RESEARCH ARTICLE

Long term simulation analysis of deceased donor initiated chains in kidney exchange programs

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ABSTRACT
Kidney exchange programs (KEPs) aim to find compatible kidneys for recipients with incompatible donors. Patients without a living donor depend upon deceased donor (DD) donations to get a kidney transplant. In India, a DD donates kidneys directly to a DD wait-list. The idea of initiating an exchange chain starting from a DD kidney is proposed in a few articles (and executed in Italy in 2018), but no mathematical formulation has been given for this merger. We have introduced an integer programming formulation that creates DD-initiated chains, considering both paired exchange registry and DD allocations simultaneously and addressing the overlap issue between the exchange registry and DD wait-list as recipients can register for both registries independently. A long-term simulation study is done to analyse the gain of these DD-initiated chains over time. It suggests that even with small numbers of DDs, these chains can significantly increase potential transplants.

1. Introduction

Transplantation is the preferred treatment over dialysis for patients with kidney failure. The limitation of this therapy is the availability of compatible donors. Waiting time for a compatible kidney is very high and varies across different blood groups (Stanford et al., 2014). If a recipient has a compatible living donor, then the transplant is performed. A blood-group incompatible pair can undergo an ABO-incompatible transplant or can register for a Kidney Exchange Program (KEP). Another way to get a compatible kidney is via non-directed donors (NDDs) like an altruistic donor or a deceased donor (DD). An altruistic donor is the one who donates one kidney to a recipient with kidney failure without receiving any incentive from this act. A DD is the one who donates organs to wait-listed patients in the DD wait-list registry once the criteria of brain stem death is satisfied. Different countries have different laws that govern these kinds of donations (Biró et al., 2021). For example, in India, altruistic donations are not permissible under the law (Bill et al., 2018; Kute et al., 2018).

KEP also known as Paired Kidney Exchange (PKE) and Kidney Paired Donations (KPD) initially considered binary swaps, but later it was recognised that more patients could benefit if swaps are extended into longer chains or cycles. Although simultaneous execution of very long exchange cycles is challenging for logistical reasons, still cycles of up to ****5 pairs have been successfully performed several times. One of the critical aspects of implementing long cycles is that all surgeries in a cycle need to be done simultaneously. It will eliminate chances of donors backing out. If any donor refuse to participate in the cycle after the linked recipient receives a kidney, then the whole cycle gets terminated. The subsequent recipient in the cycle will lose a paired donor and also the chance of participating in another exchange at a latter stage. Although the non-simultaneous paired exchange is permissible under the law in North America, in countries like India, paired exchanges have to be simultaneous. A few non-simultaneous exchanges have also been done in exceptional circumstances.

NDD chains have also become part of KEPs, where an altruistic or a DD starts a chain of exchanges when a kidney is donated to a pair in the KEP registry. Now, the donor of that pair will donate a kidney to the next pair in the chain, and this will go on till a donor fails to donate (Roth et al., 2006; Wallis et al., 2011). These transplants are performed in segments and the donor of the last pair becomes a bridge donor for the next segment. The longest NDD chain performed in the US had more than 100 transplants (University of Alabama at Birmingham, 2018).

Another possibility of exchange is known as list exchange or indirect exchange. It is an exchange

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This article has been corrected with minor changes. These changes do not impact the academic content of the article.

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mechanism between a Donor–Recipient (DR) pair and a recipient in the DD wait-list. Here, when the donor of an incompatible pair donates a kidney to a recipient in the DD wait-list and, in return, the intended recipient gets a high priority in that DD wait-list. It improves the chances of the recipient of that pair getting a compatible DD kidney sooner as compared to a long waiting time for a usual DD kidney. However, this process also has challenges in implementation because the arrival of a DD kidney is random. A paired recipient may have to wait for a long time to get a compatible kidney, and in the meantime, the patient might become too ill for a transplant or even die, so even after the paired donor donates a kidney, the recipient may not get a compatible kidney. Also, such a patient will not be able to take part in possible future KEP and will lose the chance of getting a living donor. These things make indirect exchange practically hard to implement.

Currently, DD allocations are done independently of the KEP in major parts of the world. An idea of initiating DD chains was proposed in the literature, and a two-length DD chain was performed in Italy in 2018 (Furian et al., 2019; Melcher et al., 2016). There are some studies done on DD chains recently, and some retrospective analysis of possibilities of such chains was also performed (Cornelio et al., 2019). Extending the analysis of such chains, a long-term simulation study of DD chains is done here on some realistic data from Indian registries. This paper proposes a mathematical model to optimise the number of transplants through DD-initiated chains (DDICs), considering recipients from both the DD wait-list and KEP registry. A model simulation is performed over time to estimate the relative benefit of creating DDIC to the independent functioning of the DD allocation and KEP. The simulations are conducted on Indian registry data with current Indian guidelines for kidney transplantation.

In the next section, a brief literature review of KEPs is given, and later, a mathematical model and analysis of DDIC are shown.

2. Literature review
KEP have emerged over the last two decades (Ashlagi & Roth, 2012, 2021; Awasthi & Sandholm, 2009; Biró et al., 2009, 2019; Klimentova et al., 2022; Nickholds & Mak-Hau, 2015; Roth et al., 2004, 2005, Mincu et al., 2021, Verma & Rangaraj, 2020). It was first introduced by Rapaport in 1986 when he proposed the idea of creating a living donor pool for kidney exchange (Ferrari et al., 2015). In 2000, the USA initiated a pilot program for paired kidney exchange, and later other countries like the UK, the Netherlands, and Italy started their KEP (Biró et al., 2019; Roth et al., 2005). Initially, the pool size of these exchange programs was small, and sometimes the proposed transplants failed due to tissue type incompatibility (J. Dickerson et al., 2013). Researchers have tried to increase the supply of donors by other mechanisms. Indirect exchange or List exchange is a mechanism where a donor from an incompatible pair will trade a kidney for a rank in the DD wait-list (Roth et al., 2004). This had some ethical concerns as DD arrivals are random, and by donating a kidney, a pair loses the possibility of further direct exchanges. ABO-incompatible or desensitised transplants can also be part of KEP where incompatible pairs can exchange their donors to improve their compatibility (Karami et al., 2019). NDD-initiated chains also became part of KEP, and several mechanisms to create NDD-initiated chains were proposed (Abraham et al., 2016; Roth et al., 2006). There are two types of NDDs, DDs, and altruistic donors. Altruistic donations provide an opportunity to create long-exchange chains because these chains can be performed in segments, and the last donor of each segment becomes a bridge donor, which can start another segment, and this chain can continue forever, in theory, (Veale & Hil, 2009).

DD chains are another possibility of exchange chains discussed in recent years. Melcher et al., (2016) proposed non-simultaneous altruistic chains starting from DDs. These DD-initiated chains would benefit DD wait-listed patients, as patients of KEP usually also register for DD kidneys. If KEP patients get a compatible kidney through chains, then it will clear the wait-list faster. It can also increase the welfare of DD patients of the chain since they will get a living donor kidney, which has greater graft survival. However, they proposed it as a non-simultaneous chain which can create issues of fairness. If a chain is not executed fully due to a donor backing out, then a DD wait-list patient will not get a compatible kidney, which would have been available if the current process of allocation was performed.

DD allocations are managed separately from living donor kidney transplantation in India. The DD organs are first allocated to the local registry if possible, otherwise it is offered to the regional registry and then to a national registry (Sahay, 2018).

Billa et al., (2018) proposed the idea of initiating DD chains in India, and they suggested simultaneous execution of DD-initiated chains where multiple alternatives can be created to increase the probability of successful execution. They also showed that there would not be any loss in terms of the number of recipients matched for different blood groups if all KEP recipients also register for a DD wait-list.

There are some ethical concerns regarding DD chains such as unfairness towards type-O recipients on the DD wait-list, the quality difference between DD and donor provided to DD wait-list, acceptance of DD kidney in return for a living donor kidney, and donor
backing out from chain which will reduce a transplant in DD wait-list (Melcher et al., 2016). Rees et al., (2016) showed that these chains would not disadvantage O-type and highly sensitised patients, but there could be other concerns in the implementation of DD chains. The major difference between the Indian and the western allocation policies is the inclusion of Altruistic donations. In India, altruistic donations are not allowed, which restricts the models from including NDD chains (Altruistic donor chains) in the system. Thus, there was a need to build a model under the current allocation rule to increase compatibility through DD-initiated chains.

A few reports of these concepts were given by Haynes & Leishman (2017) and Xavier (2017), and a similar study was conducted on the US data by Wang et al. (2022). The significant difference between these reports and the current work is the allocation approach and the study data. In developing countries, the DD rates are significantly lesser in developed countries, which makes the utility of a DD kidney even more critical as compared to these countries. Also, blood group distribution varies across countries which suggest that the benefit may vary across countries, and it could become more important for some countries to include these DDICs as compared to some other country. This paper gives us the long-term simulation study of DDIC in Indian settings.

In the next section, the idea in Billa et al., (2018) is extended and provides an integer programming formulation and a long-term simulation analysis of the simultaneous execution of DD chains.

3. DD-initiated chains

In the currently existing scheme of organ allocation in India, both kidneys of a DD are allotted to the DD wait-list recipients. We propose that (a) the first DD kidney goes to a recipient in the DD wait list registry and (b) the second kidney goes to the KEP registry and the paired donor of that recipient donates a kidney to the next recipient in the same KEP registry, to create a paired exchange chain. See Figure 1 for a schematic view of such a scheme. Several such donor–recipient pairs can potentially be added to this chain. The last donor of the pair then donates his kidney to the next patient on the DD wait list. Thus, from a single DD, two patients in the DD wait-list receive kidneys (as is the case currently), while some more patients in the paired exchange registry could also simultaneously receive compatible kidneys.

The main objective of the scheme is to increase the number of valid donor kidneys that will become available to potential recipients, both in the PK registry as well as the DD wait-list (we note that most intended recipients in the PKE will also be part of DD waitlists). This increase in the number of kidneys has a direct impact on waiting times and the number of dropouts. It turns out that the overall quality of matches that can be achieved also increases, as we find during our simulation results, subject to assuming the comparable quality of DD kidney (if done immediately after death) versus a living donor.

We emphasise that there will not be any loss to the DD wait-list per se (i.e., in terms of the number of transplants) as the last donor of the chain donates a kidney back to the DD waitlist. In terms of specific blood groups, O-type recipients who only register on the DD wait-list might suffer a longer wait time as the kidney offered to the DD wait-list may not be an O-type kidney, but that is the trade-off (optimality vs. fairness) one has to encounter while merging the two allocation mechanisms. In our model, it is proposed that one of the two kidneys from a DD should be allocated directly to the DD wait-list to ensure that the most needful recipient (i.e., first ranked recipient in that blood group category) gets the compatible kidney (i.e., fairness to the DD wait-list recipients) and then the second kidney can be used to increase the transplant possibilities (i.e., optimality with the remaining DD kidney). In the trade-off between fairness (in terms of waiting times) and optimality in terms of the number of transplants, the approach proposed by Melcher et al., (2016) starts chains from

![Figure 1. Deceased donor allocation in proposed mechanism, one of the deceased donor kidneys offered directly to the deceased donor wait-list, and the second kidney was used to initiate a DDIC length 3 (Billa et al., 2018).](image-url)
all the DD kidneys, which would be more unfair to DD wait-list recipients but will have more transplants as well. The current set-up is fairer for the DD wait-list but does not take the opportunity of more transplants. The proposed approach attempts to identify a compromise solution between these two approaches.

Also, the recipient who gets the O-type kidney in KEP will also be on the DD wait-list or will soon join the DD wait-list to increase his chances of getting a compatible kidney. Thus, it can be seen as the recipient trading his donor’s kidney for getting a DD kidney earlier than the standard procedure while allowing a few more incompatible pairs to get a compatible kidney. In any case, the burden on the DD wait-list will reduce, but there will be some impact on O-type recipients in the DD wait-list in terms of waiting time.

A bound-on chain length is required as the last donor of the chain needs to donate a kidney to a DD wait-list patient to ensure that the DD wait-list does not lose any transplant. In this paper, multiple chain lengths were considered for simulations to analyse the effect of chain length in DDICs. We consider chain length up to 3 (considering simultaneous exchanges) and also 6, keeping in mind future developments that allow for more non-simultaneous exchanges driven by NDDs.

In the next section, we will discuss an Integer Programming model for DD-initiated chains, and subsequently, we present simulation results comparing DDICs with the current allocation process.

### 3.1. IP model for DD-initiated chains

Consider a directed graph \( G = (N, E) \) with a set of nodes \( N \) consisting of four subsets of nodes, a set of DDs, a set of incompatible DR pairs that only register for living donor kidney exchanges (P), set of incompatible DR pairs who register for both registries (PWL) and set of DD wait-list (WL) recipients who does not have any willing donor. The edge set \( E \) consists of all directed edges in the graph, and an edge is formed from one node to another if the donor at the first node is compatible with the recipient at the other node. So each node in DD will have only outgoing edges from it, and each node in WL will have only incoming edges. Nodes in P and PWL will have both incoming and outgoing edges. A weight \( w \) is associated with each edge where weights are obtained by considering two factors HLA mismatch and the age difference between donor and recipient. A compact formulation is proposed for creating DDICs, which is one of the first models designed for it as per our knowledge. For compact formulation, \( L \) copies of the graph were created, where \( L \) is the sum of the number of DD and half of the number of pair nodes.

Let the variables be

\[
x^l_{ij} = \begin{cases} 1 & \text{If edge } (i,j) \text{ is selected in the } l^{th} \text{ copy of the graph} \\ 0 & \text{otherwise} \end{cases}
\]  

(1)

\[
f^l_i = \text{Sum of all outgoing edges for a node } i \text{ in } l^{th} \text{ copy of graph} 
\]

\[
g^l_i = \text{Sum of all incoming edges to a node } i \text{ in } l^{th} \text{ copy of graph} 
\]

An integer programming formulation for DD initiated chains is as follows:

\[
\begin{align*}
\max & \sum_{l \in L} \sum_{(i,j) \in E} w^l_{ij} x^l_{ij} \\
\text{s.t.} & \sum_{j \in (i,j) \in E} x^l_{ij} = f^l_i \quad \forall i \in N, \forall l \in L \\
& \sum_{j \in (i,j) \in E} x^l_{ij} = g^l_i \quad \forall i \in N, \forall l \in L \\
& f^l_i = g^l_i \quad \forall i \in P, \forall l \in L \\
& f^l_i \leq g^l_i \quad \forall i \in PWL, \forall l \in L \\
& \sum_{(i,j) \in E} x^l_{ij} \leq k \quad \forall l \in L \\
& \sum_{l \in L} f^l_i \leq 1 \quad \forall i \in N \\
& \sum_{l \in L} g^l_i \leq 1 \quad \forall i \in N \\
& x^l_{ij} \in \{1,0\}, \quad \forall (i,j) \in E, \forall l \in \{1..L\}
\end{align*}
\]  

Here, the objective is to maximise the weighted sum of the total number of edges over all replications. Each edge represents a compatible match, and weights are calculated based on a scoring system which is given in the appendix. Thus, it is maximising the number of feasible transplants while considering the quality of a match.

Constraint 5 ensures that the sum of incoming edges must be equal to the sum of outgoing edges in each replication for all pair nodes. It means a pair will only donate his donor’s kidney if his intended recipient receives a compatible kidney in that replication else it won’t donate.

Now for those recipients who are on both the DD wait-list and swap registries, a new constraint was introduced. Constraint 6 ensures that the sum of all outgoing edges should be less than the sum of all
incoming edges in replication for a PWL pair, this will mean that whenever a PWL pair donates his donor’s kidney, then the recipient also gets a compatible kidney in the same replication but it is not necessary vice-versa. Note here that since these pairs are registered for both registries, thus they should get a chance to receive a compatible kidney either via a living donor or via a DD kidney, depending upon their ranks in both registries. This was done by separating out those pairs who registered for both registries and defining a new variable for them. It ensures that there is no loss to recipients who registers for both registries in the merging registry.

Constraint 7 ensures that maximum donation in replication is bounded by k. Thus, a chain or cycle can be formed with a maximum length of k. Constraint 8 ensures that for a node i, the maximum donation overall replications can maximum be 1, and constraint 9 ensures that a maximum of 1 kidney can be received by a recipient over all replications.

This IP model can be considered as a combination and extension of earlier discussed models by (Anderson et al., 2015; Constantino et al., 2013; J. P. Dickerson et al., 2016). The major difference between the proposed model and earlier models is the inclusion of different types of nodes and constraints. Constantino’s model is designed for cycle formulation, while Anderson’s model talks about finding long chains initiated by altruistic donors. We have proposed a model considering both PKE and DD wait-list registries simultaneously. This creates a possibility of overlap between both registries, so we considered this possibility as well and defined a new variable that represents a pair in both registries. Our model has a non-directed donor node (DD node) which does not have any incoming edges and a DD wait-list node which does not have any outgoing edges. A few additional constraints were also added to create a bound on-chain and cycle length as we are considering simultaneous executions of these exchange transplants.

Melcher et al., (2016) proposed that these DD-initiated chains can be non-simultaneous, and every DD kidney can be considered as a NDD’s kidney. Our scheme addresses this differently and tries to retain fairness for all groups of recipients by donating one of the two DD kidneys directly to the DD wait-list.

4. Variants of the DDIC scheme

Two variants of the DD-initiated chains are discussed as follows: (a) patients with multiple, incompatible donors and (b) patients with a low-quality compatible donor.

4.1. DD-initiated chains with multiple donors

A patient may have more than one willing, incompatible donor with different blood groups and ages. Having more than one willing donor will increase the chances of getting a compatible kidney. For such recipients, the network that is created considers all willing donors and edge weights are calculated for each edge. The algorithm considers all edges and tries to maximise the overall weight.

4.2. DD-initiated chains with compatible pairs

Compatible pairs can also be part of a DD-initiated chain. Pairs with low HLA match or large age difference or HIV positivity between donor and recipient could participate in a KEP to increase the recipient’s post-transplant benefits. A few compatible pairs with O donors also join the registry because O donors are especially valuable since they are the only possible donors for O recipients. The corresponding donor of the O recipient could provide a better match. For all such pairs, to ensure fairness only edges with weights greater than a threshold (their own edge weight) are considered in the network. This condition can be modelled via the following constraint:

Let CP be the set of pairs in which the donor is compatible with the recipient,

\[ w_{(i,j)}^l x_{(i,j)}^l \geq w_{(i,j)}^l x_{(i,j)} \quad \forall j \in CP, \forall l \in \{1...L\} \] (11)

However, while creating the graph, for recipients in the set CP, only the edges with higher edge scores than the own edge score were considered. This will be done to reduce constraints in the model.

In this work, compatible pairs were part of the simulations as there were data available for compatible pairs in the KEP registry. However, the data distribution for multiple donors were unavailable, which restricts our model only to consider one donor for one recipient.

5. Simulation plan

In this paper, a simulation study is conducted to analyse the behaviour of DDICs as compared to standalone functioning of the current allocation processes for KEP and DD allocations. The simulation is based on representative data from Indian registries of KEP and DD wait-list. Since NDD chains have not been performed in India, several assumptions were required to make this comparison realistic. The following assumptions on various parameters were considered for the simulations.

(1) Blood Group distribution of pairs follows Apex Swap Transplant Registry (ASTRA) registry distribution.
(2) DDs’ blood group distribution follows general Blood Group distribution in India.

(3) The simulation is for a period of 3 years – the outcome of the PKE is computed every 3 months, and DDICs are created with the merged registry (12 rounds of simulations).

(4) The model was replicated 20 times to average out the randomness of the process.

(5) Two instances of arrival rates were considered for paired patients (who are willing to accept only living donors) and paired cum wait-list patients (who are willing to accept both living and DD kidneys) as Uniform(1,5), and Uniform (5,10).

(6) Two instances of DD arrival rates were considered as Uniform(1,5), and Uniform(5,10).

(7) It is assumed that there is a large wait-list for DD kidneys, so all the kidneys offered to them will be utilised (This was due to the lack of data availability for the DD wait-list and its related parameters).

(8) Probability of failure for an unmatched pair in the PKE registry to go to the next round was considered to be 0.2 and 0.4 (Dropout Probability – DP).

(9) Bound on cycle/chain length was considered to be 3 and 6.

In the next section, various results of DDIC comparison with independent functioning PKE and DD allocation are shown.

6. Results

Under the above assumptions, the following parameters were compared for the two processes: (a) the number of possible transplants, (b) the average quality of matches (i.e., average edge score), (c) average waiting time per recipient, (d) effective dropout probability (i.e., the proportion of unmatched pairs to the total number of pair available at the end of any round’s dropout probability). These parameters will give insight into the overall performances of both processes. Also, a blood group-wise comparison of waiting time was made. In the following tables, "DDIC sol" refers to the DDIC solution where both registries are considered simultaneously, and "Ind PKE and DD sol" refers to the combined solution of independent functioning of the PKE registry and DD allocations. Dropout numbers for the DDIC solution are the total number of recipients who dropped out from the combined registry, and the Ind solution consists of the sum of dropout numbers from the PKE and DD wait-list registry.

Table 1 shows that even with modest arrival rates of DD and PKE participants, and the relative gain of DDIC to the current process is significant (about 30%). The results suggest that large PKE registries would benefit from participation in DDICs as significant improvements can be achieved for them even with a small number of DD arrivals. In general, for a given PKE size, the benefits will increase with increased DD arrival rates. (This is true for other parameters also.) The above analysis was done with bound on cycle and chain length to be 3.

If DDICs can be performed non-simultaneously, then larger DDICs can be formed and executed over time. However, the last transplant of DDIC will be to a patient on the DD wait-list and this should be performed so that the patient should not have to wait for too long. So a bound of 6 on chain length was considered, and a simulation was conducted to observe the effect of bounds on DDICs. It is intuitive that with lesser restrictions on chain length, the relative gain of DDIC should increase, and our simulations also confirm it.

Similarly, the average edge score for DDIC improves as compared to the current allocation process, considering the average weights for DD edges. With higher arrival rates for PKE recipients, average edge score improvement also increases and this shows that with higher arrivals of PKE recipients, DDIC will provide better quality solutions. Now with higher DD and PKE arrivals, the benefit in average edge score improves to 10.8%. The increase in average edge score also improves with lesser bound chain lengths, which is intuitive as more flexibility creates opportunities for better matches.

Figures 2 and 3 show the comparison of DDIC to the current process over 12 rounds of simulations. These values were averaged out over 20 replications, and the mean results were compared in the graph. Here, it can be

| Arrival rate | DDIC Sol | Ind PKE and DD sol | Relative Gain in % |
|--------------|----------|--------------------|--------------------|
|                | Number of Transplants | Avg Edge Score | Number of Transplants | Avg Edge Score | Transplants, Edge Score |
| P=U(1,5), PWL=U(1,5) DD=U(1,5), bound =3 | 75.2 | 76.2 | 56.6 | 74.3 | 33%, 2.6% |
| P=U(5,10), PWL=U(5,10) DD=U(1,5), bound =3 | 153.8 | 79.9 | 112 | 77 | 37.3%, 3.7% |
| P=U(5,10), PWL=U(5,10) DD=U(5,10), bound =3 | 228 | 84.5 | 162.7 | 76.3 | 40.2%, 10.8% |
| P=U(1,5), PWL=U(1,5) DD=U(5,10), bound =3 | 138.9 | 82.6 | 107.8 | 74.2 | 28.9%, 11.3% |
| P=U(1,5), PWL=U(1,5) DD=U(1,5), bound =6 | 73.9 | 76.9 | 55.1 | 74.8 | 34%, 2.7% |
| P=U(1,5), PWL=U(1,5) DD=U(5,10), bound =6 | 155.8 | 82.7 | 113 | 79.5 | 37.8%, 4% |
| P=U(1,5), PWL=U(1,5) DD=U(5,10), bound =6 | 229 | 86.7 | 168.3 | 78.1 | 36%, 11% |
| P=U(1,5), PWL=U(1,5) DD=U(1,5), bound =6 | 140.8 | 82.4 | 108.8 | 74.5 | 29.4%, 10.6% |
observed that DDIC performed better than the current process in all the rounds, both in terms of the number of transplants and a lesser number of dropouts. As the number of rounds increased, the slope for the number of dropouts in DDICs becomes smaller than the current process. This suggests that fewer recipients will drop out of DDICs over time. Also, with higher arrival rates of PKE recipients, the difference between DDIC solutions to independent PKE and DD solutions will increase over time, which will encourage practitioners to consider implementing DDICs.

In India, as in many other countries, waiting times for recipients can be high and the average wait time for a kidney is an important parameter. The DDIC scheme can decrease the waiting time significantly even for small numbers of DD arrivals and it ranges between 6 and 12 months for different arrival rates of DD and PKE recipients (Table 2).

The proportion of recipients who drop out after every round (time period) also comes down, and this is related to the number of matches successfully achieved in a round (Table 2).

An analysis of waiting times for recipients of different blood groups in Table 3 reveals the following. As is well-known, AB recipients have the lowest waiting times and O recipients the highest. In the DDIC, a small increase in waiting times for AB recipients is offset by a much larger overall decrease in all other blood groups, especially the hard-to-match O group recipients for recipients in the PKE registry. Overall, the impact on waiting times is significant, reducing from up to 44 months to 2.3 months for O-type recipients. As expected, the improvements are more with higher arrival rates. However, for recipients who only registered for the DD waitlist, O-type recipients might have a higher waiting time in DDIC than independent allocation. The comparison of waiting times for such recipients could not be made due to a lack of data (as mentioned in assumption 7).

Please refer to appendix A for scoring method, appendix B for simulations on higher dropout probability and appendix C for data distribution.
Figure 3. Comparison of DDIC solution to individual solution with varying arrival rates for PKE recipients and DD, Bound on cycle and chain length = 6.

Table 2. Comparison of DDIC solution to individual (Ind) solution of PKE and DD allocation for PKE recipients in terms of effective Dropout (DO) probabilities and average Waiting Time (WT, in months) for different bound on cycle and chain lengths.

| Arrival rate | DDIC Sol | Ind KPE and DD sol | Relative Gain |
|--------------|----------|--------------------|---------------|
|              | Avg WT/recipient | Effective DO Probability | Avg WT/recipient | Effective DO Probability | Avg WT, DO probability |
| P=U(1,5), PWL=U(1,5) DD=U(1,5), bound =3 | 2.5 | 0.10 | 12.4 | 0.17 | 9.9, 0.07 |
| P=U(5,10), PWL=U(5,10) DD=U(1,5), bound =3 | 3.2 | 0.11 | 8.7 | 0.15 | 5.5, 0.04 |
| P=U(5,10), PWL=U(5,10) DD=U(5,10), bound =3 | 1.5 | 0.07 | 9.2 | 0.15 | 7.7, 0.08 |
| P=U(1,5), PWL=U(1,5) DD=U(5,10), bound =3 | 0.5 | 0.03 | 11.8 | 0.16 | 11.3, 0.13 |
| P=U(1,5), PWL=U(1,5) DD=U(5,10), bound =6 | 2.5 | 0.10 | 11.1 | 0.16 | 8.6, 0.06 |
| P=U(5,10), PWL=U(5,10) DD=U(1,5), bound =6 | 2.9 | 0.11 | 8.7 | 0.15 | 5.8, 0.04 |
| P=U(5,10), PWL=U(5,10) DD=U(5,10), bound =6 | 1.3 | 0.07 | 8.1 | 0.15 | 6.8, 0.08 |
| P=U(1,5), PWL=U(1,5) DD=U(5,10), bound =6 | 0.5 | 0.04 | 12.3 | 0.17 | 11.8, 0.13 |

Table 3. Blood group-wise comparison of waiting time (in months)/recipient of DDIC to individual (Ind) KEP and DD allocation for PKE registry recipients.

| Arrival rate | O type | A type | B type | AB type |
|--------------|--------|--------|--------|---------|
| P=U(1,5), PWL=U(1,5) DD=U(1,5), bound =3 | 2.3/44 | 0.4/1.6 | 0.4/1.7 | 0.2*/0 |
| P=U(5,10), PWL=U(5,10) DD=U(1,5), bound =3 | 5.4/32.7 | 0.4/0.9 | 0.3/0.8 | 0.2*/0 |
| P=U(5,10), PWL=U(5,10) DD=U(5,10), bound =3 | 1.5/34.4 | 0.2/0.9 | 0.2/1 | 0.2*/0 |
| P=U(1,5), PWL=U(1,5) DD=U(5,10), bound =3 | 0.3/48.2 | 0.1/1.5 | 0.1/1.4 | 0/0 |
| P=U(1,5), PWL=U(1,5) DD=U(5,10), bound =6 | 2.2/30.7 | 0.3/1.3 | 0.4/1.6 | 0.3/0 |
| P=U(5,10), PWL=U(5,10) DD=U(1,5), bound =6 | 5/34.2 | 0.4/1 | 0.3/0.7 | 0.7*/0 |
| P=U(5,10), PWL=U(5,10) DD=U(5,10), bound =6 | 1.4/31.5 | 0.2/1 | 0.1/0.9 | 0.1*/0 |
| P=U(1,5), PWL=U(1,5) DD=U(5,10), bound =6 | 0.3/47.3 | 0.1/1.6 | 0.1/1.4 | 0/0 |
7. Technical information regarding the simulations

The integer programming model was written in Python-Pulp and solved using the state-of-art CPLEX solver operating under a windows 11 environment. The desktop configuration was i5 -10,210 U CPU @ 1.60 GHz with 8Gb ram, and it took an average of about half a minute to solve each instance. Since the arrival rates were low for our model, the problem size never becomes exponentially large, but for higher arrival rates, the problem size can grow exponentially, and the CPLEX solver directly may not be able to solve it. Thus, more sophisticated approaches like column generation might be required for larger-size problems.

8. Conclusion and discussion

Shortages of kidney donors have been a significant concern in providing compatible kidney transplants to needy recipients. KEPs were developed to increase the supply of compatible kidneys to the pool of incompatible donor—recipient pairs. Even with increasing kidney exchange pools, not every recipient gets a compatible kidney quickly, especially for O-type recipients. The average waiting time to get a compatible kidney in a KEP registry is increasing over the years. However, in the last few years, deceased donations have increased steadily, and it is expected that with an increase in awareness about organ donation, it will increase further in the country. With this prospect, the idea of DD-initiated chains could increase the supply of compatible kidneys to a PKE registry and improve the waiting time to get a compatible kidney in both the PKE and DD wait-list registries.

An integer programming model is proposed in this paper, which allows us to create DD-initiated chains. A long-term simulation study is also done to analyse the gain that can be achieved through this. Results show that a significant gain in the number of transplants, waiting times, average edge scores, and effective dropout probabilities can be achieved for each blood group. Even with small DDICs, the benefit that can be achieved is around 30–40% in terms of the number of transplants and 3–11% in terms of the quality of matches under various scenarios. The acceptance of a DD kidney in return for a living donor kidney is still a debatable topic, but as the demand for a kidney is very high, patients are willing to accept any possible transplant opportunity. Larger DDICs with more benefit can be achieved if non-simultaneous execution can be done.

DDICs can include multi-hospital/registry set-up as well, but that brings more logistical complexity into the system as managing multi-hospital registries comes with its own challenges of data sharing and different objectives and constraints for each registry. ABO-incompatible transplants can also be part of DDICs which will increase the compatibility within the registry; however, it will require individual preferences of recipients among available transplant choices.

In conclusion, DDIC seems to be one way forward to increase the utility of DD kidneys, and the long-term analysis shows that there will be a significant benefit in all the parameters in comparison to the current process.

Acknowledgments

We would like to acknowledge Zonal Transplant Co-ordination Centre (ZTCC), Mumbai, for their feedback and data distributions.

Disclaimer

Only the blood group data number of the wait-listed patients has been shared by ZTCC, and the contents are not verified or ratified by that ZTCC.

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Data availability statement

The authors confirm that the data supporting the findings of this study are available within the article [and/or] its supplementary materials.

Code availability

The code that supports the findings of this study is available from the corresponding author upon request.

References

Abraham, G., Vijayan, M., Gopalakrishnan, N., Shroff, S., Amalorpavanathan, J., Yuvaraj, A., Sundararajan, S. . . . Sundararajan, S. (2016). State of deceased donor transplantation in india: A model for developing countries around the world. World Journal of Transplantation, 6 (2), 331–335. https://doi.org/10.5500/wjt.v6.i2.331

Anderson, R., Ashlagi, I., Gamarnik, D., & Roth, A. (2015). Finding long chains in kidney exchange using the traveling salesman problem. Proceedings of the National Academy of Sciences of the United States of America, 112 (3), 663–668.

Ashlagi, I., & Roth, A. (2012). New challenges in multi-hospital kidney exchange. The American Economic Review, 102(3), 354-259. https://doi.org/10.1257/aer.102.3.354

Ashlagi, I., & Roth, A. (2021). Kidney exchange: An operations perspective. Management Sciences.

Awasthi, P., & Sandholm, T. (2009). Online stochastic optimization in the large: Application to kidney exchange. IJCAI’09 Proceedings of the 21st international joint conference on Artificial intelligence, 405–411.
Karami, Billa, V., Verma, U., Usulumarty, D., Rangaraj, N., Sanap, G., Kothari, J., Bichu, S., Bichu, S. (2018). A novel method to increase the kidney donor pool: A fusion model linking the deceased donor waitlist to a paired kidney exchange program. Indian Journal of Transplantation, 12, 187–192. https://doi.org/10.4103/ijot.ijot_44_18

Biró, P., Klundert, J., Manlove, D., Pettersson, W., Andersson, T., Burnapp, L., Viana, A. … Viana, A. (2021). Modeling and optimization in European kidney exchange programs. European Journal of Operational Research, 291 (2), 447–456. https://doi.org/10.1016/j.ejor.2019.09.006

Biró, P., Kromwijk, B., Andersson, T., Åsgeirsson, E., Baltesová, T., Boletis, I., Böhög, M. … Böhmig, G. (2019). Building kidney exchange programmes in Europe – An overview of exchange practice and activities. Transplantation, 103(7), 1514–1522. https://doi.org/10.1097/TP.0000000000002432

Biró, P., Manlove, D., & Rizzi, R. (2009). Maximum weight cycle packing in directed graphs, with application to kidney exchange programs. Discrete Mathematics, Algorithms and Applications, 01, 499–517. https://doi.org/10.1142/S1793830900000373

Constantino, M., Klimentova, X., Viana, A., & Rais, A. (2013). New insights on integer-programming models for the kidney exchange problem. European Journal of Operational Research, 231(1), 57–68. https://doi.org/10.1016/j.ejor.2013.05.025

Cornelio, C., Furian, L., Nicol’o, A., & Rossi, F. (2019). Using deceased-donor kidneys to initiate chains of living donor kidney paired donations: Algorithms and experimentation. AIES ’19: Proceedings of the 2019 AAAI/ACM Conference on AI, Ethics, and Society, (pp. 477–483).

Dickerson, J. P., Manlove, D. F., Plaut, B., Sandholm, T., & Trimble, J. (2016). Position-indexed formulations for kidney exchange. In Proceedings of the 2016 ACM Conference on Economics and Computation (EC ’16).

Dickerson, J., Procaccia, A., & Sandholm, T. (2013). Failure-aware kidney exchange. EC ’13: Proceedings of the fourteenth ACM conference on Electronic commerce, 323–340.

Ferrari, P., Weimar, W., Johnson, R., Lim, W., & Tinckam, K. (2015). Kidney paired donation: Principles, protocols and programs. Nephrolgy, Dialysis, Transplantation: Official Publication of the European Dialysis and Transplant Association - European Renal Association, 30(8), 1276–1285. https://doi.org/10.1093/ndt/gfu309

Furian, L., Cornelio, C., Silvestre, C., Neri, F., Rossi, F., Rigotti, P., Nicol’o, A. … Nicol’o, A. (2019). Deceased donor-initiated chains: first report of a successful deliberate case and its ethical implications. Transplantation, 103(10), 2196–2200. https://doi.org/10.1097/TP.0000000000002645

Haynes, C., & Leishman, R. (2017). Allowing deceased donor-initiated kidney paired donation (kpd) chains. OPTN/UNOS Kidney Transplantation Committee, https://optn.transplant.hrsa.gov/media/2219/kidneypcdncepts201707.pdf

Karami, F., Gentili, M., Nayebpour, M., Koizumi, N., & Melancon, J. (2019). Optimal integration of desensitization protocols into kidney paired donation (kpd) programs. Operations Research for Health Care, 22. https://doi.org/10.1016/j.orhc.2019.100198

Klimentova, X., Biró, P., Viana, A., Costa, V., & Pedroso, J. (2022). Novel integer programming models for the stable kidney exchange problem. European Journal of Operational Research, 307, 1391–1407. https://doi.org/10.1016/j.ejor.2022.09.031

Kute, V., Agarwal, S., Sahay, M., Kumar, A., Rathi, M., Prasad, N., Rees, M. … Rees, M. (2018). Kidney-paired donation to increase living donor kidney transplantation in India: Guidelines of Indian society of organ transplantation – 2017. Indian Journal of Nephrology, 28(1), 1–9. https://doi.org/10.4103/ijn.IJN_365_17

Melcher, M., Roberts, J., Leichtman, A., Roth, A., & Rees, M. (2016). Utilization of deceased donor kidneys to initiate living donor chains. American Journal of Transplantation, 16(5), 1367–1370. https://doi.org/10.1111/ajt.13740

Mincu, R., Biró, P., Gyetvai, M., Popa, A., and Verma, U. (2021). IP solutions for international kidney exchange programmes. Cent Eur J Oper Res, 29(2), 403–423. 10.1007/s10100-020-00706-5

Nickholds, L., & Mak-Hau, V. (2015). Heuristic approaches for multi-criteria optimisation in kidney exchange programs. Proceedings of the 21st International Congress on Modelling and Simulation, Modelling and Simulation Society of Australia and New Zealand, 1780–1786.

Rees, M., Roberts, J., Lentine, K., Roth, A., Leichtman, A., Xiao, H., Melcher, M. … Melcher, M. (2016). Nead chains do not disadvantage blood type o, black, or highly sensitized patients. 16(3). American Journal of Transplantation. (Abstract).

Roth, A., Sönmez, T., & Ünver, M. (2004). Kidney exchange. The Quarterly Journal of Economics, 119(2), 457–488. https://doi.org/10.1162/0033550041382157

Roth, A., Sönmez, T., Ünver, M., Delmonico, F., & Saidman, S. L. (2006). Utilizing list exchange and nondirected donation through ‘chain’ paired kidney donations. American Journal of Transplantation, 6(11), 2694–2705. https://doi.org/10.1111/j.1600-6143.2006.01515.x

Roth, A., Ünver, S. T. M., & Utku Ünver, M. (2005). Pairwise kidney exchange. Journal of Economic Theory, 125(2), 151–188. https://doi.org/10.1016/j.jet.2005.04.004

Sahay, M. (2018). Transplantation of human organs and tissues act-“simplified”. Indian Journal of Transplantation, 12, 84–89. https://doi.org/10.4103/ijot.ijot_31_18

Stanford, D., Lee, J., Chandok, N., & Melcher, V. (2014). A queueing model to address waiting time inconsistency in solid-organ transplantation. Operations Research for Health Care, 3(1), 40–45. https://doi.org/10.1016/j.orhc.2014.01.001

University of Alabama at Birmingham. (2018). Nation’s longest single-site kidney chain reaches 100. nation-s-longest-single-site-kidney-chain-reaches-100.

Veale, J., & Hii, G. (2009). The National Kidney Registry: Transplant chains – beyond paired kidney donation. Clinical Transplants, Clinical transplants, 253–264.

Verma, U., and Rangaraj, N. (2020). Analysis of multi-register kidney exchange program with individual rationality constraints. https://arxiv.org/abs/2012.06647

Wallis, C., Samy, K., Roth, A., & Rees, M. (2011). Kidney paired donation. Nephrology Dialysis Transplantation, 26 (7), 2091–2099. https://doi.org/10.1093/ndt/gfr155

Wang, W., Leichtman, A., Rees, M., Song, P., Ashby, V., Shearon, T., & Kalbfleisch, J. (2022). Kidney paired donation chains initiated by deceased donors. Kidney International Reports, 7(6), 1278–1288. https://doi.org/10.1016/j.ekir.2022.03.023

Xavier, C. (2017). Joint management models of kidney exchange program and deceased donor waiting list. Master’s thesis. https://repositorio.ul.pt/bitstream/10451/40495/1/ulfc125594tmCarolinaXavier.pdf
Appendix A

This section has additional information regarding the simulations. The parameter considered for creating edge score consist of two parameters which directly affects the quality of matches, i.e. HLA matches and age difference between donor and recipient. The scoring system used to create the edge score is shown below.

**HLA parameters** – There are several types of HLA antigens in a human body of which some are more considerable than the others. Here six HLA antigen types namely – HLA A1, A2, B1, B2, DR1, and DR2 are considered for defining the quality of a match. HLA matches are usually counted in mismatches of antigens between donor and recipient, and lesser the mismatch indicated, the better is the quality of the match. A total score of 100 is assigned to HLA mismatches and the scoring criteria is shown in Table A1.

| Table A1. HLA scoring system for quality of match. |
|-----------------------------------------------|
| Number of HLA mismatch | Score |
|------------------------|-------|
| 0                      | 100   |
| 1                      | 85    |
| 2                      | 70    |
| 3                      | 55    |
| 4                      | 40    |
| 5                      | 25    |
| 6                      | 10    |

Age parameter – Another important parameter considered for quality of the match is the age difference between the donor and recipient. Graft survival of kidney increase with a decrease in age difference. Since age difference is a continuous variable, a function was defined to calculate the score for each compatible edges. It is assumed that score increased linearly with a decrease in age difference, and the function was truncated at a difference of 40. If the age difference between a donor and recipient is less than 40, then it gets a 0 age score otherwise, the score function is the following:

\[ f(x) = \begin{cases} 
50 & \text{if } x \leq 40 \\
0 & \text{otherwise} 
\end{cases} \]  

(A1)

1 where x is the age difference between donor and recipient.

These two parameters are the ones that affect the quality of a match, other parameters like vascular access failure, waiting time of dialysis, hypertension, and previously failed transplants are considered for fairness of the allocation. For simulations, only HLA and age parameters were considered for edge weights and other parameters can be included in the scoring system when allocation will be done in practice.

Appendix B Simulation with higher dropout probability

The simulation results mentioned in the paper are for a dropout probability of 0.2 for a potential recipient who is unmatched at the end of a round. The simulations were repeated with a higher dropout probability of 0.4 and the results are similar (Tables B2, B3, and B4).

| Table B2. Comparison of DDIC solution to individual (Ind) solution of PKE and DD allocation in terms of number of transplants and optimal score for different bound on cycle and chain lengths, and dropout probability = 0.4. |
|-----------------------------------------------|
| Arrival rate | DDIC Sol | Ind PKE and DD sol | Relative Gain |
| Transplants | Transplants | Transplants | Transplants |
| Avg Edge Score | Avg Edge Score | Score | Score |
|-----------------|-----------------|-----------------|-----------------|
| P=U(1,5), PWL=U(1,5), DD=U(1,5), bound =3 | 73.4 | 75.9 | 53.5 | 72.8 | 37.3% | 4.3% |
| P=U(5,10), PWL=U(1,5), DD=U(5,10), bound =3 | 140.8 | 78.7 | 106.2 | 75.9 | 32.6% | 3.7% |
| P=U(5,10), PWL=U(5,10), DD=U(5,10), bound =3 | 216.2 | 84.2 | 158.4 | 75.8 | 36.5% | 11.1% |
| P=U(1,5), PWL=U(1,5), DD=U(1,5), bound =3 | 139.4 | 82.5 | 107 | 73.7 | 30.2% | 11.9% |
| P=U(1,5), PWL=U(1,5), DD=U(1,5), bound =6 | 73.4 | 76.7 | 54.8 | 73.5 | 33.9% | 4.4% |
| P=U(5,10), PWL=U(1,5), DD=U(5,10), bound =6 | 144.1 | 82.1 | 105.6 | 78.1 | 36.5% | 5.1% |
| P=U(5,10), PWL=U(1,5), DD=U(5,10), bound =6 | 220.2 | 85.7 | 162.7 | 77.3 | 35.4% | 10.8% |
| P=U(1,5), PWL=U(1,5), DD=U(1,5), bound =6 | 136.8 | 82.6 | 105.3 | 74.4 | 29.9% | 11% |

| Table B3. Comparison of DDIC solution to individual (Ind) solution of PKE and DD allocation in terms of average number of dropouts and waiting time (in months) for different bound on cycle and chain lengths, and dropout probability = 0.4. |
|-----------------------------------------------|
| Arrival rate | DDIC Sol | Ind PKE and DD sol | Relative Gain |
|-----------------|-----------------|-----------------|-----------------|
| P=U(1,5), PWL=U(1,5), DD=U(1,5), bound =3 | 1.7 | 0.09 | 6.4 | 0.16 | 4.7, 0.07 |
| P=U(5,10), PWL=U(1,5), DD=U(1,5), bound =3 | 1.9 | 0.10 | 4.6 | 0.14 | 2.7, 0.04 |
| P=U(1,5), PWL=U(1,5), DD=U(1,5), bound =6 | 0.4 | 0.04 | 6.9 | 0.16 | 6.5, 0.12 |
| P=U(1,5), PWL=U(1,5), DD=U(1,5), bound =6 | 1.7 | 0.09 | 6.3 | 0.15 | 4.6, 0.06 |
| P=U(5,10), PWL=U(1,5), DD=U(1,5), bound =6 | 1.9 | 0.10 | 4.8 | 0.14 | 2.9, 0.04 |
| P=U(5,10), PWL=U(5,10), DD=U(5,10), bound =6 | 0.8 | 0.06 | 4.3 | 0.14 | 3.5, 0.08 |
| P=U(1,5), PWL=U(1,5), DD=U(1,5), bound =6 | 0.4 | 0.03 | 6.8 | 0.15 | 6.4, 0.12 |
Appendix C Data distribution

The blood group distribution of the recipient–donor pairs used for the simulations is shown in Table C5. This distribution is based on 211 pairs of data from the ASTRA registry. In a typical registry of incompatible donor–recipient pairs in India, there were many O-type recipients and only a few O-type donors because the compatible pairs with the O-type blood group do not usually join the exchange registry, and the vice versa case happens with AB-type donors and recipients. Thus, merging deceased donor chains into kidney exchange programs creates more possibilities of a compatible match for such pairs.

Table C5. Percentage of different blood type pairs used for simulation.

| Patient and donor pairs blood group (ABO) | Percentage (%) of pairs |
|-----------------------------------------|-------------------------|
| A-A                                     | 1.9                     |
| A-B                                     | 19                      |
| A-AB                                    | 7.1                     |
| A-O                                     | 0.5                     |
| B-A                                     | 19.9                    |
| B-B                                     | 0.9                     |
| B-AB                                    | 5.2                     |
| B-O                                     | 1.9                     |
| AB-A                                    | 0.5                     |
| AB-B                                    | 0.5                     |
| AB-AB                                   | 0.4                     |
| AB-O                                    | 0.5                     |
| O-A                                     | 15.6                    |
| O-B                                     | 20.9                    |
| O-AB                                    | 4.7                     |
| O-O                                     | 0.5                     |

Age distribution

Table C6 shows the age distribution of donor and recipient based on the available data. This age distribution was used in the simulation to generate the age of donors and recipients.

Table C6. Age distribution for Donor and Recipient in paired exchange registry.

| Age range (in years) | Donor | Recipient |
|----------------------|-------|-----------|
| 10–20                | 0%    | 1%        |
| 20–30                | 5%    | 17%       |
| 30–40                | 14%   | 25%       |
| 40–50                | 39%   | 26%       |
| 50–60                | 31%   | 24%       |
| 60–70                | 11%   | 7%        |