; and the Scientific Registry of Transplant Recipients (SRTR) currently held by the

Minneapolis Medical Research Foundation. Input is solicited from the transplantation community with oversight provided by the Division of Transplantation within the Health Resources and Services Administration (HRSA) of the US Department of Health and Human Services (HHS)[18-20]. The current geographic structure for the OPTN divides the US into 11 regions, each of which is a grouping of several neighboring states. These regions are further subdivided into 58 Donor Service Areas (DSAs) total with the DSAs not necessarily having boundaries that correspond with state borders. Each DSA has a designated Organ Procurement Organization (OPO) that facilitates local procurement and allocation procedures. Allocation of livers is based primarily on a three-tier geographic system – local/regional/national (local refers to the DSA of the procuring OPO) [21].

The OPTN follows certain policies in its operations. These policies mainly prioritize which candidates on the waitlist are offered an organ for transplantation in the three-tier system. The recent liver allocation policies and its history are summarized in[22,23]. Current policy adheres to the principles of transplanting "*the sickest first*" and that "*organs and tissues ought to be distributed on the basis of objective priority criteria and not on the basis of accidents of geography*" as promulgated by HRSA and refined by the, Institute of Medicine, into the HHS Final Rule[18]. Compliance with the regulations is ongoing and has resulted in several incremental changes to liver allocation policy (e.g. Status 1, MELD, Share 15, Share 35)[4,24,25]. The Model for End-stage Liver Disease (MELD) score, a predictor of 3-month mortality without liver transplantation, currently serves as the key metric for assessing medical urgency[26-29]; however, there is no similarly established standard for assessing geographic disparity in organ transplantation although several possibilities have been proposed[30]. MELD scores range from 6-40 points (more points implying greater urgency) and are based on laboratory values (INR, bilirubin, creatinine, and as of January 2016, sodium[31-33]). However, point assignment is not purely model-based, as candidates may receive additional 'exception points' that augment their

MELD score based on circumstantial criteria (of which hepatocellular carcinoma (HCC) is a prominent example[34]).

Table 1.1 provides an overview of current liver allocation. The geographic structure of the OPTN and the sharing policies together comprise how deceased donor-livers are allocated to recipients.

Policy Initiatives:

Despite existing organ sharing policies, there continues to be discrepancies across the 58 DSAs in a number of metrics such as the mean MELD score at transplant (>10 points), transplant rates (> 20-fold)[6], placement on waitlist (>14-fold)[7], and deaths due to ESLD (> 19-fold)[35]. The redistricting plan under consideration involves regrouping the DSAs into 8 districts instead of the current 11 UNOS regions[10-14]. The proposal has evolved over the past four years and was simulated under different sharing policies and compared with various alternatives. The redistricting plan is based on an optimization model that solves for a new grouping of DSAs into districts where MELD at transplant across the DSAs in the district is as equal as possible [10]. The plan is projected to reduce total mortalities while slightly increasing organ transport distances and times[14].

The methodology for redistricting demonstrates the value of optimization techniques, but some of its limitations ought to be addressed[10]. We confine the critique to the proposed geographic structure (i.e. regrouping the 58 DSAs into 8 instead of 11 districts) rather than any specific sharing policy that was tested. Figure 1 demonstrates the chief structural shortcoming of the redistricting solution and the concept of districting in general. We use Tennessee as an example. According to the redistricting plan, the OPO serving Western Tennessee will share organs with parts of Arkansas and Missouri rather than with Eastern Tennessee during regional allocation. Eastern Tennessee will instead share with parts of Illinois, Indiana, Kentucky, Ohio, and Wisconsin[16].Since redistricting partitions the country into geographically disjoint subsets,

organs procured near district boundaries may be transported to recipients farther away whereas candidates with greater medical urgency who are also closer to the procuring DSA, but are out-of-district, will not receive the organ. Unfortunately, this lack of connectivity among neighboring DSAs will be symptomatic of any redistricting plan. Concentric circles (where candidates within a specified physical radius of the donor hospital or procuring OPO are given additional priority) or momentarily granting out-of-district candidates that are closer to the donor hospital additional MELD points have been suggested to remedy this deficiency. Additionally, the example also demonstrates that districts are imbalanced in the numbers of OPOs within the district and in the population sizes necessary for supporting donor pools.

Interestingly, Tennessee in 1992 implemented a statewide sharing variance for kidney allocation (which proceeds similarly to liver allocation, but more closely follows a local-regional-national setup without MELD-scoring). The policy variance reduced geographic disparities in kidney transplant rates and ischemic times by allowing the OPOs in Tennessee to preempt regional allocation and share with each other before sharing with OPOs out-of-state[36]. This historical incident further motivates the value of the notion of a DSA's neighborhood discussed in the following section.

A second major structural deficiency of any districting solution is its inability to locally respond to changes in policies and/or practices that may occur within an ever evolving transplant system. The OPTN is a dynamic system in which the behaviors of OPOs and transplant centers change over time. For example, the number of newly listed candidates needing a liver for transplant in each DSA from 2005-2015 fluctuated by approximately 15% year-to-year on average[3]. Any revision to the districts in response to these inevitable organ supply-demand imbalances will simultaneously affect multiple DSAs.

We present an approach that retains attractive features of both redistricting and concentric circles and is also amenable to the current operation of the OPTN. The framework is

based on mathematical theory in operations research that surmounts some of the aforementioned limitations of redistricting.

Materials and Methods

DSA/OPO Neighborhoods:

The core concept of our proposal is to define regions as a specified set of neighboring DSAs for each DSA, instead of DSAs in a fixed district. A DSA's set of neighbors is called that DSA's *neighborhood.* Liver allocation may proceed just as before, except that during regional allocation, organs are shared with the procuring OPO's set of neighboring DSAs; thus maintaining the current local-regional-national hierarchy.

Figure 1.2 depicts an example of a neighborhood for Western Tennessee. In contrast to Figure 1.1, where Eastern and Western Tennessee are separated during regional allocation under redistricting, Figure 1.2 shows that the DSAs in Western Tennessee's neighborhood include its geographically immediate neighbors among others. The figure illustrates a neighborhood for a single DSA; each of the 58 DSAs has its own neighborhood. OPOs in each of these respective neighborhoods can be made to share with their geographically-immediate neighbors among others during regional allocation. This requirement forces neighborhoods of adjacent DSAs to "overlap", i.e. two adjacent DSAs will have some neighbors in common. This feature has an underpinning in the operations research literature on the theory of the design of manufacturing systems that are resilient to demand and supply uncertainty [37] [38] [39] [40]. This literature discusses manufacturing systems and networks abstractly, but when translated into the context of the OPTN, recommends the following: Increasing a DSA's connectivity and creating overlapping neighborhoods promotes resilience in responding to demand and supply uncertainty; and balancing supply and demand across neighborhoods ensures greater equity. Interconnectivity is achieved by having each DSA's neighborhood contain other nearby DSAs. Supply-demand balancing is discussed in the following subsection.

The neighborhoods concept provides additional rigor to and generalizes the concept of concentric circles, as geographically immediate neighbors of a procuring OPO are within its neighborhood during regional allocation. Regions in the current OPTN and districts in the redistricting proposal are special types of neighborhoods that do not overlap; hence the neighborhoods framework also generalizes districting.

Constructing the Neighborhoods:

Selecting which DSAs belong in each DSA's neighborhood using multiple years of supply and demand data requires solving an optimization model. The neighborhood of a DSA identified from the optimization model forms the DSA's region in a local-regional-national policy. An explicit mathematical formulation of the optimization model is included in the Supplement.

Much like the geographic structure used in districting[10], the neighborhoods can be constructed so that each of them has attractive properties. Table 1.2 summarizes the most important properties of the neighborhoods that were included in the modeling framework. They include that a neighborhood for each DSA contains its geographically-immediate neighbors; has relationships that are reciprocal or symmetric (i.e. DSA *A* is in DSA *B*'s neighborhood if and only if DSA *B* is in DSA *A's* neighborhood); has a minimum and a maximum number of DSAs inside of it; attains a minimum population size; includes a minimum number of transplant centers; has bounded average organ travel distance/time; and is geographically contiguous. In the spirit of concentric circles, once geographically-immediate neighbors are included in a specific DSA's neighborhood, the model will then consider including the geographically-immediate neighbors of those immediate neighbors, and so on; however, not all such neighbors are necessarily included and the model does not discriminate among neighbors at each stage. These properties promote resilience in the solution.

In addressing disparity, we adopt a Rawlsian[41] principle of justice in ensuring that the worst-off neighborhood is as close to the best-off neighborhood as possible. The model's

objective is to balance the ratio of supply and demand across neighborhoods (not for a specific DSA). Additionally, the model departs from that used in Gentry et al. in four important ways[10]. First, the model uses 10 years of historical supply and demand data to mitigate the uncertainty of annual changes in donor and listing rates. Second, demand in a specific year is measured by the number of waitlist additions to the liver transplantation list during that year. Other definitions for demand are possible. Third, the objective of the optimization model in Gentry et al. [10] minimizes the sum of absolute deviations in the number of donors from demand across districts; it is preferable to minimize the ratios of supply and demand to avoid penalizing DSAs based on the number of donors and candidates that they have[15]. Thus, for each neighborhood, the model considers the ratio of the supply of demand and its deviation from the ratio of the expected value of the nationally aggregated supply and demand. Fourth, it minimizes the expected value of the maximum of these deviations, where the expectation is taken over the years 2005-2014.

We used Julia 0.3.10 and a commercial solver Gurobi 6.5 to solve the optimization model[42,43]. Hawaii and Puerto Rico were excluded from the model and their neighborhoods were defined to include the 4 closest DSAs in California and Florida respectively. Data on the numbers of transplant centers (as of 2015), population sizes (as of 2013), historical transplant volumes, and the numbers of organs recovered for transplant and the number of waitlist additions from 2005-2014 were obtained from UNOS and SRTR. Transport distances (miles) were calculated using latitudes and longitudes of donor hospitals and transplant centers via the method of geodesics in SAS 9.4[44].

Simulating Neighborhood Solutions:

We test the performance of a neighborhoods solution from the optimization model in a simulation environment. Unfortunately, to our knowledge, the architecture of the simulation tool used in the transplantation community, the Liver Simulated Allocation Model (LSAM v Aug

2014), does not allow for neighborhoods[45]. We therefore programmed a discrete-event liver allocation simulator in Python 3, hereafter referred to as LivSim.

LivSim approximates LSAM from information available in publically released sources. LivSim begins with an initial waitlist and takes three input streams: additions to the liver transplant waitlist, status updates of waitlist candidates; and arrivals of donors. LivSim then processes each of these events. When candidates arrive to a particular DSA, they are assigned a MELD score, ABO blood type, Status 1 exception (yes or no), and HCC exception (yes or no). During a status update, LivSim updates the candidate's MELD score and potentially removes the candidate from the waitlist or indicates their death. After a donor arrives, the liver is assigned an ABO blood type and is offered to ABO blood type-compatible candidates in accordance with the sharing policies and geographic structure in place. The current version of LivSim uses a reduced form of LSAM's organ acceptance model to calculate whether a candidate accepts a liver for transplant. The acceptance model uses LSAM's coefficients for whether the potential recipient is Status 1, the potential recipient's waiting time, whether the potential recipient is listed in the DSA of the procuring OPO, and donor blood type and assumes all other patient attributes are held at the baseline. These four sets of coefficients included are also the four most significant predictors in LSAM's acceptance model. After LivSim processes these streams, it will calculate the post-transplant deaths and the average organ transport distance. Organ transport distances are calculated by assuming that any organ traveling between any two DSAs travel (including within a DSA) the historical average amount of distance; distances are not calculated using donor hospitals and transplant centers. The current version of LivSim operates at the DSA level and does not incorporate re-lists, re-transplants, and multiple transplants; it also assumes candidates will remain active on the waitlist once they are assigned a MELD score.

The input files generated by LSAM input generator modules for waitlist, patient listing, patient status updates, and post-transplant survival are used. LivSim incorporates Status 1, HCC exceptions, Share 15, and Share 35 sharing policies in addition to MELD scoring with and without sodium.

We calibrate LivSim against LSAM by comparing results generated by both simulators on the same input data for the current geographic structure and sharing policies. 5-year (January 2010- December 2014) patient listing data and status updates were generated by the LSAM Candidate Generator and organ donor data were generated by the LSAM Donor Generator.

Simulation Experiment for Comparing Geographic Structures:

The simulation experiments using LivSim compare the performance of the geographic structures under the current allocation system, redistricting, the specific neighborhoods solution obtained, and national allocation. For each system, we assume that Status 1, Share 15, and Share 35 policies are in place; the experiment only varies the geographic structure employed.

Performance Measures:

We measure disparity by DSA mean transplant MELD standard deviation. DSA mean transplant MELD aims to measure the overall medical urgency of patients being transplanted and its standard deviation across DSAs measures geographic disparity in access to transplant. Additional important performance measures are waitlist and post-transplant mortalities, waitlist removals, and average organ transport distance. Average organ transport distances have implications for costs. The simulation experiment is conducted on the same input data used in the calibration with a 5-year run-length (January 2010- December 2014). Differences in the performance measures relative to current allocation and between redistricting and neighborhoods were computed and significance was assessed using two-tailed z-tests on

differences between replication means. We performed 5 replications (25 replication-years) and modeled two cases:

1) MELD without sodium: No candidate was excluded, even those with MELD exception points. HCC exceptions were included but the recent cap and delay policy was not incorporated[46].
2) MELD with sodium: No candidate was excluded and it was assumed no exception points for non-HCC candidates were awarded, HCC exceptions were included but the recent cap and delay policy was not incorporated[46].

Results

Calibration Results:

Table 1.3 presents the results of the calibration of LivSim against LSAM for current allocation. LivSim's results for all performance metrics except for average organ transport distance are within 10% relative error of LSAM. LivSim overestimates average organ transport distances because it uses right-skewed DSA-to-DSA historical averages of distances rather than donor-hospital-to-transplant center distances. Actual distances are likely to be less than those reported.

Neighborhood Solution Found:

We found a neighborhood solution where each neighborhood had at least 9 transplant centers and population of 25 million; and the volume-weighted organ transport distance was less than 400 miles. Each DSA had at least 5 neighbors including itself and no more than 20 neighbors including itself. Table 4 provides a listing of the DSA's in each DSA's neighborhood. Bounds on distance, transplant centers, population, and number of DSAs in the neighborhood may be adjusted.

Simulation Experiment Results:

Tables 1.5 and 1.6 present the 5-year comparative performances of the current allocation, redistricting, the neighborhood solution found, and national allocation for the cases of using MELD without sodium and with sodium respectively. We emphasize results for the latter case since it is more representative of the most recent liver allocation policy. All estimates are differences relative to current allocation.

For standard deviation in DSA mean transplant MELD, in the case of MELD without sodium, redistricting and neighborhoods both achieve significant reductions in the standard deviation of mean transplant MELD of 0.48 and 0.50 points respectively (a 24% and 25% reduction with respect to current allocation) when compared to current allocation ($p < 0.05$). In the case of MELD with sodium, both achieve significant reductions of 0.50 and 0.59 points respectively (a 25% and 29% reduction with respect to current allocation) ($p < 0.05$). Compared to redistricting in this case, neighborhoods significantly reduced disparity by an additional 17% ($p < 0.05$).

Experiment results for either case demonstrate that both redistricting and neighborhoods achieve significant annual reductions in the total of post-transplant and waitlist mortalities compared to current allocation ($p < 0.05$), with neighborhoods saving an additional 20-25 lives annually compared to redistricting in both cases ($p < 0.05$). MELD with sodium scoring improves mortality reductions for all structures. Both redistricting and neighborhoods reduce waitlist removals by 40-55 each year compared to current allocation, but the finding was not significant ($p > 0.05$); additionally no significant difference was found between redistricting and neighborhoods in this regard.

Redistricting will increase DSA mean transplant MELD by approximately 0.6 points in either case ($p < 0.05$), and neighborhoods will do so by 0.8 points in the case of MELD without sodium and 0.9 points in the case of MELD with sodium ($p < 0.05$) when compared with current allocation. The differences between redistricting and neighborhoods are also statistically

significant ($p < 0.05$). Both structures will increase average organ transport distances compared to current allocation; redistricting by approximately 36 miles per organ, and neighborhoods by approximately 24 miles, or 33% less in the case of MELD without sodium while MELD with sodium scoring shows an increase of 43 and 36 miles respectively. All differences in transportation distances between redistricting and neighborhoods with current allocation and among each other were significant ($p < 0.05$).

Further analysis of the simulation results show that the benefits of neighborhoods are also borne more uniformly. For both the cases of MELD without sodium and MELD with sodium respectively, we calculated the DSA-ranges for waitlist mortalities; total miles procured organs are transported; and MELD at transplant. The DSA-ranges are defined as the difference of the minimum number of waitlist mortalities (resp. total miles transported, average MELD at transplant) across DSAs from the maximum number of waitlist mortalities (resp. total miles transported, average MELD at transplant) across DSAs averaged over all replications. For MELD without sodium and with sodium, DSA-ranges for mortalities decreased by 13% and 15% respectively for neighborhoods relative to current allocation. This decrease is 11% and 12% respectively for redistricting. Ranges in total miles transported fell by 12% in both cases for neighborhoods. However, they rose by 3% and 2% respectively for redistricting. The ranges for MELD at transplant fell by 12% and 17% respectively for neighborhoods. This reduction is 8% and 9% respectively for redistricting. All changes were statistically significant ($p < 0.001$) relative to current allocation. Differences between redistricting and neighborhoods were significant for ranges of MELD at transplant in the case of MELD with sodium ($p = 0.004$) and ranges of total miles transported for both cases ($p < 0.001$).

Discussion

Optimally designed districts and neighborhoods both further the goals of transplanting the sickest first, reducing total mortalities, and promoting fairness in transplant access when

compared with the current allocation system. However, as the particular neighborhood solution demonstrates, interventions that exceed the redistricting structure in these aims are possible. Moreover, the neighborhood solution, while exhibiting smaller increases in average organ transport distances, exceeds redistricting in improvements on average DSA transplant MELD (especially in the MELD with sodium case where exceptions were not granted to most candidates); total mortalities; and DSA transplant MELD standard deviation.

These advantages stem from the structural design. A neighborhood for a given DSA expands the DSA's regional allocation and thereby results in more organs being directed to sicker candidates by sharing policies (e.g. Share 35). The inclusion of geographically immediate neighbors of that DSA helps forestall rising organ transport distances. The neighborhoods are optimally constructed so that available organs for transplantation relative to demand are as equal as possible – thereby resulting in reductions to geographic disparity. We emphasize that the framework is not specifying the number of organs an OPO will send to its region but merely ensuring similar opportunities to access organs from regional allocation. Also, the shapes of each neighborhood (with respect to compactness in historical-transplant volumes) may be further constrained with guidance from policymakers (e.g. use forecasted transplant volumes, contain a limited number of US states, have maximum geographic areas, etc.).

The underlying optimization model confers the neighborhoods with additional resilience against uncertainty. Several trends (e.g. acute alcoholic hepatitis transplantation, healthcare reform, ex vivo liver perfusion, varying organ refusal rates, evolving community demographics, etc.) can cause unforeseen changes in donor organ supply and demand. Historical variability in procurement rates and listing rates are incorporated so that a particular neighborhood solution remains the same as long as the ratios of donors to candidates at individual DSAs remain close to their 2005-2014 historical averages. An advantage of using a stochastic rather than a

deterministic optimization methodology is that data forecasting procurement and listing rates may be used in lieu of historical data to construct the neighborhoods in future work – and such solutions would remain similarly stable during the forecast period. Should supply and demand change significantly from the forecasted values, the model can be adaptively used to specify a new set of neighbors without redesigning the borders.

We emphasize that the results herein demonstrate the promise of the neighborhood framework more so than that of the particular geographic structure obtained. This framework is quite general and alternative solutions meeting different requirements of stakeholders may arise from it in future refinements. It is advisable for the transplantation community to compare the advantages and disadvantages of the neighborhood and redistricting frameworks relative to current allocation before enacting policy changes. Notably, neighborhoods are perhaps also amenable to current OPTN practice. From the perspective of an individual OPO, their activities remain much the same in relation to sharing, albeit with different neighbors. The only major operational change for the DSAs would be where the sharing of organs might occur during regional allocation. Moreover, a remarkable advantage of the neighborhoods is that should the neighborhoods ever be modified in the future, it can be done so one OPO at a time and without disrupting the ongoing practices of other OPOs, whereas changing the districts in redistricting affects the operations of every OPO in the district. However, whether such modifications can be made systematically and regularly is influenced by the culture of the OPTN and the ease of securing reform[47]. Inertia in this regard only underscores the importance of having the best possible solution at the outset.

Limitations:

This study has some limitations. Foremost, the results asserting the improved performance of neighborhoods were based on our own simulator that only approximates LSAM. Differences in mortality and disparity estimates were due to omission of re-transplants/re-lists

and the use of less patient and donor characteristics in the current version of LivSim. Transport distances provided by LivSim are conservative overestimates, so actual distances will be smaller. However, we treated all geographic structures consistently in the simulation experiment. Lastly, the simulation experiment results are based on sharing policies at the time of writing. Modifications of the sharing policies affect the performance of the geographic structures tested and the validity of comparisons among them.

Future Work:

This work focused on the geographic aspects of the OPTN's design in a local-regional-national framework under current policy at a systems-level. It did not consider changes in transplant centers' and patients' behaviors in response to the neighborhoods design. Incorporating behavioral models into the optimization framework to obtain a more refined solution requires further investigation. We believe, however, that the flexibility provided by the neighborhood structure will be an important factor in developing such a model. This flexibility can also be used for developing an allocation design that judiciously directs low quality livers to DSAs for rapid placement to reduce discards. Sharing policies are also the counterparts of the geographic structures and help perfect liver allocation. For example, boosting local priority by assigning temporary MELD exception points is a possibility. Such policies should be studied in conjunction with the geographic structures – and ideally, optimized with them simultaneously.

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The authors assume responsibility for the integrity of this work and all views expressed herein.

Table 1.1: Overview of Deceased Donor Liver Allocation Policy for Adult[1] Recipients

Deceased Donor Liver Prioritization[2]
Local and Regional Status 1A or 1B Candidates
Regional and Local Candidates with MELD 35-40
(i.e. local 40, regional 40, local 39, …)
Local Candidates with MELD $\geq$ 15
Regional Candidates with MELD $\geq$ 15
National Status 1A or 1B Candidates
National Candidates with MELD $\geq$ 15
Local Candidates with MELD < 15
Regional Candidates with MELD <15
National Candidates with MELD <15

[1]Pediatric candidates are prioritized differently

[2]Table presents overview of prioritization. Rules shown have minor modifications based on ABO blood type, donor-recipient compatibility, and multiple transplant recipients.

Table 1.2: Properties Ensured in Neighborhood Solutions

✓ ***Formed using 10-year historical data:*** The DSA-neighborhoods are formed using a 10-year period (2005-2014) and hence incorporate uncertainty in organ availability and needs
✓ ***Immediate Neighbors*****:** DSAs have their geographically immediate neighbors in their neighborhood
✓ ***Population:*** Each DSA's neighborhood has a minimum population
✓ ***Symmetry in DSA Relationships*****:** DSA *A* has DSA *B* in its neighborhood if and only if DSA *B* has DSA *A* in its neighborhood[1]
✓ ***Density:*** Each DSA has a minimum and a maximum number of neighbors
✓ ***Contiguity:*** Each DSA's neighborhood is geographically contiguous[1]
✓ ***Compactness:*** The average transport distance/time for a DSA's neighborhood is bounded[1]
✓ ***Transplant Centers:*** Each DSA's neighborhood has a minimum number of transplant centers[1]
✓ ***Possibility to generate a spectrum of solutions, instead of one:*** By parameter specifications, it is possible to generate many alternative solutions with different properties (e.g. average distance, mortality, disparity, etc.) to facilitate decision making.

[1]Property also possessed by redistricting[10].

Table 1.3: Calibration Results of LivSim vs. LSAM

	LSAM	**LivSim**
Category	Current Allocation	Current Allocation
Annualized Waitlist and Post Transplant Deaths	2301.9	2181.9
Annualized Waitlist Deaths	1230.8	1149.8
Annualized Post Transplant Deaths	1071.1	1032.1
Annualized Waitlist Removals	3453.4	3091.0
DSA Mean Transplant MELD	23.32	24.30
DSA Mean Transplant MELD Standard Deviation	2.00	2.03
Average Organ Transport Distance (miles)	257	332

Input data generated by LSAM Candidate and Donor generators for 2010-2014

Table 1.4: Example Neighborhoods Solution[1]

Procuring OPO	DSAs Belonging to Procuring OPO's Neighborhood																			
ALOB-OP1 Alabama Organ Center	ALOB	AROR	FLUF	GALL	KYDA	LAOP	MOMA	MSOP	NCNC	TNDS	TNMS	VATB								
AROR-OP1 Arkansas Reg. Organ Recovery Agency	ALOB	AROR	AZOB	CORS	IAOP	ILIP	INOP	KYDA	LAOP	MOMA	MSOP	MWOB	NEOR	NMOP	OKOP	TNDS	TNMS	TXGC	TXSA	TXSB
AZOB-OP1 Donor Network of Arizona	AROR	AZOB	CADN	CAGS	CAOP	CASD	CORS	NMOP	NVLV	OKOP	ORUO	TXGC	TXSA	TXSB	UTOP	WALC				
CADN-OP1 Donor Network West	AZOB	CADN	CAGS	CAOP	HIOP	NVLV	ORUO	WALC												
CAGS-OP1 Sierra Donor Services	AZOB	CADN	CAGS	CAOP	CASD	HIOP	NVLV	ORUO	UTOP	WALC										
CAOP-OP1 OneLegacy	AZOB	CADN	CAGS	CAOP	CASD	HIOP	NVLV	ORUO	UTOP											
CASD-IO1 Lifesharing - A Donate Life Org.	AZOB	CAGS	CAOP	CASD	HIO	NVLV	UTOP													
CORS-OP1 Donor Alliance	AROR	AZOB	CORS	IAOP	MNOP	MOMA	MWOB	NEOR	NMOP	NVLV	OKOP	ORUO	TXGC	TXSA	TXSB	UTOP	WALC	WIUW		
CTOP-OP1 LifeChoice Donor Services	CTOP	MAOB	NJTO	NYAP	NYFL	NYRT	NYWN	OHLP	PADV	PATF										
DCTC-OP1 Washington Reg Transplant Community	DCTC	MDPC	NCNC	NJTO	NYRT	PADV	PATF	TNDS	VATB											
FLFH-IO1 TransLife	FLFH	FLMP	FLUF	FLWC	GALL	PRLL														
FLMP-OP1 Life Alliance Organ Recovery Agency	FLFH	FLMP	FLUF	FLWC	GALL	PRLL														
FLUF-IO1 LifeQuest Organ Recovery Services	ALOB	FLFH	FLMP	FLUF	FLWC	GALL	PRLL	SCOP	TNMS											
FLWC-OP1 LifeLink of Florida	FLFH	FLMP	FLUF	FLWC	GALL	PRLL														
GALL-OP1 LifeLink of Georgia	ALOB	FLFH	FLMP	FLUF	FLWC	GALL	KYDA	MDPC	MSOP	NCCM	NCNC	PATF	SCOP	TNDS	TNMS	VATB				
HIOP-OP1 Legacy of Life Hawaii	CADN	CAGS	CAOP	CASD	HIOP															
IAOP-OP1 Iowa Donor Network	AROR	CORS	IAOP	ILIP	INOP	MNOP	MOMA	MWOB	NEOR	OKOP	WALC	WIDN	WIUW							
ILIP-OP1 Gift of Hope	AROR	IAOP	ILIP	INOP	MIOP	MNOP	MOMA	NEOR	OHLC	OHOV	TNMS	WIDN	WIUW							
INOP-OP1 Indiana Donor Network	AROR	IAOP	ILIP	INOP	KYDA	MIOP	MOMA	MWOB	OHLB	OHLC	OHLP	OHOV	TNMS	WIDN	WIUW					
KYDA-OP1 KY Organ Donor Affiliates	ALOB	AROR	GALL	INOP	KYDA	MDPC	MOMA	NCCM	NCNC	NYFL	NYWN	OHLB	OHLC	OHLP	OHOV	PATF	TNDS	TNMS	VATB	
LAOP-OP1 Louisiana Organ Procurement Agency	ALOB	AROR	LAOP	MOMA	MSOP	MWOB	NMOP	OKOP	TNDS	TNMS	TXGC	TXSA	TXSB							
MAOB-OP1 New England Organ Bank	CTOP	MAOB	NJTO	NYAP	NYFL	NYRT	NYWN	OHLP	PADV	PATF										
MDPC-OP1 The Living Legacy Foundation of MD	DCTC	GALL	KYDA	MDPC	NCNC	NJTO	NYAP	NYFL	NYRT	NYWN	OHLB	OHLP	PADV	PATF	TNDS	VATB				
MIOP-OP1 Gift of Life Michigan	ILIP	INOP	MIOP	OHLB	OHLC	OHLP	OHOV	WIDN	WIUW											
MNOP-OP1 LifeSource Upper Midwest OPO	CORS	IAOP	ILIP	MNOP	MOMA	MWOB	NEOR	OKOP	ORUO	WALC	WIDN	WIUW								
MOMA-OP1 Mid-America Transplant Svcs	ALOB	AROR	CORS	IAOP	ILIP	INOP	KYDA	LAOP	MNOP	MOMA	MWOB	OHLC	OHLP	OHOV	OKOP	TNMS	WIDN	WIUW		
MSOP-OP1 Mississippi Organ Recovery Agency	ALOB	AROR	GALL	LAOP	MSOP	NCNC	OKOP	PATF	TNDS	TNMS	TXGC	VATB								
MWOB-OP1 Midwest Transplant Network	AROR	CORS	IAOP	INOP	LAOP	MNOP	MOMA	MWOB	NEOR	OKOP	TXGC	TXSB	WALC	WIUW						
NCCM-IO1 LifeShare of the Carolinas	GALL	KYDA	NCCM	NCNC	PATF	SCOP	TNDS	TNMS	VATB											
NCNC-OP1 Carolina Donor Services	ALOB	DCTC	GALL	KYDA	MDPC	MSOP	NCCM	NCNC	OHLB	PATF	SCOP	TNDS	TNMS	VATB						
NEOR-OP1 Nebraska Organ Recovery System	AROR	CORS	IAOP	ILIP	MNOP	MWOB	NEOR	OKOP	WALC	WIUW										
NJTO-OP1 NJ Organ and Tissue Sharing Network	CTOP	DCTC	MAOB	MDPC	NJTO	NYAP	NYFL	NYRT	NYWN	OHLP	PADV	PATF								
NMOP-OP1 New Mexico Donor Services	AROR	AZOB	CORS	LAOP	NMOP	NVLV	OKOP	TXGC	TXSA	TXSB	WALC									
NVLV-OP1 Nevada Donor Network	AZOB	CADN	CAGS	CAOP	CASD	CORS	NMOP	NVLV	ORUO	UTOP	WALC									
NYAP-OP1 Ctr for Donation and Transplant	CTOP	MAOB	MDPC	NJTO	NYAP	NYFL	NYRT	NYWN	OHLB	OHLP	PADV	PATF	TNDS	VATB						
NYFL-IO1 Finger Lakes Donor Recovery Network	CTOP	KYDA	MAOB	MDPC	NJTO	NYAP	NYFL	NYRT	NYWN	OHLB	OHLP	PADV	PATF	TNDS	VATB					
NYRT-OP1 LiveOnNY	CTOP	DCTC	MAOB	MDPC	NJTO	NYAP	NYFL	NYRT	NYWN	PADV	PATF	VATB								
NYWN-OP1 Upstate NY Transplant Svcs	CTOP	KYDA	MAOB	MDPC	NJTO	NYAP	NYFL	NYRT	NYWN	OHLB	OHLP	PADV	PATF	TNDS	VATB					
OHLB-OP1 LifeBanc	INOP	KYDA	MDPC	MIOP	NCNC	NYAP	NYFL	NYWN	OHLB	OHLC	OHLP	OHOV	PADV	PATF	TNDS	VATB				
OHLC-OP1 Life Connection of Ohio	ILIP	INOP	KYDA	MIOP	MOMA	OHLB	OHLC	OHLP	OHOV	WIUW										
OHLP-OP1 Lifeline of Ohio	CTOP	INOP	KYDA	MAOB	MDPC	MIOP	MOMA	NJTO	NYAP	NYFL	NYWN	OHLB	OHLC	OHLP	OHOV	PADV	PATF	TNDS	TNMS	VATB
OHOV-OP1 LifeCenter Organ Donor Network	ILIP	INOP	KYDA	MIOP	MOMA	OHLB	OHLC	OHLP	OHOV	TNMS										
OKOP-OP1 LifeShare Transplant Donor Svcs of OK	AROR	AZOB	CORS	IAOP	LAOP	MNOP	MOMA	MSOP	MWOB	NEOR	NMOP	OKOP	ORUO	TNMS	TXGC	TXSA	TXSB	UTOP	WALC	
ORUO-IO1 Pacific NW Transplant Bank	AZOB	CADN	CAGS	CAOP	CORS	MNOP	NVLV	OKOP	ORUO	UTOP	WALC	WIUW								
PADV-OP1 Gift of Life Donor Program	CTOP	DCTC	MAOB	MDPC	NJTO	NYAP	NYFL	NYRT	NYWN	OHLB	OHLP	PADV	PATF	TNDS	VATB					
PATF-OP1 Center for Organ Recovery and Educ.	CTOP	DCTC	GALL	KYDA	MAOB	MDPC	MSOP	NCCM	NCNC	NJTO	NYAP	NYFL	NYRT	NYWN	OHLB	OHLP	PADV	PATF	TNDS	VATB
PRLL-OP1 LifeLink of Puerto Rico	FLFH	FLMP	FLUF	FLWC	PRLL															
SCOP-OP1 LifePoint, Inc.	FLUF	GALL	NCCM	NCNC	SCOP	VATB														
TNDS-OP1 Tennessee Donor Svcs	ALOB	AROR	DCTC	GALL	KYDA	LAOP	MDPC	MSOP	NCCM	NCNC	NYAP	NYFL	NYWN	OHLB	OHLP	PADV	PATF	TNDS	TNMS	VATB
TNMS-OP1 Mid-South Transplant Foundation	ALOB	AROR	FLUF	GALL	ILIP	INOP	KYDA	LAOP	MOMA	MSOP	NCCM	NCNC	OHLP	OHOV	OKOP	TNDS	TNMS	VATB		
TXGC-OP1 LifeGift Organ Donation Ctr	AROR	AZOB	CORS	LAOP	MSOP	MWOB	NMOP	OKOP	TXGC	TXSA	TXSB									
TXSA-OP1 Texas Organ Sharing Alliance	AROR	AZOB	CORS	LAOP	NMOP	OKOP	TXGC	TXSA	TXSB											
TXSB-OP1 Southwest Transplant Alliance	AROR	AZOB	CORS	LAOP	MWOB	NMOP	OKOP	TXGC	TXSA	TXSB										
UTOP-OP1 Intermountain Donor Services	AZOB	CAGS	CAOP	CASD	CORS	NVLV	OKOP	ORUO	UTOP	WALC										
VATB-OP1 LifeNet Health	ALOB	DCTC	GALL	KYDA	MDPC	MSOP	NCCM	NCNC	NYAP	NYFL	NYRT	NYWN	OHLB	OHLP	PADV	PATF	SCOP	TNDS	TNMS	VATB
WALC-OP1 LifeCenter Northwest	AZOB	CADN	CAGS	CORS	IAOP	MNOP	MWOB	NEOR	NMOP	NVLV	OKOP	ORUO	UTOP	WALC	WIUW					
WIDN-OP1 Wisconsin Donor Network	IAOP	ILIP	INOP	MIOP	MNOP	MOMA	WIDN	WIUW												
WIUW-IO1 UW Health Organ and Tissue Donation	CORS	IAOP	ILIP	INOP	MIOP	MNOP	MOMA	MWOB	NEOR	OHLC	ORUO	WALC	WIDN	WIUW						

[1]Neighborhood solution found with requirements that neighborhoods have average volume-weighted organ transport distance less than 400 miles; and have at least 9 transplant centers and population of 25 million. Each DSA has at least 5 neighbors including itself and no more than 20 neighbors including itself. Bounds on distance, transplant centers, and number of DSAs in the neighborhood may be adjusted.

Table 1.5: 5-Year Comparative Performance of Allocation Systems (MELD without sodium case) [1]

	Current	Redistricting[2]	Neighborhoods[2]	Difference (Neighborhoods-Redistricting)	National[2]
Annualized Waitlist and Post Transplant Deaths	--	-23.1 *(0.050)*	-48.2 *(p < 0.001)*	-25.1 *(0.038)*	-237.6 *(p < 0.001)*
Annualized Waitlist Deaths	--	-32.6 *(0.005)*	-45.2 *(p < 0.001)*	-12.6 *(0.160)*	-155.3 *(p < 0.001)*
Annualized Post Transplant Deaths	--	+9.5 *(0.060)*	-3.0 *(0.314)*	-12.4 *(0.021)*	-82.3 *(p < 0.001)*
Annualized Waitlist Removals	--	-53.2 *(0.113)*	-46.7 *(0.144)*	+6.5 *(0.441)*	-143.2 *(p < 0.001)*
DSA Mean Transplant MELD	--	+0.6 *(p < 0.001)*	+0.8 *(p < 0.001)*	+0.2 *(p < 0.001)*	+1.6 *(p < 0.001)*
DSA Mean Transplant MELD Standard Deviation	--	-0.48 *(p < 0.001)*	-0.50 *(p < 0.001)*	-0.02 *(0.274)*	-0.8 *(p < 0.001)*
Average Organ Transport Distance (miles)	--	+35.5 *(p < 0.001)*	+24.3 *(p < 0.001)*	-11.3 *(p < 0.001)*	> +300 *(p < 0.001)*

[1] P-Values in parentheses.

[2]All results obtained from LivSim for 2010-2014 and relative to current allocation. Input data generated by LSAM Candidate and Donor generators.

Table 1.6: 5-Year Comparative Performance of Allocation Systems (MELD with sodium case) [1]

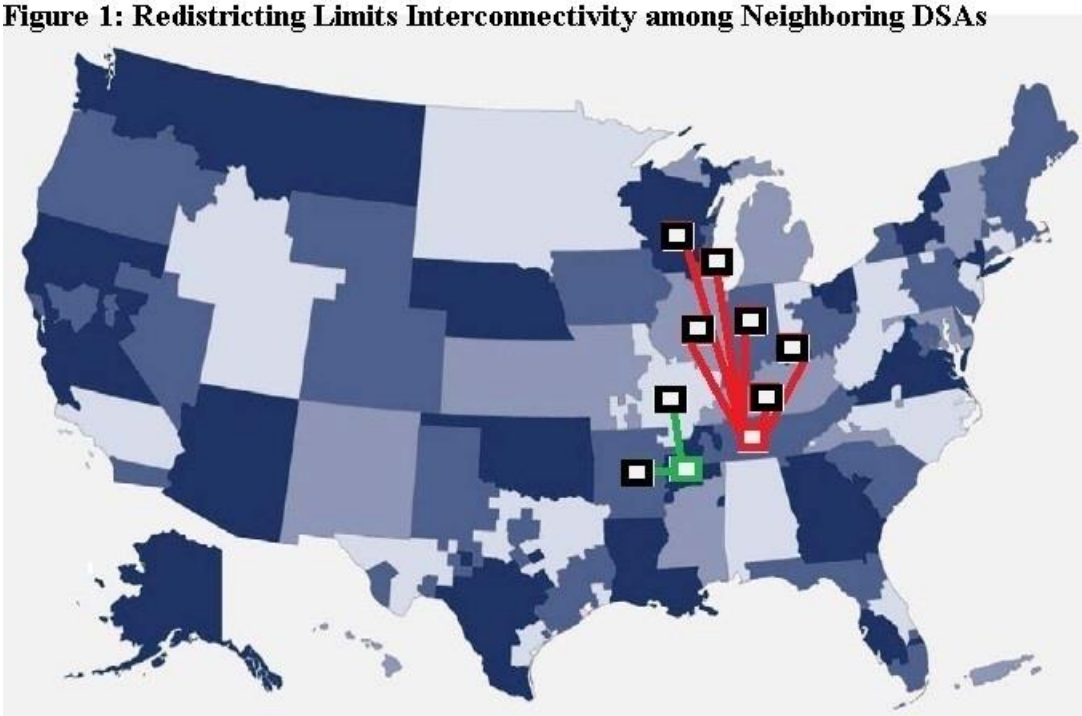
	Current	Redistricting[2]	Neighborhoods[2]	Difference (Neighborhoods-Redistricting)	National[2]
Annualized Waitlist and Post Transplant Deaths	--	-45.8 *(p < 0.001)*	-64.2 *(p < 0.001)*	-18.4 *(0.014)*	-272.4 *(p < 0.001)*
Annualized Waitlist Deaths	--	-41.0 *(p < 0.001)*	-56.2 *(p < 0.001)*	-15.1 *(0.004)*	-142.7 *(p < 0.001)*
Annualized Post Transplant Deaths	--	-4.8 *(0.218)*	-8.1 *(0.093)*	-3.3 *(0.293)*	-129.7 *(p < 0.001)*
Annualized Waitlist Removals	--	-41.3 *(0.174)*	-46.8 *(0.144)*	-5.5 *(0.450)*	-116.2 *(0.004)*
DSA Mean Transplant MELD	--	+0.6 *(p < 0.001)*	+0.9 *(p < 0.001)*	0.3 *(p < 0.001)*	+1.7 *(p < 0.001)*
DSA Mean Transplant MELD Standard Deviation	--	-0.50 *(p < 0.001)*	-0.59 *(p < 0.001)*	-0.09 *(p < 0.001)*	-0.9 *(p < 0.001)*
Average Organ Transport Distance (miles)	--	+43.4 *(p < 0.001)*	+36.1 *(p < 0.001)*	-7.3 *(p < 0.001)*	> +300 *(p < 0.001)*

[1] P-Values in parentheses.

[2]All results obtained from LivSim for 2010-2014 and relative to current allocation. Input data generated by LSAM Candidate and Donor generators.

Figure 1.1: Redistricting Limits Interconnectivity among Neighboring DSAs

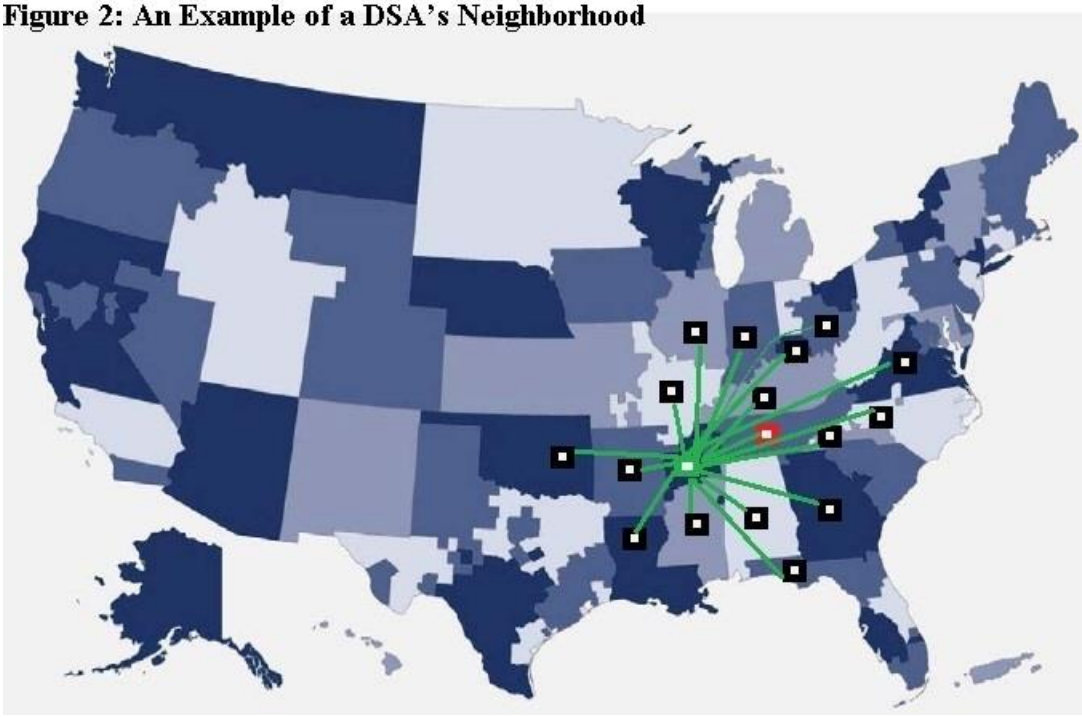
Figure 1: Redistricting Limits Interconnectivity among Neighboring DSAs



The OPO serving primarily Western Tennessee (green) also shares with OPOs in Arkansas and Eastern Missouri during regional allocation but not with the OPO serving primarily Eastern Tennessee (red) in the current 8-district redistricting plan. The OPO in Eastern Tennessee will potentially send organs as far as Wisconsin before Western Tennessee in the redistricting plan.

Figure 1.2: An Example of a DSA's Neighborhood

Figure 2: An Example of a DSA's Neighborhood



The OPO serving primarily Western Tennessee (green) now shares with neighboring DSAs including Eastern Tennessee (red) during regional allocation under the neighborhoods framework in contrast to redistricting in Figure 1.1.

Supplement: Formulation of Optimized Neighborhoods

Improved Liver Allocation with Optimized Neighborhoods
Technical Appendix

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The neighborhood optimization model forms neighborhoods around each DSA with certain desired properties. The neighborhood of a DSA identified from the optimization model forms this DSA's region in a local-regional-national policy. For the results presented in the article, this is done so that the combined DSA neighborhood organ need (demand) and organ availability (supply) ratio is as close as possible to the national organ need and availability ratio, while other structural requirements (described below) are ensured. We emphasize that the output from the model is a neighborhood structure to be used in the local-regional-national framework, i.e., *neither the optimization model nor its output specify the number of organs an OPO could be sending to its region.*

We now provide the mathematical details of the neighborhood approach to achieve greater equity and efficiency in the liver allocation system.

1. Mathematical Formulation of the Neighborhood Model

Let $I = \{1, 2, ...n\}$ be the set of DSAs and $\{1, 2, ...T\}$ be the years in the study period. We formulate a stochastic program that minimizes the expected disparity in organ supply and demand over T years. Moreover, we assume that I carries with it an adjacency matrix that identifies whether $i \in I$ and $j \in I$ share physical boundaries.

1.1. **Decision Variables.** The binary decision variables are x_{ij}, which take the value 1 if DSA $j \in I$ is linked to DSA $i \in I$.

1.2. **Parameters.** Let $s_i(t)$ be the number of livers recovered in DSA i in year t; Let $d_i(t)$ be the number of organs demanded in DSA i in year t. We measure $d_i(t)$ as the number of waitlist additions in DSA i in year t; Let c_i and p_i be the number of active transplant centers and population respectively in DSA i; $\underline{C}$ is the minimum allowable number of transplant centers that can be in a neighborhood; $\underline{P}$ is the minimum allowable population in a neighborhood; $\underline{M}$ and $\bar{M}$ are lower and upper bounds respectively on the number of DSAs that can be in a neighborhood. Let θ be the target for the ratios of neighborhood supplies and demands to be achieved. Specifically, we take $\theta = \frac{1}{T}\sum_{t-1}^{T} \frac{\sum_{j=1}^{n} d_j(t)}{\sum_{j=1}^{n} s_j(t)}$, that is, θ is the expected value of the ratio of nationally aggregated organ supply and demand, where the expectation is taken over T years.

Define v_{ij} to be the historical volumes of organs procured in DSA i and transplanted in DSA j and similarly define τ_{ij} to be the historical average transport distances (or times) of organs procured in DSA i and transplanted in DSA j. Let $\bar{\tau}$ be the desired bound for average organ-transport distance or time.

1.3. **Neighborhood Structure.** In order to impose a specific type of contiguity and geographic immediacy requirements, for each DSA i, we define a relation such that for each $j, k \in I$, $j \prec_i k$ if and only if the minimum number of adjacent DSAs required to traverse from DSA i to DSA j is less than the minimum number of adjacent DSAs required to traverse from DSA i to DSA k.

1.4. **Objective.** The objective is to minimize the expected value of the maximum absolute deviation of the ratios of the number of organs available to a DSA's neighborhood (not a specific DSA) and the number of organs needed in a DSA's neighborhood from the target value, the national ratio θ. In the specific output used for the results presented in the article, the number of waitlist additions each year is used to estimate organ need.

1.5. **Description of Constraints.** The constraints enforce that a DSA has a minimum and a maximum number of neighbors that it can be linked to (Density); the average volume-weighted transport distance or time in a neighborhood is bounded (Compactness); neighborhoods are contiguous and DSAs that are geographically immediate to a given DSA are in its neighborhood (Contiguity); neighborhoods have a minimum number of transplant centers and population (Centers; Population respectively); each DSA is in its own neighborhood (Reflexivity); and DSA i is in DSA j's neighborhood if and only if DSA j is in i's neighborhood (Symmetry).

(Neighborhoods)

$$\min_{x_{ij}} \quad \frac{1}{T}\sum_{t=1}^{T}\max_{i\in I}\left|\frac{\sum_{j=1}^{n} d_j(t)x_{ij}}{\sum_{j=1}^{n} s_j(t)x_{ij}} - \theta\right|$$

$$\text{s.t.} \quad \underline{M} \le \sum_{j=1}^{n} x_{ij} \le \bar{M} \qquad \forall i \in I \ \textit{(Density)}$$

$$\sum_{j=1}^{n}(\tau_{ij} - \bar{\tau})v_{ij}x_{ij} \le 0 \qquad \forall i \in I \ \textit{(Compactness)}$$

$$x_{ij} \ge x_{ik} \qquad \forall i,j,k \in I \text{ with } j \prec_i k \ \textit{(Contiguity)}$$

$$\sum_{j=1}^{n} c_j x_{ij} \ge \underline{C} \qquad \forall i \in I \ \textit{(Centers)}$$

$$\sum_{j=1}^{n} p_j x_{ij} \ge \underline{P} \qquad \forall i \in I \ \textit{(Population)}$$

$$x_{ii} = 1 \qquad \forall i \in I \ \textit{(Reflexivity)}$$

$$x_{ij} = x_{ji} \qquad \forall i,j \in I \ \textit{(Symmetry)}$$

$$x_{ij} \in \{0,1\} \qquad \forall i,j \in I \ \textit{(Integer)}$$

A Concentric-Neighborhoods Solution to Disparity in Liver Access that contains current UNOS Districts

Addressing geographic disparities in access to liver transplantation has been a weighty predicament for policymakers in recent years[48]. Since liver transplant is the unique restorative therapy for irreversible and progressive liver failure[1,2], members of the transplantation community are understandably distressed that the current liver allocation system permits those with similar medical urgency in different parts of the US to experience varying transplant rates, waiting times, and mortality[6-8]. However, the provision of this therapy relies almost exclusively on scarce deceased-donor resources (about 95% of all liver transplants annually since 2014[3]), which are acquired through the generosity of organ donors and their families, in addition to the actions of donor hospitals and transplant centers and the efforts of 58 organ procurement organizations (OPOs) across the country. There are numerous publications detailing the extent of disparity in access[6,7,35]. Notwithstanding an increase in the total number of organ donors, any liver redistribution policy must confront the dilemma between reducing geographic disparity in access through the reallocation of organs from regions of high supply relative to demand and mitigating reductions in local access to the resource for those sharing more, especially in rural and under-resourced parts of the country[49]. Moreover, since redistribution likely entails more non-local transportation of organs, the latter half of the dilemma also includes controlling organ transport times, distances, availability of aircraft/crews, organ quality, and costs.

The United Network for Organ Sharing (UNOS), the organization responsible for the organ procurement and transplantation network (OPTN) and for promoting organ donation, is keenly aware of these issues. The UNOS Liver and Intestinal Committee[9] has the unenviable task of resolving the aforementioned dilemma. In August 2016, they put forth as a public comment a proposal to redistrict the OPTN into 8 districts in order to promote a fairer distribution of transplanted organs[10-14]. The new proposal was polarizing[48] in the liver

transplantation community with 8 of the 11 UNOS regions rejecting the proposal with nearly unanimous votes while 2 of 11 regions showed nearly unanimous voting in support of the proposal. Fervent denials arose from transplant centers, health-care professionals, and individuals from areas where transplant volumes were expected to decline and patient mortality to increase after redistricting[50]. Mehrotra et al.[16,51], numerous public comments[50], and recent meetings of the UNOS Liver and Intestinal Committee[48] held that additional modeling frameworks warranted consideration.

Besides the redistricting and concentric circles proposals, another framework considered for further development by the members of the committee[48] was a proposal of optimized neighborhoods[52]. The proposal introduced a framework that possessed concepts from both redistricting and concentric circles. The framework yielded an alternative design of the OPTN that would be more resilient to regional changes in demand and supply of deceased donor organs while also mitigating rising transport costs and reducing geographic disparity and annual mortalities. The work provided a demonstrative example of its conceptual promise but did not recommend a particular geographic structure or sharing policy for consideration. This article presents a specific specialized neighborhoods construction that can become a potential starting point for a systematic development of a solution for resolving a complex problem that has polarized the community. The presented design incorporates feedback from members of the transplantation community and many aspects of the public comments. However, further refinements will be needed with better quantification of the community's concerns, but they can be made within the framework of concentric neighborhoods presented here. Below, we summarize liver allocation; briefly recapitulate the concept of neighborhoods; describe refinements of the neighborhood concept that define concentric neighborhoods; and review the performance of concentric neighborhoods under different sharing policies using simulation.

Summary of Liver Allocation

The current geographic structure for the OPTN divides the US into 11 UNOS regions and those regions are further subdivided into 58 Donor Service Areas (DSAs). Each DSA has a designated OPO that facilitates local procurement and allocation procedures. Allocation of deceased-donor livers is based upon a three-tier geographic system –- local/regional/national (local refers to the DSA of the procuring OPO) [21]. Coupled with the geographic structure, the OPTN follows specific allocation rules or sharing policies that mainly prioritize which candidates are offered an organ for transplant. These sharing policies and their accompanying rationale are detailed in Elwir and Lake[22,23] and Trotter[22].

Patients are prioritized by their Model for End-stage Liver Disease (MELD) scores. MELD scores (ranging from 6-40 points) are predictors of 3-month mortality without liver transplantation and presumably indicate medical urgency[26-29] based on lab values (INR, bilirubin, creatinine, and sodium[31-33]). Within the allocation framework, more than one-third of candidates receive additional points, known as exception points, because their original MELD scores may not accurately reflect their mortality risk. Exception points are given to patients diagnosed with hepatocellular carcinoma (HCC) or hepatopulmonary syndrome along with other uncommon indications[34,53]. Collectively, liver allocation proceeds roughly as follows: (1) an offer is first made to Status 1 candidates regionally; (2) an offer is then made to regional candidates with the highest MELD scores $\geq$ 35 with local priority if the top 2 candidates share the same MELD score but only one is in the allocating OPO [Share 35 policy]; (3) an offer is then made to local candidates with MELD scores 15-34 in the same DSA as the procuring OPO; (4) an offer is then made to regional candidates with MELD scores 15-34 in the same UNOS region as the procuring OPO; (5) an offer is then made to national candidates with Status 1 and then MELD scores 15-40; (6) an offer is then made to local candidates, followed by regional candidates, and lastly national candidates with MELD scores less than 15. The threshold MELD score of 15 used in these sharing policies is known as the Share 15 policy.

Explanation of an OPO's Concentric Neighborhood

A concentric neighborhood is a special type of neighborhood[52]. The center of a concentric neighborhood is the OPO where an organ is procured. A concentric neighborhood is constructed by adding OPOs/DSAs around the procuring OPO in a circular fashion until it meets the maximum distance and/or minimum population requirements. Geographic proximity is imposed to reduce travel distance and address concerns regarding local prioritization. The procuring OPO and the surrounding OPOs that define the concentric neighborhood acts as the region in the current local-regional-national allocation system –- that is, allocation proceeds as before with the exception that the OPOs and DSAs involved in this "regional allocation" are defined by the procuring OPO. Different relational requirements among the OPOs in a neighborhood can be incorporated using a general framework that yields several alternative designs for the OPTN. However, concentric neighborhoods are of particular interest because they allow OPOs to maintain relationships with nearby OPOs and transplant centers and they possess other benefits that may not be easily quantifiable.

Materials and Methods

Development of the Concentric Neighborhoods Structure:

The UNOS Liver and Intestinal Committee requested the first author to provide neighborhoods satisfying the following constraints:

1. Each DSA's neighborhood has a minimum population of 12 million.
2. Each neighborhood should be contiguous and avoid holes (i.e. each neighborhood ought to be as convex as possible).
3. The average organ transport time for each neighborhood should be less than or equal to 3 hours. Observed average transport times may be less when sharing policies are applied.

Other public comments[50] and notes from the UNOS Liver and Intestinal Committee[48] were further incorporated. The public comments and notes reveal an apprehension for enacting sweeping structural changes to the OPTN. Unfortunately, redistricting[10] or the demonstrative example of optimized neighborhoods provided by Kilambi and Mehrotra[52] disrupt the existing regional relationships among OPOs and transplant centers.

After conversations with several members of the liver transplantation community, we imposed the additional requirement on the neighborhoods solution:

4. Every neighborhood of an OPO contains the OPO itself and the DSAs in its current UNOS Region. For example, the DSA for Oregon is currently in UNOS Region 6 with the DSA serving Washington, Idaho, Alaska, and Montana. This particular solution has the feature that the neighborhood for Oregon includes this DSA in addition to other nearby DSAs (e.g. Northern California in region 5).

By ensuring that each neighborhood of an OPO contains its original UNOS region, all OPOs and transplant centers that work together in the current system for regional allocation may continue working together in the future albeit with some new relationships. This requirement is included more so for facilitating implementation of a solution and it should not be construed that honoring extant OPO boundaries is in itself optimal.

Since the public comments also raised concerns about organ supply and demand estimates used in the design of any "optimized" system, we combined the concept of neighborhoods with the concept of concentric circles. Concentric circles use constant radii that do not rely on estimates for organ supply and demand. Given the expressed concerns regarding organ transport times in the public comments[50] and the notes of the UNOS Liver and Intestinal Committee[48], we introduced the following two versions of the proposed concentric neighborhoods structure:

5a. An OPO is allowed to have as many neighbors as possible. If an OPO's physical address is within *r* (*r* = 400, 500, or 600) miles of a procuring OPO, then the former will be in the latter's neighborhood and vice versa.

5b. An OPO is allowed to have at most *n* (*n*=10) neighbors, including itself and the OPOs of the same UNOS region. If an OPO's physical address is within *r* (*r* = 400, 500, or 600) miles of a procuring OPO, then the former will be in the latter's neighborhood as long as it does not exceed the limit.

In later discussion, we refer 5a as the unconstrained concentric neighborhoods structure and 5b as the constrained concentric neighborhoods structure.

Possible values for *r* that we selected are 400, 500, or 600 miles. These values represent the flight distances for a standard jet used in procurement with a flight time less than 2 hours. For example, with this feature, the direct distance between the LifeNet Health OPO serving Virginia in Virginia Beach, VA, and the Gift of Life Donor OPO serving Eastern Pennsylvania in Philadelphia, PA, is approximately 250 miles. Thus, Eastern Pennsylvania will be a potential neighbor of Virginia and Virginia will be a potential neighbor of Eastern Pennsylvania.

The value for *n* that we selected is 10 since UNOS Region 3 has 10 OPOS, the most number out of the other regions. When implementing the constrained concentric neighborhoods structure, if an OPO has more than 10 potential neighbor OPOs, the potential neighbors are added to the OPO's neighborhood in the following order until the limit is met: (1) the OPO itself, (2) OPOs of the same UNOS region, and (3) closest OPOs outside the UNOS region.

By including nearby OPOs in the neighborhood, organs may be transported to candidates with higher MELD scores nearer to the procuring OPO during regional allocation without being transported farther away to candidates with lower MELD scores. With some

exceptions, DSAs will have their geographically immediate neighbors in their neighborhood. Second, this requirement helps avoid neighborhoods with 'holes'.

The structural properties of the concentric neighborhoods solution are summarized in Table 2.1. Figure 2.1 presents an example of the proposed concentric neighborhood for the OPO based in Eastern Pennsylvania using a radius of 600 miles and containing its current UNOS Region (Region 2). It is important to note that unlike the earlier optimized neighborhoods proposal[52], these particular concentric neighborhood solutions are fully described by the requirements that OPOs within a specified radii are connected as in concentric circles and that each OPO's neighborhood contains its original UNOS region. Therefore, there is no optimization employed nor does any particular solution herein allude to any metric for organ supply and demand. Moreover, for assessing geographic disparity, we follow the recent policy literature and consider equalizing average/median MELD at transplant across DSAs and reducing its standard deviation[13].

Two further changes are investigated within the concentric neighborhoods design obtained from the imposed requirements above. The first is to grant a 3- or 5-point proximity boost to MELD scores for patients listed in the OPO where the organ is procured. The reasons for this include the following: (1) avoiding unnecessary travel; (2) providing a buffer for possible differences in increased mortality arising from lower access to transplant in less populated areas; and (3) maintaining the viability of low-volume transplant centers. The need to address such issues were raised in the public comments[50]. The second change is to increase the threshold in the Share 15 policy to a higher value. Since patients with lower MELD scores are expected to have longer survival times, geographic equity may be better served by directing organs to non-local candidates with greater MELD scores sooner. The effect of changing this threshold value is counterbalanced by the aforementioned conferral of proximity boosts to local candidates.

Simulating Neighborhoods Solutions:

As previously described[52], the Liver Simulated Allocation Model (LSAM v Aug 2014) [45], to our knowledge, cannot accommodate neighborhoods. We therefore tested the performance of the proposed concentric neighborhoods solution (relative to the current system) using an open-source discrete event simulator LivSim. For more information about LivSim, please refer to our previous work and the LivSim User Guide[18,54]. The software and the manual are accessible at https://github.com/kbui1993/LivSim-Codes. The current version of LivSim uses the same acceptance model as LSAM along with inactive waitlist candidates, relists, and re-transplants. Our simulation experiment is also similar to that of the previous publication[52] and utilizes the same input data experimented in it. Specifically, we used input data on patient listing, MELD progression, and organ donors from the LSAM Candidate Generator and the LSAM Donor Generator (v Aug 2014). The run-length was 5-years (Jan 2010 – Dec 2014) with 5 replications (25 replication-years). We incorporated MELD-Na (i.e. MELD with sodium) and HCC exceptions including the cap-and-delay policy[46]. We assumed no exceptions (i.e. used lab MELD scores with sodium) for non-HCC candidates. Therefore, the MELD scores used in the simulation are adjusted for sodium and roughly correspond to using lab MELD scores for everyone except HCC patients (whose allocation MELD follows a predictable schedule). We focus our results on overall system performance rather than on specific diagnosis groups. The simulation measures disparity by standard deviation of DSA mean transplant MELD across DSAs and other important statistics such as waitlist and post-transplant mortalities, waitlist removals, average organ transport distances/times, and percentage of organ travelled by mode of transit. Differences in the non-transport performance measures between the current allocation system, neighborhoods, and redistricting were computed, and significance was assessed using two-tailed t-tests on differences between replication means with 24 degrees of freedom for the 25 replication-years. In particular, differences in the average of standard

deviations of mean and median DSA-MELD at transplant across replication-years were also computed using two tailed t-tests with 24 degrees of freedom. Average transport metrics (e.g. mean distance traveled, mean travel time, mean share transported by airplane, etc.) were calculated over each 5-year replication and differences in means were assessed using two-tailed t-tests with 4 degrees of freedom. We also compute percentage changes in each DSA's transplant volume relative to its volume under the current system.

Sharing Policies:

We simulated the proposed concentric neighborhoods solution with several variations of the sharing and boosting policies. Additionally, we simulated 8-district redistricting[10,12] with the same variations. We used the current system (i.e. the current 11 UNOS regions with the Share 15 and Share 35 policies and no proximity boosts) for making baseline comparisons of the performance of the concentric neighborhoods. Specifically, for the Share 35 policy, we consider the current value of 35 and a value of 29, which is being considered by UNOS at the time of writing[55]. For the Share 15 and boosting policies, we consider changing the thresholds to 18 and 20 with 3- and 5-point boosts respectively to counterbalance increased travel with local priority. To assess the effects on geographic disparity of only changing the sharing policies for the current system, we conducted simulations of the current geographic structure (11 districts/regions) with different values of the thresholds for Share 35 and Share 15 and of the proximity boosts.

We stress the importance of selecting the appropriate sharing in conjunction with some specificity to preserve the core geographical arrangement. In summary, we simulated various policies listed in Table 2.2.

Results

Part (a) of Tables 2.3-9 summarize simulation results for interventions (i)-(xlvii). Part (b) of Tables 2.3-9 present the respective differences of the simulation results relative to the current system in addition to p-values for assessing statistical significance.

Modifications to Current System Policy without Neighborhoods. Tables 2.3a and 2.3b present the performance and comparative performances respectively for the current 11-districts with changes to the Share 15 policy and proximity boosts (Block I). Increasing the Share 15 thresholds to either 18 or 20 decreases the number of waitlist deaths, significantly for policy (iii) ($p < 0.05$), and does not affect the number of post-transplant deaths significantly. Standard deviations in DSA-mean and median MELD at transplant are significantly reduced ($p < 0.05$). DSA-mean and -median MELD at transplant increase significantly as do the shares of organs transported by airplane and their travel distance ($p < 0.05$). Therefore, the simulation results show that the applications of 3-point and 5-point proximity boosts mitigate the rising shares of organs traveling by airplane and dampen mortality and geographic disparity reductions.

Share 29/Share15/0-Point Boost on 8 Districts and Concentric Neighborhoods. Tables 2.4a and 2.4b present the performance and comparative performances respectively for 8-district redistricting and unconstrained and constrained concentric neighborhoods with the Share 35 policy threshold changed to 29 and no proximity boosts (Block II). The simulation results show important improvements by using the concentric neighborhoods structure. Unconstrained concentric neighborhoods of any radius further reduce total mortalities when compared to redistricting or the current system. However, the constrained versions nearly reduce as much total mortalities as the redistricting policy. Both unconstrained and constrained neighborhoods reduce geographic disparity compared to the current system at various levels of significance. DSA-mean and -median MELD at transplant increase significantly as do the shares of organs transported by airplane. However, transport distances and times by airplane are reduced in all policies of Block II.

Share 29/Share 18/3-Point Boost on 8 Districts and Concentric Neighborhoods. Tables 2.5a and 2.5b present the performance and comparative performances respectively for 8-district redistricting and concentric neighborhoods with the Share 35 policy threshold changed to 29, Share 15 threshold raised to 18, and 3-point proximity boosts (Block III). Simulation results convey similar trends as the results for Block II. The unconstrained concentric neighborhoods of any radius further reduce total mortalities when compared to redistricting or the current system, but the constrained concentric neighborhoods do not save as many lives as redistricting unless the radius is either 500 or 600 miles. All policies reduce geographic disparity compared to the current system at various levels of significance. DSA-mean and -median MELD at transplant increase significantly as do the shares of organs transported by airplane. However, transport distances and times by airplane are significantly reduced by the concentric neighborhoods solutions ($p < 0.05$).

Share 29/Share 20/5-Point Boost on 8 Districts and Concentric Neighborhoods. Tables 2.6a and 2.6b present the performance and comparative performances respectively for 8-district redistricting and concentric neighborhoods with the Share 35 policy threshold changed to 29, Share 15 threshold raised to 20, and 5-point proximity boosts (Block IV). Simulation results show similar trends as the results of Blocks II and III. Unconstrained concentric neighborhoods of any radius further reduce total mortalities when compared to redistricting or the current system, but the constrained neighborhoods of radii 400, 500, and 600 miles do not save as many lives as the redistricting policy. Nevertheless, all policies reduce geographic disparity compared to the current system at various levels of significance. DSA-mean and -median MELD at transplant increase significantly as do the shares of organs transported by airplane. However, transport distances and times by airplane are significantly reduced by the unconstrained concentric neighborhoods solutions ($p < 0.05$), but they increase for the constrained versions.

Share 35/Share 15/0-Point Boost on 8 Districts and Concentric Neighborhoods. Tables 2.7a and 2.7b present the performance and comparative performances respectively for 8-district redistricting and concentric neighborhoods with no sharing policy changes (Block V). The simulation results highlight important improvements especially for the constrained neighborhood solutions compared to the Share 29 policies. Both unconstrained and constrained concentric neighborhoods of any radius further reduce total mortalities when compared to redistricting or the current system and reduce geographic disparity compared to the current system at various levels of significance. DSA-mean and -median MELD at transplant increase significantly as do the shares of organs transported by airplane. However, transport distances and times by airplane are significantly reduced in all policies of Block V ($p < 0.05$).

Share 35/Share 18/3-Point Boost on 8 Districts and Concentric Neighborhoods. Tables 2.8a and 2.8b present the performance and comparative performances respectively for 8-district redistricting and concentric neighborhoods with the Share 15 threshold raised to 18, and 3-point proximity boosts (Block VI). The simulation results show similar improvements as the results of Block V. Both unconstrained and constrained concentric neighborhoods of any radius further reduce total mortalities when compared to redistricting or the current system and reduce geographic disparity compared to the current system at various levels of significance. DSA-mean and -median MELD at transplant increase significantly as do the shares of organs transported by airplane. However, transport distances and times by airplane are significantly reduced for concentric neighborhoods solutions ($p < 0.05$).

Share 35/Share 20/5-Point Boost on 8 Districts and Concentric Neighborhoods. Tables 2.9a and 2.9b present the performance and comparative performances respectively for 8-district redistricting and concentric neighborhoods with the Share 15 threshold raised to 20, and 5-point proximity boosts (Block VII). Simulation results show similar trends in non-transport statistics but different trends in transport statistics compared to the results for Blocks V and VI. The

unconstrained and constrained concentric neighborhoods of any radius further reduce total mortalities when compared to redistricting or the current system and reduce geographic disparity compared to the current system at various levels of significance. DSA-mean and -median MELD at transplant increase significantly for both versions of concentric neighborhoods solutions. While the shares of organs transported by airplane increase significantly for the unconstrained concentric neighborhood solutions, they increase by less than a minimal value of 0.15% for the constrained versions. Moreover, transport distances and times by airplane are significantly reduced for unconstrained concentric neighborhoods solutions ($p < 0.05$), but they increase significantly for the constrained versions ($p < 0.05$).

Figures 2.2-4 depict the distribution of average MELD at transplant across DSAs for all of the above interventions. Figures 2.5-7 depict the percentage changes in DSA transplant volume for each policies. The changes in transplant volume are more compact in the concentric neighborhoods than in the 8-district redistricting, and depending on the radius and sharing policies selected, no DSA experience a loss of transplant volume greater than 25%. Although the 8-district solutions manage to save lives and reduce geographic disparity, the major disadvantage is its detrimental shift in the sharing of livers between DSAs within a district. This is indicated by the maximum organ volume gain/loss as we see from Figures 2.5-7 that a DSA can gain nearly 40% more organs while a DSA can lose at least 25% of its organs. On the other hand, the constrained concentric neighborhood structures with the Share 35 policy manage to cap losses at approximately 16%.

Table 2.10 presents a subset of the concentric neighborhoods solutions with different levels of organ volume loss along with their statistics. We show that it is possible to obtain a solution where the organ volume loss is as low as nearly 10% while reduction in total mortalities, geographic disparity, and airplane travel time is possible. However, when trying to attain a more satisfactory reduction in one of these values, tradeoff between these values are inevitable. For

example, when relaxing the constraint of 10 DSAs per neighborhoods for the Share 35/Share 15/0-Point Boost policy on the constrained 500-miles concentric neighborhoods map, the total mortalities, geographic disparity, and airplane travel time do decrease, but the organ volume loss increases. Therefore, reduction in total mortalities, geographic disparity, and airplane travel time requires shifts in the organ sharing flow between DSAs, but both reduction and organ volume change can be managed by tuning the parameters and combinations in concentric neighborhoods model.

Discussion

With the feature that each OPO continues to work with its current regional partners and some nearby OPOs, a concentric neighborhoods solution serves to transplant the sickest candidates more quickly, reduce geographic disparity in access to liver transplant, and decreases annual mortalities regardless of the adjunct sharing policy tested. Allowing current transplant centers and OPOs to continue working with those with whom they have existing relationships is expected to make actual implementation easier. The essence of concentric circles also appears in the solution –- as the neighborhoods' maps show that each OPO can share with several surrounding DSAs to extend supply. Despite a considerable increase in the geographic size of regions for many DSAs, which thereby increases in the percentage of organs transported by airplanes, the number of miles traveled by airplanes decreases significantly for most of the concentric neighborhoods solutions. For a given sharing policy, using larger radii for the concentric neighborhoods usually further reduced geographic disparity. These particular concentric neighborhoods solutions were not constructed from a specific optimization model and also do not rely on demand or supply metrics which have changed considerably in the last 2 years -- when record increases in OPO donation rates with absolute liver deceased donor numbers increasing from 6,744 donors in 2013 to 8,151 donors in 2016 (https://optn.transplant.hrsa.gov/). It is important to reemphasize that unlike the redistricting

proposal[52], this neighborhood solution was not obtained with reference to a mathematical model that optimized deviations in organ demand and supply rates. The advantage of this position is that it avoids addressing contentious issues such as how to measure the need for organs at each DSA.

The choice of the sharing policy reflects a balance between equity in access and resource utility. Raising the Share 15 threshold to either 18 or 20 may significantly reduce total mortalities and geographic disparity regardless of the geographic structure employed. Consequently, the policy change induces a larger percentage of organs traveling by airplane and possibly longer travel distances and times. The inclusion of proximity boosts aims to counterbalance the rising transport distances and times. Using concentric neighborhoods and raising the Share 15 threshold along with providing a proximity boost offered the greatest reduction in geographic disparity of the interventions tested. Including the boost points when increasing the Share 15's threshold attenuates the negative impact of broader sharing upon disadvantaged parts of the country where the population is medically underserved and potentially faces greater mortality when the local supply of organs is diminished. We strove to find a solution whose observed performance reduced disparity and mortality without significantly increasing logistic burden in the simulations. Moreover, the geographic structure obtained (i.e. the membership relations for each neighborhood) is itself agnostic to how MELD scores are used. The impact of MELD scores and sharing policies, and thereby the observed performance of the entire intervention (i.e. geographic structure + sharing policy changes), are reflected in the simulation results and subject to the limitations thereof.

Losses in transplant volume were of interest and concern in public comments[50]. When a fixed resource is being rationed, there will be net-gainers and net-losers with shifts in allocation. The Share 35 unconstrained concentric-neighborhoods solution with the 5-point proximity boost and Share 20 shows losses in transplant volumes for any DSA up to 20% of its current volume

from among the DSAs who will become the net supplier. The validity of this prediction depends on current organ acceptance behaviors being maintained. A significant loss in transplant volume may not be acceptable for transplant centers in certain DSA for several reasons, such as financial viability or access to transplants for the patients. However, the authors suggest that if an *a priori* cap on the losses is specified, refinements can be made to the concentric-neighborhoods and the sharing policy presented here in order to reduce disparity while maintaining transplant volume losses within a specified range.

On the other hand, the authors consider a simple refinement to the unconstrained concentric-neighborhoods solution, especially to address the issue of organ volume loss. Since the number of sharing partners per DSA resulting from the unconstrained concentric-neighborhoods solution may be of concern, we impose the constraint that each DSA may have up to 10 sharing partners, resulting in the constrained concentric neighborhoods solution. From the simulation results, we observe that these solutions serve as intermediate solutions between their District 11 counterparts and their unconstrained counterparts. The constrained concentric-neighborhoods solution managed to save more lives and reduce geographic disparity. For the most part, they also decreased the transport distance by airplanes. More significantly, while achieving these desired improvements, most of constrained concentric-neighborhoods solutions with Share 35 policy were able to cap their organ volume losses to at most 12%.

Two additional contentious issues warrant additional comments. The first of these is how to *expressly* reward or penalize OPOs for their performance. A major assumption in the simulation modeling is that the organ procurement and placement performance of high performing OPOs will not deteriorate due to sharing with additional partners. The quantitative modeling of this issue is desirable. Since the concentric neighborhoods design presented here only adds OPOs to the current 11-districts, it does not change any existing relationships an OPO leadership may have built with respect to organ procurement and placement. It only augments this relationship.

Additionally, a high-performing OPO may find it easier to share and help implement its best practices and share resources needed for organ procurement with its added neighbors due to geographical proximity. The second contentious issue is the use of allocation MELD at transplant as a metric for evaluating disparity. Alternative metrics are being developed by the liver transplant community, and the baseline solution presented here may be further refined with respect to these metrics. Since concentric neighborhoods preserve the OPO-OPO relationships and build additional relationships with the proximal neighbors, the concentric-neighborhoods approach has a distinct advantage over redistricting generated from an optimization model since in the latter case the districts can change significantly with the disparity metric used to generate demand for the objective function in an optimization model.

We present the specific combinations of 3-point boosts/Share 18 and 5-point boosts/Share 20 because they maintain a symmetric change to the current sharing policies and they have reduced geographic disparity compared to the current system in the simulations. Different combinations of the boosts and thresholds may be tested further. Furthermore, more specific "boost" might be created for each DSA, or even for specific ranges of MELD scores, when further considering this neighborhoods approach in the future. Ultimately, the choices for the radii between OPOs in this neighborhood solution, the appropriate value for the Share 15 threshold, and magnitude of the proximity boosts all reflect a delicate balancing act.

Since the volume of organs traveled by road may be of concern as indicated in the most recent Liver Committee discussion, a further refinement can be made by imposing a road distance radii within the concept of concentric neighborhood. For example, while the patients in the organ procuring OPO receive a 3- or 5-point boost, the patients listed within certain mile radius (or the immediate surrounding OPO's) of the procuring OPO may be given a 2- or 3-point boost. In our testing, we were limited by the features implemented in LivSim.

The principal contributions of this article are that reducing the number of deaths, geographic disparity, and transport distance by airplanes with slight organ volume losses are possible without dismantling the current 11-UNOS regions but by augmenting them using the concept of concentric neighborhoods and/or by adjusting the Share 15 policy.

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Table 2.1: Structural Properties of Concentric Neighborhood Solutions[1]

✓ ***Maintains existing regional relationships:*** DSAs have their current UNOS region inside their neighborhood
✓ ***Nearby and Immediate Neighbors*****:** DSAs have all DSAs with OPO locations that are within *r* (*r*=400,500, or 600) miles in their neighborhood. DSAs usually have their geographically immediate neighbors in their neighborhood.
✓ ***Population:*** Each DSA's neighborhood has a minimum population of 12 million
✓ ***Contiguity:*** Each DSA's neighborhood is geographically contiguous
✓ ***Compactness:*** The average transport time for a DSA's neighborhood is within 3 hours
✓ ***Transplant Centers:*** Each DSA's neighborhood has at least 8 transplant centers[2]

[1] Hawaii and Puerto Rico were not included in the model. Their neighborhoods were defined as their current UNOS region. Neighborhoods do not refer directly to an optimization model.

[2] With exception for LifeCenter Northwest OPO (WALC) whose neighborhood contains 5 transplant centers.

Table 2.2: List of Policies Simulated

Policies Simulated					
	Current System		(IV)	**Share 29/Share 20/5-Point Boost on 8 Districts and Concentric Neighborhoods**	
	(i)	Share 35/Share 15 with 0 point boost and 11 districts		(xx)	Share 29/Share 20 with 5 point boost and 8 districts
				(xxi) (xxii)	Share 29/Share 20 with 5 point boost and 400-mile Nbhd. (U) Share 29/Share 20 with 5 point boost and 400-mile Nbhd. (C)
				(xxiii) (xxiv)	Share 29/Share 20 with 5 point boost and 500-mile Nbhd. (U) Share 29/Share 20 with 5 point boost and 500-mile Nbhd. (C)
				(xxv) (xxvi)	Share 29/Share 20 with 5 point boost and 600-mile Nbhd. (U) Share 29/Share 20 with 5 point boost and 600-mile Nbhd. (C)
(I)	**Modifications to 11-District Policy without Neighborhoods**		(V)	**Share 35/Share 15/0-Point Boost on 8 Districts and Concentric Neighborhoods**	
	(ii) (iii) (iv) (v)	Share 35/Share 18 with 0 point boost and 11 districts Share 35/Share 20 with 0 point boost and 11 districts Share 35/Share 18 with 3 point boost and 11 districts Share 35/Share 20 with 5 point boost and 11 districts		(xxvii)	Share 35/Share 15 with 0 point boost and 8 districts
				(xxviii) (xxix)	Share 35/Share 15 with 0 point boost and 400-mile Nbhd. (U) Share 35/Share 15 with 0 point boost and 400-mile Nbhd. (C)
				(xxx) (xxxi)	Share 35/Share 15 with 0 point boost and 500-mile Nbhd. (U) Share 35/Share 15 with 0 point boost and 500-mile Nbhd. (C)
				(xxxii) (xxxiii)	Share 35/Share 15 with 0 point boost and 600-mile Nbhd. (U) Share 35/Share 15 with 0 point boost and 600-mile Nbhd. (C)
(II)	**Share 29/Share15/0-Point Boost on 8 Districts and Concentric Neighborhoods**		(VI)	**Share 35/Share 18/3-Point Boost on 8 Districts and Concentric Neighborhoods**	
	(vi)	Share 29/Share 15 with 0 point boost and 8 districts		(xxxiv)	Share 35/Share 18 with 3 point boost and 8 districts
	(vii) (viii)	Share 29/Share 15 with 0 point boost and 400-mile Nbhd. (U) Share 29/Share 15 with 0 point boost and 400-mile Nbhd. (C)		(xxxv) (xxxvi)	Share 35/Share 18 with 3 point boost and 400-mile Nbhd. (U) Share 35/Share 18 with 3 point boost and 400-mile Nbhd. (C)
	(ix) (x)	Share 29/Share 15 with 0 point boost and 500-mile Nbhd. (U) Share 29/Share 15 with 0 point boost and 500-mile Nbhd. (C)		(xxxvii) (xxxviii)	Share 35/Share 18 with 3 point boost and 500-mile Nbhd. (U) Share 35/Share 18 with 3 point boost and 500-mile Nbhd. (C)
	(xi) (xii)	Share 29/Share 15 with 0 point boost and 600-mile Nbhd. (U) Share 29/Share 15 with 0 point boost and 600-mile Nbhd. (C)		(xxxix) (xl)	Share 35/Share 18 with 3 point boost and 600-mile Nbhd. (U) Share 35/Share 18 with 3 point boost and 600-mile Nbhd. (C)
(III)	**Share 29/Share 18/3-Point Boost on 8 Districts and Concentric Neighborhoods**		(VII)	**Share 35/Share 20/5-Point Boost on 8 Districts and Concentric Neighborhoods**	
	(xiii)	Share 29/Share 18 with 3 point boost and 8 districts		(xli)	Share 35/Share 18 with 3 point boost and 8 districts
	(xiv) (xv)	Share 29/Share 18 with 3 point boost and 400-mile Nbhd. (U) Share 29/Share 18 with 3 point boost and 400-mile Nbhd. (C)		(xlii) (xliii)	Share 35/Share 18 with 3 point boost and 400-mile Nbhd. (U) Share 35/Share 18 with 3 point boost and 400-mile Nbhd. (C)
	(xvi) (xvii)	Share 29/Share 18 with 3 point boost and 500-mile Nbhd. (U) Share 29/Share 18 with 3 point boost and 500-mile Nbhd. (C)		(xliv) (xlv)	Share 35/Share 18 with 3 point boost and 500-mile Nbhd. (U) Share 35/Share 18 with 3 point boost and 500-mile Nbhd. (C)

[1]Unconstrained concentric neighborhood is abbreviated as Nbhd. (U).

[2]Costrained concentric neighborhood is abbreviated as Nbhd. (C).

Table 2.3a: 5-Year Performances of Current System and Current System with Modified Sharing Policies without Neighborhoods (Block I)

Category	Current System (Share 15, Share 35) (i)	Share35, Share18, 11 district, Local MELD Boost+0 (ii)	Share35, Share20, 11 district, Local MELD Boost+0 (iii)	Share35, Share18, 11 district, Local MELD Boost+3 (iv)	Share35, Share20, 11 district, Local MELD Boost+5 (v)
Annualized Waitlist Removals	3128.60	3078.16	3044.2	3114.68	3113.32
Annualized Total Deaths	2243.28	2218.36	2208.76	2249.52	2247.96
Annualized Waitlist Deaths	1173.68	1127.2	1093.56	1165.16	1159.4
Annualized Waitlist Relist Deaths	23.92	23.8	23.56	23.92	23.6
Annualized Post Tx Deaths	996.12	1016.4	1038.92	1009	1014.36
Annualized Post Re-Tx Deaths	49.56	50.96	52.72	51.44	50.6
DSA Mean Transplant MELD	23.09	24.03	24.66	23.34	23.41
DSA Mean Transplant MELD Std.	1.88	1.48	1.35	1.78	1.76
DSA Median Transplant MELD	24.48	25.67	26.53	24.83	25.09
DSA Median Transplant MELD Std.	2.84	2.06	1.55	2.65	2.59
Avg. Organ Transport Distance (mi.)					
Ground Vehicle	33.34	33.77	34.20	33.01	32.62
Helicopter	100.99	99.31	100.36	102.12	101.22
Airplane	525.87	612.02	693.51	563.24	589.92
Avg. Organ Transport Time (hr.)					
Ground Vehicle	0.78	0.79	0.80	0.78	0.77
Helicopter	1.22	1.21	1.22	1.23	1.22
Airplane	2.48	2.65	2.80	2.55	2.60
Percentage of Organs Transported					
Ground Vehicle	46.94%	40.04%	33.92%	47.81%	48.41%
Helicopter	0.68%	0.57%	0.41%	0.75%	0.75%
Airplane	52.23%	59.24%	65.53%	51.30%	50.70%

Table 2.3b: 5-Year Comparative Performance between Current System and Current System with Modified Sharing Policies without Neighborhoods (Block I)

Annualized Post Re-Tx Deaths	---	+1.4	+3.16*	+1.88*	+1.04
DSA Mean Transplant MELD	---	+0.94*	+1.57*	+0.26*	+0.32*
DSA Mean Transplant MELD Std.	---	-0.40*	-0.53*	-0.11	-0.12*
DSA Median Transplant MELD	---	+1.19*	+2.04*	+0.35*	+0.61*
DSA Median Transplant MELD Std.	---	-0.78*	-1.29*	-0.19*	-0.26*
Avg. Organ Transport Distance (mi.)	---				
Ground Vehicle	---	+0.43*	+0.86*	-0.33	-0.72*
Helicopter	---	-1.67	-0.63	+1.14	+0.23
Airplane	---	+86.15*	+167.64*	+37.37*	+64.05*
Avg. Organ Transport Time (hr.)	---				
Ground Vehicle	---	+0.01*	+0.02*	-0.01	-0.01*
Helicopter	---	-0.01	0	+0.01	0
Airplane	---	+0.17*	+0.33*	+0.07*	+0.12*
Percentage of Organs Transported	---				
Ground Vehicle	---	-6.90%*	-13.02%*	+0.87%*	+1.46%*
Helicopter	---	-0.12%*	-0.27%*	+0.06%*	+0.07%*
Airplane	---	+7.02%*	+13.30%*	-0.93%*	-1.52%*

*This indicates that difference has p-value less than 0.05 ($p < 0.05$).

Table 2.4a: 5-Year Performances of Current System and Share 29/Share 15/0-Point Boost Policy on 8 Districts and Concentric Neighborhoods (Block II)

Category	Current System (Share 15, Share 35) (i)	Share 29, Share 15, 8 district, Boost+0 (vi)	Share 29, Share 15, 400 mi. Nbhd. (U) Boost+0 (vii)	Share 29, Share 15, 400 mi. Nbhd. (C) Boost+0 (viii)	Share 29, Share 15, 500 mi. Nbhd. (U) Boost+0 (ix)	Share 29, Share 15, 500 mi. Nbhd. (C) Boost+0 (x)	Share 29, Share 15, 600 mi. Nbhd. (U), Boost+0 (xi)	Share 29, Share 15, 600 mi. Nbhd. (C), Boost+0 (xii)
Annualized Waitlist Removals	3128.60	3086.52	3101.84	3100.76	3077.48	3093.48	3062.20	3091.84
Annualized Total Deaths	2243.28	2216.24	2220.32	2215.56	2190.24	2208.68	2173.76	2215.2
Annualized Waitlist Deaths	1173.68	1128.04	1150.28	1138.88	1111.64	1134.56	1097.84	1134.16
Annualized Waitlist Relist Deaths	23.92	23.52	24.04	22.76	22.88	23.40	22.20	23.24
Annualized Post Tx Deaths	996.12	1014.60	997.72	1003.68	1003.88	1003.64	1002.28	1009.44
Annualized Post Re-Tx Deaths	49.56	50.08	48.28	50.24	51.84	47.08	51.44	48.36
DSA Mean Transplant MELD	23.09	23.76	23.26	23.61	23.87	23.61	24.08	23.64
DSA Mean Transplant MELD Std.	1.88	1.59	1.80	1.77	1.70	1.83	1.64	1.83
DSA Median Transplant MELD	24.48	26.01	24.92	25.59	26.27	25.61	26.69	25.73
DSA Median Transplant MELD Std.	2.84	2.34	2.68	2.75	2.48	2.76	2.19	2.77
Avg. Organ Transport Distance (mi.)								
Ground Vehicle	33.34	34.21	33.04	34.71	34.32	34.63	33.77	34.70
Helicopter	100.99	103.96	103.89	105.54	104.66	104.40	103.77	105.47
Airplane	525.87	507.88	454.37	468.38	451.53	469.74	465.80	468.56
Avg. Organ Transport Time (hr.)								
Ground Vehicle	0.78	0.80	0.78	0.81	0.80	0.81	0.79	0.81
Helicopter	1.22	1.24	1.24	1.25	1.25	1.25	1.24	1.25
Airplane	2.48	2.44	2.33	2.37	2.33	2.37	2.36	2.37
Percentage of Organs Transported								
Ground Vehicle	46.94%	39.39%	44.33%	38.22%	35.03%	37.90%	33.75%	37.63%
Helicopter	0.68%	0.63%	0.71%	0.69%	0.52%	0.67%	0.50%	0.71%
Airplane	52.23%	59.86%	54.81%	60.97%	64.34%	61.31%	65.65%	61.55%

Table 2.4b: 5-Year Comparative Performance between Current System and Share 29/Share 15/0-Point Boost Policy on 8 Districts and Concentric Neighborhoods (Block II)

Category	Current System (Share 15, Share 35) (i)	Share29, Share15, 8 district, Boost+0 (vi)	Share29, Share15, 400 mi. Nbhd. (U) Boost+0 (vii)	Share29, Share15, 400 mi. Nbhd. (C) Boost+0 (viii)	Share29, Share15, 500 mi. Nbhd. (U) Boost+0 (ix)	Share29, Share15, 500 mi. Nbhd. (C) Boost+0 (x)	Share29, Share15, 600 mi. Nbhd. (U), Boost+0 (xi)	Share29, Share15, 600 mi. Nbhd. (C), Boost+0 (xii)
Annualized Waitlist Removals	---	-42.08	-41	-27.84	-51.12	-35.12	-66.4	-36.76
Annualized Total Deaths	---	-27.04	-22.96	-27.72	-53.04	-34.6	-69.52	-28.08
Annualized Waitlist Deaths	---	-45.64	-49.84	-34.8	-62.04	-39.12	-75.84*	-39.52
Annualized Waitlist Relist Deaths	---	-0.4	-0.8	-1.16	-1.04	-0.52	-1.72	-0.68
Annualized Post Tx Deaths	---	+18.48*	+12.28	+7.56	+7.76	+7.52	+6.16	+13.32
Annualized Post Re-Tx Deaths	---	+0.52	+0.52	+0.68	+2.28	-2.48*	+1.88	-1.2
DSA Mean Transplant MELD	---	+0.68*	+0.62*	+0.52*	+0.78*	+0.52*	+0.99*	+0.56*
DSA Mean Transplant MELD Std.	---	-0.29*	-0.13*	-0.11	-0.18*	-0.06	-0.25*	-0.05
DSA Median Transplant MELD	---	+1.52*	+1.44*	+1.10*	+1.79*	+1.13*	+2.21*	+1.24*
DSA Median Transplant MELD Std.	---	-0.51*	-0.21*	-0.09*	-0.36*	-0.08	-0.65*	-0.08
Avg. Organ Transport Distance (mi.)	---							
Ground Vehicle	---	+0.88*	+0.78*	+1.37*	+0.98*	+1.29*	+0.43*	+1.36*
Helicopter	---	+2.98*	+4.01*	+4.55*	+3.67*	+3.41*	+2.79*	+4.49*
Airplane	---	-17.99*	-80.26*	-57.50*	-74.34*	-56.14*	-60.07*	-57.31*
Avg. Organ Transport Time (hr.)	---							
Ground Vehicle	---	+0.02*	+0.02*	+0.03*	+0.02*	+0.02*	+0.01*	+0.03*
Helicopter	---	+0.02*	+0.03*	+0.03*	+0.03*	+0.02*	+0.02*	+0.03*
Airplane	---	-0.04*	-0.16*	-0.11*	-0.15*	-0.11*	-0.12*	-0.11*
Percentage of Organs Transported	---							
Ground Vehicle	---	-7.55%*	-10.46%*	-8.72%*	-11.92%*	-9.04%*	-13.19%*	-9.32%*
Helicopter	---	-0.05%	-0.12%*	+0.01%	-0.17%*	0%	-0.19%*	+0.03%
Airplane	---	+7.63%*	+10.61%*	+8.74%*	+12.11%*	+9.08%*	+13.42%*	+9.32%*

*This indicates that difference has p-value less than 0.05 ($p < 0.05$).

Table2. 5a: 5-Year Performances of Current System and Share 29/Share 18/3-Point Boost Policy on 8 Districts and Concentric Neighborhoods (Block III)

Category	Current System (Share 15, Share 35) (i)	Share29, Share18, 8 district, Boost+3 (xiii)	Share29, Share18, 400 mi. Nbhd. (U), Boost+3 (xiv)	Share29, Share18, 400 mi. Nbhd. (C), Boost+3 (xv)	Share29, Share18, 500 mi. Nbhd. (U), Boost+3 (xvi)	Share29, Share18, 500 mi. Nbhd. (C), Boost+3 (xvii)	Share29, Share18, 600 mi. Nbhd. (U), Boost+3 (xviii)	Share29, Share18, 600 mi. Nbhd. (C), Boost+3 (xix)
Annualized Waitlist Removals	3128.60	3077.56	3083.56	3091.48	3072.92	3090.60	3053.76	3092.36
Annualized Total Deaths	2243.28	2224.12	2207.72	2235.6	2193.92	2220.8	2179.56	2214.6
Annualized Waitlist Deaths	1173.68	1130.04	1120.60	1141.28	1112.80	1132.72	1100.12	1135.72
Annualized Waitlist Relist Deaths	23.92	23.12	23.40	22.40	23.04	22.88	22.40	23.32
Annualized Post Tx Deaths	996.12	1020.12	1012.04	1019.48	1009.60	1015.00	1007.48	1004.96
Annualized Post Re-Tx Deaths	49.56	50.84	51.68	52.44	48.48	50.20	49.56	50.60
DSA Mean Transplant MELD	23.09	23.89	23.89	23.72	24.00	23.78	24.13	23.78
DSA Mean Transplant MELD Std.	1.88	1.54	1.64	1.70	1.66	1.75	1.57	1.72
DSA Median Transplant MELD	24.48	26.18	26.14	25.80	26.39	25.84	26.74	25.90
DSA Median Transplant MELD Std.	2.84	2.18	2.38	2.53	2.25	2.54	2.02	2.51
Avg. Organ Transport Distance (mi.)								
Ground Vehicle	33.34	33.61	33.49	33.92	33.44	33.84	33.20	33.84
Helicopter	100.99	103.79	104.27	104.11	104.08	103.87	103.16	105.31
Airplane	525.87	532.09	472.57	503.91	474.91	502.44	482.86	501.79
Avg. Organ Transport Time (hr.)								
Ground Vehicle	0.78	0.79	0.79	0.80	0.79	0.79	0.78	0.79
Helicopter	1.22	1.24	1.24	1.24	1.24	1.24	1.24	1.25
Airplane	2.48	2.48	2.37	2.43	2.37	2.43	2.39	2.43
Percentage of Organs Transported								
Ground Vehicle	46.94%	42.15%	39.69%	41.40%	38.16%	41.15%	36.96%	40.78%
Helicopter	0.68%	0.69%	0.58%	0.71%	0.54%	0.72%	0.56%	0.72%
Airplane	52.23%	57.04%	59.62%	57.78%	61.19%	58.00%	62.37%	58.37%

Table 2.5b: 5-Year Comparative Performances between Current System and Share 29/Share 18/3-Point Boost Policy on 8 Districts and Concentric Neighborhoods (Block III)

Category	Current System (Share 15, Share 35) (i)	Share29, Share18, 8 district, Boost+3 (xiii)	Share29, Share18, 400 mi. Nbhd. (U), Boost+3 (xiv)	Share29, Share18, 400 mi. Nbhd. (C), Boost+3 (xv)	Share29, Share18, 500 mi. Nbhd. (U), Boost+3 (xvi)	Share29, Share18, 500 mi. Nbhd. (C), Boost+3 (xvii)	Share29, Share18, 600 mi. Nbhd. (U), Boost+3 (xviii)	Share29, Share18, 600 mi. Nbhd. (C), Boost+3 (xix)
Annualized Waitlist Removals	---	-51.04	-45.04	-37.12	-55.68	-38	-74.84	-36.24
Annualized Total Deaths	---	-19.16	-35.56	-7.68	-49.36	-22.48	-63.72	-28.68
Annualized Waitlist Deaths	---	-43.64	-53.08	-32.4	-60.88	-40.96	-73.56*	-37.96
Annualized Waitlist Relist Deaths	---	-0.8	-0.52	-1.52	-0.88	-1.04	-1.52	-0.6
Annualized Post Tx Deaths	---	+24*	+15.92*	+23.36*	+13.48	+18.88*	+11.36	+8.84
Annualized Post Re-Tx Deaths	---	+1.28	+2.12	+2.88*	-1.08	+0.64	0	+1.04
DSA Mean Transplant MELD	---	+0.81*	+0.80*	+0.63*	+0.91*	+0.69*	+1.05*	+0.70*
DSA Mean Transplant MELD Std.	---	-0.34*	-0.24*	-0.18*	-0.22*	-0.13*	-0.31*	-0.16*
DSA Median Transplant MELD	---	+1.69*	+1.65*	+1.31*	+1.90*	+1.36*	+2.25*	+1.42*
DSA Median Transplant MELD Std.	---	-0.67*	-0.46*	-0.31*	-0.60*	-0.31*	-0.82*	-0.33*
Avg. Organ Transport Distance (mi.)	---							
Ground Vehicle	---	+0.27	+0.15	+0.58*	+0.10	+0.50*	-0.14	+0.50*
Helicopter	---	+2.81*	+3.29*	+3.12*	+3.09*	+2.88*	+2.17	+4.32*
Airplane	---	+6.22*	-53.30*	-21.96*	-50.97*	-23.43*	-43.01*	-24.08*
Avg. Organ Transport Time (hr.)	---							
Ground Vehicle	---	0	0	+0.01*	0	+0.01*	0	+0.01*
Helicopter	---	+0.02*	+0.02*	+0.02*	+0.02*	+0.02*	+0.02	+0.03*
Airplane	---	+0.01	-0.10*	-0.04*	-0.10*	-0.04*	-0.08*	-0.04*
Percentage of Organs Transported	---							
Ground Vehicle	---	-4.80%*	-7.26%*	-5.55%*	-8.78%*	-5.80%*	-9.98%*	-6.16%*
Helicopter	---	+0.01%	-0.11%*	+0.02%	-0.14%*	+0.04%	-0.12%*	+0.04%
Airplane	---	+4.81%*	+7.40%*	+5.55%*	+8.96%*	+5.78%*	+10.14%*	+6.15%*

*This indicates that difference has p-value less than 0.05 ($p < 0.05$).

Table2. 6a: 5-Year Performances of Current System and Share 29/Share 20/5-Point Boost Policy on 8 Districts and Concentric Neighborhoods (Block IV)

Category	Current System (Share 15, Share 35) (i)	Share29, Share20, 8 district, Boost+5 (xx)	Share29, Share20, 400 mi. Nhbd. (U), Boost+5 (xxi)	Share29, Share20, 400 mi. Nhbd. (C), Boost+5 (xxii)	Share29, Share20, 500 mi. Nbhd. (U), Boost+5 (xxiii)	Share29, Share20, 500 mi. Nbhd. (C), Boost+5 (xxiv)	Share29, Share20, 600 mi. Nbhd. (U), Boost+5 (xxv)	Share29, Share20, 600 mi. Nbhd. (C), Boost+5 (xxvi)
Annualized Waitlist Removals	3128.60	3078.24	3079.52	3092.44	3066.56	3090.60	3066.28	3087.16
Annualized Total Deaths	2243.28	2220	2215.56	2227.64	2200.96	2220.8	2182.16	2227.6
Annualized Waitlist Deaths	1173.68	1130.56	1125.12	1138.96	1116.80	1132.72	1098.20	1136.76
Annualized Waitlist Relist Deaths	23.92	23.12	22.88	23.12	22.36	22.88	22.36	23.00
Annualized Post Tx Deaths	996.12	1014.16	1016.20	1013.60	1011.12	1015.00	1012.32	1015.96
Annualized Post Re-Tx Deaths	49.56	52.16	51.36	51.96	50.68	50.20	49.28	51.88
DSA Mean Transplant MELD	23.09	23.90	23.93	23.81	24.03	23.78	24.18	23.86
DSA Mean Transplant MELD Std.	1.88	1.55	1.66	1.69	1.66	1.75	1.54	1.67
DSA Median Transplant MELD	24.48	26.26	26.22	25.94	26.50	25.84	26.77	26.03
DSA Median Transplant MELD Std.	2.84	2.09	2.19	2.36	2.07	2.54	1.86	2.35
Avg. Organ Transport Distance (mi.)								
Ground Vehicle	33.34	33.33	33.07	33.42	33.23	33.84	32.79	33.48
Helicopter	100.99	104.00	104.56	104.29	103.51	103.87	103.32	103.96
Airplane	525.87	556.97	498.81	532.22	495.42	502.44	501.03	530.13
Avg. Organ Transport Time (hr.)								
Ground Vehicle	0.78	0.78	0.78	0.79	0.78	0.79	0.78	0.79
Helicopter	1.22	1.24	1.25	1.24	1.24	1.24	1.24	1.24
Airplane	2.48	2.53	2.42	2.49	2.41	2.43	2.42	2.48
Percentage of Organs Transported								
Ground Vehicle	46.94%	43.70%	41.46%	43.19%	40.04%	41.15%	38.89%	42.69%
Helicopter	0.68%	0.70%	0.60%	0.76%	0.60%	0.72%	0.56%	0.74%
Airplane	52.23%	55.47%	57.82%	55.94%	59.25%	58.00%	60.44%	56.44%

Table 2.6b: 5-Year Comparative Performances between Current System and Share 29/Share 20/5-Point Boost Policy on 8 Districts and Concentric Neighborhoods (Block IV)

Category	Current System (Share 15, Share 35) (i)	Share29, Share20, 8 district, Boost+5 (xx)	Share29, Share20, 400 mi. Nhbd. (U), Boost+5 (xxi)	Share29, Share20, 400 mi. Nhbd. (C), Boost+5 (xxii)	Share29, Share20, 500 mi. Nbhd. (U), Boost+5 (xxiii)	Share29, Share20, 500 mi. Nbhd. (C), Boost+5 (xxiv)	Share29, Share20, 600 mi. Nbhd. (U), Boost+5 (xxv)	Share29, Share20, 600 mi. Nbhd. (C), Boost+5 (xxvi)
Annualized Waitlist Removals	---	-50.36	-49.08	-36.16	-62.04	-40.08	-62.32	-41.44
Annualized Total Deaths	---	-23.28	-27.72	-15.64	-42.32	-22.48	-61.12	-15.68
Annualized Waitlist Deaths	---	-43.12	-48.56	-34.72	-56.88	-39.52	-75.48*	-36.92
Annualized Waitlist Relist Deaths	---	-0.8	-1.04	-0.8	-1.56	-0.32	-1.56	-0.92
Annualized Post Tx Deaths	---	+18.04*	+20.08*	+17.48*	+15	+25.12*	+16.2*	+19.84*
Annualized Post Re-Tx Deaths	---	+2.6*	+1.8*	+2.4	+1.12	+1	-0.28	+2.32
DSA Mean Transplant MELD	---	+0.82*	+0.85*	+0.73*	+0.95*	+0.75*	+1.09*	+0.77*
DSA Mean Transplant MELD Std.	---	-0.34*	-0.22*	-0.19*	-0.22*	-0.22*	-0.34*	-0.21*
DSA Median Transplant MELD	---	+1.78*	+1.74*	+1.46*	+2.02*	+1.50*	+2.29*	+1.54*
DSA Median Transplant MELD Std.	---	-0.75*	-0.66*	-0.49*	-0.77*	-0.50*	-0.98*	-0.49*
Avg. Organ Transport Distance (mi.)	---							
Ground Vehicle	---	-0.01	-0.27	+0.08	-0.11	+0.04	-0.55*	+0.14
Helicopter	---	+3.02*	+3.58*	+3.31*	+2.53*	+4.17*	+2.34	+2.98*
Airplane	---	+31.10*	-27.06*	+6.35*	-30.45*	+3.33	-24.84*	+4.26*
Avg. Organ Transport Time (hr.)	---							
Ground Vehicle	---	0	0	0	0	0	-0.01*	0
Helicopter	---	+0.02*	+0.03*	+0.02*	+0.02*	+0.03*	+0.02	+0.02*
Airplane	---	+0.06*	-0.05*	+0.01*	-0.06*	+0.01*	-0.05*	+0.01*
Percentage of Organs Transported	---							
Ground Vehicle	---	-3.25%*	-5.48%*	-3.76%*	-6.90%*	-4.12%*	-8.06%*	-4.25%*
Helicopter	---	+0.02%	-0.09%*	+0.07%*	-0.09%*	-0.06%*	-0.12%*	+0.06%*
Airplane	---	+3.25%*	+5.60%*	+3.72%*	+7.02%*	+4.09%*	+8.21%*	+4.22%*

*This indicates that difference has p-value less than 0.05 ($p < 0.05$).

Table 2.7a: 5-Year Performances of Current System and Share 35/Share 15/0-Point Boost Policy on 8 Districts and Concentric Neighborhoods (Block V)

Category	Current System (Share 15, Share 35) (i)	Share35, Share15, 8 district, Boost+0 (xxvii)	Share35, Share15, 400 mi. Nbhd. (U), Boost+0 (xxviii)	Share35, Share15, 400 mi. Nbhd. (C), Boost+0 (xxix)	Share35, Share15, 500 mi. Nbhd. (U), Boost+0 (xxx)	Share35, Share15, 500 mi. Nbhd. (C), Boost+0 (xxxi)	Share35, Share15, 600 mi. Nbhd. (U), Boost+0 (xxxii)	Share35, Share15, 600 mi. Nbhd. (C), Boost+0 (xxxiii)
Annualized Waitlist Removals	3128.60	3106.92	3101.84	3113.40	3094.64	3107.64	3086.56	3108.72
Annualized Total Deaths	2243.28	2238	2220.32	2224.6	2214.6	2225.2	2209.68	2224.36
Annualized Waitlist Deaths	1173.68	1153.68	1150.28	1157.16	1139.56	1159.00	1135.32	1160.64
Annualized Waitlist Relist Deaths	23.92	23.92	24.04	24.08	23.92	23.72	23.60	23.88
Annualized Post Tx Deaths	996.12	1010.40	997.72	992.68	1002.16	992.52	1002.44	991.08
Annualized Post Re-Tx Deaths	49.56	50.00	48.28	50.68	48.96	49.96	48.32	48.76
DSA Mean Transplant MELD	23.09	23.31	23.26	23.23	23.39	23.26	23.53	23.27
DSA Mean Transplant MELD Std.	1.88	1.64	1.80	1.84	1.80	1.84	1.73	1.83
DSA Median Transplant MELD	24.48	24.98	24.92	24.74	25.14	24.83	25.40	24.81
DSA Median Transplant MELD Std.	2.84	2.54	2.68	2.75	2.63	2.74	2.53	2.73
Avg. Organ Transport Distance (mi.)								
Ground Vehicle	33.34	33.18	33.04	33.28	32.90	33.22	32.68	33.29
Helicopter	100.99	103.40	103.89	102.97	103.51	104.22	102.60	104.89
Airplane	525.87	499.26	454.37	483.38	457.60	484.42	464.96	478.58
Avg. Organ Transport Time (hr.)								
Ground Vehicle	0.78	0.78	0.78	0.78	0.78	0.78	0.77	0.78
Helicopter	1.22	1.24	1.24	1.24	1.24	1.24	1.23	1.25
Airplane	2.48	2.42	2.33	2.39	2.34	2.40	2.35	2.38
Percentage of Organs Transported								
Ground Vehicle	46.94%	46.60%	44.33%	45.05%	43.62%	45.03%	43.34%	44.95%
Helicopter	0.68%	0.80%	0.71%	0.80%	0.70%	0.78%	0.69%	0.77%
Airplane	52.23%	52.47%	54.81%	54.02%	55.55%	54.05%	55.85%	54.14%

Table 2.7b: 5-Year Comparative Performances between Current System and Share 35/Share 15/0-Point Boost Policy on 8 Districts and Concentric Neighborhoods (Block V)

Category	Current System (Share 15, Share 35) (i)	Share35, Share15, 8 district, Boost+0 (xxvii)	Share35, Share15, 400 mi. Nbhd. (U), Boost+0 (xxviii)	Share35, Share15, 400 mi. Nbhd. (C), Boost+0 (xxix)	Share35, Share15, 500 mi. Nbhd. (U), Boost+0 (xxx)	Share35, Share15, 500 mi. Nbhd. (C), Boost+0 (xxxi)	Share35, Share15, 600 mi. Nbhd. (U), Boost+0 (xxxii)	Share35, Share15, 600 mi. Nbhd. (C), Boost+0 (xxxiii)
Annualized Waitlist Removals	---	-21.68	-26.76	-15.2	-33.96	-20.96	-42.04	-19.88
Annualized Total Deaths	---	-5.28	-22.96	-18.68	-28.68	-18.08	-33.6	-18.92
Annualized Waitlist Deaths	---	-20	-23.4	-16.52	-34.12	-14.68	-38.36	-13.04
Annualized Waitlist Relist Deaths	---	0	+0.12	+0.16	0	-0.2	-0.32	-0.04
Annualized Post Tx Deaths	---	+14.28	+1.6	-3.44	+6.04	-3.6	+6.32	-5.04
Annualized Post Re-Tx Deaths	---	+0.44	-1.28	+1.12	-0.6	+0.4	-1.24	-0.8
DSA Mean Transplant MELD	---	+0.22*	+0.18*	+0.14*	+0.31*	+0.18*	+0.44*	+0.18*
DSA Mean Transplant MELD Std.	---	-0.24*	-0.08	-0.04	-0.08	-0.04	-0.15*	-0.05
DSA Median Transplant MELD	---	+0.49*	+0.44*	+0.26*	+0.66*	+0.34*	+0.91*	+0.33*
DSA Median Transplant MELD Std.	---	-0.30*	-0.16*	-0.09*	-0.21*	-0.11*	-0.31*	-0.12*
Avg. Organ Transport Distance (mi.)	---							
Ground Vehicle	---	-0.16	-0.30*	-0.06	-0.44*	-0.12	-0.66*	-0.05
Helicopter	---	+2.41*	+2.91*	+1.99*	+2.52*	+3.23*	+1.61	+3.91*
Airplane	---	-26.61*	-71.50*	-42.49*	-68.27*	-41.45*	-60.91*	-47.29*
Avg. Organ Transport Time (hr.)	---							
Ground Vehicle	---	0	-0.01*	0	-0.01*	0	-0.01*	0
Helicopter	---	+0.02*	+0.02*	+0.01*	+0.02*	+0.02*	+0.01	+0.03*
Airplane	---	-0.06*	-0.14*	-0.08*	-0.14*	-0.08*	-0.12*	-0.09*
Percentage of Organs Transported	---							
Ground Vehicle	---	-0.35%*	-2.61%*	-1.90%*	-3.33%*	-1.91%*	-3.61%*	-2.00%*
Helicopter	---	+0.12%*	+0.03%*	+0.12%*	+0.01%*	+0.10%*	+0.01%*	+0.09%*
Airplane	---	+0.24%*	+2.58%*	+1.79%*	+3.32%*	+1.82%*	+3.62%*	+1.92%*

*This indicates that difference has p-value less than 0.05 ($p < 0.05$).

Table 2.8a: 5-Year Performances of Current System and Share 35/Share 18/3-Point Boost Policy on 8 Districts and Concentric Neighborhoods (Block VI)

Category	Current System (Share 15, Share 35) (i)	Share35, Share18, 8 district, Boost+3 (xxxiv)	Share35, Share18, 400 mi. Nbhd. (U), Boost+3 (xxxv)	Share35, Share18, 400 mi. Nbhd. (C), Boost+3 (xxxvi)	Share35, Share18, 500 mi. Nbhd. (U), Boost+3 (xxxvii)	Share35, Share18, 500 mi. Nbhd. (C), Boost+3 (xxxviii)	Share35, Share18, 600 mi. Nbhd. (U), Boost+3 (xxxix)	Share35, Share18, 600 mi. Nbhd. (C), Boost+3 (xl)
Annualized Waitlist Removals	3128.60	3094.64	3100.40	3103.68	3088.36	3108.72	3091.04	3101.92
Annualized Total Deaths	2243.28	2239.68	2223.12	2232.44	2214.68	2226.36	2215.08	2238.6
Annualized Waitlist Deaths	1173.68	1153.68	1149.32	1154.52	1139.48	1148.56	1134.56	1153.68
Annualized Waitlist Relist Deaths	23.92	23.60	23.88	23.72	23.64	23.08	23.08	24.24
Annualized Post Tx Deaths	996.12	1012.36	1000.92	1003.92	1002.16	1005.72	1008.76	1009.28
Annualized Post Re-Tx Deaths	49.56	50.04	49.00	50.28	49.40	49.00	48.68	51.40
DSA Mean Transplant MELD	23.09	23.49	23.45	23.39	23.49	23.41	23.55	23.41
DSA Mean Transplant MELD Std.	1.88	1.64	1.74	1.76	1.74	1.78	1.72	1.73
DSA Median Transplant MELD	24.48	25.20	25.21	25.05	25.33	25.05	25.48	25.08
DSA Median Transplant MELD Std.	2.84	2.47	2.54	2.62	2.54	2.60	2.52	2.59
Avg. Organ Transport Distance (mi.)								
Ground Vehicle	33.34	32.93	32.82	32.94	32.82	32.93	32.62	32.99
Helicopter	100.99	102.30	103.26	103.45	102.46	103.81	102.41	104.06
Airplane	525.87	529.59	488.15	516.15	480.73	515.56	482.89	512.27
Avg. Organ Transport Time (hr.)								
Ground Vehicle	0.78	0.78	0.77	0.78	0.77	0.78	0.77	0.78
Helicopter	1.22	1.23	1.24	1.24	1.23	1.24	1.23	1.24
Airplane	2.48	2.48	2.40	2.46	2.38	2.46	2.39	2.45
Percentage of Organs Transported								
Ground Vehicle	46.94%	47.19%	45.10%	46.16%	44.50%	46.09%	43.95%	45.95%
Helicopter	0.68%	0.78%	0.74%	0.79%	0.71%	0.83%	0.71%	0.82%
Airplane	52.23%	51.90%	54.01%	52.91%	54.66%	52.94%	55.19%	53.10%

Table 2.8b: 5-Year Comparative Performances between Current System and Share 35/Share 18/3-Point Boost Policy on 8 Districts and Concentric Neighborhoods (Block VI)

Category	Current System (Share 15, Share 35) (i)	Share35, Share18, 8 district, Boost+3 (xxxiv)	Share35, Share18, 400 mi. Nbhd. (U), Boost+3 (xxxv)	Share35, Share18, 400 mi. Nbhd. (C), Boost+3 (xxxvi)	Share35, Share18, 500 mi. Nbhd. (U), Boost+3 (xxxvii)	Share35, Share18, 500 mi. Nbhd. (C), Boost+3 (xxxviii)	Share35, Share18, 600 mi. Nbhd. (U), Boost+3 (xxxix)	Share35, Share18, 600 mi. Nbhd. (C), Boost+3 (xl)
Annualized Waitlist Removals	---	-33.96	-28.2	-24.92	-40.24	-19.88	-37.56	-26.68
Annualized Total Deaths	---	-3.6	-20.16	-10.84	-28.6	-16.92	-28.2	-4.68
Annualized Waitlist Deaths	---	-20	-24.36	-19.16	-34.2	-25.12	-39.12	-20
Annualized Waitlist Relist Deaths	---	-0.32	-0.04	-0.2	-0.28	-0.84	-0.84	+0.32
Annualized Post Tx Deaths	---	+16.24*	+4.8	+7.8	+6.04	+9.6	+12.64	+13.16
Annualized Post Re-Tx Deaths	---	+0.48	-0.56	+0.72	-0.16	-0.56	-0.88	+1.84
DSA Mean Transplant MELD	---	+0.40*	+0.36*	+0.30*	+0.41*	+0.32*	+0.46*	+0.32*
DSA Mean Transplant MELD Std.	---	-0.24*	-0.14*	-0.12	-0.14*	-0.10	-0.17*	-0.15*
DSA Median Transplant MELD	---	+0.71*	+0.73*	+0.56*	+0.85*	+0.57*	+0.99*	+0.60*
DSA Median Transplant MELD Std.	---	-0.38*	-0.30*	-0.23*	-0.31*	-0.24*	-0.33*	-0.26*
Avg. Organ Transport Distance (mi.)	---							
Ground Vehicle	---	-0.41*	-0.52*	-0.40*	-0.52*	-0.41*	-0.72*	-0.35
Helicopter	---	+1.31	+2.27	+2.47	+1.47	+2.82*	+1.42	+3.08*
Airplane	---	+3.72	-37.72*	-9.72*	-45.14*	-10.31*	-42.98*	-13.60*
Avg. Organ Transport Time (hr.)	---							
Ground Vehicle	---	-0.01*	-0.01*	-0.01*	-0.01*	-0.01*	-0.01*	-0.01
Helicopter	---	+0.01	+0.02	+0.02	+0.01	+0.02*	+0.01	+0.02*
Airplane	---	0	-0.08*	-0.02*	-0.09*	-0.02*	-0.09*	-0.03*
Percentage of Organs Transported	---							
Ground Vehicle	---	+0.25%	-1.84%*	-0.79%*	-2.44%*	-0.85%*	-2.99%*	-1.00%*
Helicopter	---	+0.09%*	+0.06%*	+0.11%*	+0.02%	+0.14%*	+0.03%	+0.13%*
Airplane	---	-0.33%*	+1.78%*	+0.69%*	+2.43%*	+0.71%*	+2.97%*	+0.87%*

*This indicates that difference has p-value less than 0.05 ($p < 0.05$).

Table 2 9a: 5-Year Performances of Current System and Share 35/Share 20/5-Point Boost Policy on 8 Districts and Concentric Neighborhoods (Block VII)

Category	Current System (Share 15, Share 35) (i)	Share35, Share20, 8 district, Boost+5 (xli)	Share35, Share20, 400 mi. Nbhd. (U), Boost+5 (xlii)	Share35, Share20, 400 mi. Nbhd. (C), Boost+5 (xliii)	Share35, Share20, 500 mi. Nbhd. (U), Boost+5 (xliv)	Share35, Share20, 500 mi. Nbhd. (C), Boost+5 (xlv)	Share35, Share20, 600 mi. Nbhd. (U), Boost+5 (xlvi)	Share35, Share20, 600 mi. Nbhd. (C), Boost+5 (xlvii)
Annualized Waitlist Removals	3128.60	3092.20	3100.96	3104.60	3083.76	3100.00	3086.36	3105.52
Annualized Total Deaths	2243.28	2246.24	2224.08	2238.44	2215.44	2238.68	2204.76	2239.6
Annualized Waitlist Deaths	1173.68	1151.88	1141.56	1151.72	1138.12	1153.88	1129.28	1153.12
Annualized Waitlist Relist Deaths	23.92	23.84	23.92	24.12	23.52	23.40	23.88	23.88
Annualized Post Tx Deaths	996.12	1020.20	1009.44	1012.36	1004.72	1010.40	1001.44	1011.96
Annualized Post Re-Tx Deaths	49.56	50.32	49.16	50.24	49.08	51.00	50.16	50.64
DSA Mean Transplant MELD	23.09	23.50	23.49	23.47	23.59	23.47	23.64	23.46
DSA Mean Transplant MELD Std.	1.88	1.70	1.69	1.75	1.75	1.74	1.72	1.75
DSA Median Transplant MELD	24.48	25.34	25.38	25.24	25.50	25.24	25.60	25.23
DSA Median Transplant MELD Std.	2.84	2.38	2.48	2.54	2.47	2.56	2.45	2.59
Avg. Organ Transport Distance (mi.)								
Ground Vehicle	33.34	32.72	32.53	32.89	32.59	32.92	32.47	33.06
Helicopter	100.99	102.05	102.33	102.65	103.20	103.88	103.04	103.50
Airplane	525.87	552.29	509.62	542.32	501.84	538.57	501.21	534.51
Avg. Organ Transport Time (hr.)								
Ground Vehicle	0.78	0.77	0.77	0.78	0.77	0.78	0.77	0.78
Helicopter	1.22	1.23	1.23	1.23	1.24	1.24	1.24	1.24
Airplane	2.48	2.52	2.44	2.51	2.42	2.50	2.42	2.49
Percentage of Organs Transported								
Ground Vehicle	46.94%	47.64%	45.82%	46.75%	45.09%	46.74%	44.45%	46.72%
Helicopter	0.68%	0.80%	0.76%	0.85%	0.73%	0.80%	0.72%	0.79%
Airplane	52.23%	51.43%	53.28%	52.26%	54.04%	52.32%	54.71%	52.34%

Table 2.9b: 5-Year Comparative Performances between Current System and Share 35/Share 20/5-Point Boost Policy on 8 Districts and Concentric Neighborhoods (Block VII)

Category	Current System (Share 15, Share 35) (i)	Share35, Share20, 8 district, Boost+5 (xli)	Share35, Share20, 400 mi. Nbhd. (U), Boost+5 (xlii)	Share35, Share20, 400 mi. Nbhd. (C), Boost+5 (xliii)	Share35, Share20, 500 mi. Nbhd. (U), Boost+5 (xliv)	Share35, Share20, 500 mi. Nbhd. (C), Boost+5 (xlv)	Share35, Share20, 600 mi. Nbhd. (U), Boost+5 (xlvi)	Share35, Share20, 600 mi. Nbhd. (C), Boost+5 (xlvii)
Annualized Waitlist Removals	---	-36.4	-27.64	-24	-44.84	-28.6	-42.24	-23.08
Annualized Total Deaths	---	2.96	-19.2	-4.84	-27.84	-4.6	-38.52	-3.68
Annualized Waitlist Deaths	---	-21.8	-32.12	-21.96	-35.56	-19.8	-44.4	-20.56
Annualized Waitlist Relist Deaths	---	-0.08	0	+0.2	-0.4	-0.52	-0.04	-0.04
Annualized Post Tx Deaths	---	+24.08*	+13.32	+16.24	+8.6	+14.28*	+5.32	+15.84
Annualized Post Re-Tx Deaths	---	+0.76	-0.4	+0.68	-0.48	+1.44	+0.6	+1.08
DSA Mean Transplant MELD	---	+0.41*	+0.40*	+0.39*	+0.50*	+0.39*	+0.55*	+0.38*
DSA Mean Transplant MELD Std.	---	-0.18*	-0.19*	-0.13*	-0.13*	-0.14*	-0.17*	-0.13*
DSA Median Transplant MELD	---	+0.86*	+0.90*	+0.76*	+1.01*	+0.76*	+1.11*	+0.75*
DSA Median Transplant MELD Std.	---	-0.46*	-0.37*	-0.30*	-0.37*	-0.29*	-0.39*	-0.25*
Avg. Organ Transport Distance (mi.)	---							
Ground Vehicle	---	-0.62*	-0.82*	-0.45*	-0.75*	-0.42*	-0.87*	-0.27
Helicopter	---	+1.07	+1.35	+1.67	+2.21*	+2.90*	+2.06	+2.52
Airplane	---	+26.41*	-16.25*	+16.45*	-24.03*	+12.70*	-24.67*	+8.64*
Avg. Organ Transport Time (hr.)	---							
Ground Vehicle	---	-0.01*	-0.02*	-0.01*	-0.01*	-0.01*	-0.02*	0
Helicopter	---	+0.01	+0.01	+0.01	+0.02*	+0.02*	+0.01	+0.02
Airplane	---	+0.05*	-0.03*	+0.03*	-0.05*	+0.02*	-0.05*	+0.02*
Percentage of Organs Transported	---							
Ground Vehicle	---	+0.69%*	-1.13%*	-0.19%*	-1.85%*	-0.21%	-2.50%*	-0.23%*
Helicopter	---	+0.12%*	+0.08%*	+0.17%*	+0.05%*	+0.12%*	+0.04%	+0.11%*
Airplane	---	-0.80%*	+1.05%*	+0.03%	+1.81%*	+0.09%	+2.48%*	+0.12%

*This indicates that difference has p-value less than 0.05 ($p < 0.05$).

Table 2.10: 5-Year Performances of Selected Policies Based on Organ Volume Loss

Policies	Organ Volume Loss Relative to Current System	Annualized Total Deaths	DSA Median Transplant MELD	DSA Median Transplant MELD Std.	Avg. Airplane Transport Time (hr.)	Percentage of Organs Transported by Airplane
(xxxi) Share 35/Share 15 0-Point Boost 500-mi. Nbhd. (C)	-9.88%	-18.08	+0.34	-0.11	-0.08	+1.82%
(xxx) Share 35/Share 15 0-Point Boost 500-mi. Nbhd. (U)	-16.30%	-28.68	+0.66	-0.21	-0.14	+3.32%
(xxxii) Share 35/Share 15 0-Point Boost 600-mi. Nbhd. (U)	-19.47%	-33.6	+0.91	-0.31	-0.12	+3.62%

Figure 2.1: Concentric Neighborhood for OPO serving Eastern Pennsylvania (PADV)

Fig. 2.1(a)

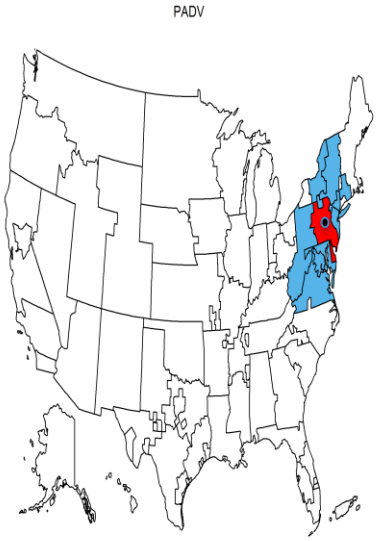


Fig. 2.1(b)

The figure shows two versions of concentric neighborhood of 500-mile radius for the OPO serving Eastern Pennsylvania.

Figure 2.1(a) shows the unconstrained concentric neighborhoods solution. This neighborhood contains the current UNOS region for the OPO (UNOS Region 2) and all OPOs whose physical addresses are within 500 miles of the OPO's main address in Philadelphia.

Figure 1(b) shows the constrained concentric neighborhoods solution. This neighborhood contains only 10 OPOs, where the first 5 are the current UNOS region for the OPO (UNOS Region 2) and the last 5 are the closest OPOs outside the UNOS region whose physical addresses are within 500 miles of the OPO's main address in Philadelphia.

Figure 2.2: Mean Transplant MELD across DSAs of Current System with Modified Sharing Policies without Neighborhoods (Block I)

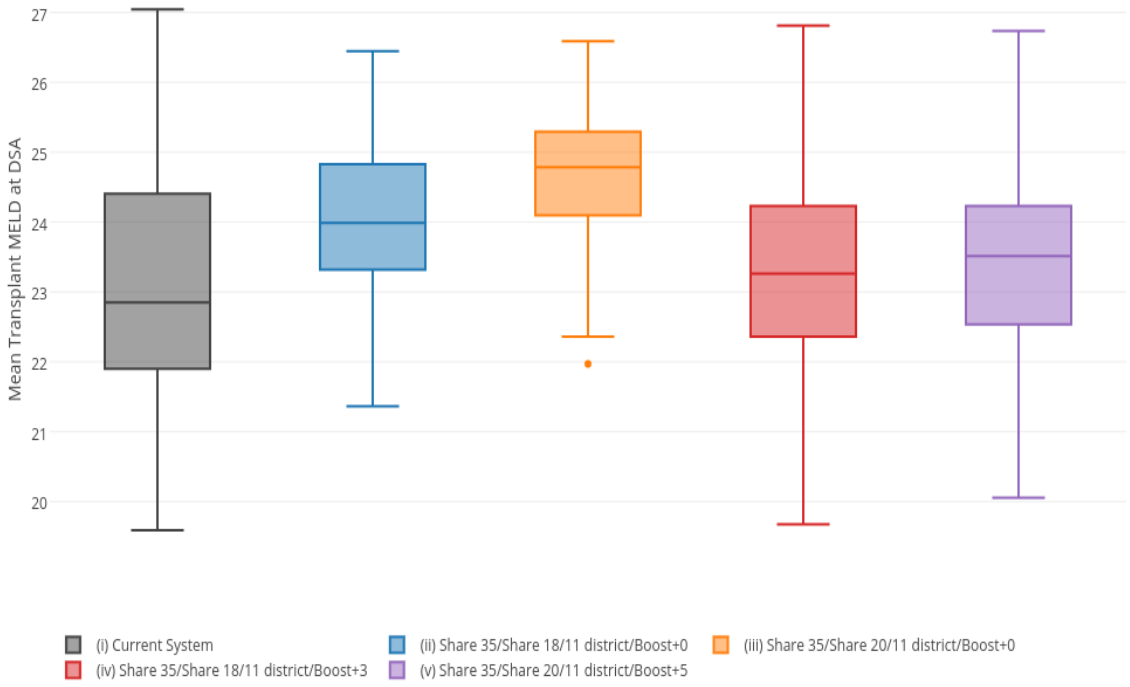


Figure 2.3: Mean Transplant MELD across DSAs for Current System and Share 29 Policies on 8 Districts and Concentric Neighborhoods (Blocks II-IV)

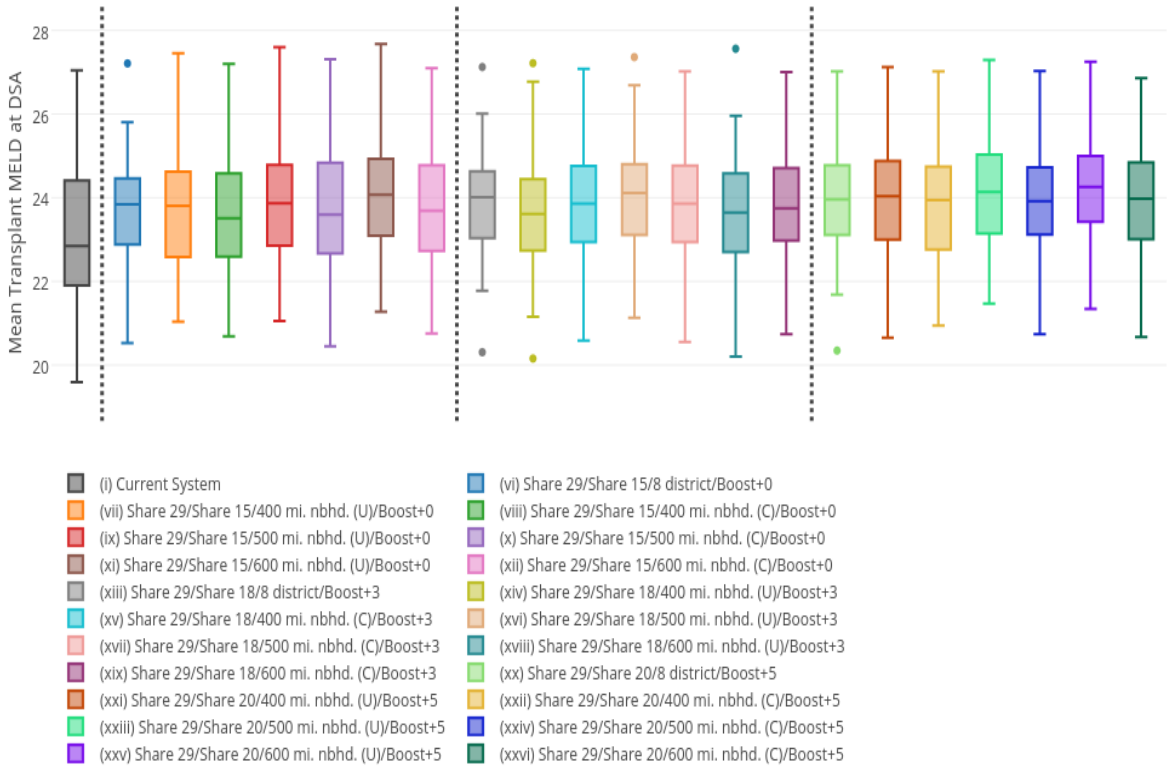


Figure 2.4: Mean Transplant MELD across DSAs for Current System and Share 35 Policies on 8 Districts and Concentric Neighborhoods (Blocks V-VII)

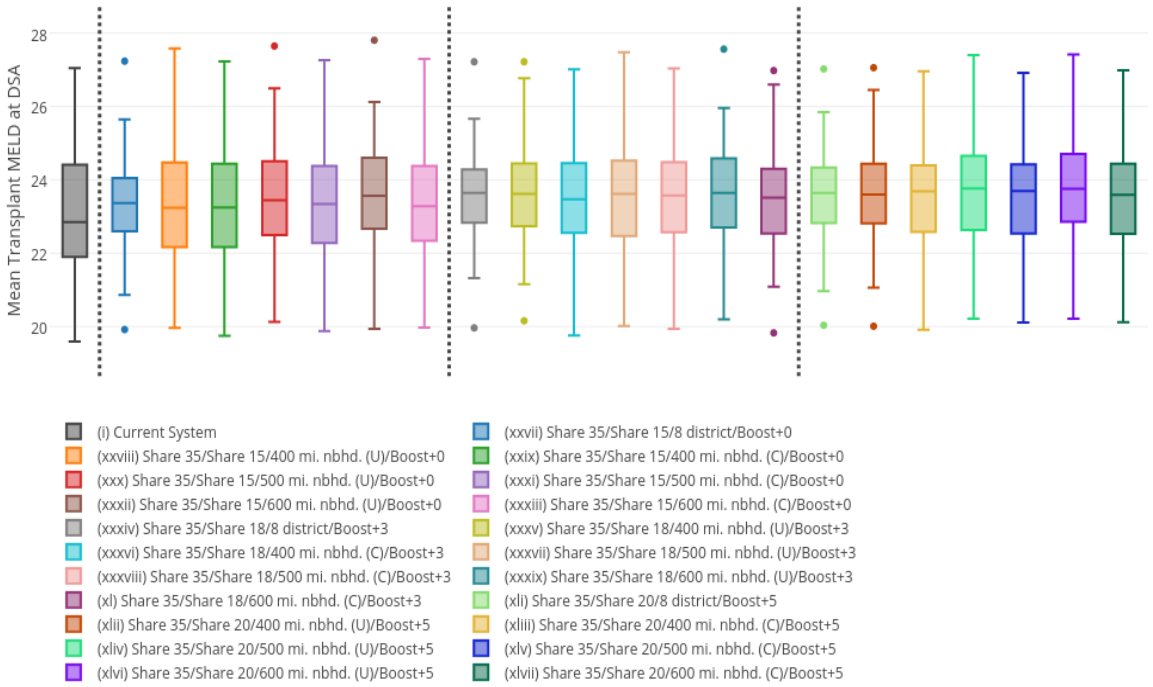


Figure 2.5: DSA Percentage Changes in Transplant Volume for Current System with Modified Sharing Policies without Neighborhoods (Block I)

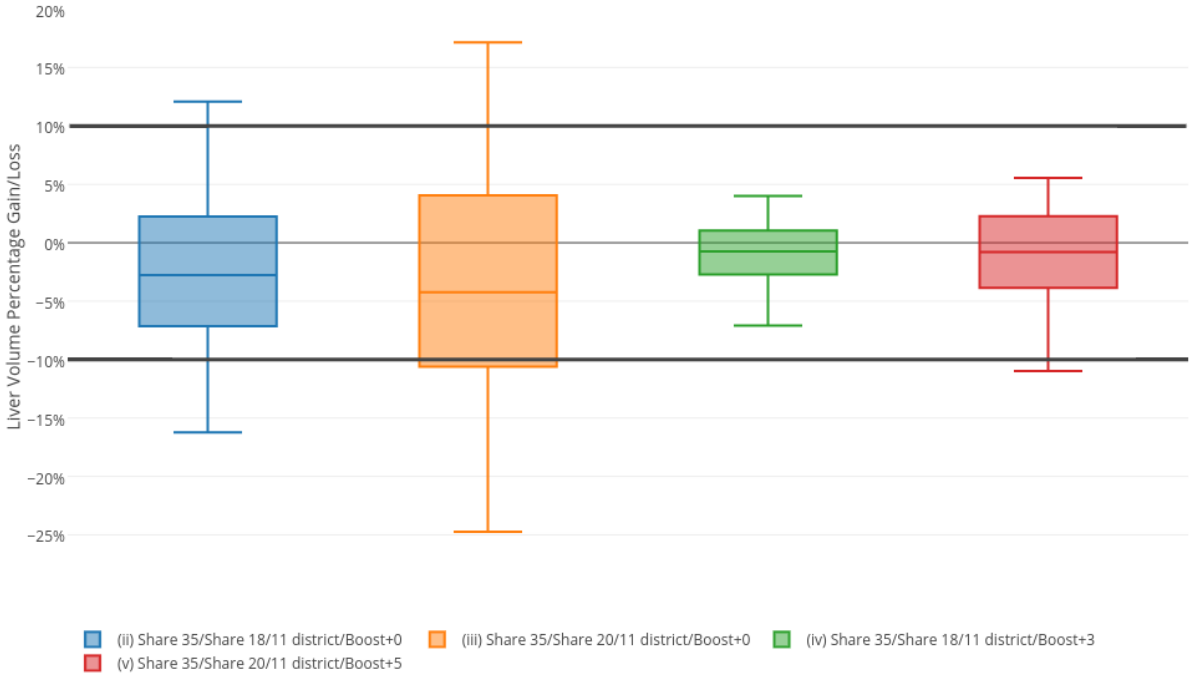


Figure 2.6: DSA Percentage Changes in Transplant Volume for Share 29 Policies on 8 Districts and Concentric Neighborhoods (Blocks II-IV)

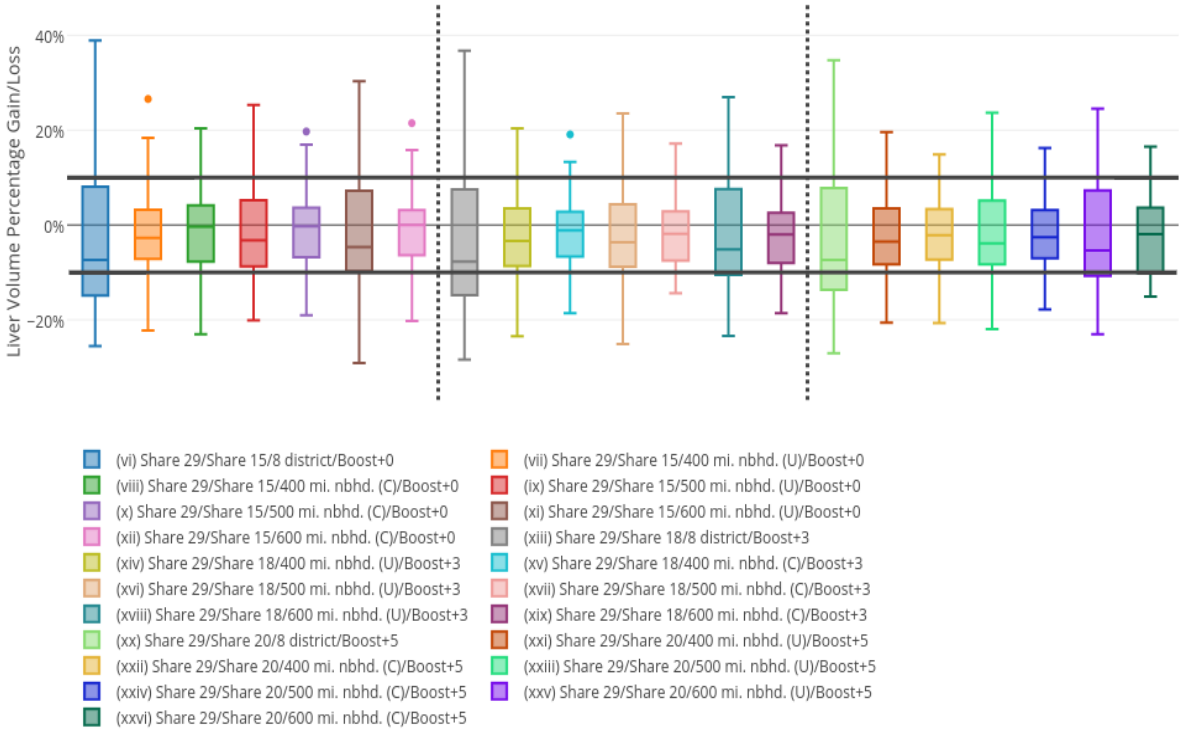
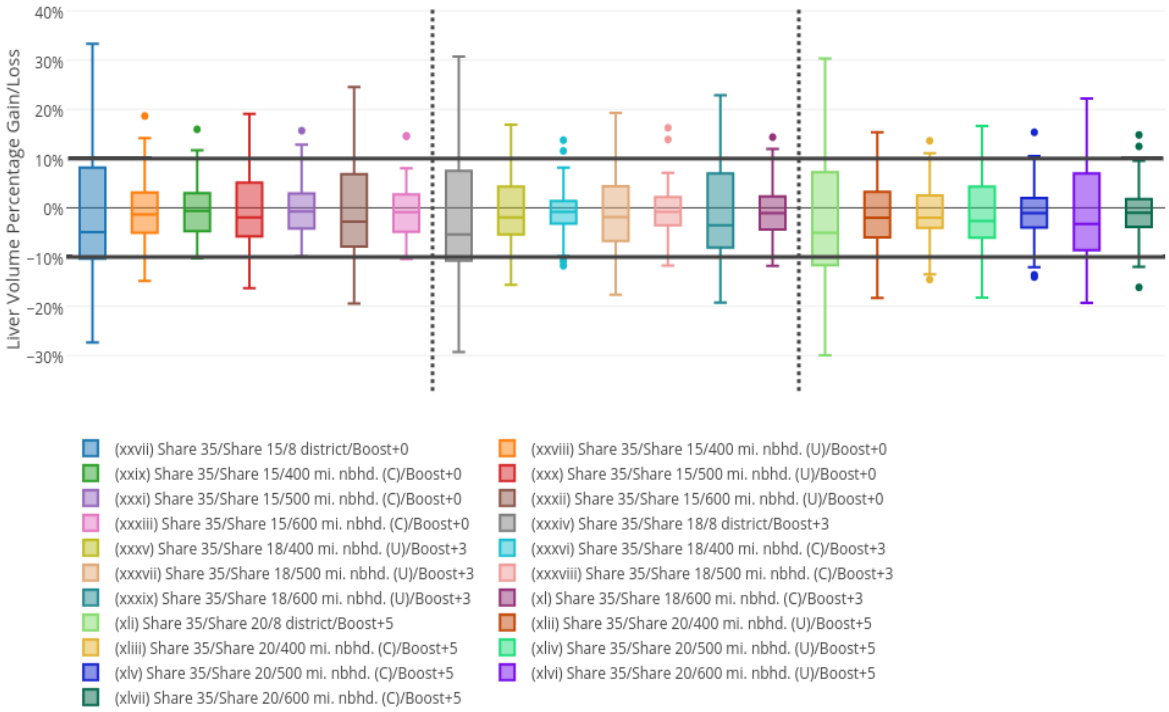


Figure 2.7: DSA Percentage Changes in Transplant Volume for Share 35 Policies on 8 Districts and Concentric Neighborhoods (Blocks V-VII)



Assessing Renal Transplant Candidate Survival at Listing Using a Risk-Adjusted Multi-State Semi-Markov Model

The experience of patients who will list for a kidney transplant in the United States is a dynamic, multifaceted process. Initially, end-stage renal disease (ESRD) etiology and individual risk factors will determine the course of treatment and whether the individual is suitable for transplantation[56]. However, once a patient lists for a deceased-donor transplant, progression is also influenced by the individual's interactions with the organ procurement and transplantation network (OPTN)[57]. The OPTN is the complex logistical system tasked with allocating organs from deceased donors to eligible recipients. Its daily operation depends on the collective decisions of organ procurement organizations (OPOs), transplant centers, donor hospitals, and supervisory bodies[57]. Thus, this system effectively decides when a patient receives an offer for a prospective graft of a given quality. Since donor quality affects transplant efficacy[58] and extended time on dialysis exacerbates waitlist and post-transplant outcomes[59-61], the characteristics of the system, in addition to individual clinical factors, necessarily also impact patient survival and predictions thereof.

Unfortunately, the system does not operate uniformly, as individuals will face varying transplant rates, waiting times, and donor qualities depending on the OPO where they list[30]. Differences among transplant centers and OPO should therefore be incorporated in an individual-specific manner akin to the standard criteria used for assessing survival-benefits and risk-adjustments[2,62]. Since these factors also affect outcomes, patients can be better informed about the consequences of listing at a particular transplant center by including them into survival time estimates.

Moreover, an assessment at listing of waitlist survival time and hence total survival time ought to adjust for the events that patients may experience throughout the process[63]. These events include removal from the waitlist, waitlist inactivity, and transplantation. Survival time estimates at listing are complicated by the various states patients must navigate over the course of their treatment and ESRD progression. A patient at the time of listing will be uncertain of his or her overall survival time and the times when a transplant will be available. At the outset, several pathways to death are possible. For example, a patient may die after listing but before receiving a graft. Alternatively, a patient may receive a graft and then perhaps die some years later. More complicated pathways, which we consider sparingly in this article and leave to future work, are also possible. For instance, a patient may alternate between being active and inactive on the waitlist a few times, receive a graft that subsequently fails, and then re-list for a transplant, receive a re-transplant, and then die (with the prospects of being inactive, being removed from the waitlist, or dying before re-transplantation). Of particular interest to a newly listed ESRD patient is the expected survival time he or she will experience regardless of the path undertaken.

This article introduces the use of a multi-state Semi-Markov process (SMP) model for calculating expected survival time at listing. The SMP abstracts the aforementioned events and consequences that a patient experiences during treatment. It incorporates risk-adjustments for relevant characteristics of transplant centers and OPOs in addition to standard criteria such as patient demographics and individual clinical factors (diagnoses, comorbidities, immunology, and functional status). Conditional on receiving a transplant, the model also adjusts for donor characteristics,

donor quality, and donor-recipient attributes. Using the model parameters, individual characteristics, potential donor characteristics, and OPO/transplant center characteristics, expected survival times are calculated. These estimates may aid patient decision making with respect to treatment or listing at a particular center.

As discussed below, a SMP is a stochastic process that generalizes continuous-time Markov chains and is used in multi-state time-to-event modeling[64,65]. The Concept section lays out the process modeling framework in a nontechnical manner and justifies the covariates used for the risk-adjustments. The Methods section and supplement summarize the mathematical model, distributional assumptions, expected survival calculations, data, and estimation. We provide results for risk-adjustments and provide example expected survival time calculations. The study population consists of all adult US kidney transplant candidates from January 2007 through December 2016 exclusive of those having prior transplants or requiring simultaneous/multiple transplants.

Concept

Multi-State Paradigm for a Waitlisted Patient

Figure 3.1 depicts an idealized, multi-state conception of the transplantation process from the waitlist candidate's perspective. Throughout this article, we maintain that the initial state is *Waitlisted* and motivate the work from the viewpoint of a newly listed kidney transplant candidate. Candidates are held to be on the waitlist for as long as they are accruing priority for transplantation. Although not shown in the figure, being waitlisted may be preceded by states describing chronic kidney disease progression into ESRD. Patients may alternately transition between inactivity and being waitlisted. A waitlisted patient may then receive a transplant, die, or be removed from the waitlist

for another reason (e.g. their condition improves). Transplanted recipients may experience graft failure and re-list (i.e. transition again to *Waitlisted*) or perhaps die. *Death* is as an absorbing state – once a candidate enters an absorbing state, he or she does not transition to other states. All other states are known as transient states.

The complexity of the model in Figure 3.1 can make estimation and mathematical analysis more difficult. Because data on patients experiencing less common transitions (e.g. a removed patient whose condition first improves but then subsequently dies) are scarce, we make the following conventions and simplifying assumptions to create a process model with unidirectional transitions and a sole absorbing state (*Death*):

1. The *Waitlist* state does not distinguish among inactive or active candidates. Time spent on the waitlist includes any time spent inactive (Convention).
2. Patients receiving a transplant are assumed to neither re-list nor receive a re-transplant (Assumption 1).
3. Waitlisted patients who are removed because they became medically unsuitable for transplantation or too sick to transplant are assumed to die (Assumption 2).

Figure 3.2 depicts the simplified modeling framework that we hereafter refer to almost exclusively. Since approximately only 13% (ca. 1990-2000) of transplant recipients need re-transplantation in practice, the model should apply to the majority of candidates [66]. Moreover, the state diagram shown in Figure 3.2 is equivalent to that of the Illness-Death model used in the multi-state modeling and epidemiological literature [64,67]. Competing risks models are also multi-state models whereby a single state may have several transitions to multiple different states [64]. This is for instance useful to model patients that are only in the *Waitlisted* state [63,68], but with the disadvantage that

subsequent transitions from the *Transplanted* state to *Death* (i.e. post-transplant survival) cannot be easily included to calculate the overall survival time.

The Semi-Markov Process Model for Waitlisted Patients

When in a particular transient state i before leaving for a state j, the amount of time a patient spends in state i is known as the sojourn time for state i given the following state j. For example, the sojourn time for the *Transplanted* state (the following state is *Death*) represents post-transplant survival time. The amount of time a patient spends in the initial state is known as the initial sojourn time, i.e. the amount of time the patient spends on the waitlist before transplantation or death. This sojourn time does not represent just waitlist survival time, as a patient on the waitlist may receive a transplant, thereby transitioning to the *Transplanted* state before dying. In fact, the notion of waitlist survival is somewhat ambiguous in the multi-state paradigm as two different pathways to death are possible and is partly the reason why competing events and multi-state time-to-event models must be considered. Sojourn times for each particular state i given the following state j may be nonnegative random variables with known distributions.

Markov processes, particularly discrete- and continuous-time Markov chains have the property that the likelihood of transitioning into state j from state i only depends on the fact that a patient is at state i at the given moment and not which states the patient was in previously or for how long – that is, the likelihood of transitioning into state j from state i does not depend on the patient's history. Imposing this requirement on the modeling framework would force all sojourn times to have exponential distributions.

Moreover, due to the memoryless property of exponential distributions, the hazard of time spent in state i before entering state j remains constant over time.

The Markov requirement is untenable. Hazards for each transition that are not constant over time are plausible and alone suffice to invalidate the assumption. For example, given that the patient is waitlisted, the hazard of entering the *Transplanted* state ought to increase with time, as OPTN policies and procedures increasingly prioritize patients who have waited longer [57]; moreover, the possibility of accelerated failure due to protracted time on dialysis or to aging challenges the assumption that transitions from either the *Waitlisted* or *Transplantation* states to *Death* have constant hazard [69,70].

At a cost of additional complexity, (time-homogenous) SMPs, also known as clock-reset models, relax the exponential property of Markov chains. While allowing for sojourn times with varying distributions and hazards for each transition, they maintain that the likelihood of transitioning into a state j depends only on the current state *at the time of transition* (hence the name Semi-Markov)[71,72]. The intuition for a SMP is as follows: a patient first enters state i and chooses to transition to some state j with probability p_{ij}. Knowing that the patient will transition to j from i, he or she will then spend a random amount of time (sojourn time) in state i that follows some probability distribution F_{ij} (e.g. exponential, Weibull, etc.). The sojourn time for each transition is governed by such a probability distribution. When the patient then enters the new state j, the clock or process resets. He or she is assigned the next state k with some probability p_{jk}, and stays in state j for a time governed by the sojourn time distribution F_{jk}. In the context of Figure 1, this means a newly listed patient may be

thought of as being assigned to a transplant or death at the outset. If the latter, the patient awaits death for a random amount of time; if the former, the patient waits for a transplant for a random amount of time, transitions to the *Transplanted* state whence the next state is chosen with some probability (here *Death* with probability 1). The patient then dies after a random amount of time (post-transplant survival).

Expected Survival Time

For newly listed patients, of particular interest is the expected amount of time that will elapse before death. The absorption time is the amount of time a patient starting in the initial state (*Waitlisted*) takes to reach an absorbing state (*Death*). The absorption time is agnostic towards the specific pathway (i.e. whether dying on the waitlist or after transplant) taken and provides an informative, prognostic assessment for individuals who are uncertain about their survival time.

Risk-Adjustments for the Transitions

For each transition (*Waitlisted -> Death, Transplanted->Death,* and *Waitlisted ->Transplanted*) we consider three classes of risk-adjustments: candidate characteristics, donor-recipient characteristics, and transplant center/OPO characteristics. The risk-adjustments indicate the relative hazard of undergoing each transition relative to the baseline. Relative risk estimates for any transition to death provide mortality hazards and estimates for the *Waitlisted ->Transplanted* transition correspond to the hazard of receiving a graft whereby the failure event is kidney transplantation.

Candidate characteristics are included as risk-adjustments for all 3 transitions. Competing risks studies of waitlist mortality and risk-modeling by the Scientific Registry

of Transplant Recipients for post-transplant survival have already identified several variables for the 2 transitions leading to death [63,68,73]. Among them we selected age, gender, ethnicity, serum albumin, calculated panel reactive antibodies (both at listing and the most recent value while on the waitlist), BMI at listing, history of diabetes, peripheral vascular disease, any previous malignancy, and the diagnosis for kidney transplant. Functional status at listing has garnered interest recently for being a significant predictor of mortality and was also added [74]. We also included the urban/rural status of the patient. Rural patients are defined as patients residing in a zip code not contained in a US metropolitan statistical area. Commonly observed disparities in access to transplantation based on ethnicity or rural status may affect the transitions from the *Waitlisted* state to the *Transplanted* state. For instance, Axelrod et al demonstrated that candidates living in rural areas have reduced access to timely transplantation despite not having different outcomes than urban candidates [49] Vranic et al showed waiting time (i.e. sojourn time) disparities among different racial groups [75].

Donor and donor-recipient characteristics are included as risk-adjustments for the *Transplanted->Death* transition. These characteristics arise mainly from post-transplant survival modeling, and include donor age, donor creatinine, whether the donor ABO blood type is identical to the recipient, the number of DR and HLA mismatches, and the kidney donor profile index (KDPI). The KDPI is a risk-score ranging from 0-100 that indicates donor quality with higher scores indicating inferior quality [76]. It is based on donor characteristics: age; height; weight; ethnicity; histories of hypertension and diabetes; cause of death, serum creatinine, Hepatitis C status, and the status of donation after circulatory death. We also include the recipient's functional

status at the time of transplant. These characteristics are exclusive to post-transplant survival and may not be known to the patient at listing. In such cases, these risk-adjustments may be fixed to the baseline or the average for that patient's transplant center or OPO when calculating expected survival times.

Studies have identified independent OPO and transplant center "effects" on patient survival and OPTN performance [77-79]. The OPO effect marks the structural influence of the allocation system on the patient, as OPOs with diverse average waiting times and transplant volumes signify variation in the times patients must wait for an organ, and hence affect their hazard of entering the *Transplanted* or *Death* states from the waitlist. In contrast to the OPO effect, the influence of transplant centers can be better described as endemic rather than structural. Notwithstanding activities undertaken to increase organ donation, OPOs mainly perform as suppliers of a fixed resource, whereas transplant centers can be more responsive to the volume and the quality of the donors they accept from their OPO and even to the patients that they list. Thus, differences in transplant center volumes and waiting times could also indicate differences in practices, willingness to treat particular patients, and resources. Additionally, transplant centers must compete with each other for their volumes. Therefore, following previous work [77-79], we include the waiting times (averages) and transplant volumes for the patient's OPO and transplant center in the risk-adjustments. We account for transplant center competition by including the number of transplant centers in the OPO in each patient's risk adjustment. Additionally, following Davis et al [77], we also included the Herfindahl-Hirschman index (HHI) of the patient's OPO, which

was calculated using the transplant centers in the OPO and their transplant volumes over the study period.

Methods

Modeling:

Multi-state survival modeling with SMPs is an established topic. The supplement provides the technical details for how the SMP is modeled; how the risk-adjustments are incorporated; and how both mean sojourn and absorption (i.e. survival) times are calculated. More detailed information about the theory of SMPs and similar stochastic processes, including competing risks and multiple-event survival models, are available in the references [64,65,71,72,80].

We assume that the probability distributions describing the sojourn times for each transition follow a Weibull distribution with respective shape and scale parameters (Assumption 3). The Weibull family is useful for a few reasons. First, it is a flexible family that allows for incorporation of risks with monotonic hazards. Second, the Weibull distribution is one of the families of distributions that satisfy both the accelerated failure and proportional hazards paradigms. Third, parametric models for survival after kidney transplant and time-to-transplant using the Weibull distribution have been used previously [70,81].

We incorporate the risk-adjustments and estimate the SMP using Cox Semi-Markov models for each transition [65]. Cox Semi-Markov models entail fitting Weibull proportional hazards models for each transition where the dependent variables are the censored times to the failure events of interest (death or transplantation). We subsequently obtain coefficients for the risk adjustments, scale parameters, and shape

parameters for each transition. Following the proportional hazards assumption on sojourn times from the risk-adjustments (Assumption 4), we calculate individualized expected survival times. The details of these calculations are also included in the appendix.

Data:

Data on all listed adult renal transplant candidates and organ donors in the US were provided by the United Network for Organ Sharing for January 2007 through December 2016 with updated statuses as of March 2017. We considered all adult candidates listed for a deceased-donor kidney transplant that had no previous transplants nor required multiple transplants.

Estimation of the SMP transition probabilities and Cox Semi-Markov models were performed using SAS 9.4 [44]. 95% confidence intervals for the shape parameters were used to assess the appropriateness of exponential distributions for the sojourn times. Goodness of fit was assessed by comparison of the fitted and unfitted model AICs.

Individualized Survival Time Calculations:

As an example, we consider a hypothetical patient profile – a 65-year old, rural, highly sensitized patient with diabetes and peripheral vascular disease. We calculate overall expected survival time, expected time to death on the waitlist conditional on waitlist mortality, and expected post-transplant survival and time-to-transplant conditional on transplantation. Moreover, we consider scenarios where this patient is choosing among a low-volume transplant center with negligible waiting time; a high-volume transplant center with a mean waiting time of 730 days; a high-volume

transplant center that is the only center in the OPO with a mean waiting time of 730 days; and a high-volume transplant center with a mean waiting time of 730 days where the patient is assumed to receive a 95+ KDPI transplant.

Results

Table 3.1 summarizes the individual characteristics of the candidates used in the study (N=306,356). Each subsection below summarizes the findings and provides some context thereof.

Semi Markov Process Parameters:

Table 3.2 presents the estimated transition probabilities and distributional fits. According to the model, a candidate at listing has an overall chance of 70.4% of ever receiving a graft and a 29.6% chance of dying on the waitlist (or being removed due to medical unsuitability or because he or she has become too sick to transplant). The confidence intervals for Weibull shape parameter estimates reject the hypothesis that time-to-transplantation or time-to-death while on the waitlist has an exponential distribution at 5% significance, hence confirming that the Markov assumption was indeed inappropriate. We did not reject that post-transplant survival time was exponentially distributed (i.e. confidence interval for respective shape parameter includes unity).

Risk-Adjustments for Transition from Waitlisted to Transplanted:

Table 3.3 presents the risk-adjustments for patients transitioning from *Waitlisted* to *Transplanted*. A positive coefficient indicates a higher hazard of receiving a graft relative to baseline (and hence shorter waiting time or time-to-transplantation). All estimates are statistically significant ($p < 0.05$). Higher initial CPRA scores and not

having blood type O decrease the risk of not receiving a graft. Moreover, patients aged 35-65 have lower chances of being transplanted and patients aged 60 or over have a greater chance relative to the baseline. Candidates with reduced functional status or not having diabetes are also more likely to receive a graft. Non-white or rural candidates have lower chances of receiving a graft, which is consistent with a previous study [49]. Candidates listing in OPOs with greater transplant volumes or longer waiting times experience increased chances of receiving a graft, but these effects are reversed at the transplant-center level. Transplant centers with lower volumes or shorter average waiting times reduced time-to-transplantation.

Risk-Adjustments for Transition from Waitlisted to Death:

Table 3.4 presents the risk-adjustments for patients transitioning from *Waitlisted* to *Death*. A positive coefficient indicates a higher mortality hazard relative to baseline (and hence shorter survival time). The diagnosis categories were omitted for model stability. Most of the estimates are statistically significant ($p < 0.05$) except for OPO waiting time, ABO blood type B, or for some of the ethnicities. Also, rural patients exhibited higher mortality risk. Otherwise, interpretations of the remaining estimates are consistent with clinical expectations except for BMI at listing; lower serum albumin levels, higher CPRAs, greater age, being male, having reduced functional status, and having peripheral vascular disease are all correlated with increased mortality risk.

Those listing at OPOs with higher volumes or at transplant centers with longer waiting times experience greater risk. Patients at centers with higher volume also exhibit increased risk, but this could be indicative of the larger, more varied populations high-

volume centers may perhaps serve. Increased concentration of transplant volume via less transplant centers are also linked to increased mortality risk.

Risk-Adjustments for Transition from Transplanted to Death:

Table 3.5 presents the risk-adjustments for patients transitioning from *Transplanted* to *Death*. A positive coefficient indicates a higher mortality hazard relative to baseline (and hence shorter post-transplant survival time). Most of the estimates are statistically significant ($p < 0.05$) except for initial CPRA, rural status, ABO blood type, functional status at listing, some ethnicity and donor age categories, and the number of DR mismatches. The non-significance of rural status is notable and consistent with Axelrod et al [49], as access to transplantation may be less relevant after transplantation. All transplant center and OPO characteristics were not statistically significant except transplant center volume, with higher volumes linked to reduced mortality. Otherwise, interpretations of the remaining estimates are consistent with expectations. Lower serum albumin levels, higher recent CPRAs, greater recipient age, being male, diabetes, having reduced functional status at the time of transplant, having peripheral vascular disease or previous malignancy are all correlated with increased mortality risk as expected. Moreover, increased HLA mismatches, donor age, recipient-donor ABO incompatibility, and higher KDPI scores also increase mortality risk as expected.

Expected Survival Times at Listing:

Table 3.6 provides example calculations using the SMP for the hypothetical patient profile. The patient faces greater waitlist mortality or time-to-transplantation at transplant centers with extended waiting times and volumes. If it is known that the patient will accept a 95+ KDPI organ, post-transplant survival is subsequently adjusted

(reduced in Table 3.6). The overall survival time is adjusted based on all of the information provided as well. Computations for other profiles are possible, and a spreadsheet calculator is available from the authors upon request.

Discussion

Factors such as increased age, comorbidities and sensitization, usually led to higher mortality risk as expected. Similarly, reduced donor quality and functional status also heightened mortality risk after transplant. Moreover, factors such as ABO blood type and sensitization, which are explicitly accounted for in OPTN guidelines in prioritizing patients for transplantation [57], also affect transplantation hazard in an intuitive manner. OPO adjustments for waiting time and transplant volume tended to have the opposite signs of their transplant center counterparts. This is perhaps suggestive of some attendant response of transplant centers to their environments. Only transplant center volume affected post-transplant survival with greater volumes leading to reduced mortality. This could reflect the greater resources of larger transplant centers and their improved performance by having additional opportunities for learning-by-doing. OPOs with increased concentration of transplant volumes with higher HHI or a fewer number of transplant centers also increased the rate at which patients are transplanted, possibly indicating that transplant centers are better at exerting influence within the OPO and obtaining organs when competition is lacking.

The risk-adjusted calculations herein facilitate individualized decision making by conferring a prognostic measurement of overall expected survival time and time-to-transplantation. This information may be deployed in two ways: 1) assessments of potential outcomes for listing in particular OPO or transplant center, possibly through a

Web tool or United Network for Organ Sharing information technology systems; and 2) identification at listing of specialized donor criteria for the patient (e.g. acceptability of KDPI 85+ organs; suitability of living donors; etc.). Lastly, the methodology of this article can be specialized to subpopulations (e.g. pediatric) or translated to other forms of transplantation (e.g. liver).

This work has a few limitations. First, while considering the bulk of a transplant candidate's experience, we made simplifying assumptions about patient removals and inactivity that warrant greater examination. Second, some of the estimates, especially the expected survival times, need to be interpreted with caution when extrapolating beyond the study period and accuracy is subject to that of the regression models. Lastly, while the SMP employed herein is a general stochastic process that perhaps captures the most salient aspects of the transplantation process, the appropriateness of the distributional assumptions and even the Semi-Markov property itself may be further challenged.

Acknowledgements

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Tables

Table 3.1: Study Population Patient Characteristics (N=306,356)[1]

Category	Value	N	%
Gender			
	Female	118,052	38.53
	Male	188,304	61.47
Ethnicity			
	White	137,127	44.76
	Black	89,353	29.17
	Hispanic	52,969	17.29
	Asian	20,889	6.82
	American Indian/Alaska Native	2,980	0.97
	Native Hawaiian/Pacific Islander	1,354	0.44
	Multiracial	1,684	0.55
Age at Listing			
	18-34	34,731	11.34
	35-44	46,994	15.34
	45-54	75,852	24.76
	55-64	93,407	30.49
	>65	55,372	18.07
Diabetes			
	No Diabetes	164,938	54.19
	Type I	19,620	6.45
	Type II	113,459	37.28
	Other Type	2,377	0.78
	Type Uknown	3,976	1.31
	Missing	1,986	
Diagnosis for Transplant			
	IGA Nephropathy	6,052	5.36
	Focal Golumerular Sclerosis	7,494	6.64
	Polycistic Kidneys	11,418	10.12
	Hypertensive Nephrosclerosis	25,289	22.42
	Diabetes Mellitus Type II	26,493	23.48
	Other	36,068	31.97
	Not reported/uknown	193,542	
Functional Status at Listing	10% - Moribund, fatal processes progressing rapidly	250	0.08
	20% - Very sick, hospitalization necessary: active treatment necessa	1,777	0.58
	30% - Severely disabled: hospitalization is indicated, death not imm	934	0.31
	40% - Disabled: requires special care and assistance	3,442	1.13
	50% - Requires considerable assistance and frequent medical care	7,005	2.29
	60% - Requires occasional assistance but is able to care for needs	18,054	5.91
	70% - Cares for self: unable to carry on normal activity or active wo	61,194	20.02
	80% - Normal activity with effort: some symptoms of disease	85,134	27.86
	90% - Able to carry on normal activity: minor symptoms of disease	77,522	25.37
	100% - Normal, no complaints, no evidence of disease	35,459	11.60
	Not reported/unknown	15,585	
Peripheral Vascular Disease	No	280,687	91.86
	Unknown	6,170	2.02
	Yes	18,707	6.12
	Missing	792	
ABO	A	99,786	32.57
	AB	11,526	3.76
	B	45,635	14.90
	O	149,409	48.77
Residence	Urban	259,217	85.09
	Rural	45,429	14.91
	Missing	1,710	
Calculated Panel Reactive Antibodies at Listing, [mean (standard deviation)]	3.92 (16.15)		
Last Known Panel Reactive Antibodies, [mean (standard deviation)]	14.09 (28.38)		

[1]The sample includes adult kidney transplant candidates from Jan 2007-Dec 2016 excluding previous or multiple transplant candidates. Percentages do not include missing values and may not sum to 100 due to rounding.

Table 3.2: Estimated Semi-Markov Process Model Parameters

Parameter	Transition	Coefficient	SE	95% CI	
Log(Scale) Parameters					
	Waitlisted -> Transplanted	4.80	0.05	4.71	4.90
	Waitlisted -> Death	8.05	0.07	7.92	8.18
	Transplanted -> Death	9.35	0.16	9.03	9.67
Shape Parameters					
	Waitlisted -> Transplanted	0.93	0.003	0.92	0.93
	Waitlisted -> Death	1.06	0.004	1.06	1.07
	Transplanted -> Death	0.9972	0.009	0.98	1.02
Transition Probabilities					
	Waitlisted -> Transplanted	0.704	0.001	---	---
	Waitlisted -> Death	0.296	---	---	---
	Transplanted -> Death	1.000	---	---	---
Goodness of Fit		AIC (no covariates)	AIC (covariates)		
	Waitlisted -> Transplanted	519311.3	344987		
	Waitlisted -> Death	237941.5	220587.8		
	Transplanted -> Death	69918.7	64771.98		

Table 3.3: Estimated Risk-Adjustments for Transition from Waitlist to Transplant

Category	Coefficient	SE	Chi-Square	P-Value
Serum Albumin Level at Listing	-0.082	0.006	172.27	<.0001
Calculated Panel Reactive Antibodies at Listing [0-100]	0.003300	0.000300	165.57	<.0001
Calculated Panel Reactive Antibodies (Last Known) [0-100]	-0.003500	0.000200	504.67	<.0001
BMI at Listing	-0.012000	0.000700	311.05	<.0001
Residence in Urban Zip Code	Reference			
Residence in Rural Zip Code	-0.024	0.010	5.55	0.018
OPO 10-year transplant volume (number of organs '000s)	0.025	0.004	38.080	<.0001
OPO mean waiting time for transplant (days)	0.0002	0.0001	11.310	0.001
Transplant center 10-year transplant volume (number of organs '000s)	-0.018	0.007	6.660	0.010
Transplant center mean waiting time for transplant (days)	-0.002	0.000	1812.80	<.0001
Transplant center HHI Index [0-1]	0.087	0.025	12.09	0.001
Number of transplant centers in the OPO	-0.006	0.002	9.11	0.003
Age at listing 18-34 years	Reference			
Age at listing 35-44 years	-0.096	0.013	53.15	<.0001
Age at listing 45-54 years	-0.096	0.013	58.80	<.0001
Age at listing 55-64 years	-0.080	0.012	41.15	<.0001
Age at listing ≥ 65 years	0.029	0.014	4.30	0.038
Male	Reference			
Female	0.034	0.008	18.63	<.0001
ABO = O	Reference			
ABO = A	0.171	0.008	462.90	<.0001
ABO = B	0.033	0.011	8.55	0.004
ABO = AB	0.433	0.016	713.44	<.0001
Functional Status at listing is 10% - Moribund, fatal processes progressing rapidly	2.128	0.124	292.90	<.0001
Functional Status at listing is 20% - Very sick, hospitalization necessary: active treatment necessary	2.636	0.040	4429.62	<.0001
Functional Status at listing is 30% - Severely disabled: hospitalization is indicated, death not imminent	2.292	0.054	1814.78	<.0001
Functional Status at listing is 40% - Disabled: requires special care and assistance	0.481	0.035	194.27	<.0001
Functional Status at listing is 50% - Requires considerable assistance and frequent medical care	0.306	0.026	137.56	<.0001
Functional Status at listing is 60% - Requires occasional assistance but is able to care for needs	0.163	0.018	82.50	<.0001
Functional Status at listing is 70% - Cares for self: unable to carry on normal activity or active work	0.084	0.013	44.28	<.0001
Functional Status at listing is 80% - Normal activity with effort: some symptoms of disease	0.075	0.012	40.95	<.0001
Functional Status at listing is 90% - Able to carry on normal activity: minor symptoms of disease	0.058	0.012	24.43	<.0001
Functional Status at listing is 100% - Normal, no complaints, no evidence of disease	Reference			
Patient has history of diabetes	Reference			
Patient does not have history of diabetes	0.181	0.012	239.23	<.0001
White	Reference			
Black	-0.312	0.009	1102.61	<.0001
Hispanic	-0.172	0.011	244.92	<.0001
Asian	-0.294	0.016	324.01	<.0001
Native American, Native Hawaiian, or Pacific Islander	-0.214	0.034	40.81	<.0001
Patient does not have peripheral vascular disease	Reference			
Patient has peripheral vascular disease	-0.076	0.015	26.54	<.0001
Patient has no history of malignancy	Reference			
Patient has history of malignancy	0.065	0.014	22.95	<.0001
Diagnosis for transplant is other	Reference			
Diagnosis for transplant is unknown	-3.871	0.018	46247.30	<.0001
Diagnosis for transplant is IGA NEPHROPATHY	0.039	0.017	5.03	0.025
Diagnosis for transplant is FOCAL GLOMERULAR SCLEROSIS	-0.042	0.016	7.20	0.007
Diagnosis for transplant is POLYCYSTIC KIDNEYS	-0.115	0.014	69.78	<.0001
Diagnosis for transplant is HYPERTENSIVE NEPHROSCLEROSIS	-0.072	0.011	43.99	<.0001
Diagnosis for transplant is DIABETES MELLITUS - TYPE II	0.067	0.014	23.79	<.0001

Table 3.4: Estimated Risk-Adjustments for Transition from Waitlist to Death

Category	Coefficient	SE	Chi-Square	P-Value
Serum Albumin Level at Listing	-0.328	0.008	1588.10	<.0001
Calculated Panel Reactive Antibodies at Listing [0-100]	0.001000	0.000300	8.79	0.003
Calculated Panel Reactive Antibodies (Last Known) [0-100]	0.000500	0.000200	8.04	0.005
BMI at Listing	-0.004700	0.000900	26.42	<.0001
Residence in Urban Zip Code	Reference			
Residence in Rural Zip Code	0.028	0.014	4.24	0.040
OPO 10-year transplant volume (number of organs '000s)	0.016	0.005	9.480	0.002
OPO mean waiting time for transplant (days)	-0.00001	0.00008	0.010	0.929
Transplant center 10-year transplant volume (number of organs '000s)	0.089	0.009	100.640	<.0001
Transplant center mean waiting time for transplant (days)	0.001	0.000	69.70	<.0001
Transplant center HHI Index [0-1]	-0.090	0.035	6.51	0.011
Number of transplant centers in the OPO	-0.012	0.002	25.04	<.0001
Age at listing 18-34 years	Reference			
Age at listing 35-44 years	0.306	0.029	110.09	<.0001
Age at listing 45-54 years	0.721	0.027	739.31	<.0001
Age at listing 55-64 years	1.070	0.026	1713.91	<.0001
Age at listing $\geq$ 65 years	1.397	0.026	2809.63	<.0001
Male	Reference			
Female	-0.095	0.011	80.52	<.0001
ABO = O	Reference			
ABO = A	-0.067	0.011	37.39	<.0001
ABO = B	-0.003	0.014	0.05	0.821
ABO = AB	-0.113	0.029	15.56	<.0001
Functional Status at listing is 10% - Moribund, fatal processes progressing rapidly	2.428	0.095	660.95	<.0001
Functional Status at listing is 20% - Very sick, hospitalization necessary: active treatment necessary	2.065	0.043	2294.67	<.0001
Functional Status at listing is 30% - Severely disabled: hospitalization is indicated, death not imminent	1.699	0.059	843.58	<.0001
Functional Status at listing is 40% - Disabled: requires special care and assistance	0.736	0.040	342.28	<.0001
Functional Status at listing is 50% - Requires considerable assistance and frequent medical care	0.608	0.028	460.13	<.0001
Functional Status at listing is 60% - Requires occasional assistance but is able to care for needs	0.428	0.022	394.37	<.0001
Functional Status at listing is 70% - Cares for self: unable to carry on normal activity or active work	0.289	0.016	318.22	<.0001
Functional Status at listing is 80% - Normal activity with effort: some symptoms of disease	0.109	0.016	47.41	<.0001
Functional Status at listing is 90% - Able to carry on normal activity: minor symptoms of disease	-0.012	0.016	0.57	0.450
Functional Status at listing is 100% - Normal, no complaints, no evidence of disease	Reference			
Patient has history of diabetes	Reference			
Patient does not have history of diabetes	-0.455	0.011	1785.26	<.0001
White	Reference			
Black	-0.015	0.012	1.72	0.190
Hispanic	-0.077	0.014	29.92	<.0001
Asian	-0.236	0.023	110.27	<.0001
Native American, Native Hawaiian, or Pacific Islander	0.012	0.038	0.10	0.754
Patient does not have peripheral vascular disease	Reference			
Patient has peripheral vascular disease	0.122	0.017	53.25	<.0001
Patient has no history of malignancy	Reference			
Patient has history of malignancy[1]	---	---	---	---
Diagnosis for transplant is other	Reference			
Diagnosis for transplant is unknown[1]	---	---	---	---
Diagnosis for transplant is IGA NEPHROPATHY[1]	---	---	---	---
Diagnosis for transplant is FOCAL GLOMERULAR SCLEROSIS[1]	---	---	---	---
Diagnosis for transplant is POLYCYSTIC KIDNEYS[1]	---	---	---	---
Diagnosis for transplant is HYPERTENSIVE NEPHROSCLEROSIS[1]	---	---	---	---
Diagnosis for transplant is DIABETES MELLITUS - TYPE II[1]	---	---	---	---

[1]Omitted for numerical stability

Table 3.5: Estimated Risk-Adjustments for Transition from Transplant to Death

Category	Coefficient	SE	Chi-Square	P-Value
Serum Albumin Level at Listing	-0.181	0.019	94.81	<.0001
Calculated Panel Reactive Antibodies at Listing [0-100]	-0.000800	0.000900	0.79	0.375
Calculated Panel Reactive Antibodies (Last Known) [0-100]	0.002700	0.000500	28.36	<.0001
BMI at Listing	-0.005300	0.002200	5.82	0.016
Residence in Urban Zip Code	Reference			
Residence in Rural Zip Code	0.042	0.029	2.03	0.154
OPO 10-year transplant volume (number of organs '000s)	0.021	0.013	2.870	0.090
OPO mean waiting time for transplant (days)	-0.00030	0.00020	1.770	0.183
Transplant center 10-year transplant volume (number of organs '000s)	-0.055	0.022	6.230	0.013
Transplant center mean waiting time for transplant (days)	-0.0002	0.0001	1.82	0.178
Transplant center HHI Index [0-1]	0.037	0.078	0.22	0.640
Number of transplant centers in the OPO	0.003	0.006	0.16	0.690
Age at listing 18-34 years	Reference			
Age at listing 35-44 years	0.354	0.068	26.95	<.0001
Age at listing 45-54 years	0.608	0.062	96.82	<.0001
Age at listing 55-64 years	1.024	0.060	288.25	<.0001
Age at listing ≥ 65 years	1.446	0.062	541.10	<.0001
Male	Reference			
Female	-0.167	0.025	45.63	<.0001
ABO = O	Reference			
ABO = A	0.025	0.025	1.04	0.307
ABO = B	0.009	0.036	0.06	0.809
ABO = AB	-0.007	0.052	0.02	0.898
Functional Status at listing is 10% - Moribund, fatal processes progressing rapidly	-0.174	0.302	0.33	0.565
Functional Status at listing is 20% - Very sick, hospitalization necessary: active treatment necessary	0.108	0.104	1.08	0.298
Functional Status at listing is 30% - Severely disabled: hospitalization is indicated, death not imminent	0.271	0.125	4.69	0.030
Functional Status at listing is 40% - Disabled: requires special care and assistance	0.225	0.101	5.02	0.025
Functional Status at listing is 50% - Requires considerable assistance and frequent medical care	0.180	0.076	5.68	0.017
Functional Status at listing is 60% - Requires occasional assistance but is able to care for needs	0.096	0.058	2.78	0.096
Functional Status at listing is 70% - Cares for self: unable to carry on normal activity or active work	0.056	0.043	1.65	0.199
Functional Status at listing is 80% - Normal activity with effort: some symptoms of disease	0.014	0.039	0.13	0.723
Functional Status at listing is 90% - Able to carry on normal activity: minor symptoms of disease	-0.039	0.039	1.01	0.316
Functional Status at listing is 100% - Normal, no complaints, no evidence of disease	Reference			
Patient has history of diabetes	Reference			
Patient does not have history of diabetes	-0.365	0.032	131.90	<.0001
White	Reference			
Black	-0.047	0.029	2.67	0.102
Hispanic	-0.325	0.038	74.16	<.0001
Asian	-0.409	0.060	46.63	<.0001
Native American, Native Hawaiian, or Pacific Islander	-0.192	0.107	3.23	0.072
Patient does not have peripheral vascular disease	Reference			
Patient has peripheral vascular disease	0.329	0.036	84.24	<.0001
Patient has no history of malignancy	Reference			
Patient has history of malignancy	0.140	0.035	15.77	<.0001
Diagnosis for transplant is other	Reference			
Diagnosis for transplant is unknown	0.098	0.048	4.13	0.042
Diagnosis for transplant is IGA NEPHROPATHY	-0.770	0.093	68.13	<.0001
Diagnosis for transplant is FOCAL GLOMERULAR SCLEROSIS	-0.174	0.061	8.21	0.004
Diagnosis for transplant is POLYCYSTIC KIDNEYS	-0.498	0.055	82.23	<.0001
Diagnosis for transplant is HYPERTENSIVE NEPHROSCLEROSIS	0.049	0.034	2.05	0.152
Diagnosis for transplant is DIABETES MELLITUS - TYPE II	0.046	0.035	1.68	0.195

Table 3.5 (Continued): Estimated Risk-Adjustments for Transition from Transplant to Death

Category	Coefficient	SE	Chi-Square	P-Value
Number of DR mismatches ≥ 0	-0.002	0.024	0.00	0.949
Number of HLA mismatches ≥ 0	0.031400	0.010500	8.90	0.003
Donor creatnine level	0.070200	0.010100	47.83	<.0001
Donor age at listing 18-34 years	Reference			
Donor age at listing 35-44 years	-0.027	0.033	0.65	0.421
Donor age at listing 45-54 years	0.111	0.031	12.91	0.000
Donor age at listing 55-64 years	0.117	0.038	9.470	0.002
Donor age at listing ≥ 65 years	0.08020	0.06100	1.730	0.189
Functional Status at transplant (recipient) is 10% - Moribund, fatal processes progressing rapidly	1.674	0.148	127.150	<.0001
Functional Status at transplant (recipient) is 20% - Very sick, hospitalization necessary: active treatment necessary	1.075	0.096	125.82	<.0001
Functional Status at transplant (recipient) is 30% - Severely disabled: hospitalization is indicated, death not imminent	0.773	0.119	41.91	<.0001
Functional Status at transplant (recipient) is 40% - Disabled: requires special care and assistance	0.364	0.090	16.39	<.0001
Functional Status at transplant (recipient) is 50% - Requires considerable assistance and frequent medical care	0.555	0.071	61.01	<.0001
Functional Status at transplant (recipient) is 60% - Requires occasional assistance but is able to care for needs	0.332	0.055	36.28	<.0001
Functional Status at transplant (recipient) is 70% - Cares for self: unable to carry on normal activity or active work	0.267	0.045	35.75	<.0001
Functional Status at transplant (recipient) is 80% - Normal activity with effort: some symptoms of disease	0.132	0.041	10.25	0.001
Functional Status at transplant (recipient) is 90% - Able to carry on normal activity: minor symptoms of disease	0.020	0.043	0.22	0.640
Functional Status at transplant (recipient) is 100% - Normal, no complaints, no evidence of disease	Reference			
Donor and Recipient have the same ABO blood type	Reference			
Donor and Recipient do not have the same ABO blood type	-0.077	0.039	3.90	0.048
KDPI is 0- <70	Reference			
KDPI is 70- <85	0.286	0.037	60.84	<.0001
KDPI is 85- <95	0.414	0.045	84.37	<.0001
KDPI is 95 or greater	0.5622	0.0619	82.6	<.0001

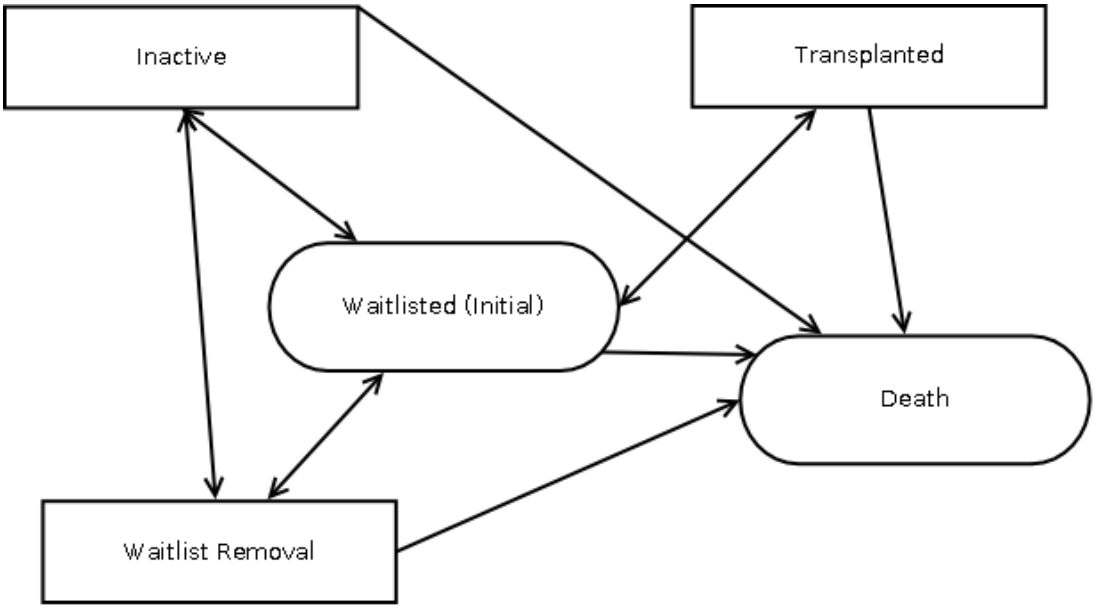
Table 3.6: Survival Time Calculations for Hypothetical Patient Profile

Hypothetical Patient Profile	Expected Time to Transplant[1]	Expected Time to Waitlist Mortality[2]	Expected Post-Transplant Survival Time[1]	Expected Absorption Time (Overall Survival Time)
65-year old rural patient, sensitized (most recent CPRA =50), peripheral vascular disease, diagnosis for transplant is diabetes, low-volume transplant center with negligible waiting time, other characteristics set to reference category or 0	153 days (0.42 years)	701 days (1.92 years)	1,549 days (4.24 years)	1,899 days (5.20 years)
65-year old rural patient, sensitized (most recent CPRA =50), peripheral vascular disease, diagnosis for transplant is diabetes, high-volume transplant center with mean waiting time of 730 days, other characteristics set to reference category or 0	710 days (1.94 years)	420 days (1.15 years)	2,004 days (5.49 years)	2,331 days (6.38 years)
65-year old rural patient, sensitized (most recent CPRA =50), peripheral vascular disease, diagnosis for transplant is diabetes, listed at only center in OPO at a high-volume transplant center, with mean waiting time of 730 days, other characteristics set to reference category or 0	650 days (1.78 years)	462 days (1.27 years)	1,926 days (5.27 years)	2,277 days (6.23 years)
65-year old rural patient, sensitized (most recent CPRA =50), peripheral vascular disease, diagnosis for transplant is diabetes, high-volume transplant center with mean waiting time of 730 days, patient will receive a KDPI 95+ transplant, other characteristics set to reference category or 0	710 days (1.94 years)	420 days (1.15 years)	1,140 days (3.12 years)	1,723 days (4.72 years)

[1]Conditional on receiving a transplant

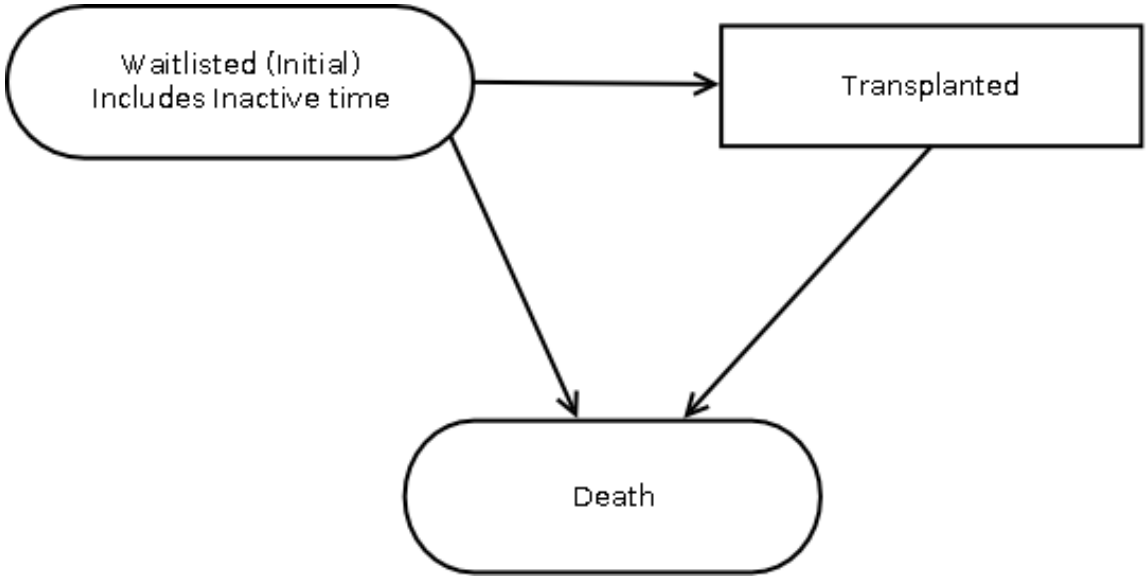
[2]Conditional on dying on the waitlist or being removed due to medically unsuitability or because too sick for transplant

Figure 3.1: Process Diagram of Candidates Listed for a Kidney Transplant



Candidates begin in the *Waitlisted* stated whence they can transition to the *Inactive, Waitlist Removal, Transplanted, or Death* states. From the *Transplanted* state candidates may transition to *Death* or re-list for a re-transplant. Candidates may also reenter the *Waitlisted* state and await transplantation after being inactive or temporarily removed. From any state, is possible to transition to *Death*.

Figure 3.2: Simplified Process Diagram Used in Study



Simplified diagram of the process shown in Figure 3.1. Time candidates spend being inactive is included during their time in the *Waitlisted* state. Removals from the waitlist due to medical unsuitability or from being too sick to transplant are considered deaths. Re-lists and re-transplants are also not considered, as indicated by the unidirectional arrows.

Supplement: Technical Methods

Multi-state survival modeling with SMPs is an established topic. For more detailed information about the theory of SMPs and similar stochastic processes, please consult the references [64,65,71,72,80]. Competing risks and multiple-event survival models are also referred to in this literature. Our brief presentation of the theory and estimation follows that of Krol and Saint-Pierre, although the notation has been altered [80].

Homogenous Semi Markov Process:

Consider a Markov renewal process (X_n, T_n) where $0 = T_0 < T_1 < T_2 < \cdots < T_n < \cdots < \infty$ and $n \in \mathbb{N}^*$denote the sequence of transition times. The sequence $X_1, X_2, \ldots, X_n, \ldots$ is the embedded, time-homogenous discrete-time Markov chain taking values over a finite state space with transition probabilities: $p_{ij} = \mathbb{P}(X_{k+1} = j | X_k = i)$. The state space being the *Waitlisted, Transplanted,* and *Death* states in Figure 2.

Define the SMP kernel function as $Q_{ij}(t) = \mathbb{P}(X_{k+1} = j, S_{k+1} \leq t | X_0, X_1, \ldots X_k = i, S_1.S_2 \ldots, S_k)$ where $S_k = T_k - T_{k-1}$ represents the k^{th} inter-arrival time $(k \in \mathbb{N})$. Moreover, from the Semi-Markov property we have that $Q_{ij}(t) = \mathbb{P}(X_{k+1} = j, S_{k+1} \leq t | X_k = i)$. A SMP is defined as $X_{Y(t)}$ where $Y(t) = \sup(n \in \mathbb{N} \mid T_n \leq t, t \in \mathbb{R}_+)$.

Suppose that given a state i and a following state j the distribution for the sojourn time for the transition is $F_{ij}(t)$. The following relates sojourn times, the SMP kernel function, and transition probabilities of the embedded discrete-time Markov chain:

$$F_{ij}(t) = \mathbb{P}(S_{n+1} \leq t | X_n = i, X_{n+1} = j) = \frac{Q_{ij}(t)}{p_{ij}}$$

Note that the sojourn time distributions do not depend on n, but do depend on the time elapsed since the previous state, the previous state, and the following state (this is

known as a homogenous SMP). Moreover, we define $\lambda_{ij}(t)$ to be the hazard function associated with the sojourn time distribution for transitions from state i to j (this notation differs from [80], where λ is used to refer to the related SMP transition-hazard rate and α to the sojourn time hazard rate.)

Cox Proportional Hazards Semi-Markov Models with Weibull Sojourn Times:

Given prior knowledge of the probability distributions describing the sojourn times for each transition, we can estimate the aforementioned transition probabilities and the parameters describing the shape and scale of the distributions. We now introduce the following assumption:

1. For each ordered pair of states i and j we require that the sojourn time for the corresponding transition be distributed Weibull with scale parameter $\sigma_{ij} > 0$ and shape parameter $\nu_{ij} > 0$ (Assumption 3). That is, the hazard function for the sojourn time distribution for transitions from state i to j may be written as:

$$\lambda_{ij}(t) = \frac{\nu_{ij}}{\sigma_{ij}}\left(\frac{t}{\sigma_{ij}}\right)^{\nu_{ij}-1}$$

The Weibull family is useful for a few reasons. First, it is a flexible family that allows for incorporation of risks with monotonic hazards. Second, the Weibull distribution is one of the families of distributions that satisfy both the accelerated failure and proportional hazards paradigms. Third, parametric models for survival after kidney transplant and time to transplant using the Weibull distribution have been used previously [70,81]. Lastly, a notable special case is when $\nu_{ij} = 1$, which corresponds to the exponential distribution with scale parameter σ_{ij}. In the unlikely case that all sojourn distributions are indeed exponential and are independent of the following state, the SMP can be reduced to a

continuous-time Markov chain. We estimate the shape and scale parameters for each transition

The risk-adjustments and any covariates that are thought to affect the sojourn times for each transition may also be incorporated into the framework with the assumption of proportional hazards (Assumption 4)[80]. Let $\boldsymbol{z}_{ij}$ be a vector of covariates for the corresponding transition and $\boldsymbol{\beta}_{ij}$ be the vector of regression coefficients describing relative risk. Covariates and risk-adjustments may differ for each transition. If $\lambda_{ij}(t)$ is understood as the baseline hazard for sojourn time given state i and entering state j, then the hazard rate may be written as:

$$\tilde{\lambda}_{ij}\left(t|\,\boldsymbol{z}_{ij}\right) = \lambda_{ij}(t)\exp\left(\boldsymbol{\beta}_{ij}{}'\boldsymbol{z}_{ij}\right), \qquad t \geq 0, i \neq j$$

Joint estimation of all the parameters in the multi-state model can be cumbersome with large datasets; so we estimate the SMP using Cox Semi-Markov models for each transition [65]. For each transition, we fit a parametric Weibull survival model where the dependent variable is the censored time to the failure event of interest (death or transplantation) and obtain estimates of the respective scale and shape parameters for that transition. Relative and baseline hazard estimates following the proportional hazards assumption are recovered from the model coefficients for each transition. The transition probabilities of the embedded discrete-time Markov Chain are calculated using the sample proportions of transitions from one state to the next.

Calculation of Mean Absorption Times:

The moments for absorption times of general SMPs can be complicated and require solving integral equations of the Laplace transformations for the sojourn times. However, for the special case with a single absorbing state, the computation is simpler.

Let 1,2,3 denote the *Waitlisted, Transplanted,* and *Death* states in the SMP respectively. Equation 1 yields the expected time until absorption:

$$Expected\ Absorption\ Time = p_{12}\ m_{12} + p_{13}\ m_{13} + p_{12}\ m_{23} \qquad (1)$$

The probabilities p_{kj} are the transition probabilities for the embedded discrete-time Markov chain. The values m_{kj} are the mean sojourn times for the transitions.

Given the Weibull parameterization, the mean sojourn times can be calculated analytically. For a Weibull distribution with scale parameter σ_{kj} and shape parameter ν_{kj}, Equation 2 computes the mean:

$$m_{kj} = \sigma_{kj}\Gamma\left(1 + \frac{1}{\nu_{kj}}\right) \qquad (2)$$

where $\Gamma(\cdot)$ is the gamma function. For calculating the mean sojourn times of a particular transition for a patient with any risk profile, consider a patient with transition-specific characteristics $\boldsymbol{z}_{kj}$ and let $c_{kj} = \exp(\boldsymbol{\beta}_{kj}{}'\boldsymbol{z}_{kj})$:

$$\tilde{\lambda}_{kj}(t) = c_{kj}\lambda_{kj}(t)$$

$$= c_{kj}\nu_{kj}{\sigma_{kj}}^{-\nu_{kj}}t^{\nu_{kj}-1}$$

$$\Longrightarrow \qquad \int_0^t c_{kj}\nu_{kj}{\sigma_{kj}}^{-\nu_{kj}}u^{\nu_{kj}-1}du = c_{kj}{\sigma_{kj}}^{-\nu_{kj}}t^{\nu_{kj}}$$

$$\Longrightarrow \qquad Expected\ Sojourn\ Time = \int_0^\infty exp\left(-c_{kj}{\sigma_{kj}}^{-\nu_{kj}}t^{\nu_{kj}}\right)dt$$

The last integral can be computed using Equation 2 by recognizing that it is the formula for the mean of a Weibull random variable with scale parameter ${c_{kj}}^{\frac{-1}{\nu_{kj}}}\sigma_{kj}$ and shape parameter ν_{kj}.

Evaluation of Accepting Kidneys of Varying Quality for Transplantation or Expedited Placement with Decision Trees

Over 20 million adult Americans suffer from some form of kidney disease [82]. When this condition progresses to End-Stage Renal Disease (ESRD), patients may receive renal replacement therapy through dialysis and/or seek a kidney for transplantation. Kidneys recovered from deceased donors are distributed by the Organ Procurement and Transplantation Network (OPTN). More than 90,000 patients are presently waiting to receive a kidney for transplant (KT)[83]. Outcomes, such as longevity, quality of life, morbidity, as well as cost are better for patients who receive a KT compared to those remaining on dialysis[61,62,84-87]. The need for kidney-organs is critical, given that only 18,598 adult and pediatric KTs occurred in 2015[88]. Surprisingly, hundreds of procured kidneys are discarded each year; 3,806 of the 14,637 kidneys recovered from adult deceased donors were discarded in 2015 [83]. In the same year, 4,981 patients died on the waitlist and 4,154 became too sick to transplant[88]. Such distressing figures compel reexamination of the decision-making for placing these organs.

The discard of a deceased-donor kidney is a potential result of the allocation process. The US is divided into 11 regions, each often a grouping of multiple states that are further subdivided into 58 Donor Service Areas (DSAs) [89]. Each DSA has a designated Organ Procurement Organization (OPO) that facilitates kidney allocation and kidney procurement within its locality. After an organ of adequate quality is recovered by an OPO, it is typically first offered to waitlisted patients within the DSA of procurement. If no recipient is found locally, the organ is offered to waitlist candidates within the same region followed by candidates waitlisted nationally. If no recipient is found, then the kidney is discarded[57]. At each step patients are ranked based on time on dialysis, sensitization, previous living kidney donation, and for potential

recipients of the highest-quality organs, estimated post-transplant survival[90]. Moreover, transplant centers and their patients may reject an offer for a KT, after which it will be offered to the next candidate. However, after actual procurement there is a limited time (0-48 hours) during which the kidney can be used and hence there is a practical limit on the number of offers that can be made. Extended ischemic times negatively impact patient outcomes after KT and thereby also affect the acceptability of a kidney once it is procured from the donor[91,92].

Causes for the Discards

Kidneys procured from deceased donors are not all of equal quality. The kidney quality presently measured and reported by the OPTN since December 2014 uses a prognostic score for kidney graft failure known as the Kidney Donor Profile Index (KDPI)[58]. The KDPI is based on donor characteristics including age, height, weight, ethnicity, hypertension status, diabetes status, Hepatitis C status, cause of death, and serum creatinine levels and ranges from 0 to 100. Higher KDPI scores signify lower kidney quality and hence worse potential graft outcomes[76]. For kidneys with KDPI 0-20, a longevity matching score estimating post-transplant survival and pediatric priority is used for allocation. For kidneys with KDPI 21-34, longevity matching and estimated post-transplant survival scores are not used, but pediatric candidates continue to receive priority. Allocation of organs with KDPI 35-85 follows the typical aforementioned sequence and organs with KDPI greater than 85 are initially offered both locally and to the region.

Deceased-donor kidneys that have been biopsied or have KDPI scores of 85 or greater exhibit significantly higher risk of discard (31.4% for biopsied kidneys and 59.1% of kidneys with KDPI 85+) relative to kidneys with KDPI scores of 0-85 (2.3-17.8%)[88]. However, there is established evidence that even high-KDPI organs confer substantial survival benefits to recipients relative to remaining on dialysis[93] –implying that routine discards are perhaps squandering an invaluable resource. While the actual reasons remain speculative, several

transplant professionals have attributed the phenomenon partly to the regulatory environment surrounding transplant centers[94-97]. Kidney transplant centers are overseen by the United States Department of Health and Human Services and by the Centers for Medicare and Medicaid Services (CMS) [20]. The conditions of participation set by CMS evaluate the performance of transplant centers regularly based on risk-adjusted 1-year patient and graft survival. The risk-adjustments are based on characteristics of the transplanted recipient and donor. There is no adjustment for the deaths of patients that occur while on the waitlist. Therefore, transplant centers may have an incentive to be cautious or risk-averse in accepting kidneys[95,96,98,99].

Suggested Solutions

Remedying the issue has led to considerable investigation over the past few years. Besides revisiting allocation rules[90] and transplant center regulations[94], two targeted interventions aimed at specific populations have been proposed. First, dual kidney transplantation (i.e. transplanting a patient in need of two kidneys) of high-KDPI organs has demonstrated success in conferring significant survival benefits to affected individuals[100-106]. Second, preemptive transplantation, dual transplantation, or expediting the placement of marginal/high-KDPI organs, particularly for those who are at increased risk of not surviving until their first offer for a KT (e.g. elderly patients, candidates at centers with long waiting times, diabetics) has also garnered interest[93,107,108].

The Need for an Individualized Decision Framework

Past work thus has convincingly shown that high-KDPI organs can benefit *some* patient and ought not to be rejected outright. We emphasize "*some"* to make the essential qualification that such a patient is not necessarily a patient who is soon due for a KT by following the typical procedures for organ allocation. The decision to accept an organ now for KT or wait for a better offer in the future is inherently an individual-level dilemma that governs the patient regardless of

whichever subpopulation he or she may belong to. For example, Massie et al calculate that it is more advantageous with respect to 5-year survival for 50-year old patients at transplant centers with median waiting times greater than 33 months to accept organs with KDPI 91-100[93]. While the authors in no way advocate doing as such, forming policy prescriptions based on such rulesets needs to be approached with caution. Although it may be true for the intended *population* of 50-year olds at such transplant centers that transplantation of high-KDPI organs leads to favorable outcomes, it may not indeed be the best course of action for an *individual* patient to accept such an organ. The individual's evaluation will depend on his or her preferences, how long he or she has already waited, and the likelihood of better opportunities that may present themselves in the future. For example, a 50-year old patient at a busy center, who has accrued sufficient priority for transplant, may be better served by rejecting an organ with KDPI 90+ at the given time because a better offer will soon become available. Massie et al recognize the importance of incorporating individual waiting time into decision analyses and correctly observe that the appropriate counterfactual for evaluating the benefit of accepting a KT offer is not survival on the waitlist, but survival accounting for future offers[93].

The individual's dilemma is defined by an inter-temporal comparison of the benefits of accepting a given offer for a KT now versus that of deferring. Because this decision is fraught with uncertainties regarding the timing of future offers and survival benefits, calculation of the opportunity cost of rejecting an offer for a KT has eluded quantification. Instead, the decision customarily relies on clinical experience and judgment. This article focuses on developing objective criteria that more accurately quantifies the consequences of that decision.

We employ a methodology using decision trees[109] – which, for example, are used by computers to make complex decisions. The aim of the analysis is to estimate 2 quantities: the value of accepting an offer for a KT of given quality now, and the value of rejecting that offer. The latter valuation is contingent on the survival benefits of offers in the future. The Concept

section and Supplement A highlight our understanding of the decision process undertaken by health-care providers, patients, and transplant professionals. It also illustrates a decision tree for accepting/rejecting a KT offer and walks the reader through a simplified decision analysis in a non-technical manner. The Methods section and Supplement B operationalize the decision analysis mathematically and explains how the valuations are computed. The valuations are linked to individual survival estimates that incorporate relevant factors including patient demographics, diagnoses, comorbidities, immunology, etc. as well as donor characteristics, donor-recipient attributes, KDPI, and transplant center/OPO characteristics. The Results section demonstrates the methodology for an actual patient. The Discussion section explains how the methodology may be used to identify candidates for expedited placement of marginal quality organs.

We emphasize that the work below outlines the construction of a computation engine that calculates the benefits of accepting a given offer or rejecting it. The goal is to provide an objective evaluation of the consequences of that decision but *not* to make a recommendation. That choice depends on the risk-attitudes of the decision maker and is ultimately left to the patient.

Concept

Prior to constructing a decision tree, it was necessary to identify the critical moments in the decisions made by transplant centers, OPOs, and the OPTN. In the autumn of 2016, we held structured and unstructured interviews with the clinical faculty, nurses, and staff of the Comprehensive Transplant Center at Northwestern University in Chicago, Illinois; organ procurement executives and administrators from the Gift of Hope OPO serving Illinois; and other transplant professionals. The purpose of the interviews was to identify the appropriate time in the process for rendering a decision analysis. Supplement A presents summaries of the

processes undergone before evaluating offers for a KT and provides flowcharts depicting the steps.

Typically before an organ is procured, DonorNet, an information technology system used by the OPTN, ranks patients for allocation based on blood type, age, sensitization, antigen compatibility, KDPI, previous transplant, prior living donor status, and post-transplant survival (if applicable) as discussed above. The system then issues provisional offers to high-ranking patients. Transplant centers for these patients then have an opportunity to respond to these offers with either a rejection or provisional acceptance. A provisional acceptance for a given patient may still not materialize into a KT if another higher ranked patient accepts; however, an affirmative reply to a provisional offer is necessary if a KT is ever to take place. Therefore, the analysis focuses on evaluating all of the provisional offers a patient may receive and thereby covers any offers that would indeed lead to a KT when no higher ranked patient accepts.

Figure 4.1 presents a simplified, 2-stage decision tree analysis of 2 provisional offers as an example. The first stage (Stage 0) represents the current offer. The second stage (Stage 1) occurs sometime after the first stage when the last offer is received. Suppose the patient currently has an offer for a high-KDPI organ but not a low-KDPI organ (i.e. receives a high-KDPI organ with probability 1 and a low-KDPI organ with probability 0). The value of accepting the high-KDPI organ now is a post-transplant survival benefit of 3 years. The value of rejecting this offer is more difficult to calculate because it depends on what may happen in Stage 1 and because getting a low-KDPI offer later or even surviving until Stage 1 is uncertain at Stage 0. Suppose that the patient knows that there is a 90% chance of reaching Stage 1 where she will receive offers for both a high-KDPI organ and low-KDPI organ with equal probability (i.e. 50%). Receiving a low-KDPI organ at this time yields a post-transplant benefit of 4 years and similarly 2 years for a high-KDPI transplant. The reduced post-transplant survival benefits at this stage may be indicative, for example, of inferior outcomes from protracted dialysis. Furthermore,

suppose that if she rejects any offer in Stage 1, that she will then survive on dialysis for only 1 year. Conditional on reaching Stage 1, the patient is better off (with respect to survival) obtaining either a high-KDPI or low-KDPI KT, as it offers an expected survival benefit of 3 years (versus the 1 year benefit from rejecting all Stage 1 offers and remaining on dialysis).

Thus, accepting the current offer for a high-KDPI KT in Stage 0 nets a 3 year benefit, and conditional on reaching Stage 1, the best course of action taken subsequently will also yield a 3 year expected benefit. However, since there is a risk of not surviving until Stage 1, the value of rejecting the current offer is discounted to 2.7 years ($3\times0.9 + 0\times0.1$) [death is assigned a value of 0]. Thus, the foregoing analysis has yielded the two quantities of interest in this study; the patient must decide between accepting the high-KDPI KT now for an immediate benefit of 3 years or deferring and obtaining an expected benefit of 2.7 years. We refrain from going further, as the decision is now left to the patient, but a risk-neutral patient interested in maximizing their expected survival ought to accept the high-KDPI KT now instead of rejecting (3 vs. 2.7)[110]. However, a patient willing to risk waiting may try for a low-KDPI KT in Stage 1 and thus reject the current offer.

Methods

The decision tree requires the following pieces of information for each stage: 1) post-transplant survival benefits; 2) waitlist survival benefits; 3) probabilities of surviving on the waitlist until the next stage; and 4) the probability distributions for KDPI. The following subsections informally describe how the information is obtained. A mathematical formulation of the tree and the technical details are available in Supplement B.

We maintain the viewpoint of a patient who has just received their first provisional offer and knows the KDPI and characteristics of the current donor. Usually, only the donor profile of the current offer will be known with certainty. We conduct a counterfactual analysis of the impact of different KDPI transplants at different times by assuming the same donor profile (except for

KDPI) for all future stages. The value of death is by convention assumed to be 0. We also use 4 KDPI quality ranges: KDPI 0-70, KDPI 70-85, KDPI 85-95, and KDPI 95+. Analyses of OPTN match-run data from 2007-2016 revealed that approximately 75% of all candidates had finished considering any provisional offers within 750 days after the first offer. They received at least 2-10 provisional offers per week over the duration. We consequently employed a 101-stage decision tree with 7 days in between stages (duration = 700 days).

Post-Transplant Survival Benefit

Post-transplant survival benefits are estimated from standard proportional hazards survival models using widely available software[44]. The model specification includes accumulated waitlist time at transplant, KDPI, and characteristics relevant to post-transplant survival such as patient characteristics (e.g. demographics, diagnoses, comorbidities, etc.) and characteristics of the patient's transplant center or OPO. Additionally, donor and donor-recipient characteristics are included; Table 4.1 provides a full list. Multiple benefit measurements are possible, such as, mean post-transplant survival, median survival, or α-quantile survival time ($\alpha = 0.5$ corresponds to median). For a given stage, KDPI-quality range, and all other characteristics, we measure the post-transplant survival benefit as the median post-transplant survival time. Moreover, the post-transplant survival benefits adjust for the amount of time the patient has spent on the waitlist until the particular stage.

Waitlist Survival Benefit and Waitlist Survival Probabilities

If the patient rejects all offers in all stages, a terminal benefit for continuing on the waitlist must be assigned. We define this terminal benefit to be the median survival time on the waitlist less the sum of accumulated waiting time and the duration of the decision tree (700 days). If this terminal benefit is 0 or negative, then the patient receives no benefit from continuing dialysis and was better off with respect to median survival time in accepting an offer for KT at some

previous stage. Moreover, the terminal benefit is conditional on the patient having already survived for some time on dialysis prior to the first provisional offer.

Waitlist survival benefits are estimated from standard proportional hazards using widely available software[44]. The model specification includes patient characteristics (e.g. demographics, diagnoses, comorbidities, etc.) and characteristics of the patient's transplant center or OPO; Table 4.1 provides a full list. Again, benefit measurements using the mean waitlist survival or different quantiles may be used. For each successive stage, we use the waitlist survival function (conditioned on the patient surviving until the first provisional offer) to calculate the probability that the given patient will survive on the waitlist until that stage.

Probability Distribution of KDPI

For each stage we compute the probability that the offer will be in a given KDPI quality range using Poisson count models with specific patient, transplant center, and OPO characteristics[111] (Table 4.1 provides a full list). The characteristics include some of the previous factors used in the preceding survival models and describe procedural aspects that influence the likelihood of receiving a provisional offer. For example, OPTN policies expressly use calculated panel reactive antibodies (CPRA) and the individual's ABO blood type to rank candidates[57]. Other related, but implicit factors might be the OPO's transplant volume or mean waiting time. KT candidates are subject to the vicissitudes of the OPTN that are driven by the complex interactions among donors, donor hospitals, transplant centers, and OPOs. These institutions and related policies effectively determine the quality of any provisional offer. Moreover, the likelihood of receiving an organ of particular quality changes in successive stages because the candidate accrues priority and is less likely to be a preempted by a higher-ranking patient seeking a better quality organ.

Computation of the Values of Accepting an Offer and Rejecting

Once the information in the preceding subsections is obtained, the decision tree can be evaluated via backwards recursion or dynamic programming[112]. We use the DTREE procedure in SAS to solve the tree[44] and obtain the two principal quantities of interest – the value of accepting the current offer for a KT and the value of rejecting it, contingent on valuations of subsequent offers at later stages.

Implementation

We programmed the decision tree including all survival-benefit computations and offer count models in SAS 9.4[44]. Survival data on all adult KT candidates and organ donors in the US were provided by the United Network for Organ Sharing (UNOS) for January 2007 through December 2016 with updated statuses as of March 2017 (10 years). The sample included all adult candidates listed for a deceased-donor KT that had no previous transplants nor required multiple transplants. Covariates shown in Table 4.1 were selected after consulting the literature[63,68,73-75,77-79,96]. The count models were estimated using match-run data for the same period. Supplement C provides the coefficients and goodness-of-fit statistics for the survival models and count models

Application of the Decision Tree

We consider a 60 year-old female candidate in the dataset that lives in an urban area and suffers from diabetes and peripheral vascular disease, but is able to carry out normal activities with minor symptoms of disease. Her most recent CPRA score is 13, serum albumin level is 3.7, and BMI is 22.1. She is currently listed at Transplant Center A and has already waited 365 days. Transplant center A has a mean waiting time of 33 months (990 days), large annual transplant volumes, and is located in an OPO with over 5 centers. This center is considering a provisional offer for this patient from an ABO-compatible donor aged 33 years old with 5 HLA mismatches and 2 DR mismatches. We consider this donor profile with different KDPI ranges and assumed that future donors have a similar profile.

Sensitivity analyses of the results were performed using the 95% confidence intervals for the pre- and post-transplant median survival times. Two additional trees, one populated with all the worst-case, lower-bound median survival times from the confidence intervals, and one similarly populated with all the best-case, upper-bound median survival times were constructed and solved. We report the ranges of the values of acceptance and rejection thereby obtained.

Results

Table 4.2 presents the patient's valuations for accepting or rejecting the current offer by the donor's KDPI, which were rendered in about 1 minute on a standard laptop (time exclusive of survival model estimation). Figure 4.2 shows the SAS output of the tree, truncated at the beginning and end. The patient's median survival time on dialysis is 1,445 days, and she will therefore obtain a terminal benefit of 380 days if she rejects all offers for the 700 days and never receives a KT, but only if she survives for the duration, for which she has a 63.7% chance of doing so.

The value of accepting the current offer for a 95+ KDPI organ, for example, is 2,961 days and the value of rejecting is 3,092 days. The best course of action will depend on her own assessment, but if she were risk-neutral or at least not too risk-averse, she ought to be inclined to reject the offer.

Table 4.3 shows the amount of time that must elapse before the acceptance value for a given KDPI KT exceeds the rejection value. This information applies in prognostic situations where the candidate is presumed to *only* receive offers of a given quality and better quality offers only much afterwards. For example, if she only receives KDPI 95+ offers from similar donors, then it will take approximately 13 weeks before the value of acceptance exceeds the value of rejection – that is, if she is not expected to receive higher quality offers for much more than 13 weeks, then she may benefit from this KT now on average. Similarly, she can afford to wait 8 more weeks for a better offer if she is only receiving offers for KDPI 85-95; and it is

usually beneficial to accept the highest-quality organs as soon as they are offered. Thus, to facilitate better decision making, it is worthwhile to communicate to her both the information in Figure 4. 2 and Tables 4.2-3.

Discussion

This patient may indeed not be best served by a well-intended policy that urges elderly diabetics at transplant centers with long waiting times to accept high-KDPI organs or something similar. Once candidates survive long enough to begin receiving provisional offers, there is lessened incentive to forego better quality offers in the near future and a strong impetus to reject low-quality organs.

This analysis may be applied in two ways. First, the usefulness of the decision tree for real-time evaluation of provisional offers is clear provided the information can be relayed to the patient or health-care provider in a timely and understandable manner. Ideally, transplant centers can integrate such an engine into their procedure for responding to offers or even have such estimates calculated in DonorNet automatically. Supplement B provides some suggestions for how the modeling may be strengthened to account for uncertainty of characteristics for future donors. However, among the donor covariates included, KDPI is exceedingly the most influential component of the donor profile that affects post-transplant survival; so, limiting the focus to KDPI alone should not severely affect the applicability of the results.

Second, the tree may be used as a prognostic tool to identify potential candidates for expedited placement of high-KDPI organs. Each stage of decision tree need not correspond to a bona fide provisional offer, but instead be interpreted as a hypothetical point in time where a patient may receive a KT. The decision tree can then still be computed when no offers are actually expected. For instance, suppose that the aforementioned patient has now been listed at Transplant Center B for 365 days instead. Moreover, we may even require that the she has the same profile as before and that Transplant Center B has the same characteristics as

Transplant Center A. However, suppose she has not yet received her first provisional offer. Her results from Figure 4.2 and Tables 4.2-3 still apply even if she receives offers only hypothetically. Since the value of acceptance of a 95+ KDPI donor will exceed the value of rejection in 13 weeks, we can deduce the following: if Transplant Center B is confident that she will not receive an offer for a better quality organ or even any offer at all for the next 13 or more weeks, then she may be a reasonable candidate for an expedited high-KDPI KT *now*. This subtle difference between these two scenarios alters her incentives (i.e. reject 95 KDPI+ at Center A, consider expedited placement of 95 KDPI+ at Center B) and underscores the essence of her dilemma.

The decision tree retains applicability despite focusing exclusively on provisional offers. Since an offer for a KT that would actually materialize will follow the first provisional offer, the patient is not harmed if she had accepted the expedited placement at Center B, as that KT would still have occurred after 13 weeks or more. Additionally, while at Transplant Center A, she has every incentive to act as if every provisional offer would materialize into a KT or otherwise lose an opportunity for a potential survival benefit.

It is the prognostic application of the decision tree that could help reduce the number of discards by bolstering expedited placements of high-KDPI organs to patients with sufficiently low priority. Candidates expected to receive offers soon may have too strong of an incentive to reject them. These patients are not bound by the need for greater efficiency in the system and perhaps should not be. A policy solution to address the discards, however, will need to balance individual autonomy and the broader welfare. At the very least, an individualized decision framework will aid transplant candidates to do the best for themselves in any likely policy environment, and if used to identify individuals, not populations, for expedited placement as just described, bolster organ utilization.

This work provides a comprehensive treatment of the patient's dilemma for accepting kidneys of varying quality that retains both methodological rigor and clinical relevance. However, we do reiterate the necessary distinction between presenting the information and making the decision; the latter should always emphasize patient preferences and the results of any decision tree should not be construed to the contrary.

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Table 4.1: List of Covariates Included in the Decision Tree Analysis

Category	Waitlist Survival Benefit	Post-Transplant Survival Benefit	Offer Count Models
Waiting time at Transplant		X	
Elapsed time since 1st Offer			X
Serum Albumin Level at Listing	X	X	
Calculated Panel Reactive Antibodies at Listing [0-100]	X	X	X
Calculated Panel Reactive Antibodies (Last Known) [0-100]	X	X	X
BMI at Listing	X	X	
Residence in Urban Zip Code	X	X	
Residence in Rural Zip Code	X	X	
OPO 10-year transplant volume (number of organs)	X	X	X
OPO mean waiting time for transplant (days)	X	X	X
Transplant center 10-year transplant volume (number of organs)	X	X	X
Transplant center mean waiting time for transplant (days)	X	X	X
Transplant center competition in OPO HHI Index [0-1]	X	X	X
Number of transplant centers in the OPO	X	X	X
Age at listing 18-34 years	X	X	X
Age at listing 35-44 years	X	X	X
Age at listing 45-54 years	X	X	X
Age at listing 55-64 years	X	X	X
Age at listing $\geq$ 65 years	X	X	X
Male	X	X	
Female	X	X	
ABO = O	X	X	X
ABO = A	X	X	X
ABO = B	X	X	X
ABO = AB	X	X	X
Functional Status at listing is 10% - Moribund, fatal processes progressing rapidly	X	X	
Functional Status at listing is 20% - Very sick, hospitalization necessary: active treatment necessary	X	X	
Functional Status at listing is 30% - Severely disabled: hospitalization is indicated, death not imminent	X	X	
Functional Status at listing is 40% - Disabled: requires special care and assistance	X	X	
Functional Status at listing is 50% - Requires considerable assistance and frequent medical care	X	X	
Functional Status at listing is 60% - Requires occasional assistance but is able to care for needs	X	X	
Functional Status at listing is 70% - Cares for self: unable to carry on normal activity or active work	X	X	
Functional Status at listing is 80% - Normal activity with effort: some symptoms of disease	X	X	
Functional Status at listing is 90% - Able to carry on normal activity: minor symptoms of disease	X	X	
Functional Status at listing is 100% - Normal, no complaints, no evidence of disease	X	X	
Patient has history of diabetes	X	X	
Patient does not have history of diabetes	X	X	
White	X	X	
Black	X	X	
Hispanic	X	X	
Asian	X	X	
Native American, Native Hawaiian, or Pacific Islander	X	X	
Patient does not have peripheral vascular disease	X	X	
Patient has peripheral vascular disease	X	X	
Patient has no history of malignancy	X	X	
Patient has history of malignancy	X	X	
Diagnosis for transplant is other	X	X	
Diagnosis for transplant is unknown	X	X	
Diagnosis for transplant is IGA NEPHROPATHY	X	X	
Diagnosis for transplant is FOCAL GLOMERULAR SCLEROSIS	X	X	
Diagnosis for transplant is POLYCYSTIC KIDNEYS	X	X	
Diagnosis for transplant is HYPERTENSIVE NEPHROSCLEROSIS	X	X	
Diagnosis for transplant is DIABETES MELLITUS - TYPE II	X	X	

Table 4.1 (Continued): List of Covariates Included in the Decision Tree Analysis

Category	Waitlist Survival Benefit	Post-Transplant Survival Benefit	Offer Count Models
Number of DR mismatches ≥ 0		X	
Number of HLA mismatches ≥ 0		X	
Donor creatnine level		X	
Donor age at listing 18-34 years		X	
Donor age at listing 35-44 years		X	
Donor age at listing 45-54 years		X	
Donor age at listing 55-64 years		X	
Donor age at listing ≥ 65 years		X	
Functional Status at transplant (recipient) is 10% - Moribund, fatal processes progressing rapidly		X	
Functional Status at transplant (recipient) is 20% - Very sick, hospitalization necessary: active treatment necessary		X	
Functional Status at transplant (recipient) is 30% - Severely disabled: hospitalization is indicated, death not imminent		X	
Functional Status at transplant (recipient) is 40% - Disabled: requires special care and assistance		X	
Functional Status at transplant (recipient) is 50% - Requires considerable assistance and frequent medical care		X	
Functional Status at transplant (recipient) is 60% - Requires occasional assistance but is able to care for needs		X	
Functional Status at transplant (recipient) is 70% - Cares for self: unable to carry on normal activity or active work		X	
Functional Status at transplant (recipient) is 80% - Normal activity with effort: some symptoms of disease		X	
Functional Status at transplant (recipient) is 90% - Able to carry on normal activity: minor symptoms of disease		X	
Functional Status at transplant (recipient) is 100% - Normal, no complaints, no evidence of disease		X	
Donor and Recipient have the same ABO blood type		X	
Donor and Recipient do not have the same ABO blood type		X	
KDPI is 0- <70		X	
KDPI is 70- <85		X	
KDPI is 85- <95		X	
KDPI is 95 or greater		X	

Table 4.2: Individualized Values of Accepting or Rejecting the Current Offer Given KDPI[1]

KDPI Range of Initial Offer	Stage	Accumulated Waiting Time (days)	Time Elapsed (days)		Value of Accepting Offer [range] (days)	Value of Rejecting Offer [range] (days)
95+	0	365	0		2961 [2774,3064]	3092 [2964,3230]
85-95	0	365	0		2995 [2930,3268]	3092 [2964,3230]
70-85	0	365	0		3042 [2989,3268]	3092 [2964,3230]
0-70	0	365	0		3268 [3072,3268]	3092 [2964,3230]
	Terminal	1065	700		---	380 [274,508]

[1]Results for a 60 year-old, diabetic female transplant candidate who has already waited 365 days at a high-volume transplant center with mean waiting time of 33 months. Value of acceptance for current offer (Stage 0) assumes transplant of given KDPI with probability 1.Ranges calculated based on sensitivity analyses using lower- and upper-bound benefit estimates.

Table 4.3: Elapsed Times Whens Value of Acceptance Exceeds Value of Rejection by KDPI Range[1]

KDPI Range	Elapsed Time When Acceptance of Offer Exceeds Rejection Value [range] (days)
0-70	0 [0,0]
70-85	28 [0,28]
85-95	56 [0,56]
95+	91 [91,133]

[1]Results for a 60 year-old, diabetic female transplant candidate who has already waited 365 days at a high-volume transplant center with mean waiting time of 33 months. Elapsed times are when value of acceptance exceeds value of rejection given all previous offers were of that quality.
Ranges calculated based on sensitivity analyses using lower- and upper-bound benefit estimates.

Figure 4.1: Example 2-Stage Decision-Tree Analysis for Evaluating Offers of Varying Quality

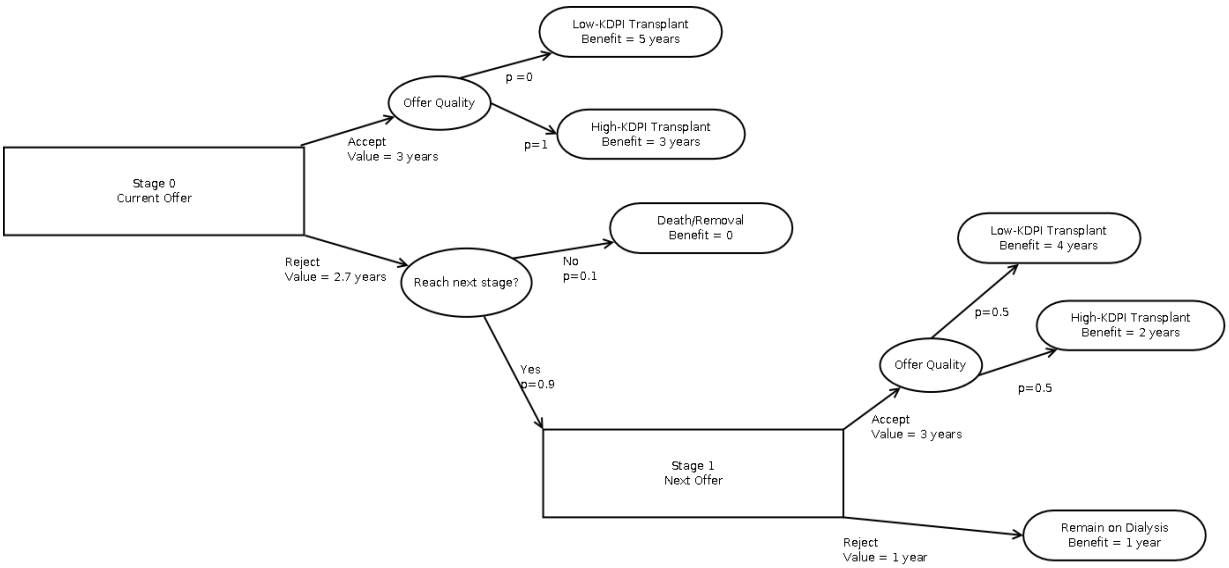
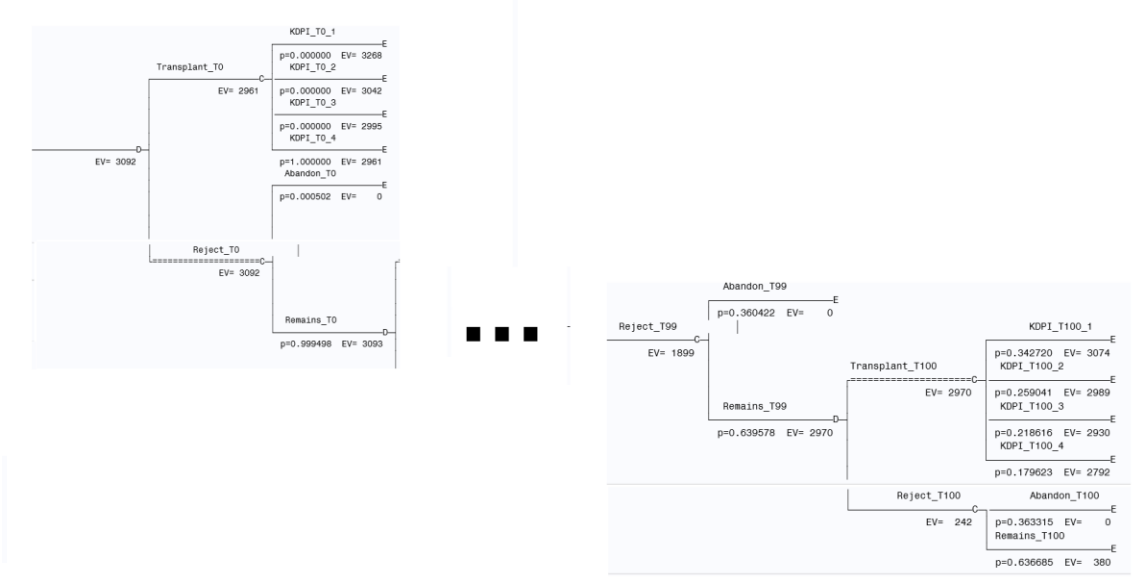


Figure 4.2: Truncated Output from Decision Tree



Truncated results for a 60 year-old, diabetic female transplant candidate who has already waited 365 days at a high-volume transplant center with mean waiting time of 33 months. Shows current offer (Stage 0) and terminal stages (Stage 100) occurring weekly 700 days later.

Supplement A: Candidate Kidney Decision Offer Process

Prior to constructing a decision model, it was necessary to identify the critical moments in the processes undertaken by transplant centers, OPOs, and the OPTN. In the autumn of 2016, we held structured and unstructured interviews with the clinical faculty, nurses, and staff of the Comprehensive Transplant Center at Northwestern University in Chicago, Illinois; organ procurement executives and administrators from the Gift of Hope OPO serving Illinois; and other transplant professionals. The purpose of the interviews was to construct flowcharts of the process.

Figure 4.3 depicts a diagram of the patient's experience from listing to receipt of an organ offer. After referral to a transplant center, multidisciplinary teams assess patients' suitability for a KT and evaluate any contraindications. If the patient is listed, a KDPI range for offers that the patient may be willing to accept in the future can be then set. After listing, the patient will be monitored in intervals chosen by both OPTN and clinical guidelines and at the discretion of transplant centers. Monitoring includes assessment of patient status and immunology including unacceptable antigens. Patients who are due for an offer soon may be monitored more frequently. During this time, patients may be temporarily deactivated from the waitlist for various reasons and even delisted if they develop conditions that prohibit transplantation. Transplant centers may have different protocols or exclude some types of donors (e.g. HIV donors). So when an organ is about to be procured by an OPO, a computer system (DonorNet) verifies that the donor meets transplant center criteria and performs a virtual cross-match. The virtual cross-match ranks patients for organ allocation based on blood type, age, sensitization, antigen compatibility, KDPI, previous transplant, prior living donor status, and post-transplant survival (if applicable) as discussed above. The system then issues provisional offers to high-ranking patients. If possible, and depending on the practices of the OPO or donor hospital, a physical cross-match of the donor's and high-ranking, potential recipients' tissues is

conducted. Information about the donor is updated in DonorNet in real-time (e.g. KDPI, donor characteristics, biopsy results if any, etc.). However, the timing of the physical cross-match or biopsy results (if even performed) may be before, after, or simultaneously occurring while provisional offers are being considered or before or after the organ is physically removed from the donor – the circumstances vary for each particular situation.

After a provisional offer, transplant center professionals (e.g. staff, nurses, nephrologists, surgeons, etc.) reassess patient suitability while considering any information about the donor that has been obtained; if the offer seems promising and likely to materialize, they will contact the patient to discuss the offer and obtain informed consent. If the patient assents, the transplant may occur if no higher-ranking patient accepts the offer. If the patient declines the offer, the transplant center or patient may reevaluate their criteria for accepting an organ in the future and potentially filter similar donors automatically in the future for that patient.

Figure 4.4 depicts more details about the offer process from the OPO's perspective. The OPO ideally obtains authorization and tissues for cross-matching from the donor before physically removing the organ. When the virtual cross-match is conducted, all transplant centers locally are notified unless 3 of the highest-ranking patients are not listed locally. Transplant centers have 1 hour to acknowledge the receipt of the provisional offer and an additional hour to deliver a provisional acceptance. Meanwhile, the OPO or sometimes donor hospital prepare the physical cross-match tray, procure the organ, and take a biopsy (the exact timing and sequence of these varies in each circumstance). If no patient is found, the OPO elects to either discard the organ or extend the match-run. Physical cross-matching may take a few hours and is limited by the number of samples that can be tested at once. Alternatively, the OPO may expedite the placement or direct the organ non-locally via UNOS and DonorNet if either a recipient is found or if some transplant center is willing to accept the organ. The organ will be discarded if no willing recipient or transplant center can be found.

We acknowledge that Figures 4.3 and 4.4 may not be representative of the practices of all transplant centers and OPOs. Processes are subject to changes in OPTN policies, information technology systems, and clinical practice. However, our discussions with professionals indicated that the foregoing described the events adequately at a high level. Most importantly, they identify that from the perspective of the patient, the most critical time for a decision evaluation is when a provisional offer is received. A provisional offer may not materialize into a KT if accepted; however, an evaluation for all provisional offers covers the offers that do indeed lead to a KT when no higher-ranking patient is found before transplantation.

Figure 4.3: Flowchart of Candidates Listed for a Kidney Transplant from Listing to Organ Offer

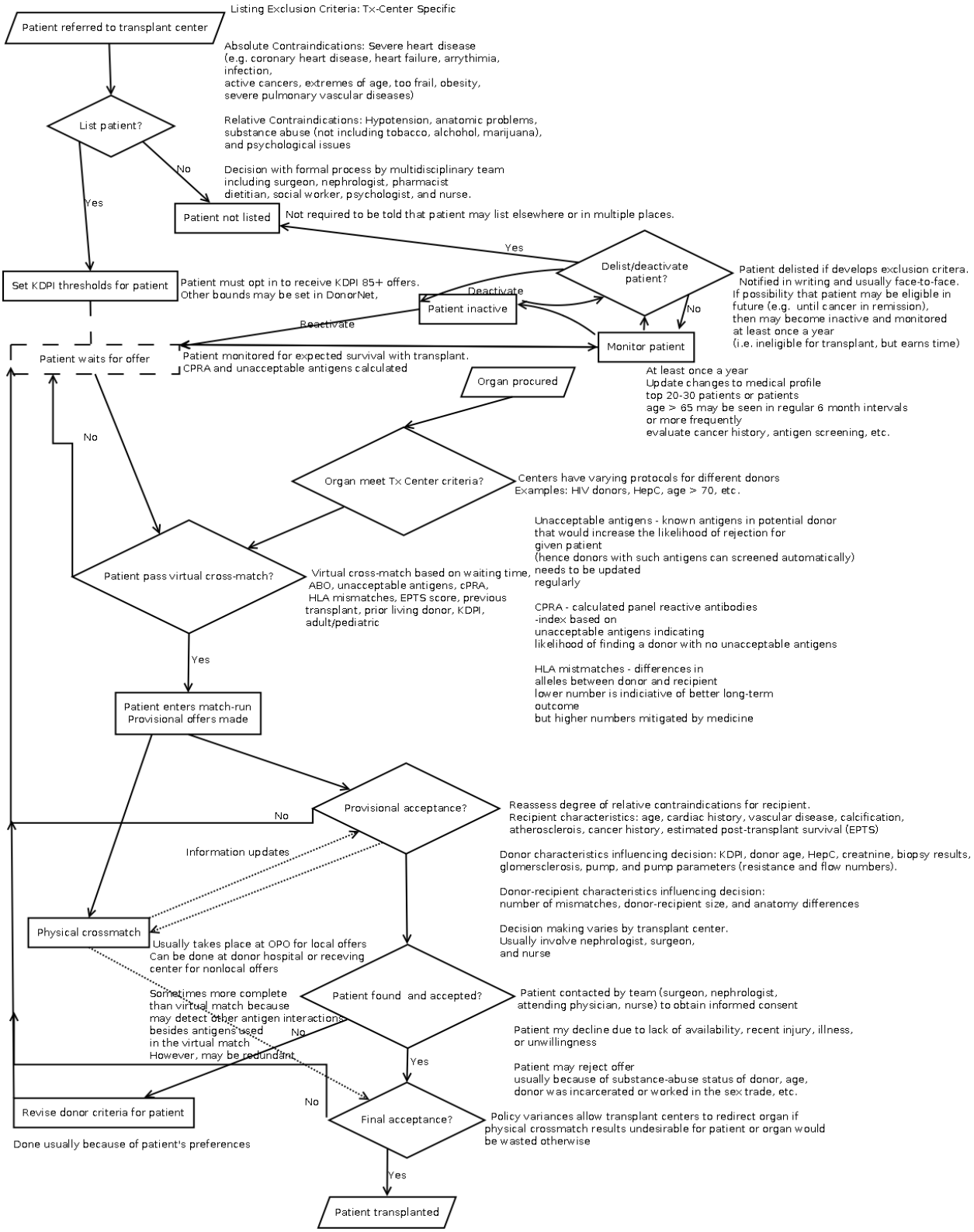


Figure based on interviews conducted with Comprehensive Transplant Center at Northwestern University and the Gift of Hope Organ Procurement Organization in Autumn 2016. May not be representative of all transplant centers or organ procurement organizations. Subject to change as processes may be modified.

Abbreviations: CPRA – calculated panel reactive antibodies; HLA – human leukocyte antigen; HepC – Hepatitis C; EPTS – Estimated post-transplant survival score; KDPI – kidney donor profile index; OPO – organ procurement organization; Tx Center – Transplant center

Dashed arrows represent variable timing in the events.

Figure 4.4: Flowchart of Organ Procurement Organization's Handling of a Donated Kidney for Transplant

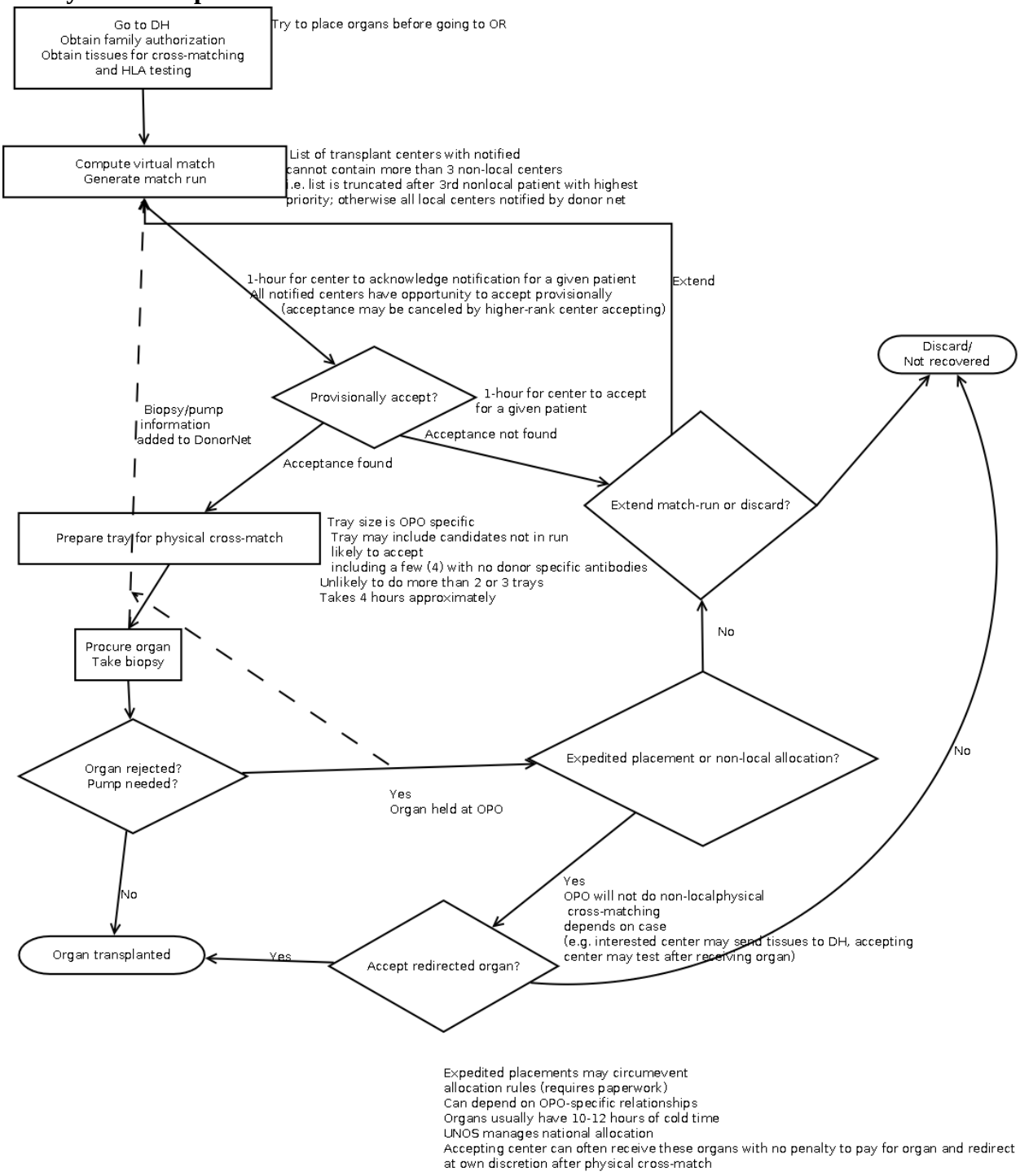


Figure based on interviews conducted with Comprehensive Transplant Center at Northwestern University and the Gift of Hope Organ Procurement Organization in Autumn 2016. May not be representative of all transplant centers or organ procurement organizations. Subject to change as processes may be modified.

Abbreviations: DH – Donor Hospital; OPO – Organ Procurement Organization; OR – operating room; UNOS – United Network for Organ Sharing

Dashed arrows represent variable timing in the events.

Supplement B: Technical Methods

The decision tree requires the following pieces of information for each stage: 1) post-transplant survival benefits; 2) dialysis/waitlist survival benefits; 3) probabilities of surviving on the waitlist until the next stage; and 4) the probability distributions for KDPI. We now extend the decision tree to any number of stages and provide the details to make the analysis clinically relevant. We maintain the viewpoint of a patient who has just received their first provisional offer and knows the KDPI and characteristics of the current donor with certainty.

Preliminaries

The value of death is by convention assumed to be 0. We measure time in days elapsed from the first provisional offer. Let $0,1,2,\dots n,\dots,N-1$ denote the N stages of the decision tree. Let $\delta > 0$ be the number of days between stages, chosen as finely as we like. Suppose the candidate has already accumulated w_0 days of time on the waitlist when the first offer is made. Let $1,2,\dots q,\dots,Q$ denote the possible KDPI quality ranges – for example, we use 4 ranges: 1 for KDPI 0-70, 2 for KDPI 70-85, 3 for KDPI 85-95, and 4 for KDPI 95+. Further, let x denote a profile vector describing any patient characteristics relevant to either post-transplant or waitlist survival except for time on the waitlist (e.g. demographics, diagnoses, comorbidities, etc.). These profiles may also include the characteristics of the patient's transplant center or OPO. Furthermore, let y denote a profile vector of donor and donor-recipient characteristics relevant to post-transplant survival except KDPI. Lastly, let α be a quantile of interest. For example, the median corresponds to $\alpha = 0.5$.

Post-Transplant Survival Benefit

Let $y_0, y_1, \dots, y_n, \dots, y_N$ be the sequence of profiles describing the donor that is considered at each stage. Usually, only the donor profile of the current offer, y_0, will be known with certainty. There are several ways to deal with unknown donor profiles at successive stages, including using simulation or the average donor profile for that patient's transplant center or

OPO. Additionally, a counterfactual analysis of the impact of different KDPI transplants at different times using similar donors can be performed by using the same donor profile for all stages – that is, by assuming $y_n = y_0$ for $1 \leq n \leq N-1$.

Let $S(t;q,w,x,y) = \mathbb{P}(S > t|q,w,x,y)$ denote the post-transplant survival for a KT with KDPI range q, performed after w days of time on the waitlist, on a patient with profile x using donor profile y. Suppose that a transplant with KDPI range q occurs after it was accepted in the n^{th} stage of the decision tree using donor profile y_n. Since the KT occurs after the patient has waited $w_0 + n\delta$ days, the survival for this patient profile at this stage would be given by $S(t;q,w_0 + n\delta,x,\ y_n)$. Consequently, multiple benefit measurements for assessing the value of a KT of given quality q at stage n can be derived as $m(n,q)$:

α-Quantile Survival Time Benefit ($\alpha = 0.5$ corresponds to median post-transplant survival time):

$$m(n,q) \coloneqq \inf\{t|S(t;q,w_0 + n\delta,x,\ y_n) \leq \alpha\}$$

Mean Survival Time Benefit:

$$m(n,q) \coloneqq \int_0^\infty S(t;q,w_0 + n\delta,x,\ y_n)dt$$

The foregoing measurements can be obtained from standard parametric and proportional hazards survival models using widely available software[44].

Waitlist Survival Benefit and Waitlist Survival Probabilities

Let R be the survival time of the candidate since being on the waitlist or on dialysis. For a patient with profile x and accumulated waiting time w_0, let $R(t;x) = \mathbb{P}(R > t|x)$ be the waitlist survival function. $R(t;x)$ may be computed using standard parametric or proportional hazards survival models using widely available software[44]. Moreover, because the patient has already

survived for some amount of time before the first offer, w_0, we condition the survival time on this fact. Suppose $t > w_0$ then:

$$\mathbb{P}(R > t | R > w_0, x) = \frac{\mathbb{P}(R > t, R > w_0 | x)}{\mathbb{P}(R > w_0 | x)} = \frac{\mathbb{P}(R > t | x)}{\mathbb{P}(R > w_0 | x)} = \frac{R(t; x)}{\mathbb{P}(R > w_0 | x)} =: \tilde{R}(t; w_0, x)$$

Thus, at the time of the current offer, the probability of surviving until stage n is defined as:

$$p_R(n) \coloneqq \tilde{R}(w_0 + n\delta; x)$$

If the patient rejects all offers in all stages, a terminal benefit for continuing on the waitlist must be assigned. Let $T = (N-1)\delta$ be the time that has elapsed after all offers have been exhausted. Let m_R denote either the mean or α-quantile survival time on dialysis (conditional on surviving for at least w_0 and calculated from $\tilde{R}$). The terminal benefit earned after rejecting offers in all N stages is:

$$V_N \coloneqq \max\{0, m_R - T - w_0\}$$

If the total of the initial waiting time and mean or α-quantile survival is less than or equal to T, then the patient receives no benefit from continuing dialysis and was better off with respect to survival time in accepting an offer for KT at some previous stage.

Probability Distribution of KDPI

Let $p_q(n)$ be the probability that an offer in stage n has KDPI range q. The value of $p_q(0)$ is presumably 0 for each range q but for the KDPI range corresponding to the current offer. Candidates are subject to the vicissitudes of the OPTN that are driven by the complex interactions among donors, donor hospitals, transplant centers, and OPOs. These institutions and related policies effectively determine the quality of any provisional offer. Moreover, the likelihood of receiving an organ of particular quality changes in successive stages because the candidate accrues priority and is less likely to be a preempted by a higher-ranking patient seeking a better quality organ. However, the probability of survival until the next will also decrease.

Let z be a vector of patient, transplant center, and OPO characteristics and $\tau > 0$ be the time that has elapsed since the first offer. The characteristics may include some of the previous factors used in the preceding survival models and ought to describe procedural aspects that influence the likelihood of entering a match-run and receiving a provisional offer. For example, OPTN policies expressly use calculated panel reactive antibodies (CPRA) and the individual's ABO blood type to rank candidates[57]. Other related, but implicit factors might be the OPO's transplant volume or mean waiting time. Unfortunately, just as for donor profiles, relevant donor-recipient characteristics for future offers, such as the number of mismatches, cannot be known with certainty. A definitive treatment of such would entail simulation of possible future match-runs; so, we therefore resort to approximations of the probabilities using Poisson count models using specific patient, transplant center, and OPO characteristics[111]:

Assumption: A patient at a transplant center and OPO with characteristics z and elapsed time τ receives provisional offers for KDPI ranges q following independent (not homogenous) Poisson Processes with mean number of offers $\lambda_q(z, \tau)$.

The probabilities of the KDPI for stages $1,2, \dots n, \dots, N-1$ may then be estimated as:

$$p_q(n) = \frac{\lambda_q(z, n\delta)}{\sum_{q=1}^{Q} \lambda_q(z, n\delta)}$$

The mean number of offers for each quality range may be estimated via Poisson regressions where β_{0q} and β_q represent the regression coefficients[44]:

$$\hat{\lambda}_q(z, \tau) = \exp(\beta_{0q}\tau + \beta_q' z)$$

Computation of the Values of Accepting an Offer and Rejecting

We now unify the preceding subsections; let $b(n) \coloneqq \sum_{q=1}^{Q} p_q(n) m(n, q)$. The function $b(n)$ represents the expected post-transplant survival benefit from a KT at stage n, and $b(0)$ in particular is one of the principal quantities of interest in the study – the value of accepting the

current offer for a KT. To obtain the value of rejecting the offer, we first compute the value function $V(n)$:

$$V(n) = \begin{cases} \max\{\ b(n),\ \ p_R(n+1)V(n+1)\ \}, & 0 \le n \le N-1 \\ V_N, & n = N \end{cases}$$

The value function encapsulates the notion that the value of the current decision is contingent on valuations of subsequent offers at later stages, i.e. $V(n)$ depends on $V(n+1)$. Evaluating the value function can be achieved via backwards recursion or dynamic programming[112]. The DTREE procedure in SAS can also be used to solve the model[44]. The computation of $p_R(1)V(1)$ yields the second principal quantity of interest – the value of rejecting the current offer. The term $V(1)$ measures the value of rejecting the offer conditional on reaching stage 1, which is subsequently discounted by the probability of surviving until Stage 1.

Supplement C: Modeling Results

Offer Models

For each of the KDPI ranges, candidates received approximately 0-10 provisional offers a week after their first offer (i.e. the computer system had selected the patient; the vast majority of the offers did not materialize into a KT). All predictors were statistically significant as were overall Pearson chi-squared and deviance statistics for goodness of fit ($p < 0.001$). Median absolute deviations in the predicted number of offers from the actual number were 23.5 per patient respectively. Median absolute percentage errors were 73.5%. Further analysis of the match-run data revealed that approximately 75% all candidates had finished considering any provisional offers within 750 days after the first one. We consequently employed a 101-stage decision tree ($N = 101$) with 7 days in between stages ($\delta = 7, T = 700$).

Analysis Of Maximum Likelihood Parameter Estimates KDPI 0-70

Parameter		DF	Estimate	Standard Error	Wald 95% Confidence Limits		Wald Chi-Square	Pr > ChiSq
Intercept		1	2.9940	0.0025	2.9891	2.9989	1447834	<.0001
Elapsed Time		1	0.0008	0.0000	0.0008	0.0008	4712173	<.0001
CPRA Listing		1	-0.0054	0.0000	-0.0055	-0.0054	28203.2	<.0001
Recent CPRA		1	-0.0119	0.0000	-0.0120	-0.0119	736903	<.0001
OPO Transplant Volume		1	0.0000	0.0000	0.0000	0.0000	194.91	<.0001
OPO Mean Waiting Time		1	0.0000	0.0000	0.0000	0.0000	18.42	<.0001
Tx Center Transplant Volume		1	0.0002	0.0000	0.0002	0.0002	187945	<.0001
Tx Center Mean Waiting Time		1	0.0003	0.0000	0.0003	0.0003	8591.08	<.0001
OPO HHI		1	-0.2046	0.0020	-0.2085	-0.2007	10531.7	<.0001
Number of Transplant Centers in OPO		1	0.0174	0.0001	0.0172	0.0177	17086.0	<.0001
Age 35-45		1	0.0147	0.0010	0.0127	0.0167	204.65	<.0001
Age 45-55		1	0.0192	0.0009	0.0174	0.0211	416.79	<.0001
Age 55-65		1	-0.0023	0.0009	-0.0041	-0.0005	6.26	0.0123
Age 65+		1	0.0159	0.0010	0.0139	0.0179	243.01	<.0001
ABO	**A**	1	0.2783	0.0006	0.2771	0.2795	198124	<.0001
ABO	**AB**	1	0.1981	0.0013	0.1956	0.2006	24106.3	<.0001
ABO	**B**	1	-0.9017	0.0010	-0.9036	-0.8998	858045	<.0001
Scale		0	1.0000	0.0000	1.0000	1.0000		

Criteria For Assessing Goodness Of Fit

Criterion	DF	Value	Value/DF
Deviance	18E4	7762750.7021	42.5531
Scaled Deviance	18E4	7762750.7021	42.5531
Pearson Chi-Square	18E4	7413186.8272	40.6369
Scaled Pearson X2	18E4	7413186.8272	40.6369
Log Likelihood		53491208.628	
Full Log Likelihood		-4372010.637	
AIC (smaller is better)		8744055.2733	
AICC (smaller is better)		8744055.2767	
BIC (smaller is better)		8744227.2145	

Analysis Of Maximum Likelihood Parameter Estimates KDPI 70-85

Parameter		DF	Estimate	Standard Error	Wald 95% Confidence Limits		Wald Chi-Square	Pr > ChiSq
Intercept		1	2.9853	0.0030	2.9794	2.9912	986653	<.0001
Elapsed Time		1	0.0007	0.0000	0.0007	0.0007	2663687	<.0001
CPRA Listing		1	-0.0050	0.0000	-0.0051	-0.0050	16899.2	<.0001
Recent CPRA		1	-0.0127	0.0000	-0.0127	-0.0127	557007	<.0001
OPO Transplant Volume		1	0.0000	0.0000	0.0000	0.0000	9542.72	<.0001
OPO Mean Waiting Time		1	-0.0003	0.0000	-0.0003	-0.0003	2464.63	<.0001
Tx Center Transplant Volume		1	0.0002	0.0000	0.0002	0.0002	148472	<.0001
Tx Center Mean Waiting Time		1	0.0001	0.0000	0.0001	0.0002	1586.33	<.0001
OPO HHI		1	-0.3980	0.0024	-0.4027	-0.3933	27467.2	<.0001
Number of Transplant Centers in OPO		1	-0.0044	0.0002	-0.0047	-0.0041	735.59	<.0001
Age 35-45		1	0.0702	0.0013	0.0677	0.0727	3026.38	<.0001
Age 45-55		1	0.1368	0.0012	0.1345	0.1391	13845.7	<.0001
Age 55-65		1	0.1469	0.0011	0.1447	0.1492	16843.8	<.0001
Age 65+		1	0.1773	0.0012	0.1748	0.1797	20548.9	<.0001
ABO	**A**	1	0.2337	0.0007	0.2323	0.2352	97782.2	<.0001
ABO	**AB**	1	0.1330	0.0015	0.1299	0.1360	7454.71	<.0001
ABO	**B**	1	-0.8199	0.0011	-0.8221	-0.8176	527249	<.0001
Scale		0	1.0000	0.0000	1.0000	1.0000		

Criteria For Assessing Goodness Of Fit

Criterion	DF	Value	Value/DF
Deviance	18E4	6393513.8341	35.0474
Scaled Deviance	18E4	6393513.8341	35.0474
Pearson Chi-Square	18E4	6116150.0161	33.5269
Scaled Pearson X2	18E4	6116150.0161	33.5269
Log Likelihood		34238731.762	
Full Log Likelihood		-3647998.513	
AIC (smaller is better)		7296031.0258	
AICC (smaller is better)		7296031.0292	
BIC (smaller is better)		7296202.9670	

Analysis Of Maximum Likelihood Parameter Estimates KDPI 85-95

Parameter		DF	Estimate	Standard Error	Wald 95% Confidence Limits		Wald Chi-Square	Pr > ChiSq
Intercept		1	2.9379	0.0037	2.9306	2.9452	622028	<.0001
Elapsed Time		1	0.0008	0.0000	0.0008	0.0008	2448612	<.0001
CPRA Listing		1	-0.0055	0.0000	-0.0056	-0.0054	14016.9	<.0001
Recent CPRA		1	-0.0132	0.0000	-0.0132	-0.0132	434078	<.0001
OPO Transplant Volume		1	0.0000	0.0000	0.0000	0.0000	914.01	<.0001
OPO Mean Waiting Time		1	-0.0009	0.0000	-0.0009	-0.0009	18457.4	<.0001
Tx Center Transplant Volume		1	0.0003	0.0000	0.0003	0.0003	162283	<.0001
Tx Center Mean Waiting Time		1	-0.0006	0.0000	-0.0006	-0.0006	18923.0	<.0001
OPO HHI		1	-0.8903	0.0029	-0.8960	-0.8845	91598.8	<.0001
Number of Transplant Centers in OPO		1	0.0023	0.0002	0.0019	0.0027	149.55	<.0001
Age 35-45		1	0.2867	0.0019	0.2830	0.2903	23885.1	<.0001
Age 45-55		1	0.6372	0.0017	0.6339	0.6404	146868	<.0001
Age 55-65		1	0.8378	0.0016	0.8346	0.8409	270146	<.0001
Age 65+		1	0.9731	0.0017	0.9698	0.9764	334863	<.0001
ABO	**A**	1	0.1272	0.0009	0.1254	0.1290	19048.4	<.0001
ABO	**AB**	1	0.0758	0.0019	0.0721	0.0796	1582.83	<.0001
ABO	**B**	1	-0.8008	0.0014	-0.8035	-0.7982	351208	<.0001
Scale		0	1.0000	0.0000	1.0000	1.0000		

Criteria For Assessing Goodness Of Fit

Criterion	DF	Value	Value/DF
Deviance	18E4	9276853.1777	50.8530
Scaled Deviance	18E4	9276853.1777	50.8530
Pearson Chi-Square	18E4	11627361.300	63.7378
Scaled Pearson X2	18E4	11627361.300	63.7378
Log Likelihood		24362612.916	
Full Log Likelihood		-5010950.801	
AIC (smaller is better)		10021935.602	
AICC (smaller is better)		10021935.606	
BIC (smaller is better)		10022107.544	

Analysis Of Maximum Likelihood Parameter Estimates KDPI 95+

Parameter		DF	Estimate	Standard Error	Wald 95% Confidence Limits		Wald Chi-Square	Pr > ChiSq
Intercept		1	3.2290	0.0043	3.2206	3.2374	568000	<.0001
Elapsed Time		1	0.0007	0.0000	0.0007	0.0007	1846130	<.0001
CPRA Listing		1	-0.0056	0.0001	-0.0057	-0.0055	11954.6	<.0001
Recent CPRA		1	-0.0132	0.0000	-0.0132	-0.0131	349746	<.0001
OPO Transplant Volume		1	0.0000	0.0000	0.0000	0.0000	542.27	<.0001
OPO Mean Waiting Time		1	-0.0012	0.0000	-0.0012	-0.0012	24870.4	<.0001
Tx Center Transplant Volume		1	0.0003	0.0000	0.0003	0.0003	232099	<.0001
Tx Center Mean Waiting Time		1	-0.0010	0.0000	-0.0010	-0.0010	44067.7	<.0001
OPO HHI		1	-1.4812	0.0034	-1.4879	-1.4745	185513	<.0001
Number of Transplant Centers in OPO		1	-0.0134	0.0002	-0.0138	-0.0130	3966.71	<.0001
Age 35-45		1	0.3984	0.0022	0.3940	0.4027	31950.4	<.0001
Age 45-55		1	0.8329	0.0020	0.8289	0.8368	173127	<.0001
Age 55-65		1	1.0673	0.0019	1.0634	1.0711	300782	<.0001
Age 65+		1	1.2309	0.0020	1.2270	1.2348	375568	<.0001
ABO	**A**	1	0.0512	0.0010	0.0493	0.0532	2618.35	<.0001
ABO	**AB**	1	0.0444	0.0021	0.0403	0.0485	457.79	<.0001
ABO	**B**	1	-0.6500	0.0014	-0.6527	-0.6473	219134	<.0001
Scale		0	1.0000	0.0000	1.0000	1.0000		

Criteria For Assessing Goodness Of Fit

Criterion	DF	Value	Value/DF
Deviance	18E4	10723438.830	58.7827
Scaled Deviance	18E4	10723438.830	58.7827
Pearson Chi-Square	18E4	14597256.172	80.0178
Scaled Pearson X2	18E4	14597256.172	80.0178
Log Likelihood		18877046.092	
Full Log Likelihood		-5653302.295	
AIC (smaller is better)		11306638.590	
AICC (smaller is better)		11306638.593	
BIC (smaller is better)		11306810.531	

Post-Transplant Survival Model

Model Fit Statistics

Criterion	Without Covariates	With Covariates
-2 LOG L	178624.79	173024.03
AIC	178624.79	173148.03
SBC	178624.79	173584.76

Testing Global Null Hypothesis: BETA=0

Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	5600.7642	62	<.0001
Score	6089.1314	62	<.0001
Wald	5240.2510	62	<.0001

Parameter	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio
Waiting Time	1	0.0002838	0.0000251	128.1480	<.0001	1.000
Serum Albumin Level at Listing	1	-0.17845	0.01847	93.3800	<.0001	0.837
Calculated Panel Reactive Antibodies at Listing [0-100]	1	-0.0004738	0.0008500	0.3107	0.5773	1.000
Calculated Panel Reactive Antibodies (Last Known) [0-100]	1	0.00286	0.0005004	32.6000	<.0001	1.003
BMI at Listing	1	-0.00485	0.00220	4.8669	0.0274	0.995
Residence in Rural Zip Code	1	0.04178	0.02910	2.0613	0.1511	1.043
OPO 10-year transplant volume (number of organs)	1	0.0000276	0.0000125	4.8474	0.0277	1.000
OPO mean waiting time for transplant (days)	1	-0.0002410	0.0001931	1.5565	0.2122	1.000
Transplant center 10-year transplant volume (number of organs)	1	-0.0000513	0.0000218	5.5310	0.0187	1.000
Transplant center mean waiting time for transplant (days)	1	-0.0003249	0.0001331	5.9589	0.0146	1.000
Transplant center HHI Index [0-1]	1	0.03282	0.07833	0.1756	0.6752	1.033
Number of transplant centers in the OPO	1	-0.00111	0.00617	0.0320	0.8580	0.999
Age at listing 35-44 years	1	0.33986	0.06788	25.0682	<.0001	1.405
Age at listing 45-54 years	1	0.58886	0.06134	92.1726	<.0001	1.802
Age at listing 55-64 years	1	1.02116	0.05933	296.2118	<.0001	2.776

Parameter	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio
Age at listing ≥ 65 years	1	1.46514	0.06053	585.9092	<.0001	4.328
Female	1	-0.17574	0.02469	50.6673	<.0001	0.839
ABO = A	1	0.03365	0.02471	1.8541	0.1733	1.034
ABO = B	1	0.00624	0.03630	0.0296	0.8635	1.006
ABO = AB	1	0.02150	0.05173	0.1728	0.6776	1.022
Functional Status at listing is 10% - Moribund, fatal processes progressing rapidly	1	0.02434	0.29915	0.0066	0.9351	1.025
Functional Status at listing is 20% - Very sick, hospitalization necessary: active treatment necessary	1	0.20148	0.10422	3.7375	0.0532	1.223
Functional Status at listing is 30% - Severely disabled: hospitalization is indicated, death not imminent	1	0.38906	0.12554	9.6049	0.0019	1.476
Functional Status at listing is 40% - Disabled: requires special care and assistance	1	0.33743	0.10046	11.2827	0.0008	1.401
Functional Status at listing is 50% - Requires considerable assistance and frequent medical care	1	0.27656	0.07580	13.3106	0.0003	1.319
Functional Status at listing is 60% - Requires occasional assistance but is able to care for needs	1	0.17617	0.05792	9.2519	0.0024	1.193
Functional Status at listing is 70% - Cares for self: unable to carry on normal activity or active work	1	0.12627	0.04319	8.5458	0.0035	1.135

Parameter	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio
Functional Status at listing is 80% - Normal activity with effort: some symptoms of disease	1	0.05832	0.03919	2.2152	0.1367	1.060
Functional Status at listing is 90% - Able to carry on normal activity: minor symptoms of disease	1	-0.00665	0.03924	0.0287	0.8654	0.993
Patient does not have history of diabetes	1	-0.36502	0.03150	134.2980	<.0001	0.694
Black	1	-0.05008	0.02854	3.0795	0.0793	0.951
Hispanic	1	-0.33320	0.03758	78.5935	<.0001	0.717
Asian	1	-0.41095	0.05957	47.5944	<.0001	0.663
Native American, Native Hawaiian, or Pacific Islander	1	-0.18182	0.10668	2.9049	0.0883	0.834
Patient has peripheral vascular disease	1	0.36666	0.03587	104.5098	<.0001	1.443
Patient has history of malignancy	1	0.16269	0.03509	21.4911	<.0001	1.177
Diagnosis for transplant is unknown	1	0.07729	0.04821	2.5706	0.1089	1.080
Diagnosis for transplant is IGA NEPHROPATHY	1	-0.75963	0.09280	67.0023	<.0001	0.468
Diagnosis for transplant is FOCAL GLOMERULAR SCLEROSIS	1	-0.17190	0.06053	8.0636	0.0045	0.842
Diagnosis for transplant is	1	-0.51347	0.05454	88.6468	<.0001	0.598

Parameter	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio
POLYCYSTIC KIDNEYS						
Diagnosis for transplant is HYPERTENSIVE NEPHROSCLEROSIS	1	0.03544	0.03376	1.1022	0.2938	1.036
Diagnosis for transplant is DIABETES MELLITUS - TYPE II	1	0.04222	0.03523	1.4364	0.2307	1.043
Number of DR mismatches ≥ 0	1	0.00418	0.02378	0.0308	0.8606	1.004
Number of HLA mismatches ≥ 0	1	0.03021	0.01056	8.1879	0.0042	1.031
Donor creatnine level	1	0.06571	0.01043	39.6845	<.0001	1.068
Donor age at listing 35-44 years	1	-0.03060	0.03320	0.8493	0.3568	0.970
Donor age at listing 45-54 years	1	0.11265	0.03073	13.4354	0.0002	1.119
Donor age at listing 55-64 years	1	0.12146	0.03808	10.1715	0.0014	1.129
Donor age at listing $\geq$ 65 years	1	0.08257	0.06110	1.8262	0.1766	1.086
Functional Status at transplant (recipient) is 10% - Moribund, fatal processes progressing rapidly	1	1.75570	0.14630	144.0073	<.0001	5.787
Functional Status at transplant (recipient) is 20% - Very sick, hospitalization necessary: active treatment necessary	1	1.13481	0.09529	141.8188	<.0001	3.111
Functional Status at transplant (recipient) is 30% - Severely disabled: hospitalization is indicated, death not imminent	1	0.84616	0.11970	49.9745	<.0001	2.331
Functional Status at transplant	1	0.37370	0.08966	17.3700	<.0001	1.453

Parameter	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio
(recipient) is 40% - Disabled: requires special care and assistance						
Functional Status at transplant (recipient) is 50% - Requires considerable assistance and frequent medical care	1	0.56096	0.07077	62.8316	<.0001	1.752
Functional Status at transplant (recipient) is 60% - Requires occasional assistance but is able to care for needs	1	0.33170	0.05507	36.2861	<.0001	1.393
Functional Status at transplant (recipient) is 70% - Cares for self: unable to carry on normal activity or active work	1	0.27597	0.04448	38.4991	<.0001	1.318
Functional Status at transplant (recipient) is 80% - Normal activity with effort: some symptoms of disease	1	0.14143	0.04103	11.8820	0.0006	1.152
Functional Status at transplant (recipient) is 90% - Able to carry on normal activity: minor symptoms of disease	1	0.02683	0.04280	0.3930	0.5307	1.027
Donor and Recipient do not have the same ABO blood type	1	-0.06632	0.03915	2.8705	0.0902	0.936
KDPI is 70- <85	1	0.26392	0.03665	51.8524	<.0001	1.302
KDPI is 85- <95	1	0.39690	0.04499	77.8163	<.0001	1.487
KDPI is 95 or greater	1	0.54758	0.06175	78.6353	<.0001	1.729

Waitlist Survival Model

Model Fit Statistics

Criterion	Without Covariates	With Covariates
-2 LOG L	873669.46	838719.60
AIC	873669.46	838799.60
SBC	873669.46	839142.25

Testing Global Null Hypothesis: BETA=0

Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	34949.8641	40	<.0001
Score	30619.4992	40	<.0001
Wald	15178.4550	40	<.0001

Parameter	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio
Serum Albumin Level at Listing	1	-0.30212	0.00867	1213.2882	<.0001	0.739
Calculated Panel Reactive Antibodies at Listing [0-100]	1	0.0003794	0.0003486	1.1842	0.2765	1.000
Calculated Panel Reactive Antibodies (Last Known) [0-100]	1	0.0006470	0.0002027	10.1851	0.0014	1.001
BMI at Listing	1	-0.00206	0.0009515	4.6982	0.0302	0.998
Residence in Rural Zip Code	1	0.01890	0.01434	1.7387	0.1873	1.019
OPO 10-year transplant volume (number of organs)	1	5.86114E-6	5.53E-6	1.1233	0.2892	1.000
OPO mean waiting time for transplant (days)	1	-0.0003561	0.0000849	17.5915	<.0001	1.000
Transplant center 10-year transplant volume (number of organs)	1	0.0001227	9.31411E-6	173.4995	<.0001	1.000
Transplant center mean waiting time for transplant (days)	1	0.0004555	0.0000583	61.0069	<.0001	1.000
Transplant center HHI Index [0-1]	1	-0.10256	0.03777	7.3723	0.0066	0.903
Number of transplant centers in the OPO	1	-0.01171	0.00260	20.2663	<.0001	0.988
Age at listing 35-44 years	1	0.38354	0.03104	152.6652	<.0001	1.467
Age at listing 45-54 years	1	0.84545	0.02808	906.6640	<.0001	2.329
Age at listing 55-64 years	1	1.21601	0.02720	1999.1702	<.0001	3.374
Age at listing $\geq$ 65 years	1	1.49923	0.02753	2964.6986	<.0001	4.478

Parameter	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio
Female	1	-0.12102	0.01129	114.7953	<.0001	0.886
ABO = A	1	-0.02541	0.01167	4.7373	0.0295	0.975
ABO = B	1	-0.00676	0.01496	0.2039	0.6516	0.993
ABO = AB	1	-0.02752	0.03053	0.8126	0.3674	0.973
Functional Status at listing is 10% - Moribund, fatal processes progressing rapidly	1	2.35792	0.10022	553.4967	<.0001	10.569
Functional Status at listing is 20% - Very sick, hospitalization necessary: active treatment necessary	1	2.01826	0.04554	1964.5368	<.0001	7.525
Functional Status at listing is 30% - Severely disabled: hospitalization is indicated, death not imminent	1	1.62487	0.06204	685.8816	<.0001	5.078
Functional Status at listing is 40% - Disabled: requires special care and assistance	1	0.69819	0.04233	272.0255	<.0001	2.010
Functional Status at listing is 50% - Requires considerable assistance and frequent medical care	1	0.54397	0.03015	325.4560	<.0001	1.723
Functional Status at listing is 60% - Requires occasional assistance but is able to care for needs	1	0.41908	0.02299	332.4243	<.0001	1.521
Functional Status at listing is 70% - Cares for self: unable to carry on normal activity or active work	1	0.27149	0.01725	247.6084	<.0001	1.312

Parameter	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio
Functional Status at listing is 80% - Normal activity with effort: some symptoms of disease	1	0.10282	0.01682	37.3632	<.0001	1.108
Functional Status at listing is 90% - Able to carry on normal activity: minor symptoms of disease	1	-0.01719	0.01743	0.9728	0.3240	0.983
Patient does not have history of diabetes	1	-0.42356	0.01124	1419.0016	<.0001	0.655
Black	1	0.03599	0.01244	8.3715	0.0038	1.037
Hispanic	1	-0.04511	0.01504	8.9945	0.0027	0.956
Asian	1	-0.15851	0.02391	43.9602	<.0001	0.853
Native American, Native Hawaiian, or Pacific Islander	1	0.04979	0.04014	1.5386	0.2148	1.051
Patient has peripheral vascular disease	1	0.21202	0.01782	141.5691	<.0001	1.236
Patient has history of malignancy	1	-14.52410	74.60811	0.0379	0.8456	0.000
Diagnosis for transplant is unknown	1	-15.22713	108.27140	0.0198	0.8882	0.000
Diagnosis for transplant is IGA NEPHROPATHY	1	-15.26794	88.93700	0.0295	0.8637	0.000
Diagnosis for transplant is FOCAL GLOMERULAR SCLEROSIS	1	-15.44090	74.60766	0.0428	0.8360	0.000
Diagnosis for transplant is POLYCYSTIC KIDNEYS	1	-15.49553	45.54913	0.1157	0.7337	0.000

Parameter	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio
Diagnosis for transplant is HYPERTENSIVE NEPHROSCLEROSIS	1	-15.95108	41.73614	0.1461	0.7023	0.000

Robust and Stochastic Scaling of the Conditional Logit Choice Model

1. Background

The need to account for heterogeneity in discrete choice modeling, particularly in data arising from discrete choice experiments, has garnered widespread interest [113-115]. Two types of heterogeneity are commonly considered, preference heterogeneity, which describes respondent-specific variations in marginal utilities for individual attributes, and scale (variance) heterogeneity (or heteroscedasticity), which is thought to describe unattributed errors to the experimental stimulus [116]. Several explanations for the errors, which are mainly of a cognitive nature, have been proposed [117-119]. These may include respondent inattention, task miscomprehension, or diffidence in alternative selection. From a mathematical standpoint, scale heterogeneity is formulated as an individual-specific, or perhaps as even an alternative- and attribute-specific heteroscedasticity in the variances of the unobserved errors of the respondent's random utility function (hence its alternative name) [120].

Heterogeneity affects the consistency of estimates retrieved from standard choice models [121]. Quantities derived from these estimates such as choice probabilities and even marginal rates of substitution (e.g. willingness-to-pay estimates) in some cases, may exhibit biases [121,122]. Models such as the conditional logit require homogeneity in order to be well-specified. Econometricians have thus devised extensions of the conditional logit in ever-increasing generality to relax assumptions. The mixed logit accommodates heterogeneity and more general substitution patterns by introducing mixing distributions for each parameter that can be used to approximate wide classes of random utility

functions [123,124]. Moreover, by allowing for general correlation structures across the unobserved errors, both scale and preference heterogeneity may indeed be accounted for by the model when applied empirically, but with the qualification that the heterogeneity cannot be attributed to either particular source [114]. Extensions of conditional logit specifically targeting various forms of scale heterogeneity include the nested logit, error-components logit, latent class models, and the generalized multinomial logit have been presented in the literature and the references therein [113,116,125-127]. While empirical estimates from these models may sometimes be interpreted to identify scale heterogeneity apart from preference heterogeneity, it is questionable whether they actually do so without making a priori assumptions about the data [128].

Given the empirical difficulty of disentangling scale heterogeneity and preference heterogeneity, this article adopts a more basic, naïve viewpoint to better understand the former. We instead pose the question, "what could happen to the conditional logit coefficients if they were all interacted with unknown, multiplicative terms that took values over some specified set?" Further, we could also examine whether the quality of the estimates, as measured by goodness-of-fit, deteriorate as these interactive terms are systematically varied. Presuming that preference heterogeneity is not present in the data, we show that this amounts to conducting a sensitivity analysis of model estimates with respect to a rescaling of the coefficients and attributes. In the setting where scale heterogeneity is individual-specific, we may explore how the estimated coefficients of the conditional logit choice model change when the normalization constants for an individual takes values from some known distribution for the population. Alternatively, we may not know the particular distribution of the constants, but still be able to claim that they lie in

some set. In this context, we can calculate conditional logit coefficients for the worst case choice of the scaling parameters – the worst case being the one that minimizes goodness-of-fit.

Computationally, choice model estimates arise as solutions to optimization problems. The fields of stochastic optimization and robust optimization allow us to assess the sensitivity of the coefficients in a precise manner. In this article, we consider the underlying likelihood maximization problem for the conditional logit and introduce parameters scaling the attribute coefficients in individuals' indirect utility functions. Variation in these parameters represents heterogeneity, specifically scale heterogeneity in some contexts when preference heterogeneity is absent. Next, we solve the likelihood maximization problem for two cases: 1) when the scaling parameters are stochastic and take values from a known distribution and 2) when the distribution of the scaling parameters are unknown, but take values over a set for which we compute the worst-case goodness-of-fit. The first case yields a stochastic optimization problem and the second case a robust optimization problem. We discuss the theory and algorithms for solving each of these problems. Using simulated discrete choice experiment data, we focus on a special case of the scaling problems that deal with the normalization constants used to obtain the standard conditional logit. For the experiments, we assess the sensitivity of the conditional logit and the scaling models as the normalization constants vary across individuals.

Throughout this article, we focus on the conditional logit due to its analytic and computational tractability. Ideally, sensitivity analyses would be performed on more sophisticated models. While treatment of preference heterogeneity rather than scale

heterogeneity is likely of greater empirical consequence [129], for clearer exposition of the ideas, we assume that preference heterogeneity does not exist in the data. Lastly, our work is primarily motivated by data typically generated in discrete choice experiments and stated-preference contexts although many of the arguments also carry over to revealed-preference settings.

2. Theory

2.1 The Conditional Logit Likelihood

A complete derivation of random utility choice models and the conditional logit model from multi-attribute utility theory are found in standard texts on the subject [120,125,130]. We denote I as the set of individuals. We assume that each individual evaluates exactly one choice task although panel data may also be incorporated. Let $\mathbb{R}^m$ be the space of attributes and C_i be a finite set of alternatives available to individual i. Next, $\forall c \in C_i$ we define $x_{ic} \in \mathbb{R}^m$ to be the attributes (including alternative-specific constants) describing alternative c for individual i. Let $y_{ic} \in \{0,1\}$ denote whether individual i chooses alternative c. Preferences are described by an indirect utility function that is linear in the parameters: U_{ic}: $\mathbb{R}^m \to \mathbb{R}$, $U_{ic} = \beta^T x_{ic} + \varepsilon_{ic}$ where $\beta \in \mathbb{R}^m$ is the parameter-vector of interest and ε_{ic} is a stochastic error term. Suppose the ε_{ic} are independent Gumbel random variables with expectation $\frac{\gamma}{\sigma_{ic}}$ and variance $\frac{\pi^2}{6{\sigma_{ic}}^2}$ where γ is the Euler-Mascheroni constant (≈ 0.57721) and σ_{ic} are positive constants. The probability that individual i selects alternative c is given as:

$$\mathbb{P}(y_{ic} = 1) = \prod\nolimits_{c \in C_i} \frac{exp(\sigma_{ic}\beta^T x_{ic})}{\sum_{d \in C_i} exp(\sigma_{ic}\beta^T x_{id})}^{y_{ic}}$$

The standard conditional logit is obtained when it is assumed $\sigma_{ic} = 1 \, \forall i \in I, \forall c \in C_i$.

The corresponding likelihood and log-likelihood functions are:

$$L(\beta) = \prod_{i \in I} \prod_{c \in C_i} \frac{\exp(\beta^T x_{ic})}{\sum_{d \in C_i} \exp(\beta^T x_{id})}^{y_{ic}}$$

$$\ell(\beta) = \sum_{i \in I} \sum_{c \in C_i} y_{ic} \left[\beta^T x_{ic} - \ln \left(\sum_{d \in C_i} \exp(\beta^T x_{id}) \right) \right]$$

and for each individual i:

$$\ell_i(\beta) = \sum_{c \in C_i} y_{ic} \left[\beta^T x_{ic} - \ln \left(\sum_{d \in C_i} \exp(\beta^T x_{id}) \right) \right]$$

Scale heterogeneity occurs when the ε_{ic} depart from standard distributional assumptions. The σ_{ic} are normalization constants necessary for normalizing the data and generally are not separately identifiable from β [113]. They may be interpreted as either scaling the coefficients β or scaling the attribute data as well.

2.2 Scaling of the Conditional Logit Likelihood

We now analyze a generalized individual-specific scaling of β and the attribute data. Let $\alpha = (\alpha_{(1)}, \alpha_{(2)}, \ldots, \alpha_{(m)})^T$ be a vector with positive components. Further, denote

$$\mathbf{A} = \begin{bmatrix} \alpha_{(1)} & & & \mathbf{0} \\ & \alpha_{(2)} & & \\ & & \ddots & \\ \mathbf{0} & & & \alpha_{(m)} \end{bmatrix}$$

as a diagonal $m \times m$ matrix and define the following functions:

$$f_i(\alpha, \beta) = \sum_{c \in C_i} y_{ic} \left[(\mathbf{A}\beta)^T x_{ic} - \ln \left(\sum_{d \in C_i} \exp((\mathbf{A}\beta)^T x_{id}) \right) \right]$$

Observe that $f_i(\alpha, \beta) = \ell_i(\mathbf{A}\beta)$. The functions f_i parameterize an arbitrary scaling of the coefficients and attributes. As a special case, $\mathbf{A} = \sigma_i \mathbf{I}$ with $\sigma_i > 0$ implements an individual-specific renormalization of the error terms in the conditional logit model. Since the variances of the error terms are never known empirically, we are particularly interested in the dependence of the maximum likelihood estimate of β when α takes values from a known distribution (the stochastic case) or when the distribution of α may not be known, but takes values in some known set (the robust case).

The function f_i is concave in β (for fixed α) and is concave in α (for fixed β). McFadden established that $\ell_i(\beta; \boldsymbol{X})$ is concave for general attribute data ($\boldsymbol{X}$ denotes the attribute data explicitly) [131]. The composition of a concave function with an affine function is concave [132], and since $f_i(\alpha, \beta) = \ell_i(\mathbf{A}\beta)$, f_i is therefore concave in β. A substitution argument that rescales the data demonstrates that f_i is also concave in α:

Proposition: $f_i(\alpha, \beta)$ is concave in α (for fixed β).

Proof:

Define $z_{(j)} \coloneqq \beta_{(j)} x_{(j)}$.

$$(\mathbf{A}\beta)^{\mathrm{T}} x = \sum_{j=1}^{m} \alpha_{(j)} \beta_{(\mathrm{j})}\, x_{(j)} = \alpha^T z$$

$$\Longrightarrow f_i(\alpha, \cdot) = \sum\nolimits_{c \in C_i} y_{ic} \left[\alpha^T z_{ic} - \ln\left(\sum\nolimits_{d \in C_i} \exp(\alpha^T z_{id}) \right) \right] = \ell_i(\alpha; \boldsymbol{Z}) \qquad \blacksquare$$

2.3 Likelihood Optimization

Let $\mathcal{D}$ be a convex subset of $\mathbb{R}^m$. Solving the following convex programming

problem yields the (possibly constrained) maximum likelihood estimate for β:

$$\max_{\beta \in \mathcal{D}} \quad \sum_{i \in I} \ell_i(\beta) \tag{1}$$

Readers familiar with predictive learning and regularization techniques may also consider an alternative formulation. If the components of β are nonzero, then the preceding problem is equivalent to minimizing the AIC loss function with a regularization term:

$$\min_{\beta \in \mathcal{D}} \quad 2\|\beta\|_0 - 2\sum_{i \in I} \ell_i(\beta)$$

where $\|\cdot\|_0$ denotes the 0-norm. This equivalent convex minimization problem alludes to an information theoretic interpretation of the optimization models in the following sections and possibly also to different algorithms for predicting choice, although such a viewpoint likely takes one outside the random utility framework.

2.4 Stochastic Scaling

Suppose that the distribution of α for a particular individual i is given by $G_i(\alpha)$ and that the distributions are independent across observations. Depending on the interpretation of heterogeneity, the G_i may characterize unobserved influences on the respondents' cognitive responses to the attribute information or on the part-worth of the attributes themselves via incorporation of random effects. The most natural approach is to maximize the expected log-likelihood with convex stochastic programming:

$$\max_{\beta \in \mathcal{D}} \quad \mathbb{E}_\alpha \left[\sum_{i \in I} f_i(\alpha, \beta) \right] \quad = \max_{\beta \in \mathcal{D}} \quad \sum_{i \in I} \int f_i(\alpha, \beta)\, dG_i(\alpha) \tag{2}$$

From an information theory perspective, the objective is to minimize the expected information loss in the data arising from variation in α or from scale heterogeneity in the appropriate contexts. This problem is not novel, as it bears strong resemblance to maximum simulated likelihood and Bayesian methods for modeling heterogeneity[124,133]. In fact, it is a very restrictive mixed model that incorporates observation-specific, random scaling of the attribute data.

2.4 Robust Scaling

Unfortunately, due to present empirical inability to distinguish preference and scale heterogeneity, it is unlikely that the exact distributions of G_i can be known with any certainty in applications. Robust optimization is applicable to situations when the data for optimization problems are uncertain[134]. Such uncertainty may arise from the impossibility of measuring characteristics of the respondents' environment, cognitive processes, and tastes without error. For example, the structural reliability of the bridge may depend on uncertain parameters with unknown distributions such as wind speed, etc. An engineer maximizing the reliability of the bridge would not only consider the average values of these parameters, but seek to ensure that reliability is maximized for a worst-case wind speed. Of course, it is too conservative to consider 'any' wind speed, but perhaps only consider speeds that can take values in some pre-specified set, known as the uncertainty set. This exercise then 'immunizes' the quality of the solution from deteriorating as long as the parameters stay within the uncertainty set, a feature referred to as 'robustness' in the literature.

Specifically, suppose $\alpha \in \mathbb{R}^m$ is allowed to take values over an uncertainty set $\mathcal{U} \subseteq \mathbb{R}^m_+$. Further, assume that $\mathcal{U}$ is a polytope (i.e. a compact, convex polyhedron that

can be described using a finite number of linear inequalities). The simplest example is when $\mathcal{U}$ is a m-dimensional hypercube, that is, each component of α is expected to be in some known interval, $\alpha_{(j)} \in [a_j, b_j]$ where $b_j > a_j \geq 0 \; \forall j \in \{1,2, \ldots m\}$. Furthermore, we assume, for reasons soon made clear, that $(1,1, \ldots ,1)^T \in \mathcal{U}$. Define $f(\alpha, \beta) := \sum_{i \in I} f_i(\alpha, \beta)$. The conditional logit model with robust scaling may be written as the following robust program:

$$\max_{\beta \in \mathcal{D}} \quad \min_{\alpha \in \mathcal{U}} \quad f(\alpha, \beta) \tag{3}$$

The max-min structure of Problem 3 is recurring feature in robust optimization. The information theory interpretation states that were are minimizing the AIC for the value of α in $\mathcal{U}$ that yields the maximum information loss. Naturally, the maximum log-likelihood value and hence goodness-of-fit for the solution β arising from the worst-case choice of α will be no better than an optimal solution for β pertaining to different values of α in $\mathcal{U}$. This is known as the 'price of robustness'. Therefore, the choice of $\mathcal{U}$ is critical in applications. A very conservative choice of $\mathcal{U}$ (i.e a large uncertainty set) could potentially result in a poor fit, although in many empirical applications, this is unlikely [134]. However, Problem 3 guarantees that the goodness-of-fit obtained from fitting this model is a lower-bound for the goodness-of-fit obtained using the actual value of α, provided the actual value of α is in $\mathcal{U}$. When $\mathcal{U} = \{(1,1, \ldots ,1)^T\}$, Problem 3 simplifies into Problem 1, the standard conditional logit choice model. This is referred to as the nominal case in the literature. The aforementioned guarantee implies that when $(1,1, \ldots ,1)^T \in \mathcal{U}$, the goodness-of-fit of the solution obtained from Problem 3 is a lower

bound for that of the standard conditional logit. If the results of the solution to Problem 3 are similar to the nominal case, and the researcher believes the actual value of α to be in $\mathcal{U}$, then the researcher can be extra confident of the quality of the model in the nominal case.

2.5 A Special Case of Scaling

Problems 2 and 3 both deal with general scaling of the choice model coefficients and attributes. A more concrete, univariate special case of the problem can provide some understanding of heterogeneity. For example, the variances of the error-terms ε_{ic} for individual i and alternative c were normalized arbitrarily by unknown positive constants σ_{ic} in the derivation of the conditional logit. We can re-parameterize the log-likelihood to assess the sensitivity of the model to this normalization:

$$\bar{f}(\sigma,\beta) = \sum\nolimits_{i\in I} \sum\nolimits_{c\in C_i} y_{ic} \left[(\sigma\beta)^T x_{ic} - \ln\left(\sum\nolimits_{d\in C_i} \exp((\sigma\beta)^T x_{id}) \right) \right]$$

Again, $\sigma = 1$ yields the standard conditional logit model. The parameter σ may be given a distribution G, yielding a special case of Problem 2:

$$\max_{\beta\in\mathcal{D}} \int \bar{f}(\sigma,\beta)\, dG(\sigma) \tag{4}$$

Empirically, such models can be motivated from combining data from various sources, such as revealed- and stated-preference data [122]. Alternatively, the variances of the error term and resulting normalization constants may be treated as having an unknown distribution. Moreover, we may wish to immunize the conditional logit against departures from the assumption that σ is indeed unity. Let $\mathcal{V}$ be an interval $[\theta_0, \theta_1]$ such that $\theta_1 \geq 1 > \theta_0 > 0$. Problem 3 specializes to:

$$\max_{\beta \in \mathcal{D}} \quad \min_{\sigma \in \mathcal{V}} \quad \bar{f}(\sigma, \beta) \tag{5}$$

3. Algorithms

This section outlines solution methods for Problems 2 and 3. Readers familiar with simulated maximum likelihood, numerical integration, and Monte-Carlo techniques will recognize the methods for Problem 2. The algorithm for Problem 3 is more involved, but still tractable due to the concavity properties of f established above.

3.1 Algorithm for Stochastic Scaling

Problem 2 is a standard convex stochastic programming problem and may be solved via the Sample Average Approximation Method (SAA) [135]. For each individual i, we sample n_i independent replications of α from $G_i(\alpha)$. We then solve the following convex programming problem:

$$\max_{\beta \in \mathcal{D}} \quad \sum\nolimits_{i \in I} \sum_{j_i=1}^{n_i} \frac{1}{n_i} f_i\left(\alpha_{j_i}, \beta\right)$$

where α_{j_i} denotes the j^{th} replication for individual i. This convex program can be solved by standard optimization solvers found in widely available software. Moreover, under some regularity conditions, by the law of large numbers, $\sum_{j_i=1}^{n_i} \frac{1}{n_i} f_i\left(\alpha_{j_i}, \beta\right)$ converges almost surely to $\mathbb{E}_{G_i(\alpha)}[f_i(\alpha, \beta)]$ as $n_i \to \infty$ [135].

3.2 Algorithm for Robust Scaling

For treatment of solution algorithms for Problem 3, the problem may be recast as the equivalent semi-infinite convex program:

$$\max_{\beta \in \mathcal{D}, t \in \mathbb{R}} \quad t$$
$$s.t. \quad f(\alpha, \beta) \geq t \quad \forall \alpha \in \mathcal{U}$$

Cutting surface algorithms for solving more general versions these problems and additional conditions required for convergence have been studied [136,137]. An outline of the method is provided below:

1. Initialize with the nominal case by setting $k = 0$ and $\mathcal{U}_k = \{(1,1,\dots,1)^T\}$.
2. Solve the following convex programming problem and obtain solutions t_k and β_k:

$$\max_{\beta \in \mathcal{D}, t \in \mathbb{R}} \quad t$$
$$s.t. \quad f(\alpha, \beta) \geq t \quad \forall \alpha \in \mathcal{U}_k$$

3. Solve $\min_{\alpha \in \mathcal{U}} f(\alpha, \beta_k)$ and obtain the solution α_k.
4. If $f(\alpha_k, \beta_k) \geq t_k$, we may terminate the algorithm and report the solutions $\alpha_k, \beta_k,$ and t_k. Otherwise, set $\mathcal{U}_{k+1} = \mathcal{U}_k \cup \{\alpha_k\}$, increment k, and go to Step 2.

The complexity of the above algorithm is determined by the difficulty of solving the optimization problem in Step 3 – which requires the minimization of a concave function. There is an extensive literature on algorithms for minimizing concave functions over convex sets [138]. Additionally, it may not always be necessary to always solve this minimization problem. An oracle that can find α_k with $f(\alpha_k, \beta_k) < t_k$ or can otherwise determine that no such α_k exists may be used in lieu of the concave minimization problem in Step 3.

The algorithm may be further simplified by exploiting that f is concave in α (for fixed β) and that $\mathcal{U}$ is a polytope. It is well-known that a concave function over a polytope attains its minimum value at one of the vertices [139]. Therefore, if we let $\mathcal{U}'$ be the set of vertices of $\mathcal{U}$, we need only to solve the following convex programming problem (with a finite number of constraints) once to obtain a solution to Problem 3:

$$\begin{aligned} \max_{\beta \in \mathcal{D}, t \in \mathbb{R}} \quad & t \\ s.t. \quad & f(\alpha, \beta) \geq t \quad \forall \alpha \in \mathcal{U}' \end{aligned}$$

Such a strategy requires prior enumeration of the vertices of the polytope. Unfortunately, enumeration is not always viable as the number of possible vertices may increase exponentially in the dimension of the polytope. However, for cases when $\mathcal{U}$ is low-dimensional, this may be a good option.

4. Experiment Methods

4.1 Choice Data Creation

We demonstrate the above methods for special-case Problems 4 and 5 using data from a simulated discrete choice experiment. We consider a two-alternative unlabeled design with three attributes (one 3-level attribute and two 2-level attributes with no alternative-specific constants). Coding the attributes using binary variables, we used SAS 9.4 to construct a D-efficient fractional factorial design consisting of 24 choice tasks under the null hypothesis that $\beta = 0$ [140]. Preferences were describe using a utility function linear in the attributes and parameters ($m = 4$). The parameter vector was normalized so that $\|\beta\|_2 = 1$.

Choice data was generated for 1000 respondents who were assumed to view the full experimental design once. Individual-specific scale heterogeneity was incorporated

into the simulation via a population-distribution for the individual-specific normalization constants σ_i. We denote the lognormal distribution with location parameter μ and shape parameter τ as $\ln \mathcal{N}(\mu, \tau^2)$. These parameters describe inherent scale heterogeneity in the population. Lesser values of μ correspond to larger expected variances in unobservable errors during utility elicitation. Greater values for τ^2 correspond to greater variability in these variances across individuals. Samples of σ_i were generated for each individual corresponding to different choices of μ and τ^2. Using the calculated utilities for each design alternative and the sampled values of σ_i, we generated the responses for each choice task[124].

We next solved Problems 4 and 5 when $\mathcal{D} = \mathbb{R}^4$ (i.e. no constraints on β) using the algorithms in Section 3. For each scaling model, we considered choice datasets arising from two scenarios, one where $\mu \to -\infty$ and one where $\tau^2 \to \infty$. Choice data generation and the optimization models below were conducted in MATLAB 2017. The code for the experiments is available on the author's website.

4.2 Experiment Methods for the Stochastic Case

For the stochastic case, Problem 4, we assumed that $G(\sigma)$ was also characterized by a lognormal distribution: $\ln \mathcal{N}(\mu', \tau'^2)$ and sampled 100 draws from $G(\sigma)$ (n_i=100). For both scenarios when $\mu \to -\infty$ or $\tau^2 \to \infty$, we assessed the behavior of the coefficients, errors, and log-likelihoods of the stochastic scaling and conditional logit models. Errors were calculated using the square roots of the trace elements of the inverse Hessian at the optimal solution for each problem. Additionally, we performed sensitivity analyses when the distribution was incorrectly specified (i.e. $\mu' \neq \mu$ or $\tau'^2 \neq \tau^2$) and when small samples (10 individuals) were used.

4.3 Experiment Methods for the Robust Case

For the robust case, Problem 5, we considered a similar experiment, albeit without being aware of suitable distributions for σ. We examined scenarios when $\mu \to -\infty$ or $\tau^2 \to \infty$. We estimate the conditional logit and robust scaling models on each of these datasets and compare the coefficients, log-likelihoods, and errors. Additionally, we consider different uncertainty sets $\mathcal{V}$ for σ, i.e. intervals $[\theta_0, \theta_1]$ with different values for θ_0 and θ_1. We chose $\theta_0 = \exp(-1.96\tau)$ and $\theta_1 = \exp(1.96\tau)$. Although any appropriate values for θ_0 and θ_1 may be chosen, we selected these because if the true population distribution of σ is indeed $\ln \mathcal{N}(0, \tau^2)$, then $\mathbb{P}[\sigma_i \in [\theta_0, \theta_1]] = 0.95$. Thus, for this experiment, we can interpret $\mathcal{V}$ as reflecting the need to immunize against departures of σ from unity 95% of the time – although a probabilistic interpretation of the uncertainty set is not necessary.

5. Results

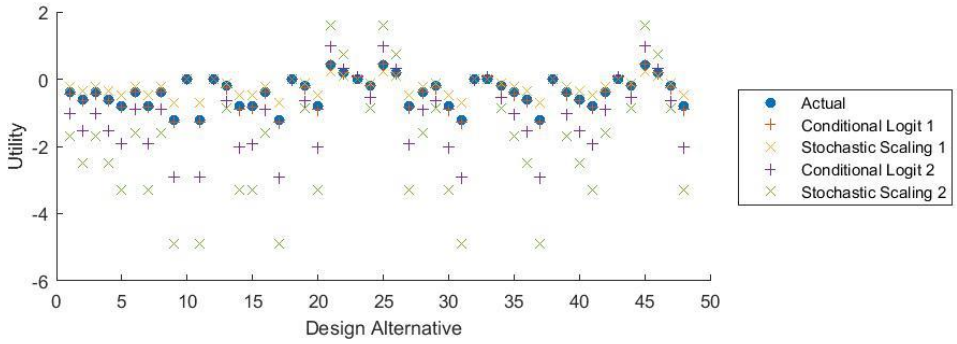
5.1 Experiment Results, the Stochastic Case

The numerical experiments suggested that as $\mu \to -\infty$, magnitudes of the coefficients of the conditional logit and stochastic scaling models increased. Calculated errors increased for the models increased as well. Coefficients for the stochastic scaling model could be farther away from the actual values unless sufficiently large samples were employed. Table 5.1 presents a representative example from this scenario. Figure 5.1 depicts the results in utility-space where calculated utilities of the design alternatives using the coefficients for each model are shown.

Table 5.1: Representative Results, Stochastic Scaling and Conditional Logit when $\mu \to -\infty$

	Actual	Conditional Logit 1	Error		Stochastic Scaling 1	Error
μ/μ'	0.00	---	---		---	---
τ^2/τ'^2	0.50	---	---		---	---
$\beta_{(1)}$	-0.80	-0.89	0.04		-0.47	0.03
$\beta_{(2)}$	-0.20	-0.25	0.03		-0.12	0.02
$\beta_{(3)}$	-0.40	-0.39	0.04		-0.23	0.03
$\beta_{(4)}$	0.40	0.44	0.05		0.23	0.03
LL(0)	---	-16635.53	---		-16635.53	---
LL(β)	---	-15413.35	---		-15839.07	---
	Actual	Conditional Logit 2	Error		Stochastic Scaling 2	Error
μ/μ'	-1.00	---				
τ^2/τ'^2	0.50	---				
$\beta_{(1)}$	-0.80	-2.02	0.04		-3.29	0.08
$\beta_{(2)}$	-0.20	-0.64	0.03		-0.87	0.05
$\beta_{(3)}$	-0.40	-0.89	0.05		-1.61	0.09
$\beta_{(4)}$	0.40	0.98	0.06		1.61	0.11
LL(0)	---	-16635.53			-16635.53	---
LL(β)	---	-12425.77			-13322.69	---

Figure 5.1: Representative Results, Stochastic Scaling and Conditional Logit when $\mu \to -\infty$



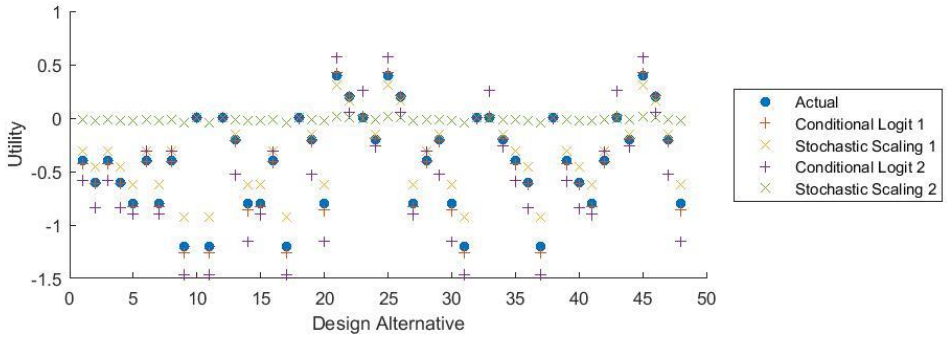
For the scenario when $\tau^2 \to \infty$, the numerical results suggest that the magnitudes of the coefficients and calculated errors for the stochastic scaling model vanish. Variability in the log-likelihoods values for the stochastic scaling model also appear to be

less than that of the conditional logit as $\tau^2 \to \infty$. Table 5.2 and Figure 5.2 similarly present representative findings.

Table 5.2: Representative Results, Stochastic Scaling and Conditional Logit when $\tau^2 \to \infty$

	Actual	Conditional Logit 1	Error		Stochastic Scaling 1	Error
μ/μ'	0.00	---	---		---	---
τ^2/τ'^2	0.25	---	---		---	---
$\beta_{(1)}$	-0.80	-0.85	0.04		-0.62	0.03
$\beta_{(2)}$	-0.20	-0.21	0.03		-0.15	0.02
$\beta_{(3)}$	-0.40	-0.40	0.04		-0.31	0.03
$\beta_{(4)}$	0.40	0.42	0.05		0.31	0.04
LL(0)	---	-16635.53	---		-16635.53	---
LL(β)	---	-15456.90	---		-15696.29	---
	Actual	Conditional Logit 2	Error		Stochastic Scaling 2	Error
μ/μ'	0.00	---	---		---	---
τ^2/τ'^2	4.00	---	---		---	---
$\beta_{(1)}$	-0.80	-1.15	0.04		-0.03	0.003
$\beta_{(2)}$	-0.20	-0.52	0.03		-0.01	0.002
$\beta_{(3)}$	-0.40	-0.31	0.04		-0.01	0.003
$\beta_{(4)}$	0.40	0.57	0.05		0.01	0.003
LL(0)	---	-16635.53			-16635.53	---
LL(β)	---	-14959.20			-16367.52	---

Figure 5.2: Representative Results, Stochastic Scaling and Conditional Logit when $\tau^2 \to \infty$



Results for misspecifications of the stochastic scaling model or behavior in small samples for either scenario were ambiguous. The stochastic scaling model is very sensitive to the choices of μ' and τ'^2 and whether these match the actual values of μ and τ^2. Under ideal conditions and sample sizes, the stochastic model can potentially match the actual values more closely than the conditional logit, a finding somewhat consistent with previous work that mixed-models incorporating some random effects can model the data better[129]. Additionally, as τ^2 increases, which represents greater heterogeneity in normalization constants across individuals, the coefficients may vanish as noted elsewhere[124]. Lesser values of μ, which may be interpreted as greater expected cognitive errors in the absence of preference heterogeneity, can potentially undermine the quality of the experimental stimulus for respondents. Comparisons of the conditional logit with the scaling model for different values of μ' and τ'^2 may be used to assess the sensitivity of the results.

5.2 Experiment Results, the Robust Case

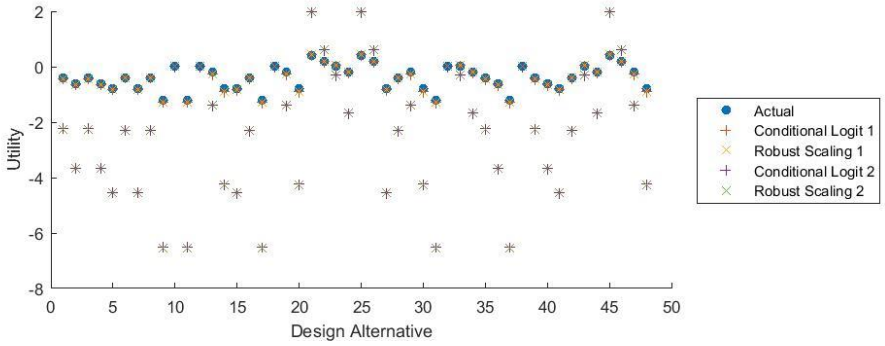
The numerical experiments suggested that as $\mu \to -\infty$, magnitudes of the coefficients and from the conditional logit and robust scaling models increased as in the stochastic case. Coefficients for the conditional logit and robust scaling model were very similar. While the calculated errors for the conditional logit decreased, it was ambiguous

how the calculated errors for the robust scaling model changed. The calculated errors for coefficients for the robust scaling model were initially smaller, but grew larger than those of the conditional logit as $\mu \to -\infty$. As expected, the log-likelihood values for the robust scaling model were less than those of the conditional logit, but the robust scaling model had less variability in the log-likelihoods than the conditional logit as $\mu \to -\infty$ for fixed τ^2. Table5. 3 and Figure 5.3 present representative results.

Table 5.3: Representative Results, Robust Scaling and Conditional Logit when $\mu \to -\infty$

	Actual	Conditional Logit 1	Error		Robust Scaling 1	Error
μ/μ'	0.00	---	---		---	---
τ^2/τ'^2	0.50	---	---		---	---
$\beta_{(1)}$	-0.80	-0.89	0.04		-0.89	0.01
$\beta_{(2)}$	-0.20	-0.25	0.03		-0.25	0.002
$\beta_{(3)}$	-0.40	-0.39	0.04		-0.39	0.01
$\beta_{(4)}$	0.40	0.44	0.05		0.44	0.01
LL(0)	---	-16635.53			-16635.53	---
LL(β)	---	-15413.35			-15424.02	---
	Actual	Conditional Logit 2	Error		Robust Scaling 2	Error
μ/μ'	-2.00	---	---		---	---
τ^2/τ'^2	0.50	---	---		---	---
$\beta_{(1)}$	-0.80	-4.23	0.08		-4.25	0.44
$\beta_{(2)}$	-0.20	-1.37	0.03		-1.37	0.07
$\beta_{(3)}$	-0.40	-2.29	0.07		-2.30	0.26
$\beta_{(4)}$	0.40	1.98	0.09		2.00	0.08
LL(0)	---	-16635.53	---		-16635.53	---
LL(β)	---	-7474.13	---		-7510.54	---

Figure 5.3: Representative Results, Robust Scaling and Conditional Logit when $\mu \to -\infty$



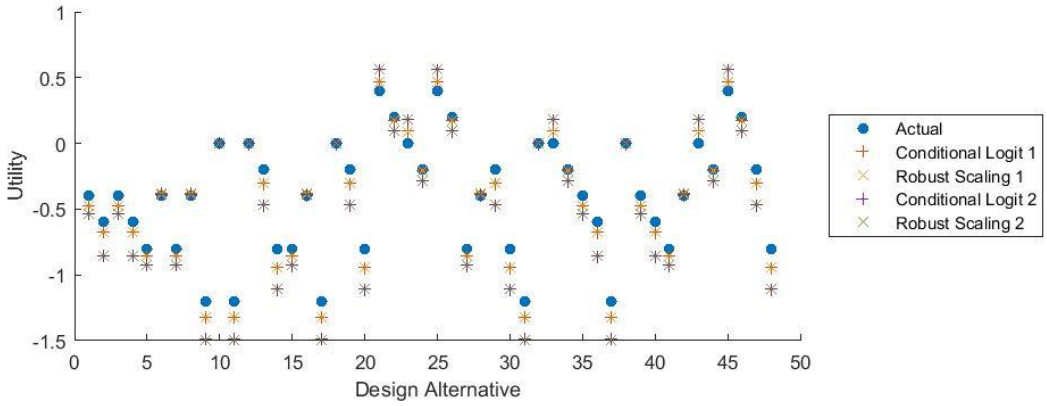
For the scenario when $\tau^2 \to \infty$, coefficients for conditional logit and robust scaling models remained very close, although were potentially different than the actual values. Calculated errors for the robust scaling model did not vary monotonically in any clear way as $\tau^2 \to \infty$; although, variability in the log-likelihoods was less than the conditional logit as $\tau^2 \to \infty$. Table 5.4 and Figure 5.4 present representative results.

Table 5.4: Representative Results, Robust Scaling and Conditional Logit when $\tau^2 \to \infty$

	Actual	Conditional Logit 1	Error		Robust Scaling 1	Error
μ/μ'	0.00	---	---		---	---
τ^2/τ'^2	1.00	---	---		---	---
$\beta_{(1)}$	-0.80	-0.94	0.04		-0.94	0.07
$\beta_{(2)}$	-0.20	-0.30	0.03		-0.30	0.07
$\beta_{(3)}$	-0.40	-0.38	0.04		-0.38	0.10
$\beta_{(4)}$	0.40	0.47	0.05		0.47	0.13
LL(0)	---	-16635.53	---		-16635.53	---
LL(β)	---	-15322.97	---		-15334.34	---

	Actual	Conditional Logit 2	Error		Robust Scaling 2	Error
μ/μ'	0.00	---	---		---	---
τ^2/τ'^2	4.00	---	---		---	---
$\beta_{(1)}$	-0.80	-1.11	0.04		-1.11	0.004
$\beta_{(2)}$	-0.20	-0.47	0.03		-0.47	0.01
$\beta_{(3)}$	-0.40	-0.38	0.04		-0.39	0.02
$\beta_{(4)}$	0.40	0.57	0.05		0.57	0.02
LL(0)	---	-16635.53	---		-16635.53	---
LL(β)	---	-14980.10	---		-14994.05	---

Figure 5.4: Representative Results, Robust Scaling and Conditional Logit when $\tau^2 \to \infty$



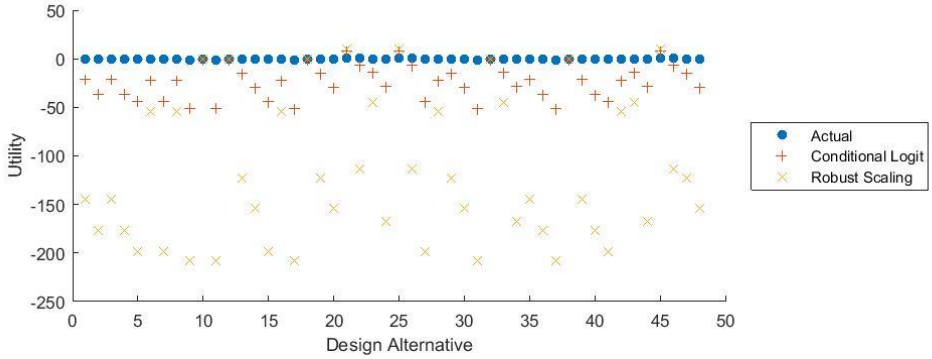
For both scenarios, the lesser variability in the log-likelihood in the robust scaling model and its similarity to the coefficients of the conditional logit seemed to hold for small samples. However, it is not always the case that the coefficients for the conditional

logit and robust scaling model will agree. Coefficients for the robust scaling model diverge from the conditional logit as $\mu \to -\infty$ and $\tau^2 \to 0$. This scenario represents a situation where variances of unobserved errors grow without bound for each individual respondent with little variation across respondents. Of course, such a scenario likely indicates some failure in the choice experiment or study design. Table 5.5 and Figure 5.5 present such a case.

Table 5.5: Example Divergence of Robust Scaling Model when $\mu \to -\infty$ and $\tau^2 \to 0$

	Actual	Conditional Logit	Error		Robust Scaling	Error
μ/μ'	-4.00	---	---		---	---
τ^2/τ'^2	0.0001	---	---		---	---
$\beta_{(1)}$	-0.80	-29.43	*		-154.04	*
$\beta_{(2)}$	-0.20	-14.46	*		-122.88	*
$\beta_{(3)}$	-0.40	-22.18	*		-54.10	*
$\beta_{(4)}$	0.40	7.95	*		9.52	*
*Large values						

Figure 5.4: Example Divergence of Robust Scaling Model when $\mu \to -\infty$ and $\tau^2 \to 0$



5.3 Discussion of Results

The above results demonstrate the well-known inconsistency of the conditional logit model in the presence of heterogeneity. The behavior of models that attempt to rescale the attributes is sensitive to the distribution of the normalization constants – which in these particular experiments signify scale heterogeneity. In the stochastic case, attempts to match the heterogeneity in the normalization constants required a priori knowledge that would likely be unavailable in empirical contexts. This sensitivity should bode caution for researchers interpreting the results of mixed models.

The divergence of the robust model from the conditional logit when $\mu \to -\infty$ and $\tau^2 \to 0$ present an interesting case when the expected unobserved errors increase for all respondents with little variation across the normalization constants. Thus, divergence of the two models can possibly serve as an empirical test for whether the normalization constants indeed depart from unity and whether individuals are even responsive to experimental stimulus.

It is important to note that these models, as noted in the literature, cannot in empirical settings separately identify from where heterogeneity arises. For the above experiments, heterogeneity may be safely interpreted as scale heterogeneity as it is being explicitly controlled as such. However, empirical confounding of preference and scale heterogeneity complicates interpretations. In fact, additional rudimentary experiments performed with preference heterogeneity (i.e. using choice data generated with stochastic β) sometimes produced similar coefficient and utility estimates in the conditional logit and scaling models. A researcher only witnessing the model estimates will not be able to ascertain the source of heterogeneity, and any subsequent explanations are subject to assumptions on the data generating process.

6. Conclusions and Future Work

This work presented models for assessing the influence of the general scaling of the attributes and parameters in the conditional logit model. Extensions of scaling to more general models such as the random parameters logit are also possible. The scaling of the parameters is treated generally and independently of any interpretation. The experiments, however, provide a concrete application of the scaling models in understanding scale heterogeneity. To our knowledge, the robust scaling model is the first introduction of robust optimization in the choice modeling literature. The purpose of robust optimization is to incorporate data uncertainty into choice model inferences without parameterizing distributions for the data. This is promising for choice models that rely on various distributional assumptions on the errors and functional forms of utility. Ongoing work in distributionally robust optimization and robust utilities may prove beneficial in the future [141-144].

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Appendix: LivSim UserGuide

For the latest version of LivSim and the UserGuide, please refer to the following link:

https://github.com/LivSim2017/LivSim-Codes.

The following is the UserGuide as of January 2017:

LivSim User Guide

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1 BACKGROUND

1.1 Purpose of Software

LivSim is an extensible, open-source discrete event simulation of the allocation of livers in the US Organ Procurement and Transplantation Network (OPTN). The most recent version, LivSim 1.11, is written for Python 3.4.2 and is designed to work in tandem with the Liver Simulated Allocation Model (LSAM) (v. Aug 2014)[45] as a separate module. LSAM is the standard simulation tool in the transplantation community used to assess alternative liver allocation policies. Unfortunately, hypothetical liver allocation policies that substantially alter the geographic aspects of organ procurement are not implementable in current versions of LSAM. Specifically, LSAM requires that transplant centers be *uniquely* assigned to a donor service area (DSA), and that DSAs be *uniquely* assigned to a region or district. Moreover, the source code for LSAM is not publicly available and therefore precludes evaluation of some designs for the OPTN such as that of optimized neighborhoods[145].

The intended purpose of LivSim is to provide an open-source alternative to LSAM that enables the testing of more general geographic structures. Like LSAM, it simulates the liver transplantation waitlist, estimates outcomes of transplant candidates and recipients, and evaluates the performance of liver allocation policies. While LivSim may be used as a standalone simulation environment, it works best when used in conjunction with LSAM input data. This guide aims to familiarize users with the architecture of LivSim.

1.2 Overview of LSAM

For a detailed description of LSAM and its architecture, please refer to[45]. LSAM is an event-sequenced Monte Carlo simulation of the OPTN. Let t_0 and t_1 be the starting time and ending times of a LSAM run respectively ($t_0 < t_1$). There are two types of input data: parameters describing the structure and policies of the system; and input streams identifying the times for

the events such as candidate arrivals, organ arrivals, candidate status progressions, deaths of graft recipients not on the waiting list, relisting of recipients whose grafts fail, and status progressions for relisted graft recipients. Every LSAM run is parameterized by the initial liver transplantation waitlist at t_0 (i.e. a list of candidates on the waitlist in addition to their individual characteristics as of t_0); the geographic relations among transplant centers, DSAs, and regions including the modes of transport, transport distances, and transport times from transplant centers to donor hospitals; allocation rules and sharing policies; organ acceptance models; and post-transplant survival/graft failure models.

LSAM executes a schedule of events in time-order through an event handler. These events are generated from schedules collated from the following input streams: 1) a schedule of arrival times for new candidates joining the waitlist during $(t_0, t_1]$ in addition to their individual characteristics at the scheduled time of listing; 2) a schedule of arrival times for new organs during$(t_0, t_1]$ and donor characteristics at time of donation. During an organ arrival event, LSAM applies the allocation rules and organ acceptance model to select a candidate on the waitlist to receive an organ; 3) a schedule of status progressions for each candidate on the waitlist during$(t_0, t_1]$. These status changes may include indications for death, removal from waitlist for any other reason except transplant, and changes to individual characteristics (e.g. model-for-end stage liver disease [MELD] scores). Moreover, if a candidate receives a transplant, all future status changes for that candidate are nullified. If the candidate is subsequently relisted after receiving a transplant, they will be randomly assigned a status change schedule from a special collection of status change schedules for this purpose.

The Scientific Registry of Transplant Recipients (SRTR) provides default input data

based on both historical data and hypothesized models in standard installations of LSAM. Users may also generate their own input data or create new input data using the separate LSAM Candidate Generator and Donor Generator modules. Also, the LSAM user guide provides a detailed description of input generation[45] and highlights some important caveats for users who generate their own input streams, especially from historical data.

At the end of a simulation-run, LSAM will output the waiting list at t_1, the characteristics of patients who had received grafts as of t_1, the characteristics of candidates who died or were removed from the waiting list for any other reason except transplantation during$(t_0, t_1]$, and the characteristics of donors whose livers were transplanted during$(t_0, t_1]$. LSAM will also produce summary statistics derivable from this information (e.g. number of discards, number of local transplants, pre-transplant mortalities at various MELD thresholds, etc.).

1.3 Other Work

Although LSAM is the simulation environment favored by the clinical community for its comprehensiveness and is the de facto benchmarking tool for liver allocation, it was the operations research community that pioneered the use of discrete event simulation for modeling OPTN performance. Pritsker et al., as early as 1995, employed an overall architecture that is similar to most implementations thereafter, including LSAM and LivSim[146]. Kreke et al., Shechter et al., and Iyer et al., have all focused on incorporating more accurate biological modeling of individual end-stage liver disease progression into the simulation logic[147-149]. Taranto et al. and Zenios et al. developed additional applications for kidney allocation prior to the introduction of the kidney-pancreas simulated allocation model (KPSAM) – the counterpart of LSAM used for kidney allocation[150,151].

1.4 LivSim versus LSAM

Please refer to the following sections for details regarding LivSim's architecture. LivSim approximates LSAM from information available in publicly released sources. LivSim, unlike LSAM, operates primarily at the DSA/OPO level. The simulation maintains lists of transplant candidates, recipients, and donors, initializes with a starting waitlist, and takes three input streams: additions to the liver transplant waitlist, status updates/progressions of waitlist candidates, and arrivals of organs. LivSim then processes each of these events similarly to LSAM.

When candidates arrive to a particular DSA, they are assigned a MELD score, ABO blood type, Status 1 exception (yes or no), and HCC exception (yes or no). During a status progression, LivSim updates the candidate's MELD score and potentially removes the candidate from the waitlist or indicates their death. After a donor arrives, the liver is assigned an ABO blood type and is offered to ABO blood type-compatible candidates in accordance with the sharing policies and geographic structure in place. Moreover, LivSim will determine whether this candidate will relist, and if necessary return the candidate to the waitlist after calculating the time until graft failure. The candidate is eligible for another transplant after this time, and as in LSAM, relists at a MELD score of 32. Other attributes for candidates and donors may be defined. LSAM (v Aug 2014) input files are compatible with LivSim 1.11, but need to be formatted prior to running LivSim.

When using LSAM input files, LivSim 1.11 will also use LSAM's organ acceptance model to calculate whether a candidate accepts a liver for transplant. It does so by scanning the LSAM input files for the potential recipient's full set of characteristics (instead of only the

selected aforementioned characteristics [MELD, ABO, Status1, HCC, etc.]) at the time of the offer and calculates the acceptance probability. If LSAM inputs are unavailable, the user may use a reduced form of LSAM's acceptance model. This reduced model uses LSAM's coefficients for whether the potential recipient is Status 1, the potential recipient's waiting time, whether the potential recipient is listed in the DSA of the procuring OPO, and donor blood type, and assumes all other patient attributes are held at the baseline. These four sets of coefficients included are also the four most significant predictors in LSAM's acceptance model.

After LivSim processes these streams, it will produce the following output:

1. DSA-average MELD at transplant and standard deviation
2. DSA-median MELD at transplant and standard deviation
3. Number of transplants by year and DSA
4. Number of waitlist mortalities by year and DSA
5. Number of waitlist removals by year and DSA
6. Average transplant waiting time by year and DSA
7. Numbers of procured organs directed or received by a specific DSA from each other DSA by year and DSA

Moreover, if using LSAM input data, LivSim can calculate the following after post-processing:

8. The number of post-transplant and post-re-transplant mortalities by year
9. Numbers of relists and re-transplants by year
10. Average organ transport distances, times, and mode of transport (drive, plane, or helicopter) by year

Details regarding these calculations are described in the following sections. LivSim shares with LSAM several important limitations. Foremost, the existence of biases or omissions in the input streams for patient arrivals, status changes, and donor arrivals affect the quality of the results. For example, users wishing to use historical data must generate hypothetical status progressions for candidates after the actual transplant date, as no such status changes would be available in historical data. Additionally, LivSim 1.10 and LSAM do not allow for multiple-organ transplants, listing at multiple centers, and split liver transplants. It is also assumed that the parameter input data governing the allocation rules and the geographic relationships among transplant centers, donor hospitals, DSAs, and OPOs do not change during a run. Different transplant centers are presumed to have the same acceptance practices. However, the author believes LivSim is extensible enough to surmount these limitations if necessary.

The primary differences between LivSim and LSAM are the former's ability to incorporate general geographic structures, its focus on OPO/DSA level modeling, simplified (but extensible) use of patient and donor characteristics, and reliance on LSAM input data for acceptance modeling and post-processing. Also, LivSim assumes a relist candidate survives until re-transplant.

2 LIVSIM

2.1 Preliminaries

2.1.1 Installing the Software

LivSim was developed in Python 3.4.2rc1 within the PyCharm Community Edition 4.03 integrated development environment. The user should be able to implement the code in most Python environments. Libraries from standard Python installations include heapq, datetime,

operator, sys, queue, csv, and copy. Additional libraries are also needed to run LivSim and are available in most standard scientific installations of Python. These include Numpy 1.9.1 and Scipy 0.14.0.

The source code is organized into the following **.py* files:

Table 1: LivSim Source Code

LIVSIM SOURCE CODE FILES
Standard Files (Require LSAM Acceptance Model)
1. LivSimPlayback_1_11.py
2. **InputData_LivPlayback_1_11.py**
Post-Processing Files (Require LSAM Input Files)
3. PostTransplantDeathsEstimator.py
4. DistanceEstimator.py
5. OutcomesEstimator_Relists_Regrafts.py
Old Standard Files (Do Not Require LSAM Input Files)
6. LivSimPlayback_1_06.py
7. **InputData_LivPlayback_1_06.py**

The most recent versions of the standard files require LSAM's acceptance model. However, this acceptance model can be replaced with a reduced-form model given in Subsection 2.5 below.

The first standard file, *LivSimPlayback_1_11.py*, is the most important component of LivSim. It contains the source code for the simulation engine, event processing, data

calculations, and output generation. The code is discussed in great detail in the sections below. The second file, *InputData_LivPlayback_1_11*, loads the input data. It is called by *LivSimPlayback_1_11.py* when the simulation initializes.

The files *PostTransplantDeathsEstimator.py*, *DistanceEstimator.py*, and *OutcomesEstimator_Relists_Regrafts.py* are used for post-processing to calculate the number of post-transplant and post-re-transplant mortalities by year, numbers of relists and re-transplants by year, and average organ transport distances, times, and mode of transport. These are described in detail in Section 3.

An older version of LivSim, as featured in *LivSimPlayback_1_06.py* and *InputData_LivPlayback_1_06.py*, are also included for reference and do not require LSAM's files for execution. Moreover, this version was used to generate the results founds in[145].

2.1.2 Input Data and Formatting

This section describes the input data for LivSim and subsequent post-processing. The following table lists the input files used by LivSim:

Table 2: LivSim Input Files

Input File	Description
distancetimes.txt	Organ transport distance/time by DSA. Used in post-processing
Donors_Accept.txt	Donor File generated by LSAM or LSAM donor generator without header. Used for acceptance model
Donors.txt	Organ arrival event input data
DSA_AvgTimes.txt	Historical average transport time by DSA
Input_Acceptance.txt	Coefficients for acceptance model
Input_Acceptance_Status1.txt	Coefficients for acceptance model for Status 1 patients
Input_Geography.txt	Geographical structure matrix. Used to define regions, neighborhoods, districts, etc.
Input_Relist.txt	Input distribution for the probability patient will relist
Input_SPartners.txt	Geographical structure matrix. Used to add sharing partners to geographical structure.
Patients.txt	Patient arrival event input data
Patients_Accept.txt	Patient File generated by LSAM or LSAM donor generator without header. Used for acceptance model
Status.txt	Patient status progression event input

The following provides detail on how each input file is formatted. Single-row tables describe

what the various data columns represent. All files are tab delimited unless specified otherwise.

0. DSAs and organ procurement organizations (OPOs) are numbered in LivSim accordingly:

Table 3: DSA Labels and ID Codes

DSA	DSA id
ALOB-OP1 Alabama Organ Center	0
AROR-OP1 Arkansas Reg. Organ Recovery Agency	1
AZOB-OP1 Donor Network of Arizona	2
CADN-OP1 Donor Network West	3
CAGS-OP1 Sierra Donor Services	4
CAOP-OP1 OneLegacy	5
CASD-IO1 Lifesharing - A Donate Life Org.	6
CORS-OP1 Donor Alliance	7
CTOP-OP1 LifeChoice Donor Services	8
DCTC-OP1 Washington Reg Transplant Community	9
FLFH-IO1 TransLife	10
FLMP-OP1 Life Alliance Organ Recovery Agency	11
FLUF-IO1 LifeQuest Organ Recovery Services	12
FLWC-OP1 LifeLink of Florida	13
GALL-OP1 LifeLink of Georgia	14
HIOP-OP1 Legacy of Life Hawaii	15
IAOP-OP1 Iowa Donor Network	16
ILIP-OP1 Gift of Hope	17
INOP-OP1 Indiana Donor Network	18
KYDA-OP1 KY Organ Donor Affiliates	19
LAOP-OP1 Louisiana Organ Procurement Agency	20
MAOB-OP1 New England Organ Bank	21
MDPC-OP1 The Living Legacy Foundation of MD	22
MIOP-OP1 Gift of Life Michigan	23
MNOP-OP1 LifeSource Upper Midwest OPO	24
MOMA-OP1 Mid-America Transplant Svcs	25
MSOP-OP1 Mississippi Organ Recovery Agency	26
MWOB-OP1 Midwest Transplant Network	27
NCCM-IO1 LifeShare of the Carolinas	28
NCNC-OP1 Carolina Donor Services	29
NEOR-OP1 Nebraska Organ Recovery System	30
NJTO-OP1 NJ Organ and Tissue Sharing Network	31

NMOP-OP1 New Mexico Donor Services	32
NVLV-OP1 Nevada Donor Network	33
NYAP-OP1 Ctr for Donation and Transplant	34
NYFL-IO1 Finger Lakes Donor Recovery Network	35
NYRT-OP1 LiveOnNY	36
NYWN-OP1 Upstate NY Transplant Svcs	37
OHLB-OP1 LifeBanc	38
OHLC-OP1 Life Connection of Ohio	39
OHLP-OP1 Lifeline of Ohio	40
OHOV-OP1 LifeCenter Organ Donor Network	41
OKOP-OP1 LifeShare Transplant Donor Svcs of OK	42
ORUO-IO1 Pacific NW Transplant Bank	43
PADV-OP1 Gift of Life Donor Program	44
PATF-OP1 Center for Organ Recovery and Educ.	45
PRLL-OP1 LifeLink of Puerto Rico	46
SCOP-OP1 LifePoint, Inc.	47
TNDS-OP1 Tennessee Donor Svcs	48
TNMS-OP1 Mid-South Transplant Foundation	49
TXGC-OP1 LifeGift Organ Donation Ctr	50
TXSA-OP1 Texas Organ Sharing Alliance	51
TXSB-OP1 Southwest Transplant Alliance	52
UTOP-OP1 Intermountain Donor Services	53
VATB-OP1 LifeNet Health	54
WALC-OP1 LifeCenter Northwest	55
WIDN-OP1 Wisconsin Donor Network	56
WIUW-IO1 UW Health Organ and Tissue Donation	57

1. distancetimes.txt

Table 4: distancetimes.txt Data

DSA id of donor hospital	DSA id of transplant center	Historical average transport distance (miles)	Historical average transport time (hours)	Transport mode *Driving =0* *Helicopter=1* *Airplane=2*

There are multiple records for each pair of DSAs corresponding to an alternate donor hospital to transplant center combinations. The source of this data is from LSAM.

2. Donors_Accept.txt

   This file is generated by LSAM. Please refer to the LSAM user guide[45] for a description of the columns. This file should have no headers. It is *"|"* delimited.

3. Donors.txt

   Table 5: Donors.txt Data

Replication #	DSA id	DSA id	Donor arrival time (years)	Donor ABO blood type *0=A* *1=AB* *2=B* *3=O*	Organ id

This input files provides the input stream for organ arrival events by describing the organ arrival time, DSA id, and donor blood type. The replication number indicates which replication the event will be read by LSAM; the DSA id indicates which DSA/OPO procures the organ, and arrival time indicates the time LivSim should schedule the event.

IMPORTANT NOTE: It is important that the organ id for the donor matches the corresponding Donor ID in the LSAM-generated Donors_Accept.txt. LivSim will rely on this correspondence to calculate a high-dimensional acceptance model using LSAM's inputs. Moreover, this file should be sorted by organ arrival times. LivSim also reads

each line individually. There is no logic for skipping lines. For example, if the file contains 2 replications of 2 year data, but LivSim is only told to perform 2 replications of 1 year using this file, then LivSim will fail because it will expect the first line after the first replication of the first year to be the first line of the second replication of the first year.

4. DSA_AvgTimes.txt

   58×58 matrix of historical average transport times. Entry a_{ij} corresponds to the transport hours from DSA with DSA id i to the DSA with DSA id j. This matrix is based on historical OPTN data for 1988-2014 and is not necessarily symmetric.

5. Input_Acceptance.txt

   Table 6: Input_Acceptance.txt Data

Coefficient	Data	LSAM Variable
-3.9696	Constant	Constant
-0.0021956	Patient	OfferNum
0.00093769	Patient	can_bili
0.13715	Patient	CANHX_EXC_DIAG_HCC2
0.0019133	Patient	can_min_wgt
-0.34554	Patient	CAN_PREV_TX
-0.0033197	Organ	don_bun
-0.00021398	Organ	don_sgpt
0.7619	Patient	local
-0.025285	Patient	traveltime
-0.00023373	Patient	t_CAN_LISTING_DT
0.6677	Organ	don_abo_b
0.75528	Organ	don_abo_ab
-0.11586	Organ	don_protein_urine_yes
0.18977	Organ	don_ebna_pos
0.27843	Organ	don_anti_hyperten_yes
0.10697	Organ	don_insulin_yes
-0.18242	Organ	don_meet_cdc_high_risk_y
-0.54685	Organ	don_non_hr_beat_y
-0.51637	Organ	don_li_biopsy_yes

0.01748	Organ	don_race_p
-0.0074625	Organ	don_race_h
0.048221	Organ	don_death_mech_gunshot
-0.082015	Organ	don_death_circum_natural
0.11223	Organ	don_hist_cancer_no
-0.050175	Patient	can_abo_o
-0.03899	Patient	can_acpt_abo_incomp_y
-0.13962	Patient	can_acpt_li_seg_y
-0.18497	Patient	can_acpt_hbc_pos_y
-0.046836	Patient	can_acpt_hcv_pos_y
0.10345	Patient	can_malig_y
-0.31748	Patient	CANHX_DIAL_PRIOR_WEEK_y
0.043042	Patient	don_pat_gender_match
0.84707	Patient	abo_compat
0.003028	Patient	labmeld
1.0889	Patient	status1b
-0.15437	Patient	don_can_wgt_ratio_gt_p50
0.0024235	Patient	labmeld_gt_p40
0.020667	Patient	labmeld_gt_p50
0.017413	Patient	labmeld_gt_p60
0.050458	Patient	match_meld_gt_p10
-0.040086	Patient	match_meld_gt_p90
-0.015695	Patient	diffmatchlabmeld_gt_p30
-0.0020132	Organ	don_age_in_months_gt_p30
-0.0000687	Organ	don_age_in_months_gt_p70
0.062528	Organ	don_li_biopsy_macro_fat_miss
-0.0000273	Patient	can_max_mile_gt_p40
0.0015365	Patient	can_min_age_gt_p40
0.0017957	Patient	can_hgt_cm_gt_p10
0.00000322	Patient	can_bili_gt_p10
-0.0101	Patient	can_sodium_gt_p10

This file contains in the leftmost column of numerical coefficients, LSAM's acceptance model.

6. Input_Acceptance_Status1.txt

Table 7: Input_Acceptance_Status1.txt Data

Coefficient	Data	Variable

-1.3617	Constant	Constant
0.0018831	Patient	can_min_age
0.0013077	Patient	can_min_wgt
-0.49647	Organ	DON_EXPAND_DON_KI
-0.088581	Patient	traveltime
0.19018	Organ	don_anti_htlv_neg
-0.024067	Organ	don_li_biopsy_yes
-0.012836	Patient	can_acpt_abo_incomp_y
0.015191	Patient	abo_compat
-0.015954	Patient	don_can_hgt_ratio_gt_p40
-0.1603	Patient	don_can_hgt_ratio_gt_p50
-0.049985	Patient	don_can_wgt_ratio_gt_p20
-0.0066923	Organ	don_wgt_kg_gt_p30
0.00011147	Patient	can_bili_gt_p50
0.0048161	Patient	can_bili_gt_p60

This file contains in the leftmost column of numerical coefficients, LSAM's acceptance model for Status 1 patients.

7. Input_Geography.txt

   This is a 58×58 matrix providing the geographical relationships amongst OPOs that defines regions, districts, or neighborhoods. Entry a_{ij} takes value 1 if DSA with DSA id j shares with the DSA with DSA id i when an organ is procured in the latter during regional allocation. This matrix is not available in LSAM in full generality and hence was the reason LivSim was created.

8. Input_Relist.txt

   This file contains the lower bound, upper bound, and mean for the uniformly distributed probability that a transplanted patient will be relisted. The current values are based on average, historical OPTN data 1988-2014.

9. Input_SPartners.txt

This is a 58×58 matrix adding DSA sharing partners to existing geographical relationships amongst OPOs. Entry a_{ij} takes value 1 if DSA with DSA id j shares with the DSA with DSA id i when an organ is procured as a sharing partner. Although this matrix is read by LivSim, it is not required to actually use it unless the user wishes to study sharing partners.

10. Patients.txt

Table 8: Patients.txt Data

Replication#	Patient id	DSA id	DSA id	Patient Arrival Time (years)	Patient ABO blood type *0=A* *1=AB* *2=B* *3=O*	Patient Allocation MELD	Patient Lab MELD	Patient HCC Status *0=No* *1=Yes*	Status1 *0=No* *1=Yes*	Sodium Score	Inact *0=N* *1=Ye*

This input files provides the input stream for patient arrival events by describing the patient arrival time, DSA id, patient blood type, starting allocation MELD (6-40), starting lab MELD, whether patient receives an HCC exception, whether the patient receives a Status 1 exception, starting lab sodium value, and whether patient is inactive. Status 1A and Status 1B patients are treated identically. The replication number indicates which replication the event will be read by LSAM; the DSA id indicates which DSA/OPO lists the patients, and arrival time indicates the time LivSim should schedule the event.

IMPORTANT NOTE: It is important that the patient id for the patient matches the

corresponding candidate ID in the LSAM-generated Patients_Accept.txt. LivSim will rely on this correspondence to calculate a high-dimensional acceptance model using LSAM's inputs. Moreover, this file should be sorted by patient arrival times. LivSim also reads each line individually. There is no logic for skipping lines. For example, if the file contains 2 replications of 2 year data, but LivSim is only told to perform 2 replications of 1 year using this file, then LivSim will fail because it will expect the first line after the first replication of the first year to be the first line of the second replication of the first year.

11. Patients_Accept.txt

    This file is generated by LSAM. Please refer to the LSAM user guide[45] for a description of the columns. This file should have no headers. It is *"|"* delimited.

12. Status.txt

    Table 9: Status.txt Data

Replication#	Patient id	Status Event Time (years)	Dies 0=No 1=Yes	Removed from waitlist 0=No 1=Yes	Updated Allocation MELD	Updated Lab MELD	Updated Sodium Score	DSA id	DSA id	Updated Inactive Status *0=No 1=Yes*

    This input files provides the input stream for status progression events for a particular patient. Each row updates a given patient's MELD scores, sodium scores, and inactive statuses at a particular DSA. Additionally, a status update event may indicate that the particular patient dies or is removed from the waitlist. Death or waitlist removal nullifies all other updates to MELD scores, sodium, etc. at the time of the death or removal and afterwards. The replication number indicates which replication the event will be read by

LSAM; the DSA id and patient id indicates which patient is to be updated, and the status event time indicates the time LivSim should schedule the update event.

IMPORTANT NOTE: This file should be sorted by status event times. LivSim also reads each line individually. There is no logic for skipping lines. For example, if the file contains 2 replications of 2 year data, but LivSim is only told to perform 2 replications of 1 year using this file, then LivSim will fail because it will expect the first line after the first replication of the first year to be the first line of the second replication of the first year.

13. status_times.txt

This file is used only for post-processing. The first column is the patient id and the second column is the status event time (years). *These columns should match the second and third columns from Status.txt*.

14. step_survival.txt

Table 10: step_survival.txt Data

This file is used only for post-processing for post-transplant outcomes. Given individual characteristics, a step probability is calculated that determines the number of days survived after transplant. Group probability can be ignored. The source of this data is from LSAM's post-transplant survival model.

Step Probability	Days Survived after Transplant	Group Probability

15. survivalcoefficents.txt

Table 11: survivalcoefficents.txt Data

Coefficient	Data	LSAM Variable
0.096521	Organ	don_race_black
0.231046	Organ	don_race_hispanic
0.136725	Organ	don_race_not_wbh
0.115276	Organ	don_cod_cerebro_stroke
0.495574	Organ	don_non_hr_beat_y
0.071974	Organ	don_li_biopsy_y
0.135386	Organ	don_diab_y
0.104547	Organ	don_anti_hcv_pos
-0.18468	Organ	don_age_lt_18
0.069699	Organ	don_age_40_50
0.215867	Organ	don_age_50_60
0.442272	Organ	don_age_60_70
0.53747	Organ	don_age_ge_70
0.048991	Organ	don_hgt_per_10cm_dec
0.187979	Patient	can_race_black
-0.12496	Patient	can_race_hispanic
-0.11149	Patient	can_race_not_wbh
0.357815	Patient	can_life_support_y
0.117489	Patient	can_prev_abdom_surg_y
0.178723	Patient	can_prev_abdom_surg_m
0.296156	Patient	can_dgn_hcv
-0.11892	Patient	can_dgn_chol
0.019462	Patient	can_dgn_ahn
0.03673	Patient	can_dgn_met_dis
0.445674	Patient	can_dgn_mal_neo
0.118069	Patient	can_dgn_other
0.206299	Patient	can_dial_y
0.111769	Patient	can_prev_malig_m
0.157912	Patient	can_prev_malig_y
0.476963	Patient	can_prev_li
-0.22144	Patient	can_ln_albumin
0.040675	Patient	can_albumin_m
0.140549	Patient	can_ln_creat
0.349983	Patient	can_creat_m
-0.10011	Patient	can_age_lt_18
0.21622	Patient	can_age_18_25
0.002244	Patient	can_age_25_35
-0.10293	Patient	can_age_45_55
-0.02486	Patient	can_age_55_65
0.165089	Patient	can_age_ge_65

0.069976 Patient regional
0.184682 Patient national
0.185855 Patient can_diab_ty_any
0.225524 Patient can_growth_fail
0.157561 Patient can_ascites_y
0.155651 Patient can_portal_vein_y

This file is used only for post-processing for post-transplant outcomes. The leftmost column of numerical coefficients is from LSAM's post-transplant survival model.

16. Waitlist_matchmeld.txt

Table 12: Waitlist_matchmeld.txt Data

Patient id	DSA id	Patient Arrival Time (years)	ABO blood type *0=A 1=AB 2=B 3=O*	Patient Starting MELD	Patient HCC Status *0=No 1=Yes*	Status1 *0=No 1=Yes*	Sodium Score	DSA id	Inactive *0=No 1=Yes*

This input files provides the initial waitlist by describing the patient arrival time, DSA id, patient blood type, starting MELD, whether patient receives an HCC exception, whether the patient receives a Status 1 exception, starting lab sodium value, and whether patient is inactive. Status 1A and Status 1B patients are treated identically. Waiting times are negative numbers, indicating that patient arrived before initialization of the simulation at time 0. The characteristics describe the patient at the initialization of the simulation. Starting MELD values may be either lab MELD or allocation MELD values depending on the user's preferences.

2.1.3 InputData_LivPlayback_1_11.py

This file loads and shapes the input data for use by the simulation. It is called by *LivSimPlayback_1_11.py* during the initialization of the simulation. The variable *i_initial* in *Line 2* toggles whether an initial waitlist should be loaded (all other input data will be loaded). *Lines 6-46* read the input files in the preceding subsection. *Lines 48-EOF* load the initial waitlist. As described in the following section, LivSim treats patients and donors as class objects. The OPTN is represented as a list of *58* lists where each list corresponds to the transplant-candidate waiting list at a particular DSA. Loading the initial waitlist instantiates patient-objects with characteristics as described by the columns of Table 12. These objects are then added to a list in the OPTN data structure.

When reading input data, LivSim follows certain conventions regarding missing values, values out of range, etc.:

1. Individuals with empty sodium scores are assigned sodium values of 137 (the highest effective sodium value as per UNOS guidelines at time of writing).
2. Allocation MELD scores range from 6-40.
3. Status 1 candidates are given allocation MELD scores of "41". This is a programming convention.
4. Lab-, allocation-, and sodium- MELD scores are assigned based on the options selected (discussed in the next subsection).
5. If patients receive HCC exceptions, they are assigned MELD scores based on the HCC MELD schedule and selected options (discussed in the next subsection).

2.1.4 Running the Software

This subsection describes running LivSim. Post-processing is described in Section 3. After ensuring that the input files have been formatted properly, the user needs to follow the following steps:

1. Ensure directory pathnames in *Lines 6-51* in *InputData_LivPlayback_1_11.py* all correspond to the appropriate input files.
2. Ensure directory pathnames in *Lines 799-825* in *LivSimPlayback_1_11.py* all correspond to the desired locations for the simulation output files.
3. Ensure pathname in *Line 689* of *LivSimPlayback_1_11.py* maps to *InputData_LivPlayback_1_11.py* or similar file.
4. In *Lines 24-43* in *LivSimPlayback_1_11.py*, select the options desired for the simulation run:
    a. *seed*: Seed for random number generation
    b. *maxtime*: Desired run-length (years)
    c. *nreps*: Number of desired replications
    d. *clock:* Starting clock time (default is *0* and should not usually be changed)
    e. *oid:* Starting organ id number (default is *0* and should not usually be changed)
    f. *maxrejects:* Maximum number of offers that should be made to eligible ABO-compatible candidates for a single donated liver before the liver is discarded.
    g. *regionalsharing:* Toggles full-regional allocation (i.e. no local allocation) if value is *1*.
    h. *sodium:* Applies MELD-Na in lieu of traditional MELD if value is *1*.

i. *capanddelay:* Applies "cap-and-delay" policy for HCC exceptions value is *1*.

j. *spartners:* Toggles sharing-partner allocation if value is *1*.

k. *localboost:* Number of boost points awarded to allocation MELD awarded to local candidates during allocation (default is *0*).

l. *regionalboost:* Number of boost points awarded to allocation MELD awarded to regional candidates during allocation (default is *0*).

Afterwards, the user may run the program by executing *LivSimPlayback_1_11.py*. The user will receive messages with time-stamps when the 1) Simulation input and initializations are complete, 2) after each replication has finished, and 3) when the simulation terminates.

2.1.5 Output Formatting

This section describes the output files generated by LivSim. Output files are usually organized by year. The following provides detail on how each input file is formatted. Single-row tables describe what the various data columns represent. All files are tab delimited unless specified otherwise. *IMPORTANT NOTE: Depending on your environment, the first row (or sometimes first 58 rows if the output file consists of concatenated matrices) may be all 0s or non-numeric values.*

1. Output_deaths.txt

Table 13: Output_deaths.txt Output

#of Deaths	Year	Replication #

2. Output_mr_disparity_mean.txt

Table 14: Output_mr_disparity_mean.txt Output

DSA Average Mortality Rate	Year	Replication #

DSA average mortality rate is calculated as the ratio of the number of deaths in a year to the sum of the waitlist arrivals that year and number of candidates at the start of the year.

3. Output_mr_disparity_std.txt

Table 15: Output_mr_disparity_std.txt Output

DSA Mortality Rate Standard Deviation	Year	Replication #

Calculated as the standard deviation of the DSA average mortality rates.

4. Output_meld_disparity_mean.txt

Table 16: Output_meld_disparity_mean.txt Output

DSA Transplant MELD Average	Year	Replication #

Output is the Average MELD at transplant over the year for non-Status 1 candidates averaged across DSAs.

5. Output_meld_disparity_std.txt

Table 17: Output_meld_disparity_std.txt Output

Standard Deviation of	Year	Replication #

Average DSA Transplant MELD		

Output is the standard deviation of DSA-average MELD at transplant for the year across DSAs (for non-Status 1 candidates).

6. Output_meld_median_mean.txt
7. Table 18: Output_meld_median_mean.txt Output

DSA Transplant MELD Median	Year	Replication #

Output is the Median MELD at transplant over the year for non-Status 1 candidates averaged across DSAs.

8. Output_meld_median_std.txt

   Table 19: Output_meld_median_std.txt Output

Standard Deviation of DSA Transplant MELD Median	Year	Replication #

Output is the standard deviation of DSA-median MELD at transplant for the year across DSAs (for non-Status 1 candidates).

9. RawOutput_ydeaths.txt

   Table 20: RawOutput_ydeaths.txt Output

Year	Replication#	Replication#	Deaths in DSA id=0	Deaths in DSA id=1	…	Deaths in DSA id=57

10. RawOutput_ytransplants.txt

Table 21: RawOutput_ytransplants.txt Output

Year	Replication#	Replication#	Transplants in DSA id=0	Transplants in DSA id=1	…	Transplants in DSA id=57

11. RawOutput_yarrivals.txt

Table 22: RawOutput_yarrivals.txt Output

Year	Replication#	Replication#	Patient Arrivals in DSA id=0	Patient Arrivals in DSA id=1	…	Patient Arrivals in DSA id=57

12. RawOutput_ycandidates.txt

Table 23: RawOutput_ycandidates.txt Output

Year	Replication#	Replication#	Candidates in DSA id=0	Candidates in DSA id=1	…	Candidates in DSA id=57

Output is the number of candidates at the beginning of the year.

13. RawOutput_yremoved.txt

Table 24: RawOutput_yremoved.txt Output

Year	Replication#	Replication#	Patients	Patients	…	Patients

			removed in DSA id=0	removed in DSA id=1		removed in DSA id=57

Output is the number of waitlist candidates removed from waitlist during the year due to any reason except death or transplant.

14. RawOutput_ywait.txt

Table 25: RawOutput_ywait.txt Output

Year	Replication#	Replication#	Accumulated total transplant waiting time in DSA id=0	Accumulated total transplant waiting time in DSA id=1	…	Accumulated total transplant waiting time in DSA id=57

Individual transplant waiting time is calculated as the difference in simulation clock times (years) between time of patient listing and time of transplant. Accumulated total transplant waiting time is the sum of all such waiting times of patients transplanted in that DSA during the year. The user must divide by the number of transplants to obtain the average waiting time per transplant.

15. RawOutput_yMELD.txt

Table 26: RawOutput_yMELD.txt Output

Year	Replication#	Replication#	Accumulated total	Accumulated total	…	Accumulated total

			transplant MELD in DSA id=0	transplant MELD in DSA id=1		transplant MELD in DSA id=57

Accumulated total transplant MELD is the sum of all MELD scores of patients transplanted in that DSA during the year. The user must divide by the number of transplants to obtain the average MELD per transplant.

16. RawOutput_DSAs.txt

    This is a 58×58 matrix summarizing organ sharing across all years and replications. Entry a_{ij} represents the number of livers procured from DSA with DSA id i that were transplanted in the DSA with DSA id j across all years and replications.

17. RawOutput_DSAs2.txt

    This is a $58 \times 58 \times N$ array where N is the number of replication-years (i.e. a 5-year 5-replication run yields 25 replication-years) summarizing organ sharing. Entry $a_{ij}(t)$ represents the number of livers procured from DSA with DSA id i that were transplanted in the DSA with DSA id j up to replication-year t. This array is provided in addition with the RawOutput_DSAs.txt so that the user may analyze organ sharing patterns over time if they so wish.

18. RawOutput_removals.txt

    Table 27: RawOutput_removals.txt Output

Year	Replication#	Removal Time	Removed Patient	Patient Allocation	Patient Lab

			ID	MELD	MELD

Output file contains information of any patient removed for any reason other than transplant/death for further analysis.

19. RawOutput_TxID.txt

Table 28: RawOutput_TxID.txt Output

Year	Replication#	Transplant Time	Transplant Patient ID	Regional Transplant *0=No* *1=Yes*	National Transplant *0=No* *1=Yes*

Output file contains information of any patient transplanted for further analysis. This does not include those who were ever or would have been relisted. Regional transplant refers to non-local but regional transplant (i.e. organ came from same region, district, or neighborhood).

20. RawOutput_DoID.txt

Table 29: RawOutput_DoID.txt Output

Year	Replication#	Transplant Time	Transplant Patient ID	Donor ID

Output file contains information of any patient transplanted (and link to corresponding donor) for further analysis. This does not include those who were ever or would have

been relisted.

21. RawOutput_yrelists.txt

Table 30: RawOutput_yrelists.txt Output

Year	Replication#	Replication#	Relists in DSA id=0	Relists in DSA id=1	…	Relists in DSA id=57

Output is the number of candidates that relisted for transplant during the year by DSA.

22. RawOutput_yregrafts.txt

Table 31: RawOutput_yregrafts.txt Output

Year	Replication#	Replication#	Regrafts in DSA id=0	Regrafts in DSA id=1	…	Regrafts in DSA id=57

Output is the number of relisted candidates that received a re-transplant during the year by DSA.

23. RawOutput_TxIDregraft.txt

Table 32: RawOutput_TxIDregraft.txt Output

Year	Replication#	Re-Transplant Time	Re-Transplant Patient ID	Regional Re-Transplant 0=No 1=Yes	National Re-Transplant *0=No* *1=Yes*

Output file contains information of any patient re-transplanted for further analysis.

Regional transplant refers to non-local but regional transplant (i.e. organ came from same region, district, or neighborhood).

24. RawOutput_DoIDregraft.txt

Table 33: RawOutput_DoIDregraft.txt Output

Year	Replication#	Re-Transplant Time	Re-Transplant Patient ID	Donor ID

Output file contains information of any patient re-transplanted (and link to corresponding donor) for further analysis.

25. RawOutput_Relistid.txt

Table 34: RawOutput_Relistid.txt Output

Year	Replication#	1st Transplant Time	Patient ID	Patient Allocation MELD at 1st Transplant Time	Patient Earliest Re-Transplant Time

Output file contains information of any patient re-listed. As described below, whether a patient will relist is determined at time of the first transplant. The earliest re-transplant time is the time that the 1st graft will fail and that the patient will be eligible for a re-

transplant.

2.2 Architecture

2.2.1 Simulation Engine

Lines 12-92 and *Lines 686-EOF* in *LivSimPlayback_1_11.py*

Figure 1 depicts the schematic for LivSim. The engine first initializes with all global variables and options set; next, calls *InputData_LivPlayback_1_11.py* to read the input data; and sets pointers for reading the patient arrival, organ arrival, and status progression input streams.

Next, the replication is initialized (clock is set to starting value and replication statistics are initialized). Prior to processing the input streams for any replication, the starting waitlist is copied from memory. The engine then reads the lines corresponding to the pointers for the patient arrival, organ arrival, and status progression input streams. Using the event times in the input files, it then determines the next event (or whether the next event is the end-of-year event). Based on the determination, the engine generates an event notice for the event and passes relevant data for the event (e.g. event type, event time, DSA event occurs, etc.). The event notice is added to a queue (called the calendar) and the pointer for the input stream from which the event was read is advanced one line. Event notices are added to the calendar until all events for the replication have been scheduled.

Lastly, once all events have been loaded onto the calendar, the engine continuously pops an event from the calendar and calls a function for the particular event as described by the event notice until it is empty. After the calendar becomes empty, the end-of-replication event is triggered and replication statistics are cleared. If all replications have finished, the engine writes all of the output files and the simulation terminates.

2.2.1 Simulation Engine Classes and Data Structures

LivSim has some object-oriented programming features and important data structures:

1. Event Object Class

   Lines 16-22 in *LivSimPlayback_1_11.py*

   This class of objects is that of the event notices that are loaded onto the calendar. They have three methods: 1) event type (e.g. "*Organ Arrival*"), 2) event time (time to be executed on the simulation clock), and 3) event information (any data that needs to passed to the event function). By default, the engine will pass the entire line read from the input stream as the event information. The user can modify the event information method to pass additional information, characteristics, etc. when the calendar calls the function associated with the event type. Provided each line of the input file for the corresponding stream has the necessary extra column data, users can refer to the appropriate column of the event information to pass additional information.

2. Global Variable Class

   Lines 24-74 in *LivSimPlayback_1_11.py*

   LivSim follows the convention of maintaining all global variables in a single object class *G*. Class *G* contains all the options listed in Section 2.1.4 in addition to the array dimensions of the output files listed in Section 2.1.5.

3. SimStat Class

   Lines 75-92 in *LivSimPlayback_1_11.py*

   This class is used to maintain performance measures and statistics during a replication. Its individual methods are the statistics such as the number of transplants that occurred during that replication-year, number of patient arrivals during that replication-year.

Instantiations of this class may be modified by other events and during the end-of-year event, however each such instantiation is deleted at the end of the replication.

4. OPTN Data Structure

   Line 724 in *LivSimPlayback_1_11.py* and *Lines 48-158* in *InputData_LivPlayback_1_11.py*

   This is a list of lists with dimension n, where n is the number of DSAs. Each element contains a list of patient-class objects that represent the candidates listed at a particular DSA. At the beginning of each replication, the data structure is initialized with a copy of the starting waitlist. During organ allocation, this data structure is temporarily copied (to pass by value in Python).

2.2.2 Entity Classes

LivSim has two important entities: *patients* and *organs* (i.e. donors):

1. Patient Object Class

   Lines 93-112 in *LivSimPlayback_1_11.py*

   Every instantiation of this class represents a patient. Upon construction, they are endowed with methods for the patient's *id*, *DSA*, and *create time*. Patient objects are created during the patient *Arrival Event* and creation of the initial waitlist. Information to populate the methods and attributes comes from the *event information* when scheduling these events and thereby the input files corresponding to the patient arrivals and initial waitlist. The *id* and *DSA* methods give the patients their unique identifiers and locations and are used to refer to the patients during various function calls. The *create time* method gives in simulation clock units, the time the patient object was created (i.e.

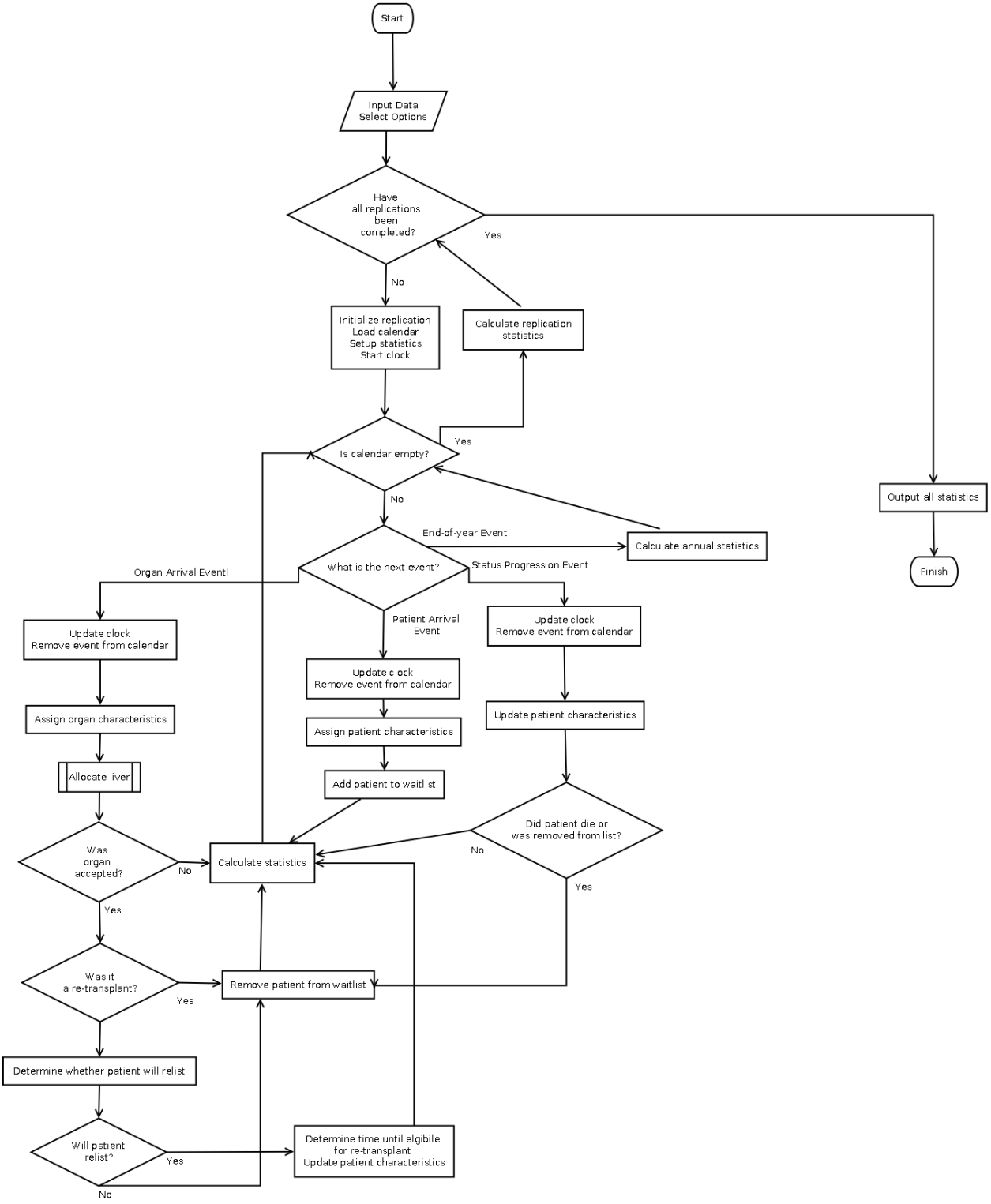
listed). Other methods describe patient characteristics and include: ABO blood type; allocation MELD score; lab MELD score; HCC exception status; Status1; sodium score; waitlist inactive status; whether the patient is a relisted patient; and the time at which a patient is eligible for a re-transplant (*relistTxTime*).

2. Organ Object Class

   Lines 113-121 in *LivSimPlayback_1_11.py*

   Every instantiation of this class represents an organ. Upon construction, they are endowed with methods for the organ's *id* and *DSA*. Organ objects are created during the *Organ Arrival Event* and exist only until the organ is either allocated or discarded. Information to populate the methods and attributes comes from the *event information* when scheduling these events and thereby the input files corresponding to the organ arrivals input stream. The *id* and *DSA* methods give the organs their unique identifiers and locations and are used to refer to the donors during various function calls. Additionally, organs are endowed for an attribute for ABO blood type.

Figure 1: LivSim Architecture



2.3 Events and Subordinate Functions

This section summarizes the various events processed by LivSim. As described above, LivSim executes each event as a function call when the corresponding event notice is retrieved from the calendar. Each event/function takes the *event information* as an input (and does not necessarily return anything).

2.3.1 Arrival (Patient)

Lines 351-403 in *LivSimPlayback_1_11.py*

This event instructs LivSim to create a patient with particular characteristics and add the patient to the waitlist. First, a patient object is created and assigned an *id*, *DSA*, and *create time* in addition to Status 1 (yes/no), ABO blood type, HCC exception status, sodium value, lab MELD, allocation MELD, and waitlist active inactive status as per the function input.

LivSim will use allocation MELD to prioritize patients for transplantation. The user may wish to incorporate sodium MELD (MELD-Na) in one of two ways 1) ensure allocation MELD corresponds to MELD-Na in input streams or 2) toggle the *sodium* option in the global variables. If using the latter, the simulation will first truncate sodium values to the interval $[125,137]$ and use lab MELD to calculated MELD-Na in accordance with the following equation[32]:

$$MELD\ Na = LabMELD + 1.32 * (137 - Na) - \left(0.033 * LabMELD * (137 - Na)\right) \qquad (1)$$

Additionally, all allocation MELD scores (regardless of the sodium update) are rounded to the nearest integer and truncated to the interval $[6,40]$. By convention, Status 1 candidates are assigned an allocation MELD of 41. If the patient is receiving an HCC exception, then either the

patient is retains their allocation MELD score, if the *cap and delay* option is also toggled, then patient's allocation MELD is the minimum of their lab MELD or 28[46]. After allocation MELD is assigned, the patient is then added to the OPTN data structure (at the place corresponding the patient's DSA) and statistics regarding the number of arrivals for the year and number of candidates currently in the OPTN are updated.

2.3.2 Progression

Lines 404-473 in *LivSimPlayback_1_11.py*

This event instructs LivSim to retrieve a particular patient from the OPTN data structure and update the patient's characteristics. These updates are passed in the *event information* for this event and thereby from the progression/status change input stream data. First, LivSim searches the element of the OPTN data structure corresponding to the patient's DSA for the patient object. If the patient has relisted for transplant, then this event is skipped. Additionally, if the patient is indicated to die or be removed from the waitlist, the patient object is deleted; statistics regarding the number of deaths/removals that year and the numbers of candidates currently in the OPTN are all updated; and the event then terminates.

Otherwise, the patient's lab MELD, allocation MELD, sodium, and inactive statuses are updated in accordance with the *event information*. If the *sodium* option is toggled, sodium values will be truncated to the interval $[125,137]$ and allocation MELD will be then updated according to Equation 1 for non-HCC and non-Status 1 candidates (and subsequently rounded to the nearest integer in $[6,40]$. If the *cap and delay* option is toggled, HCC patients' allocation MELD will be updated according the following schedule[46]:

Table 35: Allocation MELD Updates for HCC Patients with Cap and Delay

Waiting Time	Allocation MELD Update
0-0.5 years	Maximum of 28 or old allocation MELD
> 0.5 years – 0.75 years	Maximum of 29 or old allocation MELD
> 0.75 years – 1.00 years	Maximum of 31 or old allocation MELD
> 1.00 years – 1.25 years	Maximum of 33 or old allocation MELD
> 1.25 years – 1.50 years	Maximum of 34 or old allocation MELD
>1.50 years	Minimum of 40 or old allocation MELD +1

2.3.3 Organ Arrival

Lines 474-581 in *LivSimPlayback_1_11.py*

This event instructs LivSim to create an organ with particular characteristics and attempt to allocate the organ. First, an organ object is created and assigned an *id*, *DSA*, and ABO blood type using the *event information*. This event then calls the *Allocate* function and the dependent *MatchRun*, *MatchCheck*, and *Offer* functions that allocate the organ. Organ allocation in LivSim follows the schematic shown in Figure 2.

If a candidate for the organ is not found, the event ends. Otherwise, the *Allocate* function will return the *id* and *DSA* of the accepting patient for transplant. The corresponding patient

object is retrieved from the OPTN data structure. If this is the 1st transplant for the patient, then using the uniform distribution provided in Item 8 of Section 2.1.2, LivSim determines whether the patient will ever relist. If the patient will not relist or just received a re-transplant, then the patient object is deleted from the OPTN data structure, statistics regarding the number of transplants, transplant MELD, waiting time, local/national transplant, supplying DSA, and transplanting DSA are recorded, and the event ends (separate statistics are kept for re-transplants). If the patient relists, the patient object's *Relist* method is updated to the value *1* and the *RelistTxTime* method is assigned a value equal to the simulation clock plus an increment. The increment represents the time until the first graft fails and whereby the patient becomes eligible for a re-transplant. This increment is assigned with the following empirical distribution based on OPTN data[5]:

Table 36: LivSim First Graft Failure Times for Re-Transplant

Increment (Graft Failure Time)	**Probability**
5 years	0.60
2 years	0.20
1 year	0.20

Thereafter, the patient is assigned an allocation MELD of 32 (as is the convention in LSAM) and the event concludes.

2.3.4 The Allocate, MatchRun, MatchCheck, and Offer Functions

Allocate (Lines 123-216), MatchRun (Lines 217-236), MatchCheck (237-259), and Offer

(Lines 260-348) in *LivSimPlayback_1_11.py*

The first of these, the *Allocate* function is called by the *OrganArrival* event. The function takes the organ object passed from the *OrganArrival* event and returns a dummy value indicating the organ was unable to be allocated or the patient *id* and *DSA* of an accepting patient. The purpose of the function is to create the match-run list for the allocation (the offer list), pass it to the *MatchRun* function, and return the results from *MatchRun*. First, this function copies the element of OPTN data structure corresponding to the DSA where the organ was procured (the local list). It adds any local score boosts (if specified in the options). Second, it copies the elements of the OPTN data structure corresponding to the DSAs in the region/district/neighborhood/sharing partner community for regional allocation and applies any regional score boosts if applicable (the regional list). Other remaining elements are copied (the national list).

The next steps depend on the sharing policy specified. If *regional sharing* is toggled, the local and regional lists are combined, sorted by allocation MELD, and then added to a sorted national list to yield the offer list. However, by default, LivSim implements the Share 15 and Share 35 policies for liver allocation[22,23]. The local and regional lists will be partitioned into three lists: one having candidates with allocation MELD $\geq$ 35, one with allocation MELD 15-34, and one with allocation MELD <15. The national list will be partitioned into a list of candidates with allocation MELD $\geq$ 15 and a list with candidates with allocation MELD <15. These lists are then sorted and recombined to yield the offer list that matches the policy.

The second function, *MatchRun*, takes the offer list and organ object from the *Allocate* function, executes the offers, and returns the results back to the *Allocate* function. A local variable, *noffers*, counts how many offers have been made. The global variable, *maxrejects*, specifies the maximum number of offers that can be made before the organ is discarded. While offers can be made, the *MatchRun* traverses the patient objects on the offer list. When doing this, it first calls the third function, *MatchCheck*, and passes the current patient object. The *MatchCheck* function's purpose is for compatibility/cross-matching/eligibility checking of patient and organ. It returns the value *0* if the patient is incompatible or ineligible or *1* if the patient is eligible in compatible. The user may specify whatever criteria they wish, but by default, the *MatchCheck* function checks whether the patient is ABO blood type compatible with the organ, the patient does not have an inactive waitlist status, and if patient has or will relist, that his or her first graft has failed (i.e. the simulation clock has exceeded *RelistTxTime*)

If *MatchCheck* returns *0*, then *MatchRun* will continue traversing the patient objects on the offer list. If *MatchCheck* returns *1*, then it will make an offer the patient, by calling the *Offer* function. The *Offer* function's role is to take the offered organ and current patient object as input, apply the acceptance model, and return the results to *MatchRun*.

IMPORTANT: *The default acceptance model is reproduction of LSAM's acceptance model and requires LSAM files to run* (Items 2, 5, 6, and 11 in Section 2.1.1). Using the *id* variables contained in the donor and patient objects, this function will retrieve additional characteristics of the organ and patient from the LSAM file that are not explicitly modeled in LivSim. If the vector of patient and organ characteristics are denoted as $\boldsymbol{x}$ (from Items 2 and 11) and the coefficients are denoted as $\boldsymbol{\beta}$ (from items 5 and 6), then the acceptance probability is

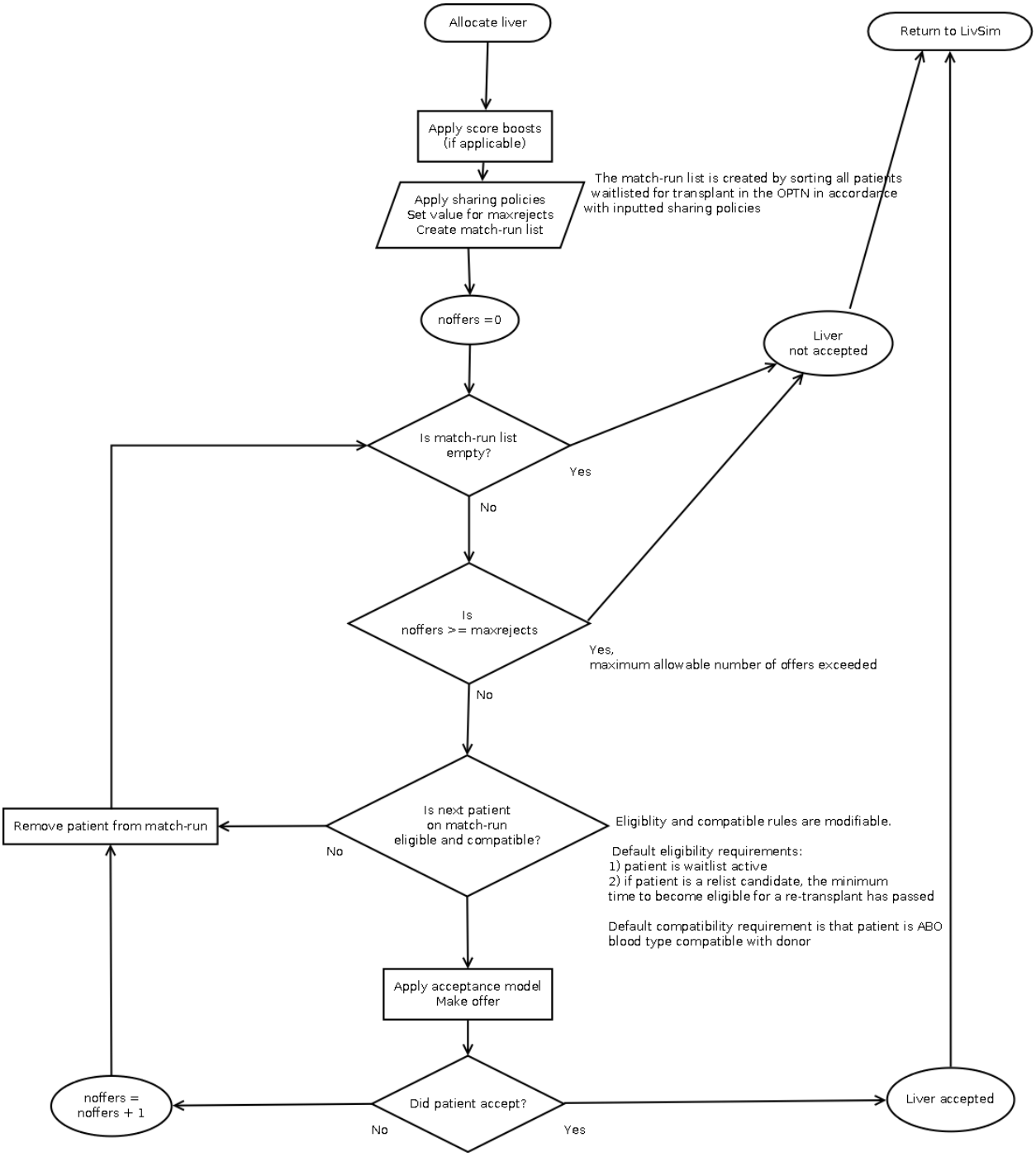
calculated using standard logistic regression:

$$Accept\ Prob = \frac{\exp(\boldsymbol{\beta^T x})}{1 + \exp(\boldsymbol{\beta^T x})} \qquad (2)$$

A separate set of patient and organ characteristics and coefficients are used for Status 1 patients; however the acceptance probability is also calculated following Equation 2. Once the acceptance probability is calculated, a random uniform number is generated. If the random number is less than or equal to $Accept\ Prob$, then the organ is accepted. Otherwise, it is rejected by the patient. A reduced-form acceptance model not requiring LSAM's inputs is provided in the Appendix.

Once an acceptance-rejection decision is made, the result is returned to the *MatchRun* function. If it is an acceptance, *MatchRun* stops traversing the offer list, returns the accepting patient's *id* and *DSA* to the *Allocate* function and thereupon to LivSim's *OrganArrival* call. If it is a rejection, *MatchRun* increments *noffers* and continues traversing the offer list or returns that it was not able to find a recipient to the *Allocate* function if the maximum number of offers were reached. Note that *noffers* is only incremented when *Offer* returns a negative decision, not when *MatchCheck* returns a negative decision – that is, offers are only counted as such if there was an opportunity for them to be rejected by the patient.

Figure 2: Organ Allocation in LivSim



2.3.4 End-of-Year

Lines 582-674 in *LivSimPlayback_1_11.py*

This event occurs after each replication-year and instructs LivSim to calculate annual statistics, to write current annual statistics to the simulation output, and to initialize annual statistics for the following replication year.

2.3.5 End-of-Replication

Lines 675-681 in *LivSimPlayback_1_11.py*

This event occurs after each replication. Currently, it only produces a time-stamp of when the replication completed. This event is included for users wishing to add extra functionality or replication-dependent statistics to LivSim.

2.4 Modifying LivSim

This section provides tips for users wishing to modify LivSim. They are not meant to be comprehensive or taken as the only way to implement the modification, but are the author's opinions on the best course of action.

1. Modifying geographic structures

   The advantage of LivSim is that geographic structures are modeled mathematically as binary relations (i.e. directed graphs) on the set of DSAs. This generality allows users to specify different regional systems, networks, topologies, etc. at the DSA/OPO level

2. Adding new events

   This has to be done carefully. The first step is to create properly formatted input

files containing the input streams. It is suggested to use a format similar to the existing input files. For example, the first columns should contain the Replication number, DSA, and the event time followed by the event information. Second, *InputData_LivPlayback_1_11.py* must be modified to read to extra input file and if necessary, format it. Third, a pointer variable and index corresponding to the dimension the input file must be created prior to scheduling in the simulation engine. Third, the scheduling logic must be modified to advance the newly created pointer, to determine the event time, determine whether this event precedes or follows other events, and to pass the *event information* and event name to the calendar. This should be straightforward and closely resemble the code for the other events. Lastly, the user has to write a new function *User_Event()* or some other valid name that will be executed each time the corresponding event notice is retrieved from the calendar.

3. Adding new donor or patient characteristics

    Adding characteristics is simple. The user can just provide additional methods to the *patient* or *organ* entity classes that correspond to the desired characteristics. Potential examples are transplant centers and donor hospitals. Although LivSim was first written and implemented at the DSA level, it is extensibility allows transplant centers and donor hospitals to be modeled as characteristics of patients and donors. This can provide additional enrichment to the acceptance models, allocation rules, and geographic sharing structures.

4. Modifying sharing policies or allocation rules

    If the user wishes to keep existing sharing policies (e.g. Share 15 and Share 35) but change the respective thresholds, this can be done my modifying the corresponding

constants in the *Allocate* function. If the user wishes to make any other changes to how the match run is created, changing how the offer list is compiled and sorted is also straightforward. The user can sort by another characteristic (instead of allocation MELD), compile lists in different order (e.g. Share 35 national, followed by MELD 15-35 local, etc.) Additionally, if the user wishes to alter compatibility/cross-matching criteria, this can be accomplished by adding additional constraints to the *MatchCheck* function.

The *Offer* function is general. The user can replace it with a very general acceptance model (e.g. transplant-center specific), function, or even another decision simulation provided that it returns the final outcome of the acceptance/rejection decision.

5. Add additional statistics

Adding additional statistics needs to be carefully done as well. First, the user will need to modify the *global variable class* and specify the dimensions of the output for the statistic. The dimensions should account for additional columns to make the output meaningful, for example, the simulation replication and year. Second, if the statistics is be updated after each replication or replication-year, it needs to be added to the *SimStat* class. Third, the statistic, if again replication- or replication-year-dependent, needs to be initialized at the beginning of each replication when an instance of *SimStat* is created. Fourth, the code for calculating the statistic will be required. This step will vary based on the purpose and nature of the statistic, but code will likely have to be added to some event call (e.g. the number of patient arrivals is updated during the patient *Arrival* event). Fifth, if the statistic is replication-year or replication dependent, the statistic will have to be processed during the *End-of-Year* or *End-of-Replication* events respectively. Processing entails the formatting the statistic (e.g. adding headers and helpful columns

such as the replication number, etc.); the writing of the statistic to the output; and clearing or re-initializing the statistic for the next replication or replication-year. If not replication-dependent, the statistic can be written directly to the output when calculated. Lastly, the user then needs to add code at the end of the simulation to write the output to the appropriate directory.

3 POSTPROCESSING

The standard files for LivSim estimate OPTN behavior and waitlist outcomes. Analysis of transplant outcomes is done outside LivSim through post-processing of LivSim output using LSAM input files. Output delivered from post-processing includes:

1. The number of post-transplant and post-re-transplant mortalities by year
2. Numbers of relists and re-transplants by year
3. Average organ transport distances, times, and mode of transport (drive, plane, or helicopter) by year

The files used for each of these items are found in *PostTransplantDeathEstimator.py*, *OutcomesEstimator_Relists_Regrafts.py,* and *DistanceEstimator.py* and are discussed below.

3.1 POST-TRANSPLANT OUTCOMES

The source code for calculating post-transplant outcomes is in *PostTransplantDeathEstimator.py*. The user will need the following files from both LivSim and LSAM to run the code:

FROM LIVSIM: Items 23, 24, and 25 from Section 2.1.3 and Items 13, 14, and 15 from Section

2.1.2

FROM LSAM: The input files for patients, status changes, and the initial waitlist.

The donor *id* and patient *id* variables in both files must match. The modules will scan the LSAM files to retrieve appropriate donor and patient characteristics for the survival computations. After obtaining the necessary files, the user will have to modify the pathnames in *PostTransplantDeathEstimator.py*. Next, the user will have to select the number of replications to bootstrap, *nreps*, and the run-length (years) in which survival will be assessed, *maxtime*. Afterwards, running the code will return the average number of post-transplant mortalities by replication and the standard error.

Calculation of post-transplant survival in LivSim matches that of LSAM[45]. The survival model is a Cox model step function that determines patient survival according to:

$$P(S > t) = f(t)^{\exp(\boldsymbol{\beta}^T \boldsymbol{x})} \qquad (3)$$

where S is the survival time, $f(t)$ is the baseline-survival step-function, $\boldsymbol{x}$ is the vector of covariates in the survival model, and $\boldsymbol{\beta}$ is the corresponding coefficient-vector for the covariates. The list of covariates and their coefficients are provided in Table 11. Consider a partition of the interval $[0, \bar{t})$ into n subintervals $[0, t_1), [t_1, t_2) \ldots [t_{n-1}, \bar{t}]$ and let each subinterval i be associated with a survival probability v_i. The step-function $f(t)$ returns v_k such that $t \in [t_{k-1}, t_k)$. Moreover, it is assumed that $v_k > v_{k+1}$, $v_0 = 1$, and v_n=0 (i.e. the set of v_i's partition the interval [0,1)).

For each transplant event, the remaining survival time is calculated by sampling value u

from a standard uniform distribution and inverting the complementary cdf of S:

$$P(S > t) = u \implies t = f^{-1}(\exp\left(\frac{\ln(u)}{\boldsymbol{\beta}^T \boldsymbol{x}}\right)) \qquad (3)$$

where f^{-1} is defined by the authors as t_k where k is $\inf\{\exp\left(\frac{\ln(u)}{\boldsymbol{\beta}^T \boldsymbol{x}}\right) \in [v_k, v_{k-1})\}$ Each replication performed will sample a different value of u and calculate the survival time t for that transplant recipient. If the sum of t and the current time of transplant is less than *maxtime*, death for the corresponding recipient during the time period is indicated.

3.2 RELIST AND RE-TRANSPLANT OUTCOMES

The source code for calculating relist and re-transplant outcomes is in *OutcomesEstimator_Relists_Regrafts.py*. The structure of the code is very similar to that of the calculation for post-transplant outcomes discussed in the previous section. The user will need the following files from both LivSim and LSAM to run the code:

FROM LIVSIM: Items 19 and 20 from Section 2.1.3 and Items 13, 14, and 15 from Section 2.1.2

FROM LSAM: The input files for patients, status changes, and the initial waitlist.

The donor *id* and patient *id* variables in both files must match. The modules will scan the LSAM files to retrieve appropriate donor and patient characteristics for the computations. After obtaining the necessary files, the user will have to modify the pathnames in *OutcomesEstimator_Relists_Regrafts.py*. Next, the user will have to select the number of replications to bootstrap, *nreps*, and the run-length (years) in which survival will be assessed, *maxtime*. These selections affect the computation for the average number of re-transplant mortalities by replication and the standard error. Also, the user will have to input the probability

that a relist candidate will die on the waitlist (*dprob*, default is about 15.2% based on OPTN data).

This code performs two calculations: the average number of mortalities for relist candidates and the average number of post-transplant mortalities for re-transplant candidates. The latter calculation proceeds exactly similar to the post-transplant survival calculation discussed in the previous section. For the former calculation, any candidate that either was relisted (but not re-transplanted) or flagged by LivSim during the main run that he or she will eventually relist will be considered. The code will first determine whether the candidate was relisted (i.e. 1st graft failed before the end of the run or equivalently that the candidate's *RelistTxTime* method is less than *maxtime*). Next, using a uniformly distributed random number u, the code will indicate that the candidate's death if $u < dprob$. The computation will be repeated for the selected number of replications and the average number of mortalities and standard errors will be reported.

3.3 DISTANCE-RELATED OUTCOMES

The source code for calculating transport times, distances, and mode is found in *DistanceEstimator.py*. The user will need the following files from both LivSim and LSAM to run the code:

FROM LIVSIM: Item 20 from Section 2.1.3

FROM LSAM: The input files for patients, status changes, the initial waitlist, and the distance/times file containing the transport distances/times/modes for each transplant center-donor hospital combination.

The donor *id* and patient *id* variables in both files must match. The modules will scan the LSAM files to retrieve appropriate donor and patient characteristics for the survival computations.

An alternative version of the code not requiring LSAM data, but using DSA-to-DSA averages instead of transplant center-donor hospital combinations is available in the Appendix. This code will only require Items 20 and 24 from Section 2.1.3 and Item 1 in Section 2.1.2. Moreover, if the user wishes to calculation distance-related measures for re-transplants, Item 20 may be replaced with Item 24 from Section 2.1.3.

After obtaining the necessary files, the user will have to modify the pathnames in *DistanceEstimator.py*. The code will then process each transplant event that occurred during the main LivSim run. For each transplant event, it will retrieve a corresponding donor hospital-transplant center combination from the LSAM files. Users may also request that a random donor hospital-transplant center combination with the constraints that the donor hospital and transplant centers are located in the DSAs corresponding to the organ's and patient's *DSA* method respectively. Using a donor hospital-transplant center combination, the code will determine the transport time, distance, and mode (helicopter, drive, and airplane) for the transplant event. After processing all the transplant events, the code will output summary statistics for the average transport distance, average transport time, percentage driven, percentage flown by helicopter, and percentage flown by airplane.

4 APPENDIX

4.1 Reduced Form Acceptance Model

This alternative acceptance model and code may be used to avoid using LSAM inputs. The acceptance model uses LSAM's coefficients for whether the potential recipient is Status 1, the potential recipient's waiting time, whether the potential recipient is listed in the DSA of the procuring OPO, and donor blood type and assumes all other patient attributes are held at the baseline. These four sets of coefficients included are also the four most significant predictors in LSAM's acceptance model.

Table 37: Reduced Form Acceptance Model Coefficients

Characteristic	Coefficient
Constant	**-2.88843**
Status 1 = True	**1.0889**
Local Transplant = True	**0.7619**
Donor Blood Type = AB	**0.75528**
Donor Blood Type = B	**0.6677**
Waiting Time (years)	**-0.08531145**

```
def Offer(offered_organ, matching_recipient):
    #This function offers an organ to a patient and returns information based
on acceptance/rejection
    accept =1
    #Generate acceptance decision
    r1 = nump.random.uniform(0,1,1)

    #Characteristcs
    patientx = [1, matching_recipient.Status1, int(matching_recipient.DSA ==
offered_organ.DSA),int(1== offered_organ.ABO),int(2==
offered_organ.ABO),(Sim.clock-matching_recipient.create_time)]
    accept_prob = nump.exp(nump.dot(patientx,AcceptanceModel)) /
(1+nump.exp(nump.dot(patientx,AcceptanceModel)))
    #accept_prob = .05
    accept = int(r1 <= accept_prob)
    #Return information based on decision
```

```
    if accept ==1:
        return [1,0,matching_recipient.DSA, matching_recipient.id]

    else:
        return [0,1,[],[]]
```

4.2 Alternative Distance Code

An alternative version of the distance code not requiring LSAM data, but using DSA-to-DSA averages instead of transplant center-donor hospital combinations is available in the Appendix. This code will only require Items 20 and 24 from Section 2.1.3 and Item 1 in Section 2.1.2.

```
#This code estimates distances, times, and mode of transport
import numpy as nump
import time
import csv
import scipy as scip
import datetime
import operator
import sys
import queue
from copy import deepcopy
from matplotlib.dates import strpdate2num

#Paramters
ndsa =58
nump.random.seed(7777)
nreps =5


#Load data from LivSimPlayback
transplants = nump.loadtxt("RawOutput_DSAs.txt")

#Load distance-time-mode data
data = nump.loadtxt("distancetimes.txt")




#Setup data
dis_data = [[[] for i in range(0,ndsa)] for j in range(0,ndsa)]
```

```
time_data = [[[] for i in range(0,ndsa)] for j in range(0,ndsa)]
mode_data = [[[] for i in range(0,ndsa)] for j in range(0,ndsa)]


for i in range(0,nump.shape(data)[0]):
    opo = int(data[i,0])
    txdsa =  int(data[i,1])
    dis_data[opo][txdsa].append(data[i,2])
    time_data[opo][txdsa].append(data[i,3])
    mode_data[opo][txdsa].append(data[i,4])

#Prepare Output
distances = []
times = []
drives =[]
helicopters = []
airplanes = []



#Perform Estimation
txtotal = (nump.sum(transplants))

for n in range(0,nreps):
    moment1_distance  =0
    moment1_time  =0

    count_drive  =0
    count_helicopter  =0
    count_airplane  =0

    for i in range(0,ndsa):
        for j in range(0,ndsa):
            if int(transplants[i,j]) <=0:
                pass
            else:
                for k in range(0,int(transplants[i,j])):
                    #Select random donor-hospital and tx-ctr combination
                    if len(dis_data[i][j]) >0:
                        randindex =
nump.random.choice(list(range(0,len(dis_data[i][j]))))

                        #Update Stats
                        moment1_distance = moment1_distance +
dis_data[i][j][randindex]

                        moment1_time = moment1_time +
time_data[i][j][randindex]


                        count_drive  =count_drive +
int(mode_data[i][j][randindex]==0)
                        count_helicopter  =count_helicopter +
int(mode_data[i][j][randindex]==1)
```

```
                        count_airplane  =count_airplane +
int(mode_data[i][j][randindex]==2)

    distances.append(moment1_distance/txtotal)
    times.append(moment1_time/txtotal)
    drives.append(count_drive/txtotal)
    helicopters.append(count_helicopter/txtotal)
    airplanes.append(count_airplane/txtotal)

#Output Results
output1 = ["Distances (Avg, SE)",
nump.mean(distances),nump.std(distances)/nump.sqrt(nreps)]
output2 = ["Times (Avg, SE)",
nump.mean(times),nump.std(times)/nump.sqrt(nreps)]
output3 = ["Drive% (Avg, SE)",
nump.mean(drives),nump.std(drives)/nump.sqrt(nreps)]
output4 = ["Helicopter% (Avg, SE)",
nump.mean(helicopters),nump.std(helicopters)/nump.sqrt(nreps)]
output5 = ["Airplane% (Avg, SE)",
nump.mean(airplanes),nump.std(airplanes)/nump.sqrt(nreps)]

final_output = [output1,output2,output3,output4,output5]

text_file = open("Output_distancestimesmodels.txt", "w")
for item in final_output:
  text_file.write("%s\n" % item)
```