TEXAS TECH UNIVERSITY

Industrial Engineering™

Optimizing Kidney Paired Donation

Shubham Singh, Dhana Gandham, Prateeksha Singh

Advisor

Dr. Hamidreza Validi

Department of Industrial, Systems, and Manufacturing Engineering

Texas Tech University

Table of Contents

1. Introduction

Kidney Paired Donation has greatly revolutionized renal transplantation, providing life-saving opportunities to patients with end-stage renal disease and having living but incompatible donors. Traditionally, transplantation has involved direct donation from a living donor to a recipient; in KPD, however, incompatible donor-recipient pairs exchange kidneys with other donor-recipient pairs. This exchange not only increases the number but also the compatibility between donors and recipients, reducing possible rejections and increasing long-time survival. Kidney exchange programs have created new hopes for thousands of patients stuck on waiting lists amidst the continuing shortage of organs around the globe.

KPD was far gathering momentum in popularity internationally, especially in the KPD programs in countries like South Korea, the Netherlands, and Australia. Each of these countries has put its distinctive mark on KPD development by shaping this model in compliance with the domestic health context and social contexts. Cultural constraints and living donor scarcity drove South Korea to stage the first paired kidney exchange in 1991. It grew rapidly and continues to serve as one of the milestones concerning societal level barriers that KPD may provide solutions for (Ellison, 2014).

In addition, the implementation of KPD in Europe was also plagued by country-specific variations-while the first national KPD program was initiated in Netherlands back in 2004. It remains one of the top performing programs internationally (Ellison, 2014). The Dutch program, run by the Dutch Transplant Foundation, has provided an example of how organ exchange systems can be much more efficient when centralized. Subsequently, other countries like Spain and Switzerland have taken similar initiatives, with variable speed. For example, Spain's high rates of deceased organ donation have given that country a unique model that integrates KPD with its larger organ donation system. Switzerland, on the other hand, has tried to maximize exchanges within a much smaller, more local network.

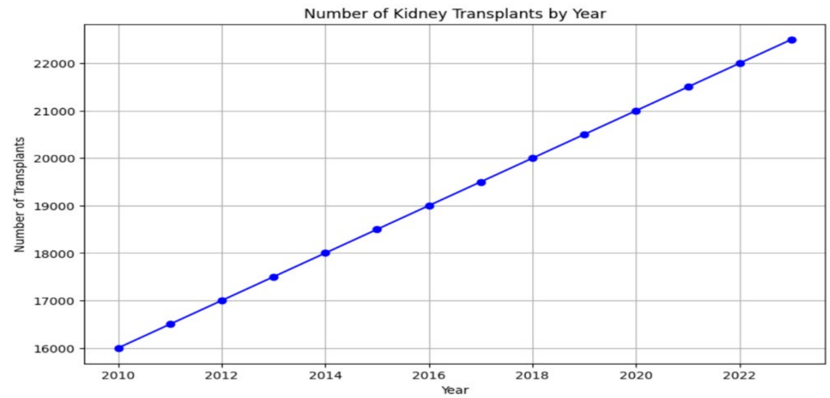
Meanwhile other countries with smaller populations, like Australia and Canada, have similarly benefited from the value in KPD. Australia's nation-wide kidney exchange program has, since its establishment in 2010, enabled very successful multi-center exchanges, putting several transplant centers within the same country in a position of optimal donor-patient compatibility, while Canada's Living Donor Paired Exchange (founded in 2009) has allowed for collaboration between several provinces through the use of a central registry, enabling life-saving matches across the country (Ellison, 2014).

These international efforts put a stamp on the flexibility of the KPD programs in the arena of overcoming challenges thrown up by organ shortages. The more countries there are to adopt and scale up the KPD systems, the more life-saving exchanges that could take place, till finally there comes a future where many more patients shall receive their transplant in time and independent of any donor compatibility issue.

KPD was first proposed by Felix Rapaport back in 1986, but it wasn't until 2000 that the first paired donation transplant was done in the USA (Wallis et al., 2011). For this case, the donors and recipients were matched based on the first computerized match run carried out by the Organ Procurement and Transplantation Network (OPTN) in October 2010 (United Network for Organ Sharing, 2010). Between 2011 and 2021, the number of KPD transplants more than doubled, and the percentage of total kidney transplants that were KPD also more than doubled (United States Renal Data System, 2023). The important legislative development came in 2007 when Congress, by passing the Charlie W. Norwood Living Organ Donation Act, finally amended NOTA by explicitly exempting paired kidney donation from its prohibition on "valuable consideration" (United Network for Organ Sharing 2010). This was, and is, the enabling legislation that allows KPD to spread nationwide.

In 2010, the United Network for Organ Sharing (UNOS) initiated the National Kidney Paired Donation Pilot Program to enable large-scale kidney exchanges among major transplant centers. This program registers donor-recipient information in a national database, where matches are run twice a week to coordinate transplants between hospitals (United Network for Organ Sharing, 2010). As it matured over the years, it has gradually scaled up participation by transplant centers and provided support to multi-center and multi-way chains of kidney exchanges that really expands the potential for matching kidneys and improving transplantation outcomes.

The UNOS pilot was succeeded by further development and increases in KPD with the assistance of national and regional programs. In 2021, KPD utilization had greatly increased in the United States, where 1 out of 5 living donor kidney transplantation (LDKT) were being made possible through KPD (Garg et al., 2024). It is reassuring to note, however, that KPD transplant opportunities are increasing for both patients and in helping eliminate disparities in transplant access, especially with regard to minority populations, as suggested by (Garg et al., 2024).Yet, serious challenges still persist, wherein a very high percentage of transplant programs still do not perform any kind of KPD transplant-a fact indicating a strong need to further efforts toward expanding the KPD at the level of centers while improving data.



Number of kidney transplants from 2010 to 2023 in the USA [6]

Project Thrust :
An optimal KPD plan is one which includes the highest number of compatible kidney transplants, ensuring that maximum numbers from a living incompatible donor-recipient pairs get matched and could eventually undergo exchanges. By and large, this work form's part and parcel for addressing the challenges experienced to this day by the United States transplant system in performing its service of saving lives by an increased number of renal transplantations, while in practice expanding the reach for its kidney exchange programs across the nation.

2. Criteria

As an operation researcher at the Kidney Paired Donation Pilot Program within OPTN, it is crucial to establish a complete comprehension of the criteria that would lead to efficient kidney exchanges. This kidney paired donation plan is developed based on the blood group compatibility of the donors and recipients. Blood type compatibility helps minimize the chances of organ rejection and thus ensures that the kidney transplantation outcome is successful. Required and prohibited criteria, additional considerations, and the relative importance of blood group compatibility in optimizing kidney exchanges are discussed below.

2.1 Required Criteria for Blood Type Compatibility

2.1.1 Matching Blood Types

The blood types between the donor and recipient should be compatible to prevent rejection of the transplanted kidney by the immune system of the recipient. The compatibility will be based on blood types A, B, AB, and O.

2.1.2 Donar Compatibility

- Type O Donor: O type is the universal donor, meaning it can be given to recipients of any blood type (A, B, AB, or O).
- Type A Donor: A type donors can only donate to recipients with blood types A and AB.

- Type B Donor: B type donors can donate to recipients with blood types B and AB.
- Type AB Donor: AB type donors can only donate to recipients with blood type AB.

2.2 Prohibited Criteria

Though some blood type combinations are compatible, others should not be matched in the kidney exchange process due to the possibility of organ rejection:

2.2.1 Type O Recipient Restrictions

A Type O recipient can only receive a kidney from a Type O donor since his blood does not match with the blood of the recipients with Types A, B, and AB. This is due to the presence of anti-A and anti-B antibodies in the plasma of the recipient that would then attack the foreign antigens of the kidneys from incompatible donors.

2.2.2 Incompatible Blood Type Pairings

Some blood types just cannot mix, due to the issues of immune rejection. These include blood from:

- A Type A donor should not give to a Type B recipient.
- A Type B donor should not give to a Type A recipient.
- A Type AB donor should not give to a Type A or Type B recipient because AB blood carries both A and B antigens.

2.3 Additional Considerations

Besides the required and prohibited criteria, a number of significant factors should be considered while determining suitable kidney exchanges.

2.3.1 Ethical Considerations

In KPD, ethical considerations are critical, especially when it comes to live donors. It is critical to ensure voluntary donations and informed permission. To ensure that all patients have equal access to organ donations, efforts must be made to reduce disparities in transplantation access (KDIGO, 2017).

2.3.2 Geographic and Logistical Factors

Geographic variations in kidney transplantation significantly affect the organ-matched donation process and outcomes. Variability among the regions leads to disparities in transplant waiting times, availability of the organ, and access to appropriate medical care and, hence, a poor outcome. Since longer transplant waiting times in a particular region could be related to reduced donor availability, better kidney allocation strategies should be developed to reduce these disparities and ensure equal access to a transplant (Kasiske et al., 2020).

2.3.3 Crossmatch Testing and Sensitized Patients

Aside from blood type compatibility, crossmatch testing is necessary to evaluate if the recipient's immune system will reject the donor kidney. Sensitization occurs when about 30% of the candidates for transplantation have antibodies that may fight a donor organ; this increases their waiting period to get a compatible kidney (Johns Hopkins Medicine, n.d.).

A crossmatch test mixes blood from recipient and donor to check for immune reactions:

- Positive Crossmatch: Indicates rejection, making the kidney unsuitable for transplant.
- Negative Crossmatch: It shows compatibility and can be transplanted.

Even in cases of compatible blood types, the transplant team has to make sure this will not be rejected, and it requires a negative crossmatch (Johns Hopkins Medicine, n.d.).

3. Problem Statement

The Organ Procurement and Transplantation Network (OPTN) has a substantial challenge in increasing the success rate of kidney transplants in circumstances when direct donor-patient matching is unavailable. The Kidney Paired Donation (KPD) initiative aims to overcome this issue by matching incompatible patient-donor pairings with other similar combinations in order to facilitate a mutually advantageous kidney exchange.

As an Operations Research consultant for the KPD Pilot Program, our goal is to create an efficient matching model for a dataset of incompatible donor-recipient couples. The goal is to maximize the number of compatible transplants by finding and implementing the best exchange cycles.

4. Description of Model

The operations research model entails determining the ideal exchanges between donor and recipient pairings in order to increase the success rate of kidney transplantation. The matching must be done under particular conditions in order for all trades to be viable, compatible, and even logistically feasible.

4.1 Participants in the Model

The model includes donor-recipient couples as participants. A donor-receiver pair comprises of a willing kidney donor who is incompatible with their intended recipient. The KPD system's purpose is to discover other donor-recipient couples with whom an exchange can take place, ensuring that all recipients receive a compatible kidney.

4.2 Exchanges Between Pairs

The model is based on exchanging pairings. A chain of exchanges in this way occurs when the donor of one pair donates to the recipient of another pair, and vice versa. These exchanges are only conceivable if the donor and recipient from another couple are immunologically compatible. The optimization model's purpose is to locate and maximize the number of exchanges that can occur while ensuring that each donor-recipient pair participates in exactly one exchange.

4.3 Binary Decision Variables

The binary decision variable denotes the decision of forming an exchange between two donor-recipient pairs. This variable takes the value of 1 if there is an exchange between two pairs and 0 otherwise. The model decides which pairs need to be matched with whom using these decision variables while optimizing the overall number of exchanges.

4.4 Objective of the Model

The goal of the model is to maximize the total number of kidney transplants by choosing pairs that can exchange kidneys in such a way that as many recipients as possible get compatible kidneys. This model maximizes the exchanges to reduce the number of patients on the waiting list and hence enhance the efficiency of the kidney transplantation process altogether.

4.5 Constraints in the Model

4.5.1 Compatibility Constraints

One of the main constraints in the KPD model is that exchanges can occur only between donor-recipient pairs who are compatible based on their blood groups. This compatibility is highly relevant to minimal organ rejection and for the assurance of maximum chances of transplant success.

4.5.2 Participation Constraints

Each donor-recipient pair may enter only one exchange. The idea behind this is that no person should be left being exchanged more than once, making the process easy to handle and less complex; this will also ensure the equity of the distribution of the kidneys to the recipients.

4.5.3 Cycle Constraints

In the KPD system, exchanges can form cycles where more than one pair is involved in a chain of kidney donations. The proposed model limits the cycle size to 3 pairs so as to keep the system workable. For sizes larger than 3, coordination and logistics become increasingly difficult since there are more participants, more variables to ensure compatibility, and greater timing challenges. Limiting cycle size to 3 provides the system with the maximum numbers of successful exchanges while keeping it feasible and efficient. Roth, Sönmez, and Ünver (2005) also note that the larger the cycle, the greater the complexity in coordination, with compatibility among a larger group of participants being increasingly hard to achieve. Correspondingly, increasing the cycle size enlarges the scope for any form of mismatch or other flaws, which increases logistical challenges during the exchange process.

4.6 Optimization Process

The optimization approach will enumerate all possible exchanges and then evaluate them for the determination of exchanges that can achieve the maximum number of transplants while satisfying the constraints put forth. The model will use a computational algorithm in finding the optimal set of exchanges, taking into account the binary decision variables, compatibility requirements, and constraints related to cycle sizes and participation.

4.7 Decision Making

Once the model has been solved, the decision makers, for example, transplant coordinators or medical professionals, can implement the exchange plan, specifying which pairs of donors and recipients should exchange kidneys in a way that maximizes the overall number of transplants. In the final solution, one can get a schedule of matchings which can be executed efficiently.

4.8 Iterative Nature of Model

Iterative processes may be required to repeat the process when more pairs become available or even the introduction of new constraints; for instance, new donor-recipient pairs enter the program, or compatibility rules change. In such cases, the model can be run again to come up with a new optimal solution incorporating these changes.

5. Mathematical Model of Problem

5.1 Decision Variables

Nodes (Patients and Donors):

a. N: Set of nodes representing incompatible patient-donor pairs.
b. Each node $i \in N$ a donor and a recipient.

Edges (Compatibility):

c. E: Set of edges, where an edge (i, j) E exists if donor i is compatible with recipient j.

Binary Decision Variable:

d. $x_{ij} = 1$ if edge (i,j) is included in the matching, 0 otherwise.

5.2 Objective Function

Maximize the total number of compatible matches:

$$Maximize \ \Sigma_{(i,j)\in E}\ x_{ij}$$

5.3 Constraints

5.3.1 Node Matching Constraint

Each node can only participate in one match (incoming or outgoing):

$$\Sigma_{(i,j)\in E}\, x_{ij} + \Sigma_{(i,j)\in E}\, x_{ji} \leq 1 \quad \forall i \in N$$

5.3.2 Cycle Constraints

Allow cycles of size 2 and 3:

- For cycles of size 2: For cycles of size 2: (i,j), (j,i)∈E:
$$x_{ij} + x_{ji} \leq 1 \quad \forall (i,j) \in E$$
- For cycles of size 3: (i,j), (j,k), (k,i)∈E:
$$x_{ij} + x_{jk} + x_{ki} \leq 1 \quad \forall (i,j,k)\ formig\ cycle$$

5.3.3 Binary Constraint

xij ∈ {0,1}   ∀(i,j)∈E

6. Python/ Gurobi Code

The Python/Gurobi code and data are available in the GitHub repository below -

https://github.com/webdeveloper31/Thematchteam.git

7. Experiments

7.1 Setup:

The optimization model was implemented using Python and solved with Gurobi Optimizer (version 11.0.3). The data consists of patient-donor pairs and their compatibility based on blood types. The compatibility graph was constructed using NetworkX, with edges representing feasible matches.

7.2 Hardware Configuration:

- Processor: 12th Gen Intel(R) Core (TM) i5-12500H
- Threads: 16 logical processors

7.3 Results

The Gurobi Solver has successfully identified a total of 322 matches, categorized by blood type as follows:

- Blood type A: 161 matches
- Blood type B: 161 matches
- Blood type AB: 0 matches
- Blood type O: 0 matches

7.3.1 Cycles of Length 2 and 3

- Identified feasible cycles of size 2 and 3 using graph traversal techniques.
- Cycles ensure maximal utilization of available pairs for transplants.

7.3.2 Optimization Outcome

- The model maximized the number of transplants matches while adhering to constraints.
- The solver efficiently handled the graph's complexity, optimizing over 40 binary variables.

7.3.3 Execution Time and Efficiency

- The optimization ran smoothly, leveraging multi-threading for speed.
- Memory usage was manageable within the student license constraints.

8. Plan

- Optimal plan for kidney transplant: The primary objective of the KPD model is to maximize the number of successful kidney transplants by identifying compatible exchanges between incompatible donor-recipient pairs.
- Maximization of Compatible Transplants: The objective of the function is to maximize the total number of successful transplants by determining viable matches between donor-recipient pairs, ensuring all compatibility requirements are met.
- Blood Type Compatibility: Matching the required blood types for successful implants like Type O donors can match with all blood types, while Type A donor's match with A and AB, Type B with B and AB, and Type AB only with AB recipients.
- Incorporation of Crossmatch Testing: Crossmatch testing is conducted to verify that the recipient's immune system will not reject the donor kidney. Donor-recipient pairs with positive crossmatches are excluded from the matching process, while those with negative crossmatches are prioritized for matching.

9. Evaluation of Plan

- Compliance with Compatibility Requirements: The model makes sure all matches are a perfect fit in terms of blood type and crossmatch compatibility, which helps keep the risk of organ rejection super low.
- Maximization of Transplant Opportunities: The solution makes the most out of the available donor-recipient pairs, ensuring we get as many successful transplants as possible.
- Efficiency and Scalability: The Gurobi optimizer can efficiently handle complex and larger datasets of donor-recipient pairs. Our kidney transplant model does not provide solutions for some of these issues.
- Geographic restrictions: Does not consider transportation time, affecting organ viability.
- Urgency of Transplants: Does not factor in the urgency of transplantation, potentially delaying critical cases.
- Post-Transplant Outcomes: Does not address potential outcomes post-transplant, which could be improved with patient health data.

10. Conclusions

The Kidney Paired Donation (KPD) optimization model successfully maximized compatible transplants by identifying feasible cycles of size 2 and 3 using Python and Gurobi Optimizer. The model handled the compatibility graph efficiently within the constraints of the student license, optimizing 40 binary variables while adhering to key operational constraints. This approach demonstrates the effectiveness of operations research in solving critical healthcare challenges. Future enhancements, such as incorporating proximity or urgency factors, could further improve the model's practical application in organ transplantation networks.

11. References

1. Ellison, B. (2014). A systematic review of kidney paired donation: Applying lessons from historic and contemporary case studies to improve the US model. Wharton Research Scholars Journal, 1, 107. Retrieved from http://repository.upenn.edu/wharton_research_scholars/107
2. Wallis, C. B., Samy, K. P., Roth, A. E., & Rees, M. A. (2011). Kidney paired donation. *Nephrology Dialysis Transplantation*, *26*(7), 2091-2099. https://doi.org/10.1093/ndt/gfr155
3. United Network for Organ Sharing. (2010, December 9). First kidney paired donor transplants performed as part of national pilot program. Retrieved from https://unos.org/news/first-kidney-paired-donor-transplants-performed-as-part-of-national-pilot-program
4. United States Renal Data System. (2023). *Annual Data Report: End-stage renal disease, transplantation*. National Institute of Diabetes and Digestive and Kidney Diseases. Retrieved from https://usrds-adr.niddk.nih.gov/2023/end-stage-renal-disease/7-transplantation
5. Garg, N., et al. (2024). "Temporal trends in kidney paired donation in the United States: 2006-2021 UNOS/OPTN database analysis." American Journal of Transplantation **24**(1): 46-56.
6. United Network for Organ Sharing (UNOS). (2020). *Kidney paired donation: Brochure 108*. https://unos.org/wp-content/uploads/Brochure-108-Kidney-paired-donation.pdf
7. Johns Hopkins Medicine. (n.d.). Incompatible kidney transplant. Retrieved from https://www.hopkinsmedicine.org/transplant/programs/kidney/incompatible
8. Kidney Disease: Improving Global Outcomes (KDIGO). (2017). Clinical practice guideline on living kidney donation. Kidney International Supplements, 7(1), 1–116. https://doi.org/10.1016/j.kisu.2017.04.001
9. Kasiske, B. L., Snyder, J. J., Skeans, M. A., Tuomari, A. V., Maclean, J. R., & Israni, A. K. (2020). The geography of kidney transplantation in the United States. *American Journal of Transplantation*, *20*(9), 2427–2434. https://doi.org/10.1111/j.1600-6143.2007.02130.x
10. Roth, A. E., Sönmez, T., & Ünver, M. U. (2005). Pairwise kidney exchange. Journal of Economic Theory, 125(2), 151–188. https://doi.org/10.1016/j.jet.2005.04.004