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A NEW SIMULATION MODEL FOR KIDNEY TRANSPLANTATION IN THE UNITED STATES

Burhaneddin Sandıkçı
Sait Tunç

University of Chicago Booth School of Business
5807 South Woodlawn Avenue
Chicago, IL 60637, USA

Bekir Tanrıöver

University of Texas Southwestern Medical Center
5939 Harry Hines Blvd. HP4
Dallas, TX 75239, USA

ABSTRACT

The United Network for Organ Sharing (UNOS) has been using simulation models for over two decades to guide the evolution of organ allocation policies in the United States. UNOS kidney simulation model (KPSAM), which played a crucial role in the 2014 U.S. kidney allocation policy update, is also available to the general public as an executable file. However, this format offers little flexibility to its users in trying out different policy proposals. We describe the development of a discrete-event simulation model as an alternative to KPSAM. It is similar to KPSAM in incorporating many clinical and operational details. On the other hand, it offers more flexibility in evaluating various policy proposals and runs significantly faster than KPSAM due to its efficient use of modern computing technologies. Simulated results closely match actual U.S. kidney transplantation outcomes, building confidence in the accuracy and validity of the model.

1 INTRODUCTION

1.1 Context

Kidney failure is a severe condition indicated by acute or gradual loss of kidney function, which is primarily measured by the level of filtering of the blood. A damaged kidney can cause wastes and unnecessary fluids to build up in the human body. Gradual loss of kidney function, called chronic kidney disease (CKD), can be fatal unless treated. Each year, kidney diseases kill more people than breast and prostate cancer combined (United States National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) 2019). When the level of damage elevates to an advanced stage, also known as the end-stage renal disease (ESRD), it must be treated via renal replacement therapy (RRT), which includes dialysis and kidney transplantation.

According to the 2018 Annual Report of the United States Renal Data System (USRDS 2018), about 15% of the U.S. adult population is affected by CKD, and almost 125,000 new cases of ESRD were reported only in 2016, corresponding to an incidence rate of 373.4 per million population per year and adding up to the U.S. ESRD prevalence of more than 726,000 cases as of the end of 2016. While the vast majority (about 70%) of ESRD patients are treated via dialysis, the preferred mode of treatment is kidney transplantation due to various reasons including longer and better quality of life as well as lower long-term costs.

In 2018, more than 20,000 kidney transplants were performed in the U.S., with an increase of more than 50% since the year 2000 (Organ Procurement and Transplantation Network (OPTN) 2018). Kidneys used in more than $2/3$ of all kidney transplants in the U.S. come from deceased donors, which is the focus of this paper. The success of this life-saving treatment is limited by the scarcity of donor organs. Allocation of deceased donor kidneys in the U.S. are managed through a nationwide waiting list. There are close to 95,000 candidates waiting for a kidney on any given day, compared to 20,000 that will receive a transplant throughout the year. More than 100 patients are added every day to the kidney waiting list, while the supply-demand imbalance results in 11 patient deaths per day while waiting for a transplant (OPTN 2018).

1.2 The Challenge

The allocation of such a scarce resource is complicated by the uncertainties involved (e.g., regarding the health progression of patients, availability of donor organs, and degree of success post-transplantation), the diversity of stakeholders involved (e.g., patients and their families, physicians, surgeons, transplant centers, organ procurement organizations, insurance companies, and transplant policy makers), as well as the multi-dimensional nature of the outcome performance measures. On a very high level, any allocation policy faces the tradeoffs involved in efficient, effective, and equitable distribution of available donor organs.

It is widely accepted that there will never be a 'perfect' allocation policy as long as the demand for transplantation far exceeds the supply (Baldwin et al. 2000; Taranto et al. 2000). What optimizes one performance metric from the perspective of a particular stakeholder may be severely suboptimal for another performance metric or even for the same performance metric from the perspective of another stakeholder. Making policy changes to a complex system of this type under such competing and conflicting objectives can result in unexpected and sometimes unintended consequences (Harper et al. 2000). Furthermore, learning the repercussions associated with a policy change can no longer be left to trial-and-error. Therefore, it is critical to gain a good understanding of the impact of a policy change prior to its implementation.

1.3 Prior Work

To help guide allocation policy changes under the complexities highlighted in Section 1.2, it is required to have an approach that is versatile, accurate, fast, and cost-conscious. It is due to the remarkable success on these aspects that simulation modeling has received acceptance among the transplant policy makers. In the U.S., the first full-blown computer simulation model was developed in 1995 for liver allocation by Pritsker Corporation, under the leadership of the late simulation pioneer Alan Pritsker, in collaboration with UNOS, which administers the U.S. organ transplantation systems. This model was named the UNOS Liver Allocation Model (ULAM) and was described in some detail in Pritsker et al. (1995). The remarkable success of this collaborative effort is best summarized by UNOS representatives in Harper et al. (2000):

> "Liver transplantation has made headline news throughout 1995-2000, with emphasis on patient waiting times and pre-transplant deaths. ULAM has been ever present in the debate, its data used by the transplant community, Department of Health and Human Services, Congress, and the media [...] During each of these proceedings, simulation was viewed as a viable, even necessary tool to evaluate the complex issues surrounding liver allocation. ULAM proved to be flexible, responsive, and able to provide vast amounts of data to its end-users. It is clear that the shape of the debate changed with the quantitative results produced by ULAM. We feel that ULAM helped to select policies that have saved patient lives and produced more quality life-years for them. UNOS continues to rely upon simulation as a tool [...] It appears that simulation is here to stay in the field of organ transplantation."

Simulation, in fact, did stay in the field of organ transplantation. The success of ULAM has energized the kidney transplant community and UNOS leadership to invest into developing UNOS Kidney Allocation Model (UKAM) (Taranto et al. 2000). ULAM and UKAM later evolved into what is known today as Scientific Registry of Transplant Recipients (SRTR) Liver and Kidney-Pancreas Simulated Allocation Models (LSAM and KPSAM, respectively), and complemented with a separate Thoracic Simulated Allocation Model (TSAM) (SRTR 2019). The original paper by Pritsker et al. (1995) was later recognized as "one of the landmark applications in the history of the Winter Simulation Conference for its very significant value and the publicity the work received in the popular press and within U.S. government policy-making and legislative organizations" by the fortieth anniversary special panel (Goldsman et al. 2007).

Several other researchers have described additional simulation modeling efforts for organ transplantation systems. Zenios et al. (1999) discuss a Monte Carlo simulation model of the U.S. kidney transplantation system. Davis et al. (2013) describe donation service area (DSA) level simulation model of the U.S. kidney

allocation system. They primarily focus on studying the input data characteristics for their simulation model, which implements a simplified version of the actual allocation policy through probabilistically identifying the DSA in which a recovered kidney would be used, allocating the kidney exclusively within the identified DSA, not allowing patients/physicians to reject kidney offers, and assuming away the complicated waiting list dynamics. Davis et al. (2014) expand Davis et al. (2013) by incorporating further details of patient demographics and organ quality. However, they incorporate these details in very coarsely aggregated groups. They present improved organ acceptance module that incorporates kidney quality as measured by the kidney donor risk index (KDRI), albeit allowing five coarsely defined KDRI ranges. Harvey and Thompson (2016) describe an agent-based discrete-event model to study the practice of 'multiple listing' in the U.S. kidney transplantation system. They also offer a simplified representation of the waiting list dynamics (e.g., each regional waiting list is implemented as a first-in-first-out queue) and kidney offer acceptance/rejection is not considered. Shechter et al. (2005) describe a discrete-event simulation model for the U.S. adult liver allocation system. The main distinction of their model from ULAM/LSAM is that it only runs on generated arrival streams and offers an alternative modeling of natural history progression of patients' health based on cubic spline modeling while falling short on modeling certain other aspects (e.g., offer acceptance). Iyer et al. (2011) offers an updated version of this model, which adds pediatric patients and donors into consideration. Baldwin et al. (2000) and Ratcliffe et al. (2001) use simulation modeling to evaluate the cost-effectiveness of alternative patient prioritization criteria for liver transplant candidates in a single transplant center in the United Kingdom. Focusing on pediatric heart transplant candidates, Crowe et al. (2015) simulate a birth-death process model with additional details such as weight and blood type compatibility considerations to study the impact of the 'bridging to transplant' practice in the UK.

1.4 Our Purpose and Contribution

As noted in Section 1.3, the U.S. transplant policy makers use a computer simulation model called KPSAM to evaluate alternative allocation strategies in kidney transplantation. KPSAM is also made available to the public but only as an executable file, offering very little flexibility to its users in evaluating different policies. Primarily to overcome this limitation, we have developed a clinically detailed simulation model for the entire U.S. kidney transplant system as an alternative to KPSAM. The code development for the main backbone of the allocation system has been completed and the resulting model is validated through closely matching the actual U.S. kidney outcomes. Upon completing the code development for auxiliary routines such as a graphical user interface and a visual animation, we hope to offer our simulation model to the general public for broader experimentation by independent researchers.

We share the basic philosophy of ULAM, UKAM, and KPSAM (Pritsker et al. 1995; Harper et al. 2000; Taranto et al. 2000; SRTR 2019) in that this simulation model is introduced to allow experimenting with various kidney allocation policy proposals, comparing alternatives to one another, estimating the effect of a policy change prior to its implementation, and, therefore, to empower transplant policy makers and researchers for kidney allocation discussions in the U.S. Similar to its predecessors, our simulation model is developed to assess the system at the national level as opposed to any particular local level (e.g., a transplant center or a DSA). The model is calibrated and validated against the national data, but its results may not be as accurate at the local level although trends observed might be useful. This setup is primarily due to several key components (particularly, survival estimation modules), which are based on national data and does not stratify by local attributes (due to lack of sufficient data at that level of granularity).

Some of the features of our simulation model include its speed that takes advantage of parallel execution of simulation replications, modularity that allows relatively easier updating with changes in the system, its portability to help minimize issues with running in different computing environments. Similar to KPSAM, key events in the simulation, such as arrivals of organs and patients, as well as status updates for candidates (including, among many other things, active/inactive status and removal from the waiting list due to death or other reasons), are linked to an actual transplant database obtained from OPTN/SRTR. This key database includes all transplant candidates that were listed in the U.S. transplant waiting lists between 1987 and 2018,

history of updates for all wait-listed candidates, follow-up records for transplant recipients, as well as all deceased donor organs that were procured during the same time frame. Our implementation corresponds to the most recent UNOS deceased-donor kidney allocation policy (OPTN 2019) and utilizes the same survival and offer acceptance models used in KPSAM. Throughout simulation progress, detailed data records are logged for each patient entering the simulation, which virtually allow analyzing and obtaining any statistical summary of practical interest.

2 THE U.S. ORGAN TRANSPLANTATION SYSTEM

2.1 Main Concepts and the Environment

A national system is employed in the U.S. for organ transplantation. This system, composed of patients, donors, and their families, transplant hospitals, physicians and surgeons, histocompatibility laboratories, organ procurement organizations (OPOs), insurance companies, law makers, and transplant policy makers, and the general public, and its data collection efforts are collectively known as the Organ Procurement and Transplantation Network (OPTN). The United Network for Organ Sharing (UNOS) is a not-for-profit administrator of this system, which operates under the regulations set forth in the Final Rule by the federal government. Final Rule (1998) sets the basic principles of organ allocation and establishes that policies

a. shall seek equitable allocation of deceased-donor organs among potential recipients,
b. shall be based on sound medical judgement,
c. shall seek to achieve the best use of donated organs,
d. shall preserve the ability to decline an offer of an organ,
e. shall be specific for each organ type,
f. shall be designed to avoid wasting organs, to promote patient access to transplantation, and to promote the efficient management of organ placement, and
g. shall be reviewed periodically and revised as appropriate.

UNOS strives to balance all aspects of this challenging mandate and sets organ-specific allocation policies through a Board of Directors receiving input from specialized committees and the general public, reviews each policy periodically and revises as needed, maintains organ-specific lists of all patients waiting for an organ transplantation in the U.S., and uses a computerized matching system to match available donors to awaiting patients in accordance with the policy in effect.

We now provide an overview of the UNOS organ allocation policies, which are described in detail in OPTN (2019). Each policy uses sophisticated algorithms, customized for the type of organ allocated, to determine the offer sequence among wait-listed candidates. A common theme in all policies, however, is to classify candidates into a number of priority groups and rank patients within and around these priority groups. The definition of priority groups depends on the type of organ allocated and its count varies between 12 and 69. Candidate and donor geographies play a significant role in this prioritization. Accordingly, the U.S. is divided into 11 mutually exclusive all encompassing geographic regions, which are subdivided into a total of 58 local donation service areas (DSAs). Each DSA is overseen by an organ procurement organization (OPO) and contains at least one transplant hospital and histocompatibility laboratory. All policies other than heart and lung allocation involve local/regional/national classification of candidates. Accordingly, for each organ recovered by an OPO, candidates are labeled as 'local' if their DSA at registration is the same as the OPO's DSA. Outside of 'local,' candidates are labeled as 'regional' if their region at registration is the same as the OPO's region, and they are otherwise labeled as 'national.' The interaction of this geographical classification with other factors determines priority groups. Although not true strictly, all allocation policies offer higher priority to local candidates, followed by regional and then by national candidates. In the case of heart and lung allocation, local/regional/national classification is replaced by Zones A, B, ..., F, in which zones are defined as concentric circles of increasing radius around the donor hospital.

2.2 The Kidney Allocation System

UNOS deceased-donor kidney allocation system (KAS) uses several candidate and donor attributes, in addition to the geographical classification described in Section 2.1, when defining priority groupings. Within each priority group, candidates are sorted in decreasing kidney allocation points, which is calculated based on candidate's waiting time, calculated Panel Reactive Antibody (cPRA) score, prior living donor status, pediatric status, and tissue mismatch with the donor. cPRA scores range from 0% (easy to match) to 100% (hard to match) and measure candidates' sensitization level (i.e., the degree of antibody incompatibility within a national donor pool). Ties in kidney points are broken by candidates' date and time of registration (oldest to most recent).

One of the factors that affect priority grouping is the quality of the donated kidney. Kidneys from deceased donors are classified according to the Kidney Donor Profile Index (KDPI) into 4 categories: those with a KDPI score of $[0\%, 20\%]$, $(20\%, 35\%)$, $[35\%, 85\%]$, and $(85\%, 100\%]$. KDPI combines ten donor characteristics (namely, age, height, weight, ethnicity, cause of death, non-heart-beating status, terminal serum creatinine level, hepatitis C status, and histories of hypertension and diabetes) into a single number that summarizes the likelihood of graft failure after deceased donor kidney transplant relative to a reference population determined by the Kidney Transplantation Committee. Lower (higher) KDPI scores are associated with longer (shorter, respectively) estimated graft function.

There are 69, 50, 47, and 32 priority groups for kidneys with a KDPI score of $[0\%, 20\%]$, $(20\%, 35\%)$, $[35\%, 85\%]$, and $(85\%, 100\%]$, respectively. The priority group of a candidate within each KDPI category is determined by the interaction of several factors: donor and candidate geographies, candidate's blood type, tissue type, Estimated Post Transplant Survival (EPTS) and cPRA scores. EPTS scores range from 0% (best) to 100% (worst) and are based on four candidate attributes: time on dialysis, diabetes status, prior organ recipient status, and age. Candidates with EPTS scores of $[0\%, 20\%]$ receive offers for kidneys from donors with KDPI scores of $[0\%, 20\%]$ before other candidates at the local, regional, and national levels of distribution. The EPTS score is not used in allocation of kidneys with KDPI scores $> 20\%$.

There are also exceptions (e.g., due to medical urgency or for double kidney allocation) in KAS that was not included in this overview. It is clear from this overview that deceased-donor kidneys in the U.S. are allocated using a highly sophisticated algorithm. We feel that analysis of such a complex system by any methodology other than simulation is bound to leave out many of its essential features.

3 OVERVIEW OF THE SIMULATION MODEL

Our objective in developing a new simulation model for the U.S. kidney transplant system is to assess and compare the impact of alternative allocation policies, which was not feasible via the KPSAM executable made available to the public. In doing so, we have independently replicated most (if not all) of the concepts framed in KPSAM (SRTR 2015) and its predecessors UKAM/ULAM.

One major issue we have faced with using KPSAM was its speed. To illustrate part of the computational burden, recall the KAS reviewed in Section 2.2. In accordance with the rules set forth by the allocation policy, KAS requires re-creating the prioritized waiting list for every donor organ arrival. Each year, approximately 15,000 kidneys arrive to the system and the size of the waiting list at the time of each organ arrival exceeds 100,000 candidate registrations. Going through just this step of re-ranking the candidates for each arriving kidney illustrates the need for efficient data structures and handling of the overall process to overcome the computational burden. For speed purposes, we chose to implement our simulation using the C/C++ programming language as it has been proven for its speed and efficiency. While our implementation offers a serial execution mode for users that do not have access to multiple CPUs, it also allows a parallel execution mode for users that have access to multiple CPUs (e.g., a modern computing grid that typically offers hundreds of CPUs). For parallel execution of simulation replications, we have used the freely available `openmpi` libraries. The execution times reported in Table 1 clearly display the significant speed advantage of our implementation over KPSAM.

Table 1: Comparison of execution time between KPSAM and our simulation model.

Simulation period	Number of replications	KPSAM (hh:mm:ss)	Our Model (hh:mm:ss)	Speedup
6 months	1 replication	01:03:57	00:05:48	11.03×
	10 replications	10:29:35	00:08:31	73.92×
	100 replications	104:19:06	00:14:08	442.86×
1 year	1 replication	02:04:40	00:10:53	11.45×
	10 replications	20:42:58	00:14:30	85.72×
	100 replications	—	00:24:22	—
3 years	1 replication	***	00:30:26	—
	10 replications	***	00:34:17	—
	100 replications	***	00:59:55	—

*** KPSAM only simulates up to 1 year.

Similar to KPSAM, we extensively utilize historical data from OPTN. As the contractor of OPTN, UNOS maintains databases that include information on every patient listed for an organ transplant as well as information on every deceased-donor seen by the system, which enables tracking each patient from listing to their removal from the waiting list. We have obtained a copy of this key database, which contains demographic and clinical information on all transplant candidates that were listed in the U.S. between 1987 and 2018, and collectively amounts to more than 30 million records and close to 1,000 variables.

We process this database using an **R** script to obtain a clean copy ready for our simulation. We will present results from running our simulation for three-year period starting in 2015 through the end of 2017. For this purpose, we filtered out records from the database that are not relevant for our simulation period. Furthermore, our current implementation exclusively models the allocation policy for single kidney only transplants, as double kidney allocation and the allocation to candidates co-listed for other organ(s) may not follow the standard allocation reviewed in Section 2.2. Accordingly, all non-kidney transplant candidate records, kidney transplant candidates simultaneously listed for other organs (e.g., kidney-pancreas, kidney-liver), and donor records that were used in double kidney transplantation were excluded. This resulted in 210,514 candidate arrival records, 584,322 patient status update records, and 25,058 donor arrival records that corresponds to 43,647 kidney arrivals. The discrepancy between the kidney and donor arrival counts is caused by unavailability or futility of some donor kidneys.

Figure 1 illustrates an overview of the key components in our simulation model.

Patient arrivals to the waiting list. Candidates arrive to the simulated waiting list in one of three ways. (*i*) Our simulation model starts with an *initial waiting list* at a specific point in time (e.g., as of the end of December 31, 2014). This initial waiting list is populated from the OPTN database and, for each record, contains a unique registration identifier and a unique patient identifier (to allow the practice of multiple listing in different transplant centers), information about the candidate such as age, gender, ethnicity, blood type, height, weight, listing center/OPO/region, HLA antigens, dialysis start date, diagnosis type, diabetes status, whether or not the individual is a primary or repeat transplant candidate, previous living donor status, cPRA score, removal reason (if removed), and so on, adding up to a total of 45 different attributes of the candidate. These data elements are used in employing the allocation policy to identify the compatible wait-listed candidates and to subsequently prioritize the list of compatible candidates for an incoming kidney and determining the outcomes for transplant recipients post-transplantation. (*ii*) Candidates can also join the waiting list after the start of the simulation according to a *patient arrivals* input file, which is again populated from the OPTN database and contains same data elements as in the initial waiting list file. (*iii*) Transplant recipients during the simulation period may experience graft failure, as determined by the post-transplantation survival module, and return back to the waiting list, forming the arrival stream

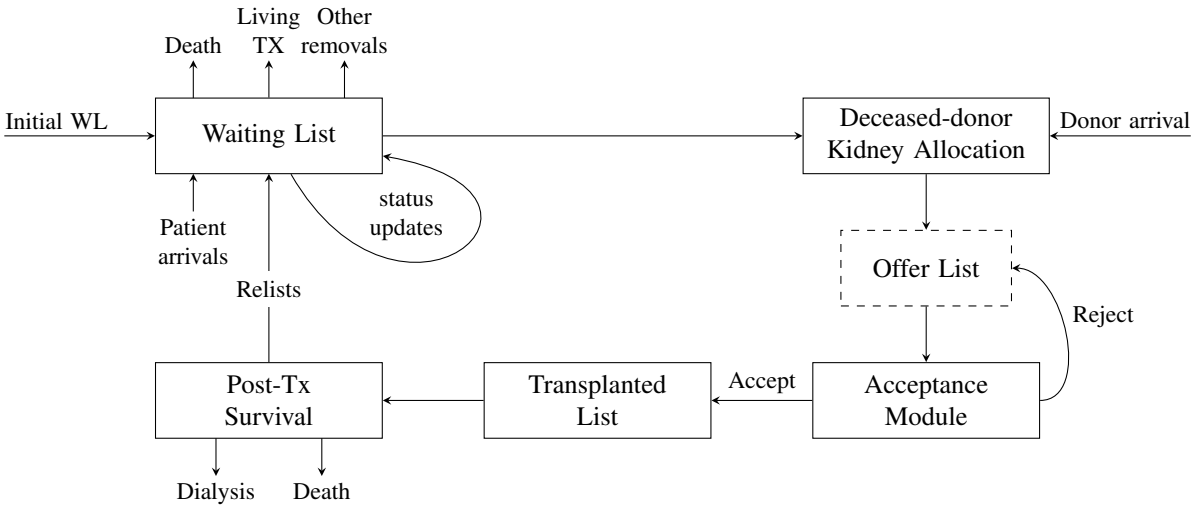

Figure 1: An overview of the simulation model.

of *relisted candidates*. It should be noted that this stream does not contain candidates who might have received a transplant prior to the start of the simulation period and are seeking a re-transplant opportunity after the start of the simulation. Such candidates would appear in one of the first two arrival streams.

Patients' status updates while waiting. Several events could take place while patients are on the waiting list. For example, patients may be removed from the waiting list, which happens due to (*i*) receiving a transplant within the simulation, or (*ii*) dying while waiting, or (*iii*) any other reason (e.g., receiving a living-donor transplant, becoming too sick for transplantation, no longer needing a transplant due to improvements in health, transplanting in another country). When a patient is transplanted within the simulation, he/she is removed from the waiting list and placed in the *transplanted list*, his/her history of updates from the status update file are deleted, and the post-transplant survival module takes over to determine the recipient's future trajectory.

Data regarding removals due to death or other reasons are provided in a *status update* input file, which is populated from the OPTN database. This input file also contains information regarding a candidate's switches between active and inactive status as well as his/her cPRA score changes.

We simulate the residual lives of candidates who received a kidney transplant in real life, had they not received this transplant, in the following manner.We first employ a Cox proportional hazard model and identify a reference pool of patients composed of individual in the database who have lived at least as long as the observed time until transplantation of the patient under consideration and are removed by reasons other than a deceased-donor kidney transplant. The results of this Cox model along with other patient attributes (i.e., diabetes status, listing age, listing waiting list status) are then compared for the patient under consideration to reference population to identify the closest matching patient in the reference pool to the patient under consideration. If such a matching is patient is found, we substitute his/her removal reason along with the removal time for the patient under consideration; otherwise, we relax our matching criteria and repeat this process until we find a matching patient from the reference pool.

Donor arrivals. Donors arrive to the system according to a *donor arrivals* input file, which is populated from the OPTN database. Each record in this data file contains a unique encrypted donor identifier and information about the donor's age, gender, ethnicity, blood type, non-heart-beating status, cause of death, history of hypertension or diabetes, KDPI score, creatinine level, HLA antigens, time, date, and center of recovery, number of kidneys, and so on, adding up to a total 33 attributes of the donor. This data is used in employing the allocation policy and predicting the post-transplant outcomes for transplant recipients.

Organ offers. Each available organ from an arriving donor are offered to the wait-listed candidates in the priority sequence determined by the allocation policy. The characteristics of the donor/organ, the

composition of the waiting list, and the allocation policy in effect determines this sequence. For this purpose, a temporary sorted 'offer list' is created for each arriving organ from the entire waiting list after filtering out incompatible candidates. Candidates are then offered the organ in the sequence dictated by the offer list. Candidates (and/or their agents acting on their behalf) accept or reject an offered kidney. Patient's likelihood of accepting an offer is determined through SRTR's kidney offer acceptance model, which is estimated from match run data for kidneys recovered between July 1, 2017 and June 30, 2018 (Wey et al. 2017; SRTR 2018). This acceptance model is based on a fairly detailed logistic regression equation that considers, among others, patient's blood type, cPRA score, diabetes status, and rank on the prioritized offer list, donor's cause of death, creatinine level and non-heart-beating status, and the interaction between the ages of the patient and the donor, their geographies, their HLA antigen (mis)match level. The result of this acceptance probability is then compared to a Uniform(0,1) number sampled at random to finalize the binary accept/reject decision. If a patient rejects the offer, the kidney is extended to the next patient in the offer list. This process repeats itself until the kidney is accepted by someone or offer count reaches a finite number (provided by user input), after which the kidney is considered discarded. This finite number of offers is used to model the phenomenon known as cold-ischemic time, which indicates the deterioration of organ quality during this offer process.

Post-transplant outcomes. We use KPSAM's parametric models to determine the post-transplant events, and to estimate the corresponding time until each event (SRTR 2015). At the core of all of these event times is an estimate of the time until graft failure, which is obtained through a Cox proportional hazard model. Given an estimate of the time until graft failure, a randomized model is used to determine the post-transplantation outcome for the recipient in questions. Accordingly, upon accepting a kidney offer, the recipient can experience one of the following outcomes: (*i*) *survival*: graft fails after the end of the simulation period (i.e., recipient survives throughout the rest of the simulation period with his/her graft), or (*ii*) *death*: graft fails *and* the recipient dies before the simulation ends, or (*iii*) *relisting*: graft fails, *but* the recipient is still alive; he/she resumes dialysis and returns back to the waiting list for another transplant opportunity, or (*iv*) *dialysis*: graft fails, *but* the recipient is still alive; he/she continues the rest of his/her life on dialysis *without* seeking another transplant opportunity.

Simulation outputs. The simulation model detailed records in output files of the 'lives' of each patient and donor that entered the simulation. These output files are analyzed using an `R` script to produce virtually any statistic of interest, some of which are listed in Table 2.

4 MODEL VERIFICATION AND VALIDATION RESULTS

We have used the detailed simulation output files to verify and validate the model on numerous performance metrics against actual transplantation outcomes observed from the OPTN database to ensure that the model is able to adequately represent the complex U.S. kidney allocation system. In doing so, we have also performed formal statistical tests to test differences between simulated and actual outcomes.

Tables 2 to 4 provide comparisons of several outcome metrics between actual OPTN data and simulated data, where simulation results are averaged across 100 independent replications of the model. They clearly illustrate that simulation outputs closely match real data.

5 CONCLUSION

In accordance with the official dictate (Final Rule 1998), organ allocation policies are periodically reviewed and revised following the advancements in medicine, technology, science, and the opinions of the transplant community. These policies in general, and the kidney allocation policy in particular, employ sophisticated algorithms reflecting the complex nature of the issues surrounding organ transplantation. Simulation modeling has been repeatedly proven influential in guiding policy decisions in organ transplantation as demonstrated by the remarkable success of ULAM, which sparked the subsequent simulation efforts by UNOS (namely, UKAM, KPSAM, LSAM, and TSAM) and others.

Table 2: Validation results for the simulation model.

Outcome	Year	Actual	Simulation	Relative error	p-value
Size of the waiting list (registrations)*	2015	104271	104239	−0.03%	0.909
	2016	102600	102290	−0.30%	
	2017	100637	100469	−0.17%	
Size of the waiting list (candidates)*	2015	96623	96680	0.06%	0.926
	2016	94888	94705	−0.19%	
	2017	92968	92900	−0.07%	
Number of living donor transplants	2015	5571	5654	1.48%	0.889
	2016	5612	5717	1.87%	
	2017	5799	5792	−0.13%	
	Total‡	16982	17161	1.06%	
Number of other removals#	2015	10812	10790	−0.20%	0.297
	2016	10767	10616	−1.40%	
	2017	11014	10600	−3.76%	
	Total‡	32593	32006	−1.80%	
1-year patient survival	2015	96.50	97.84	1.39%	0.999
	2016	97.25	97.86	0.63%	
	Overall	96.89	97.85	0.99%	
1-year graft survival	2015	93.69	94.91	1.30%	0.998
	2016	94.67	94.99	0.34%	
	Overall	94.20	94.96	0.81%	

* As of the end of the year.
‡ From January 1, 2015 to January 1, 2018.
# Including removal due to refused transplant, transferred to another center, transplant not needed anymore, too sick to transplant, removed in error, changed to kidney-pancreas, unable to contact, and other.

In this paper, we described a new discrete-event simulation model for the U.S. kidney transplantation system as an alternative to KPSAM. In our model development, we share many of the same design concepts with KPSAM, but offer a more flexible and faster model than the KPSAM executable provided to public. Our model implements the most recent UNOS deceased-donor kidney allocation policy (OPTN 2019) and is validated through closely matching the actual outcomes indicated from the OPTN database.

This simulation model is also utilized in Tunç et al. (2019), which offers a theoretical model to analyze an incentive mechanism to alleviate the burden of organ shortages. The theoretical analysis in Tunç et al. (2019) emphasizes reducing organ discard rates through offering to preserve previously accumulated waiting times of *eligible re-listed* patients, who are defined as those that have accepted a pre-defined set of organs (e.g., marginal organs) to start with. Using the simulation model described in this paper, Tunç et al. (2019) demonstrated that if the allocation policy is modified as they suggest, kidney discard rate could be reduced from it's baseline value of 17.4% down to 5.4% if the policy change is reciprocated with a strong response in the population, 9.5% if moderate response, or 15.7% if weak response, which translates to 1746, 1148, or 241 more transplants per year, respectively.

As noted in Pritsker et al. (1996), policy issues involve a broad spectrum of participants with diverse viewpoints and expectations. Given such a challenging environment, we believe in marginal improvements in an existing system; our simulation model is accordingly designed around the currently existing system and our modular setup allows for easy testing of implementable changes. On the other hand, the nature of radical changes in a system is hard to guess and such modifications almost always require a complete overhaul of an existing simulation model, possibly leading to re-building the entire model from the beginning.

Table 3: Number of deceased donor kidney transplant in adult candidates.

Grouped by	Type	Actual	Simulation	Relative error	p-value
Year	2015	10604	10224	−3.58%	0.267
	2016	11659	11775	0.99%	
	2017	12168	12234	0.54%	
Blood type	O	15769	15596	−1.10%	0.429
	A	12182	12034	−1.22%	
	B	4628	4688	1.30%	
	AB	1852	1916	3.45%	
Age	$18-34$	3976	4133	3.96%	<0.01
	$35-49$	9531	10483	9.99%	
	$50-64$	14001	13647	−2.53%	
	$65-74$	6318	5497	−12.99%	
	≥ 75	605	472	−21.93%	
Race	White	12460	12582	0.98%	<0.01
	Black	12238	12576	2.76%	
	Hispanic	6459	6035	−6.57%	
	Other	3274	3040	−7.14%	
KDPI	$\leq 20\%$	6832	6793	−0.57%	0.115
	$21-34\%$	5236	5059	−3.38%	
	$35-85\%$	19557	19444	−0.58%	
	$>85\%$	2806	2938	4.69%	

Table 4: Number of pre-transplant deaths among adult candidates.

Grouped by	Type	Actual	Simulation	Relative error	p-value
Year	2015	4626	4635	0.20%	0.852
	2016	4475	4406	−1.55%	
	2017	3895	3834	−1.58%	
Age	$18-34$	417	454	8.92%	0.349
	$35-49$	2177	2059	−5.44%	
	$50-64$	6179	6143	−0.59%	
	$65-74$	3785	3781	−0.11%	
	≥ 75	438	438	0.11%	
Race	White	5371	5328	−0.80%	0.957
	Black	4266	4188	−1.82%	
	Hispanic	2150	2151	0.03%	
	Other	1209	1208	−0.12%	
Diagnosis	Diabetes	6428	6261	−2.60%	0.546
	Polycystic kidney disease	443	472	6.64%	
	Hypertension	2564	2594	1.17%	
	Glomerular diseases	1343	1360	1.27%	
	Other	2218	2187	−1.39%	

Our framework shares several of the limitations stated for KPSAM. First, while relying on historical data is a major strength of our approach in terms of accurate modeling of arrivals to the system, it also raises concerns about the validity of the statistical predictions used within the simulation that rely on such data (e.g., the logistic regression model for offer acceptance behavior, the survival model for predicting how long an actual transplant recipient would have lived had he/she not received the transplant). Second, the actual time lapse between subsequent offers of an available organ and the associated deterioration of organ quality is currently modeled through allowing the organ to be offered a fixed number of times regardless of its characteristics. Third, our current implementation does not consider double kidney allocation or allocation of kidneys to patients simultaneously listed for other organs. Finally, we acknowledge that there might be slight variations in practice across how OPOs and/or transplant centers implement ambiguous aspects of the allocation policy. Our model is unable to capture such variations observed in practice.

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AUTHOR BIOGRAPHIES

BURHANEDDİN SANDIKÇI is Associate Professor of Operations Management at the University of Chicago Booth School of Business. He holds a PhD in industrial engineering from the University of Pittsburgh. His research interests span decision-making problems under uncertainty with particular focus on problems in healthcare policy, medical decision-making, and healthcare operations. His email address is burhan@chicagobooth.edu.

SAİT TUNÇ is a postdoctoral researcher at the University of Chicago Booth School of Business. His research focuses on application-driven theoretical problems and utilizes large-scale real-world databases, with an emphasis on medical decision-making and operational efficiency in health care delivery systems. He holds a PhD in industrial engineering from the University of Wisconsin-Madison. His email address is sait.tunc@chicagobooth.edu.

BEKİR TANRIÖVER is Associate Professor of Internal Medicine at the University of Texas Southwestern Medical School in Dallas and the Medical Director of Kidney Transplant Program at the Clements University Hospital. He earned his medical degree from Hacettepe University in Turkey. Following a residency in internal medicine at Tulane University, he completed fellowships in nephrology at the University of Alabama–Birmingham and transplant nephrology at Vanderbilt University. He also holds a master degree in public health in "Cost Effectiveness and Outcomes" tract from Columbia University. Dr. Tanriover is board certified in internal medicine and nephrology. His research interests include cost-effectiveness of immunosuppressive medications, marginal kidney utilization, and minimization of discard in renal transplantation. His email address is Bekir.Tanriover@UTSouthwestern.edu.