

A KIDNEY PAIRED DONATION PROGRAM SIMULATION

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ABSTRACT

The Organ Procurement and Transplantation Network (OPTN) Kidney Paired Donation (KPD) Program, managed by the United Network for Organ Sharing (UNOS), supports patients with end-stage renal disease who have incompatible living donors. By widening the donor pool through recipient-donor pair exchanges, KPD increases the chance of finding compatible donors. We present a simulation model that combines KPD with desensitization treatments to assess the risks and benefits for matched donors and patients. The simulation model incorporates combinatorial optimization algorithms to match patients with the most compatible donors, considering potential donation declines and simulating the outcomes of successful matches. The simulation output includes patient longevity and desensitization-related adverse effects to help analyze the benefits of the KPD program for those patients facing donor incompatibility.

1 INTRODUCTION

Kidney transplantation is the best treatment for patients with end-stage renal disease (Abecassis et al. 2008), but there is an acute shortage in the supply of kidney donations from both deceased and living donors (Abouna 2008). An additional complicating factor is the compatibility issue, which precludes certain types of kidney transplantations. The most significant barriers are ABO (blood type) or human leukocyte antigen (HLA tissue type) incompatibility (Zachary and Leffell 2014; Mattsson et al. 2008; Marfo et al. 2011). Patients with a willing living donor may not undergo a transplantation due to incompatibility. There are two major ways to overcome compatibility issues and enable more kidney transplants: (i) Kidney Paired Donation programs allow patients with incompatible living donors to swap with a compatible donor in the pool; (ii) Desensitization therapy removes antibodies from the patient's body, allowing for the transplantation of an incompatible kidney. These two are currently administered in living-donor transplants and are done independently. Our approach would allow the desensitization option to be considered in the KPD program.

UNOS, operating under a federal contract as the OPTN, runs the KPD Pilot Project, allowing patients with a willing, but blood- or tissue-type incompatible, living donor to swap their incompatible donor with a more compatible donor also in the KPD donor-patient pool. As an example (United Network for Organ Sharing 2021), Mary, with a type A kidney, cannot donate to type B Carlos, and Amir, a type B donor, cannot donate to type A Shauna. Through KPD, Mary can donate to Shauna, and Amir to Carlos, allowing both transplants to proceed, as illustrated in Figure 1. KPD are usually run locally and the size of a typical KPD patient pool is smaller than 200 at any given time.

Desensitization treatments, on the other hand, allow patients with an incompatible donor to undergo transplantation with the assistance of drugs that suppress the obstructing antibodies. However, organ transplants with desensitization carry higher risks of delayed graft function, quick graft failure, and developing cancer. In Figure 1, Mary can donate to Carlos if Carlos receives proper desensitization treatment. In current practice, desensitizing the HLA tissue type mismatch is more common than the

ABO blood type mismatch shown in the figure. We assume the patients' willing living donors are very incompatible, so they will only consider receiving a donation from their living donors if they are not offered a satisfactory swap donation. Receiving a donation by desensitizing with the living donor is considered "leaving" from the KPD perspective and is not distinguished from other types of departure in later discussions.

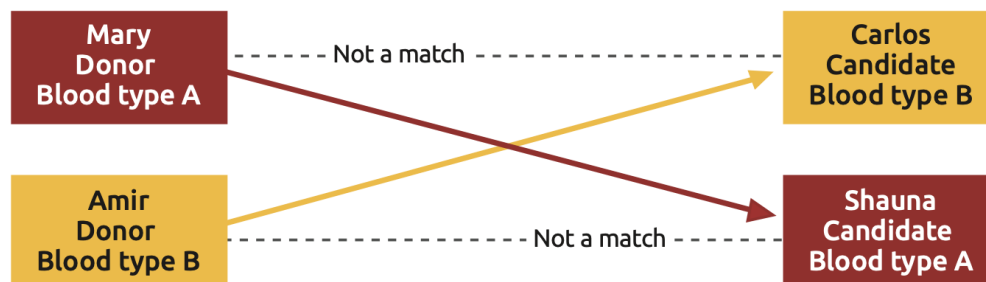


Figure 1: Switching donors and recipients in this case allows both transplants to happen.

KPD desensitization significantly broadens the pool of donors and recipients, but it also requires a complex chain of pairing decisions that take into account multiple donors and patients biomarkers, preferences, and risks. Recently, a new framework with three algorithmic modules has been developed to support decision making in kidney paired donation with desensitization. Module 1 is a machine learning algorithm developed by Shams Eddin et al. (2024) to identify the best desensitization method for an individual patient receiving an incompatible organ to minimize the risks of adverse post-transplant events. The algorithm estimates the probability of these adverse events, such as the graft failure rate, chance of cancer development, and chance of re-hospitalization. Module 1 addresses the desensitization treatment aspect of a combined KPD-desensitization model.

Module 2, developed by Serra et al. (2024), is based on combinatorial optimization algorithms that work on graphs representing donor-patient compatibility to optimize the number of donors and patients getting matched and receiving a donation. Module 2 addresses the problem of matching patients with donors, which is the core of a KPD program.

Module 3, developed by Ren et al. (2023), Ren et al. (2022), provides decision rules based on Markov decision process models of the individual organ recipient (patient and surgeon). This results in an optimized patient/surgeon decision policy on whether to accept a proposed donation offer or reject and wait for future offers. Module 3 addresses the concern of patients who participate in the combined KPD-desensitization model by providing decision support on whether or not they should accept a donation offer.

The objective of the KPD program is to facilitate donor-patient matching in order to improve post-transplant longevity and quality of life for as many patients as possible. Modules 1, 2, and 3 address specific aspects towards achieving this objective, and the goal of the simulation model is to integrate all of them for system-wide KPD program performance evaluation, as well as enable overall system optimization through new simulation optimization approaches.

The simulation model generates patient-donor pair arrivals and estimates patient life expectancy, incorporating all three modules. The simulation model allows one to test and assess the utility of the individual modules in the integrated system. For example, sensitivity analysis can be used to test the effect of perturbing parameters in one of the modules on the overall KPD performance, in terms of comparing (simulated) patient outcomes.

One of the performance measure outputs of the KPD program has to do with patient outcomes in terms of life expectancy, for which we use the estimated 5-year survival rates of patients if they receive a transplant

or if they don't receive a transplant at all during simulation run as a key performance metric. The estimation is done using a machine learning algorithm developed by Bae et al. (2019). The machine learning algorithm uses OPTN's KDPI and EPTS scores (The Organ Procurement and Transplantation Network 2020b; The Organ Procurement and Transplantation Network 2020a) to estimate the 5-year survival rates of patients with and without transplant.

2 THE SIMULATOR

The simulator is designed to project the dynamics within a KPD program's patient pool over various time periods while incorporating desensitization treatments. Figure 2 illustrates the simulator's structure.

At each time period's inception, the simulator introduces a group of patients with profiles into the pool. This pool of patients is generated by sampling from a probability distribution provided by the user. Since the KPD program focuses on swap donations, these generated patients all have their living donors who are willing to donate to the respective patient but are incompatible.

After some data preprocessing, the pool of patients becomes the input of the module "Desensitization planning" (an implementation of module 1). This module chooses the best desensitization plan to reduce risk of re-hospitalization, and also reports the risks of other adverse events. The patients' compatibility information based on their HLA mismatch levels are forwarded to the module "Patient matching" (an implementation of module 2). This module maximizes the number of matched patients based on the constraint that all donations must be compatible. This module also provides a recourse policy in case some patients reject the swap donation offer.

Patients and their surgeons receive these matching plans and evaluate them to make a decision to either accept or reject this matching plan according to the module "Patients/Surgeons' decisions" (an implementation of module 3). These decisions are made to maximize the expected life years of the patients, considering the possibility to receive an organ with higher quality later. If a transplant offer is declined, the matching plan's recourse policy will re-calibrate the plan, excluding the rejecting patient for the current period. If the second attempt is also rejected, then every patient associated with this rejecting patient will have to wait for the next period.

The simulator then simulates the outcome of the transplant surgery for successfully matched patients. The outcome involves the expected life years and the occurrences of various adverse events such as graft failure. At the end of this period, unmatched patients need to wait until the beginning of the next matching cycle, when the next batch of patients arrive to the KPD program. During the waiting period, some existing patients may depart from the pool for various reasons, such as alternative donation sources, loss of interest in the program, or mortality.

The simulation then proceeds to the next time period with the arrival of new patients. The newly arrived patients are added to the existing pool and the aforementioned procedures are invoked again. The simulation is then run for a specified number of periods, after which a report of final results is generated.

3 AN ILLUSTRATIVE EXAMPLE

3.1 Donors and Patients

This part simulates the characteristics of donor/patient pairs, effectively representing patients who participate in the Kidney Paired Donation (KPD) program at a transplant center. We use the words "patient" and "recipient" interchangeably, although we try to use "recipient" when talking about organ transplantation and "patient" when discussing general medical conditions.

3.1.1 Donor Information

Figure 3 summarizes the donor information modeled in the simulation together with the probability distribution models used to generate characteristics of donors that arrive at the pool at the beginning of

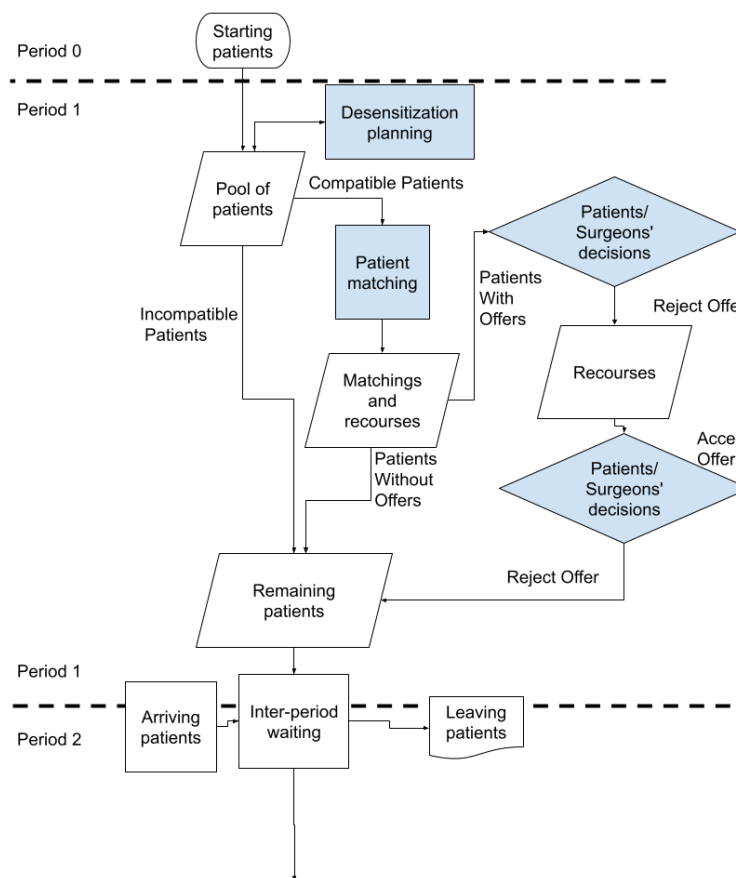


Figure 2: The structure of the simulator.

| Donor Information Distributions Example | |
|-----------------------------------------|--------------------------------------------------------------------------------|
| Variable Name | Random Generation Method |
| Age | Uniform integer in the range [25, 40] |
| Height | Normal with mean 170 cm and SD 5 cm |
| Weight | Normal with mean 80 kg and SD 10 kg |
| Gender | Bernoulli with a probability of 0.5 (Male or Female) |
| Race | Uniform integer in the range [0, 4] (Black, White, Hispanic, Asian, or Others) |
| Hypertension | Bernoulli with a probability of 0.1 (10% chance for hypertension) |
| Creatinine | Uniform in the range [0, 6] |
| Diabetes | Bernoulli with a probability of 0.1 (10% chance for diabetes) |
| Blood Type | Uniform integer in the range [0, 3] (A, B, AB, or O) |
| HCV | Bernoulli with a probability of 0.8 (80% chance for HCV history) |
| BMI | Calculate from above information |
| KDPI | Calculate from above information |

Figure 3: Example of donor information distributions.

each simulation time period. In the example are displayed information about ten donors generated by the simulator in a table shown in Figure 4.

“KDPI” stands for Kidney Donor Profile Index (The Organ Procurement and Transplantation Network 2020b), a numerical score that summarizes the quality of a deceased donor kidney on a scale from 0% to

| ID | Current Status | Donor Age | Donor Height(cm) | Donor Weight(kg) | Donor Race | Donor Hypertension | Donor HCV History | Donor Blood Type | Donor KDPI(%) |
|----|----------------|-----------|------------------|------------------|------------|--------------------|-------------------|------------------|---------------|
| 0 | Waiting | 29.0 | 178.122 | 73.882 | Asian | No | Yes | A | 0.0 |
| 1 | Waiting | 37.0 | 177.311 | 59.399 | Black | No | No | O | 0.0 |
| 2 | Waiting | 25.0 | 169.138 | 71.221 | Asian | Yes | Yes | B | 0.0 |
| 3 | Waiting | 25.0 | 169.386 | 70.642 | Others | Yes | Yes | A | 0.0 |
| 4 | Waiting | 25.0 | 169.041 | 71.124 | Hispanic | No | Yes | O | 0.0 |
| 5 | Waiting | 32.0 | 164.287 | 76.507 | Asian | Yes | Yes | A | 0.0 |
| 6 | Waiting | 30.0 | 175.658 | 95.198 | Black | No | Yes | AB | 0.0 |
| 7 | Waiting | 34.0 | 168.469 | 88.280 | Others | Yes | No | O | 0.0 |
| 8 | Waiting | 40.0 | 166.647 | 83.776 | Hispanic | No | Yes | O | 0.0 |
| 9 | Waiting | 27.0 | 168.281 | 80.436 | Others | No | Yes | A | 0.0 |

Figure 4: 10 randomly generated donors.

100%. The KDPI score represents the proportion of other kidneys with a better quality than this kidney. The KDPI is based on ten donor factors such as age, cause of death, history of hypertension and diabetes, serum creatinine, height, weight, ethnicity, Hepatitis C status, and donation after cardiac death. A lower KDPI (close to 0%) indicates a higher-quality kidney that is expected to function for a longer time, while a higher KDPI (closer to 100%) indicates a lower-quality kidney that may not function as long. For example, if a donor has a kidney with score 10%, then the donor’s kidney is only worse than 10% of other kidneys. KDPI is the most commonly used metric for calculating the quality of organs from deceased donors and living donors provides better organs than deceased donors so 0’s means the donors are better than 99% of deceased donors. “Current Status” indicates if this donor is still waiting in the KPD or has already left the KPD. “Creatinine” is a waste product that comes from the normal wear and tear on muscles of the body. The kidneys filter out this waste, and it leaves the body in the urine. A high level of creatinine in the blood is a marker of potential kidney disease or impairment. “HCV” stands for Hepatitis C Virus, a viral infection that causes liver disease, this indicator is for the history of getting HCV in the past.

3.1.2 Recipient Information

Figure 5 summarizes the patient information modeled in the simulation together with the probability distribution models used to generate characteristics of patients that arrive at the pool at the beginning of each simulation time period. The example displays information about ten recipients generated by the simulator in a table shown in Figure 6.

“EPTS” stands for Estimated Post Transplant Survival (The Organ Procurement and Transplantation Network 2020a), which is a numerical score used in kidney transplantation to rank adult candidates (age 18 and older) on the kidney waiting list. EPTS score is a percentage between 0% and 100% that represents the proportion of other patients who are estimated to live longer than this patient after a kidney transplant. The calculation of EPTS score is based on four factors: candidate’s time on dialysis, current age, whether the candidate has diabetes, and the candidate’s previous history of solid organ transplant (such as a kidney or liver transplant). If a patient has a high EPTS score, then the patient has a bad health status and is in urgent need of kidney transplant. For example, if a patient has a EPTS of 70(%), then this patient has a severe condition and will live shorter than 70% of other patients after a transplant. So “Recipient EPTS” indicates the urgency of the patient’s condition. “Recipient Age” is uniformly 70 because that is the age such that the patient decision rule is defined by module 3. With more computational resources to calculate more decision rules for different patients, this simulator can simulate more patients with and their decisions. “Receive From ID” gives the donor ID matched with this patient, which will be empty if the patient is not

| Recipient Information Distributions Example | |
|---------------------------------------------|--------------------------------------------------------------------------------|
| Variable Name | Random Generation Method |
| Age | Fixed at 70 |
| Height | Normal with mean 170 cm and SD 5 cm |
| Weight | Normal with mean 80 kg and SD 10 kg |
| Gender | Bernoulli with a probability of 0.5 (Male or Female) |
| Race | Uniform integer in the range [0, 4] (Black, White, Hispanic, Asian, or Others) |
| Dialysis | Bernoulli with a probability of 0.5 (50% chance to be on dialysis) |
| Dialysis Time | Conditional Uniform in the range [0, 10] multiplied by the dialysis variable |
| Diabetes | Bernoulli with a probability of 0.8 |
| Blood Type | Uniform integer in the range [0, 3] |
| Creatinine | Uniform in the range [0, 6] |
| CPRA | Uniform in the range [40, 100] |
| Probability | Uniform in the range [0, 0.1] |
| Previous Transplant | Fixed at 0 |
| BMI | Calculate from above information |
| EPTS | Calculate from above information |

Figure 5: Example of recipient information distributions.

yet matched. “Entry Time” indicates the time for the patient to join the KPD and the “Exit Time” indicates the time for the patient to leave the KPD for any reason. “Rewards” gives the cumulative life time from the entry time until the earlier of now or death plus the expected life years if the patient has undergone a transplant inside or outside of the KPD program. The “Rewards without Transplant” column predicts the expected life years if the patient does not attempt to get any kidney transplantation. “Probability” stands for the probability of getting an organ from a deceased donor. “CPRA”, or Calculated Panel Reactive Antibody, is expressed as a percentage. A CPRA of 0 would mean that the individual does not have any detectable antibodies to the HLA (human leukocyte antigen) proteins that are commonly found in the population. In other words, this person’s immune system is less likely to reject a transplanted organ based on HLA compatibility. On the other hand, a CPRA of 100% would mean that the individual has antibodies against all HLAs in the reference panel, making it much more difficult to find a compatible organ donor. This is because the person’s immune system is more likely to see a transplanted organ as foreign and attack it, a process known as organ rejection.

3.1.3 Desensitization

With all the information of a donor and a patient, the desensitization module estimates the risks associated with a desensitization treatment. Figure 7a shows the HLA mismatch level, the probability of malignancy in 1, 3, 5 years, the probability of delayed graft function, the probability of graft failure in 1, 3 years, and the probability of re-hospitalization in 1 year.

3.1.4 Compatibility

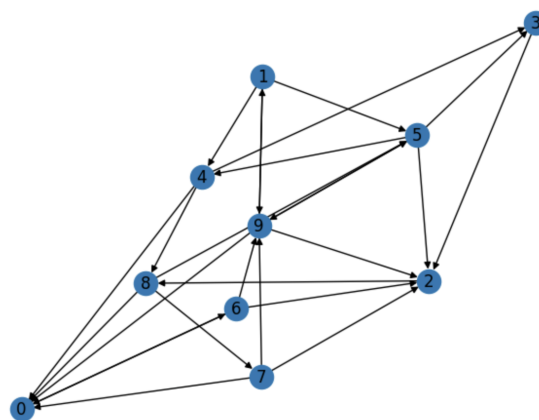
Based on the pairing information between patients, some patients may be incompatible due to the HLA mismatch level or ABO blood types. Compatibility is directed and the direction is from potential donor to a receiving patient represented by a graph. In this illustrative example, we explicitly define donor-patient pairs with HLA mismatch level < 4 to be compatible, while HLA level is a randomly generated from a $Binomial(6, 0.7)$ random variable.

Given the patients, donors, and compatibility information, we can visualize a pool of KPD participants on a graph. The rule of KPD requires the patient to get a kidney when his/her living donor donates to

| ID | Current Status | Rewards | Rewards without Transplant | Entry Time | Exit Time | Receive From ID | Recipient Age | Recipient on Dialysis | Recipient Dialysis Time | Recipient Diabetes | Recipient Blood Type | Recipient CPRA(%) | Recipient EPTS(%) |
|----|----------------|---------|----------------------------|------------|-----------|-----------------|---------------|-----------------------|-------------------------|--------------------|----------------------|-------------------|-------------------|
| 0 | Waiting | 0.0 | 4.388575 | 1.0 | | | 70.0 | No | 0.000 | Yes | O | 52.267 | 68.0 |
| 1 | Waiting | 0.0 | 3.369984 | 1.0 | | | 70.0 | Yes | 8.946 | Yes | O | 50.190 | 99.0 |
| 2 | Waiting | 0.0 | 4.752012 | 1.0 | | | 70.0 | No | 0.000 | No | A | 56.827 | 52.0 |
| 3 | Waiting | 0.0 | 4.388575 | 1.0 | | | 70.0 | No | 0.000 | Yes | O | 75.358 | 68.0 |
| 4 | Waiting | 0.0 | 3.961413 | 1.0 | | | 70.0 | Yes | 5.866 | No | B | 48.357 | 82.0 |
| 5 | Waiting | 0.0 | 3.509819 | 1.0 | | | 70.0 | Yes | 3.489 | Yes | A | 65.685 | 95.0 |
| 6 | Waiting | 0.0 | 3.439667 | 1.0 | | | 70.0 | Yes | 5.737 | Yes | B | 59.599 | 97.0 |
| 7 | Waiting | 0.0 | 3.404761 | 1.0 | | | 70.0 | Yes | 6.968 | Yes | A | 85.233 | 98.0 |
| 8 | Waiting | 0.0 | 3.369984 | 1.0 | | | 70.0 | Yes | 8.420 | Yes | AB | 75.146 | 99.0 |
| 9 | Waiting | 0.0 | 3.685664 | 1.0 | | | 70.0 | Yes | 1.365 | Yes | O | 42.673 | 90.0 |

Figure 6: 10 randomly generated patients.

| | Field Name | Value |
|---|------------|----------|
| 0 | HLA | 2.000000 |
| 1 | denovo1Y | 0.000000 |
| 2 | denovo3Y | 0.031579 |
| 3 | denovo5Y | 0.063158 |
| 4 | dgf | 0.221053 |
| 5 | gtime_1y | 0.052632 |
| 6 | gtime_3y | 0.326316 |
| 7 | hosp1Y | 0.305263 |



(a) Risks for desensitizing a transplant from donor 7 to patient 2.

(b) Compatible edges among 10 pairs.

Figure 7: Desensitization and compatibility.

someone else simultaneously. For this reason, we should put a patient and a donor with the same ID on the same node. Each directed edge of the graph represents a compatible donation.

Figure 7b represents the compatibility relationships among a group of 10 patients index from 0 to 9. We can demonstrate the meaning of this graph by an example. Looking at the node representing patient and donor with ID 3, the edge pointing from 5 to 3 means donor with ID 5 is compatible with patient 3. The edge pointing from 3 to 2 means donor 3 is compatible with patient 2. Donor 4 is also compatible with patient 3. These are all the edges related to patient/donor 3, so they are not compatible with anyone else. In addition, the double arrow between 1 and 9 means donor 1 can donate to patient 9, while donor 9 can also donate to patient 1.

3.2 Patient Matching

Module 2 takes the patient pool (including the compatibility information described previously) as input and generates a matching plan for them. The goal is to transform the patient pool into multiple chains/cycles of

matched patients, with some patients potentially remaining unmatched. Additionally, this plan incorporates a recourse option to address cases where patients reject their transplant offers.

Cycles ensure simultaneous donations that include all donor-patient pairs. There are multiple objectives for a matching strategy, including minimizing the HLA mismatch levels, maximizing the number of participating patients, and maximizing the expected life years of patients. In the current implementation of our simulator, we only considers the number of participating patients.

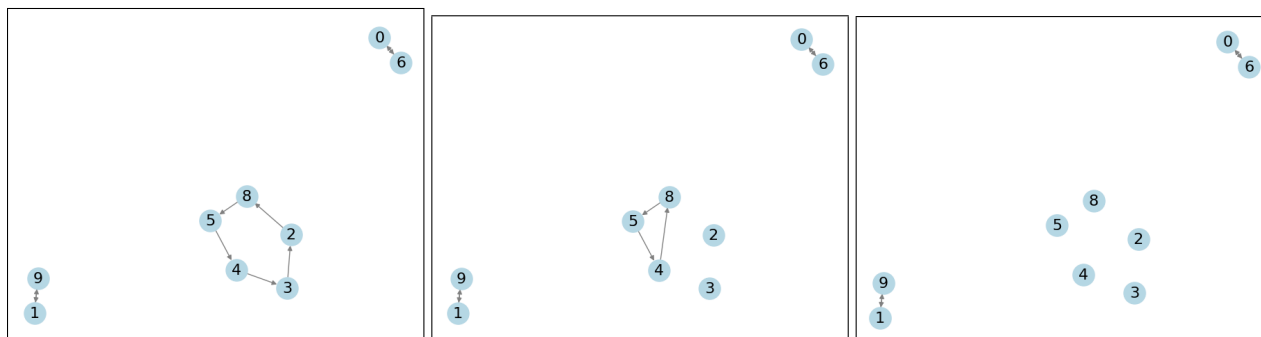


Figure 8: (a) The matching plan.

(b) The recourse plan.

(c) The final plan.

Figure 8(a) shows a graph of three chains/cycles involving all pairs in the KPD program. The chain/cycle at the bottom means, upon acceptance, donor 3 will donate to patient 2, donor 2 will donate to patient 8, 8 to 5, 5 to 4, and 4 back to 3. The chain on the upper left corner means donor 0 and donor 6 will swap their kidney donation.

3.3 Patients' Decisions

This part simulates the decisions of patients/surgeons by module 3. In an ideal scenario, these patients and doctors aim to maximize the expected life years of the patients when considering whether to accept or reject a donation offer. This decision involves assessing the likelihood of receiving a better offer in the future. The current version of the simulator employs a decision rule tailored for 70-year-old patients without diabetes based on past data from deceased donors.

3.3.1 Rejections

Based on the EPTS, KDPI, and HLA mismatch level information associated with the donor-patient pair, patients/surgeons can make their decisions to accept or reject the offered kidney transplant. The easiest case is if all patients involved in the matching accept their respective donations.

To see the consequence of a rejection, see Figure 8(a), where if patient 8 rejects the donation from donor 2, then donor 8 can't donate either. If donor 8 donates to patient 5 but patient 8 can't accept the donation from donor 2, then patient 8 becomes an "orphan" patient, a person less likely to get a good donation. The current version of the simulator doesn't incorporate "altruistic" donations to "orphan" patients. If donor 8 can't donate to patient 5, then donor 5 wouldn't donate to patient 4, then donor 4 wouldn't donate to patient 3. The entire chain involving the rejecting patient 8 would be deleted.

3.3.2 Recourses

The entire chain involving patient 8 needs to be deleted if patient 8 rejects unless there is a backup plan, so the patient matching algorithm provides an algorithm that takes in the list of rejecting patient and returns a new matching plan called a recourse plan. This recourse matching plan will be local, meaning if a chain is not deleted completely, then the chain in the recourse plan only includes a subset of the original chain. This means a chain without any rejection will be preserved in the recourse. A chain containing rejections

will not include the rejecting patients in the recourse plan, it can only contain patients in the same chain in the original plan (or it may be completely deleted).

In Figure 8(b), there is a recourse matching plan after the deletion of patient 2. This new matching has to remove patient 2 due to rejection and patient 3 due to compatibility concerns. It tries to keep the recourse local, meaning minimizing the number of patients who need to decide on this recourse plan and trying to ensure all patients except the rejecting patients get a new matching (unfortunately, it can't find a matching for patient 3).

We can't move forward with this plan since the matchings have changed and patient 8 has not yet agreed to take the donation from donor 4. Other patients still receive from the same donors they are assigned in the original plan so they shouldn't change their mind in such a short period of time. If patient 5 accepts then this recourse plan is the final plan.

3.3.3 The Final Decision

If patient 8 rejects, the simulator will not generate further recourses. Instead, the simulator will exclude the entire chain involving patient 8. In Figure 8(c), after the rejection of patient 8, the chain involving patients 8,5,4 is deleted, and there are two chains remaining with the patients 0,6,1,9 and their respective donors.

3.4 Transplant Surgeries

This part of the simulator simulates the transplant surgery. The transplant surgery may cause various complications and thus give various rewards. The current version of simulator gives 2 major surgery outcomes: Surgery successful and surgery failed (delayed graft function). In case of a failed transplant, we estimate the expected life years assuming the patient doesn't benefit from the transplant at all.

The current version of simulator is using a regression model (Bae et al. 2019) to estimate the 5-year survival rate after a surgery. Assuming the survival time follows an exponential distribution, the 5-year survival rate implies a rate of death per year. Since this rate of death can't be constant for all ages, we add another natural rate of death that increase as the patient ages. We therefore have a discrete random variable for the expected life years of this patient, and are able to calculate this patient's expected life years. In this simulation demonstration, the natural rate of death per year segmented by age groups in terms of percentage is 0.1% for those older than 18, 0.2% for those older than 30, 2% for those older than 50, 5% for those older than 70, 10% for those older than 85, 20% for those older than 95, and with a cap set at 110 years.

Looking at the patient Figure 9. Patients 0, 1, and 9 have undergone a successful surgery almost immediately after they arrive. Patient 6 has a failed transplant surgery, the newly transplant kidney is not functioning as expected. They all get a "Rewards" number to indicate their expected life years moving on. Because of a failed surgery, patient 6 has an expected life years equaling that without a transplant, while the expected life years of those with successful transplant are more than two times the expected years without a transplant.

When we look at the Figure 10, which includes the information of both the donor and the patient, we see the expected life years equals the "Rewards" column in the patient table. There are also indication of different post-surgery events, which are generated based on their probabilities predicted by the desensitization model (module 1). Patient 6 experienced delayed graft function, re-hospitalization, and malignancy within 1 year after surgery.

3.5 Waiting Periods and Subsequent Periods

This part simulates the events happening during the waiting time between patient arrivals. For example, if a patient/donor pair arrives in January, and the next pair arrives in February, there is about one month of waiting period.

| ID | Current Status | Rewards | Rewards without Transplant | Entry Time | Exit Time | Receive From ID | Recipient Age | Recipient on Dialysis | Recipient Dialysis Time | Recipient Diabetes | Recipient Blood Type | Recipient CPRA(%) | Recipient EPTS(%) |
|----|----------------|---------|----------------------------|------------|-----------|-----------------|---------------|-----------------------|-------------------------|--------------------|----------------------|-------------------|-------------------|
| 0 | Succeeded | 10.751 | 4.388575 | 1.0 | 1.0 | 6.0 | 70.0 | No | 0.000 | Yes | O | 52.267 | 68.0 |
| 1 | Succeeded | 8.063 | 3.369984 | 1.0 | 1.0 | 9.0 | 70.0 | Yes | 8.946 | Yes | O | 50.190 | 99.0 |
| 2 | Waiting | 0.000 | 4.752012 | 1.0 | | | 70.0 | No | 0.000 | No | A | 56.827 | 52.0 |
| 3 | Waiting | 0.000 | 4.388575 | 1.0 | | | 70.0 | No | 0.000 | Yes | O | 75.358 | 68.0 |
| 4 | Waiting | 0.000 | 3.961413 | 1.0 | | | 70.0 | Yes | 5.866 | No | B | 48.357 | 82.0 |
| 5 | Waiting | 0.000 | 3.509819 | 1.0 | | | 70.0 | Yes | 3.489 | Yes | A | 65.685 | 95.0 |
| 6 | Failed | 3.440 | 3.439667 | 1.0 | 1.0 | 0.0 | 70.0 | Yes | 5.737 | Yes | B | 59.599 | 97.0 |
| 7 | Waiting | 0.000 | 3.404761 | 1.0 | | | 70.0 | Yes | 6.968 | Yes | A | 85.233 | 98.0 |
| 8 | Waiting | 0.000 | 3.369984 | 1.0 | | | 70.0 | Yes | 8.420 | Yes | AB | 75.146 | 99.0 |
| 9 | Succeeded | 8.925 | 3.685664 | 1.0 | 1.0 | 1.0 | 70.0 | Yes | 1.365 | Yes | O | 42.673 | 90.0 |

Figure 9: Patients after the first surgery.

| Recipient EPTS(%) | ID | HLA | Expected Life Years After Surgery | Delayed Graft Function | Hospitalization in 1Y | Receive From ID | Donor KDPI(%) |
|-------------------|----|-----|-----------------------------------|------------------------|-----------------------|-----------------|---------------|
| 68.0 | 0 | 2 | 10.751 | False | False | 6 | 0.0 |
| 99.0 | 1 | 3 | 8.063 | False | False | 9 | 0.0 |
| 97.0 | 6 | 2 | 3.440 | True | True | 0 | 0.0 |
| 90.0 | 9 | 3 | 8.925 | False | False | 1 | 0.0 |

Figure 10: Paired information for patients participating in the first surgery.

| ID | Current Status | Rewards | Rewards without Transplant | Entry Time | Exit Time | Receive From ID | Recipient Age | Recipient on Dialysis | Recipient Dialysis Time | Recipient Diabetes | Recipient Blood Type | Recipient CPRA(%) | Recipient EPTS(%) |
|----|----------------|---------|----------------------------|------------|-----------|-----------------|---------------|-----------------------|-------------------------|--------------------|----------------------|-------------------|-------------------|
| 0 | Succeeded | 10.751 | 4.388575 | 1.0 | 1.0 | 6.0 | 70.0 | No | 0.000 | Yes | O | 52.267 | 68.0 |
| 1 | Succeeded | 8.063 | 3.369984 | 1.0 | 1.0 | 9.0 | 70.0 | Yes | 8.946 | Yes | O | 50.190 | 99.0 |
| 2 | Dead | 3.000 | 4.556900 | 1.0 | 4.0 | | 73.0 | No | 0.000 | No | A | 56.827 | 61.0 |
| 3 | Dead | 3.000 | 4.217854 | 1.0 | 4.0 | | 73.0 | No | 0.000 | Yes | O | 75.358 | 74.0 |
| 4 | Left | 8.600 | 3.580159 | 1.0 | 4.0 | | 73.0 | Yes | 8.866 | No | B | 48.357 | 93.0 |
| 5 | Succeeded | 9.821 | 3.404761 | 1.0 | 3.0 | 15.0 | 72.0 | Yes | 5.489 | Yes | A | 65.685 | 98.0 |
| 6 | Failed | 3.440 | 3.439667 | 1.0 | 1.0 | 0.0 | 70.0 | Yes | 5.737 | Yes | B | 59.599 | 97.0 |
| 7 | Succeeded | 9.638 | 3.335330 | 1.0 | 3.0 | 14.0 | 72.0 | Yes | 8.968 | Yes | A | 85.233 | 100.0 |
| 8 | Dead | 1.000 | 3.369984 | 1.0 | 2.0 | | 71.0 | Yes | 9.420 | Yes | AB | 75.146 | 99.0 |
| 9 | Succeeded | 8.925 | 3.685664 | 1.0 | 1.0 | 1.0 | 70.0 | Yes | 1.365 | Yes | O | 42.673 | 90.0 |

Figure 11: The first 10 patients, 3 years after joining the KPD program.

During this time period, some waiting patients may die, and others may receive deceased donations and leave this KPD program. The death rate per year is described in the “Transplant Surgeries” section. The actual death probability is scaled by the waiting time. For example, if the waiting period is a month, then the chance of death is 1/12 of the death rate per year. The same calculation applies to the probability of receiving outside donation and leaving this KPD program.

In this illustrative example, new patients arrive once a year, so the waiting period length is 1 year. In the patient table 11, we show the result of these patients 3 years later. During these 3 years, 30 more patients arrive at the KPD program. Patient 2, 3 died after 3 years of waiting while patient 8 died after

1 year of waiting. Patient 4 left the KPD program after 3 years of waiting. Patient 5 and 7 both got a successful transplant 2 years later.

4 ONGOING RESEARCH

4.1 Simulation Environment

The probability distribution models used to generate donors and patients variables are based on domain expert input and some medical literature to facilitate the development of the simulator. To more accurately represent real world patient profiles, one viable approach is to perform regression analysis on actual patients and donors participating in the KPD program to determine the distribution of these profiles. Population synthesis(Huynh et al. 2013) methods may be useful in this ongoing research.

Additionally, the algorithm to convert a 5-year survival rate into expected life years is a rough approximation. Given that this is a key component of the simulator for evaluating the performance of other modules, further refinement is critical.

4.2 Module Updates

The overall KPD framework incorporates three optimization modules that can be updated. Enhancing a module's functionality may improve the performance of the entire KPD framework. Module 1 could be updated to produce not only probabilities of adverse events but also joint and conditional probabilities, given that some events are inherently correlated. Module 3 could be updated to offer personalized suggestions to a wider variety of patients, as it currently only handles 70-year-old patients. Module 3 can also consider the possibility of desensitizing and receive transplantation from the incompatible willing living donor, who is always available as a worse-case backup option.

4.3 Simulation Optimization

Modules 1 and 2 both have configurable parameters that are set to default values in this version of the simulator. The desensitization module can generate multiple desensitization plans with different priorities, such as prioritizing rehospitalization risks over graft failure risks. This richer output can provide the matching algorithm with more options to consider and select from. The matching algorithm could prioritize certain patients over others, whereas it currently maximizes the total number of matched patients. By tuning weights assigned to each patient, we can further enhance the performance or fairness of this matching algorithm. This weight tuning can be accomplished through simulation optimization.

To choose the best matching plan, we can formulate and solve a Markov Decision Process problem. We define the entire patient pool as a state and a matching plan as an action. Since selecting from all the matching plans is impractical, we can choose a few generated with several parameter-setting heuristics. The task is then to select the best matching plan for now that maximizes the sum of expected life years for all patients arriving in a period. This task requires us to balance matching as many patients as possible now to gain more expected life years and waiting for the possibility that new arriving patients may offer better matches that could be missed if we act too hastily. A simulation optimization approach with the help of this simulator will assist us in determining the best matching plan. This is our ongoing research direction.

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REFERENCES

- Abecassis, M., S. T. Bartlett, A. J. Collins, C. L. Davis, F. L. Delmonico, J. J. Friedewald *et al.* 2008. “Kidney transplantation as primary therapy for end-stage renal disease: a National Kidney Foundation/Kidney Disease Outcomes Quality Initiative (NKF/KDOQIM) conference”. *Clinical Journal of the American Society of Nephrology* : *CJASN* 3(2):471–480 <https://doi.org/10.2215/CJN.05021107>.
- Abouna, G. M. 2008. “Organ Shortage Crisis: Problems and Possible Solutions”. *Transplantation Proceedings* 40(1):34–38.
- Bae, S., A. B. Massie, A. G. Thomas, G. Bahn, X. Luo, K. R. Jackson *et al.* 2019. “Who can tolerate a marginal kidney? Predicting survival after deceased donor kidney transplant by donor-recipient combination”. *American Journal of Transplantation* : *Official Journal of the American Society of Transplantation and the American Society of Transplant Surgeons* 19(2):425–433 <https://doi.org/10.1111/ajt.14978>.
- Huynh, N., M. Namazi-Rad, P. Perez, M. J. Berryman, Q. Chen and J. Barthelemy. 2013. “Generating a synthetic population in support of agent-based modeling of transportation in Sydney”. *20th International Congress on Modelling and Simulation (MODSIM 2013)* 20:1357–1363 <https://doi.org/https://ro.uow.edu.au/eispapers/1737>.
- Marfo, K., A. Lu, M. Ling, and E. Akalin. 2011. “Desensitization protocols and their outcome”. *Clinical Journal of the American Society of Nephrology* 6(4):922–936.
- Mattsson, J., O. Ringdén, and R. Storb. 2008. “Graft failure after allogeneic hematopoietic cell transplantation”. *Biology of Blood and Marrow Transplantation* 14(1):165–170.
- Ren, X., M. C. Fu, and S. I. Marcus. 2022. “Optimal Acceptance of Incompatible Kidneys”.
- Ren, X., M. C. Fu, and S. I. Marcus. 2023. “Stochastic Control for Organ Donations: A Review”. *Systems & Control Letters* 173.
- Serra, D., C. Sorgente, M. Gentili, and R. Cerulli. 2024. “Kidney Exchanges with Desensitization and Orphans: A Matheuristic Approach”.
- Shams Eddin, M., H. El-Amine, N. Koizumi, and M.-H. Li. 2024. “Nearest neighbor approach for the optimal desensitization of kidney transplant recipients”.
- The Organ Procurement and Transplantation Network 2020a. “A Guide to Calculating and Interpreting the Estimated Post-Transplant Survival (EPTS) Score Used in the Kidney Allocation System (KAS)”. https://optn.transplant.hrsa.gov/media/1511/guide_to_calculating_interpreting_epts.pdf.
- The Organ Procurement and Transplantation Network 2020b. “A Guide to Calculating and Interpreting the Kidney Donor Profile Index (KDPI)”. https://optn.transplant.hrsa.gov/media/1512/guide_to_calculating_interpreting_kdpi.pdf.
- United Network for Organ Sharing 2021. “Kidney Paired Donation”. <https://unos.org/transplant/kidney-paired-donation/>.
- Zachary, A. A. and M. S. Leffell. 2014. “Desensitization for solid organ and hematopoietic stem cell transplantation”. *Immunological Reviews* 258(1):183–207.

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