Dynamic simulations of kidney exchanges

M. Beccuti, V. Fragnelli, G. Franceschinis and S. Villa

Abstract In this paper we develop a simulator modeling a kidney exchange program, in which donor-recipient pairs with characteristics drawn from a distribution based on real data join the system over time, and a centralized authority organizes a suitably chosen set of exchanges among the pairs in the pool at regular intervals of time, as it happens in the Netherlands or in the US. We compare and discuss the results of numerical simulations on this model varying the matching policy.

1 Introduction

Kidney transplantation is the elective treatment for patients with irreversible kidney failure. Recently, kidney exchanges are emerging as a viable option for utilizing live donor kidneys from those who are incompatible with their intended recipients. Such exchanges involve two or more incompatible pairs for which a reciprocal compatibility holds, and were first suggested by the medical community, allowing to increase the number of transplants [7]. Nowadays kidney exchange programs (KEP) have been started and are currently going on in many countries, the leading examples being the US and the Netherlands, and including Germany, New Zealand, Australia, Italy among other [3] [4], [6].

The organization of KEP raises several questions that can be addressed from a mathematical perspective, and, starting from [8], a wide literature is devoted to the study of the optimal organization of such exchanges in a static situation, see [9],

M. Beccuti
Università degli Studi di Torino, Torino, Italy, e-mail: beccuti@di.unito.it

V. Fragnelli and G. Franceschinis
Università degli Studi del Piemonte Orientale, Alessandria, Italy, e-mail: {vito.fragnelli, giuliana.franceschinis}@mfn.unipmn.it

S. Villa
Università degli Studi di Genova, Genova, Italy, e-mail: villa@dima.unige.it

[5], [2] and references therein. Considerably less attention has been devoted to the dynamic setting, though the latter is fairly more realistic than the static model, since donor-recipient pairs join the system over time and not all at the same moment. The main question to be answered is how to find an optimal matching policy, i.e. a suitable scheduling of the exchanges in order to maximize a properly chosen objective.

A theoretical analysis of the dynamic problem is carried out in [11], under some “long run” assumptions. More precisely, it is proved that if only paired exchanges are considered and if there is an unlimited availability of the so called “underdemanded pairs” (pair types that are difficult to match) then the policy maximizing a discounted sum of the total number of exchanges is the one organizing exchanges as soon as they become available.

In this work we develop a simulation tool which models a realistic dynamic situation, in which a centralized authority organizes a suitably chosen set of exchanges among the pairs in the pool at regular intervals of time. The goal is to determine the potential impact of a long term organization of kidney exchanges: we discuss the results of numerical simulations obtained using the proposed model, analyzing the performance of a given exchange policy, in terms of some relevant quantities such as the number of matched and unmatched patients, and the average waiting time w.r.t. the pair characteristics. Moreover, a comparison of the performance corresponding to different choices of the time interval between one slot of exchanges and the next one is presented. Our work is related to the results in [10, 1], where an experimental analysis of different matching policies is presented. In particular, for evaluating the policy, we account the average waiting time for pairs in the system, an aspect which is not considered in [1]. On the other hand they propose a (sub)optimal policy that in terms of total number of performed transplants behaves better than ours. A careful study of the waiting times corresponding to a fixed policy belonging to the class described in our work can be found in [10]. Our contribution w.r.t. this paper is the long term perspective and a more extensive comparison among different policies. In [12] a different context is considered, where pairs can choose among paired exchanges and the waiting list from deceased donors. A simplified version of the real situation is taken into account, with only two possible pair types and an optimal decision strategy is proposed.

The paper is organized as follows: we start introducing the static kidney exchange problem together with the compatibility assumptions in Section 2, then we describe the dynamic case and the experimental analysis in Section 3, Section 4 concludes.

2 General setting

As it happens in the real world, we assume that only incompatible pairs are admitted to KEP. Incompatibility between donor and recipient has two sources: a blood type incompatibility or a tissue type incompatibility (also called positive crossmatch). While the first one is simple to check, the second is difficult to predict, but the probability of positive crossmatch between two unrelated individuals is 11%. The composition of the pool for kidney exchange programs is obtained combining the known probability distribution over blood types with the probability of positive crossmatch, according to the model proposed in [12, 10], and is reported in Tab. 1.

Table 1 Blood type characteristics of Simulated Pairs (pair percentage)

Blood Type	Recipient 0		Recipient A		Recipient B		Recipient AB	
Donor 0	[1]	14.0	[2]	6.3	[3]	2.4	[4]	0.5
Donor A	[5]	37.8	[6]	6.8	[7]	6.1	[8]	0.5
Donor B	[9]	12.0	[10]	5.1	[11]	1.2	[12]	0.2
Donor AB	[13]	2.0	[14]	2.8	[15]	2.1	[16]	0.1

We assume that each patient is indifferent among two compatible kidneys and we do not take into account the possibility of having a positive crossmatch when organizing the exchanges, so that subsequent results overestimate the number of possible exchanges. This assumptions, while simplifying the real situation, are considered acceptable also from a medical point of view and are common in the literature studying KEPs [9]. We therefore deal with a set of pair types $T = \{1,\ldots,t\}$ (in our situation $t = 16$ according to the numbers in square brackets in Tab. 1).

We model the compatibility by introducing a non-negative symmetric compatibility matrix R, where $R_{ij} > 0, i, j \in T$ means that an exchange between pairs of type i and j is possible with a *revenue* R_{ij} (e.g. the compatibility level); by the symmetry of R, we can restrict to the upper triangle, i.e. $i \leq j$. Mathematically speaking a *static kidney exchange problem* consists of a compatibility matrix R and a set of pairs, that can be identified with a tuple $(s_1,\ldots,s_t)$ describing the number of pairs of each type. A feasible set of exchanges can be found solving the following integer linear programming problem:

$$
\begin{aligned}
\max \quad & \sum_{\substack{i,j\in T \\ \text{s.t. } R_{ij}>0}} R_{ij}x_{ij} \\
\text{s.t.} \quad & \sum_{\substack{i=1,\ldots,k \\ \text{s.t. } R_{ik}>0}} x_{ik} + \sum_{\substack{j=k,\ldots,t \\ \text{s.t. } R_{kj}=1}} x_{kj} \leq s_k \qquad k \in T \\
& x_{ij} \in \mathbb{N} \qquad\qquad\qquad\qquad i \leq j, \quad i,j \in T
\end{aligned}
$$

where $x_{ij}, i \leq j, i, j \in T$ is the number of exchanges involving one pair of type i and one pair of type j. Hereafter, we use a 16×16 matrix where $R_{ij} \in \{0,1\}$ (pairs are compatible or not); this leads to a solution that maximizes the number of performed transplants.

A similar formulation of a kidney exchange problem is given in [9] using an undirected unweighted graph whose vertices represent the pairs in the system, and the edges connect compatible pairs; they look for a maximum cardinality matching, in order to provide a transplant to as many participants as possible.

The dynamic situation is more complicated and only partial solutions have been proposed so far to tackle it. We describe our approach in the next section.

3 The dynamic model: experimental analysis

We start this section by describing the dynamic model we simulate, under the compatibility assumptions described above. We assume that each pair enters in the KEP at a certain time, and leaves the system only when receiving a kidney. The arrival rates are based on the Italian situation, and the pair types are randomly chosen on the basis of the distribution in Tab. 1.

A *matching policy* is a procedure that at each time unit $t > 0$ selects a (possibly empty) set of matching pairs from the pool. Once a pair is matched at time t by a matching mechanism, it leaves the pool and its patient receives the assigned kidney. The matching policies we consider belong to a very special class. More precisely we suppose that the central authority decides to organize optimal matchings at regular intervals of time. The frequency of the exchanges remains fixed and is chosen in advance, and the matching policy organizing the optimal matching every τ units of time is denoted by π_τ. We experimentally compare exchange policies π_τ for different values of τ using the simulator we have developed in C++ using the LPsolve library (http://lpsolve.sourceforge.net) for the solution of the optimization problem every τ units of time. The comparison is made in terms of the number of matched pairs, the average waiting time and other aspects we now describe.

In order to get results easy to interpret from a practical viewpoint, we fix the time unit to be one month, and we choose the other parameters consequently. The arrival rate is of 3 pairs per time unit, which corresponds to a realistic scenario for the Italian situation, for instance. We ran the simulations adopting the policies π_τ for $\tau = 1, 2, 3, 4, 6, 12$. Each experiment is replicated 20 times (for different arrivals) to get more robust results. Confidence intervals are computed for each selected index, setting the confidence level to 95% and achieving an accuracy of at least 0.37. The time horizon is 240 time units (20 years), to which we added an initial transient period.

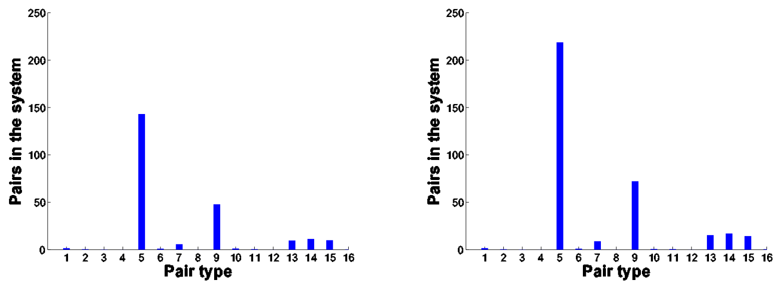

Fig. 1 Average number of pairs in the system for each type, obtained using policy π_6. Results for $TP = 36$ (left) and $TP = 120$ (right).

We start to evaluate the quantities we are interested in after the initial transient period. We analyze the results of two groups of experiments: in the first group the transient period (TP) is 36 months, and in the second one is 120 months. This choice is due to the fact that this system does not have a steady state since the *underdemanded pairs* form an increasing queue in the system (see [11] and [9]). Therefore choosing the length of the transient period has the effect of determining a different distribution on the initial state. We are interested in showing the dependence of the performances of the same policy under different initial conditions. The accumulation effect appears, as can be seen clearly in Fig. 1, no matter which policy is adopted. If the transient period is longer, the average number of pairs in the system increases and goes to infinity. This problem is a key point that must be addressed in practice and has also ethical implications. A possible solution would be not to admit to such programs a number of pairs of underdemanded types above a given threshold, since in any case the transplant would be unachievable for them.

It turns out that the average number of pairs in the system per time unit remains practically constant for underdemanded pairs (types $5,6,9,13,14,15$, see Tab. 1) and it increases only slightly for the remaining types if τ varies. For instance the average number of pairs of type 1 passes from 0.5 in the case matchings are organized every month to 2.8 in the case they are organized only once a year.

Now, we discuss how the parameter τ affects the percentage of performed transplants using the policy π_τ.

Table 2 Average number of transplanted patients (left). Average waiting time for pairs (0,A) and (A,0), types 2 and 5, respectively (right)

τ	1	2	3	4	6	12
TP=36	52.6	52.5	52.8	53.0	53.4	54.6
TP=120	53.0	52.9	53.3	53.5	53.9	55.3

τ		1	2	3	4	6	12
TP=36	Type 2	0	0.4	0.9	1.3	2.3	4.9
	Type 5	110.2	110.1	110.6	111.0	111.9	115.0
TP=120	Type 2	0	0.3	0.7	1.0	1.6	3.6
	Type 5	128.5	128.1	128.4	128.6	129.3	131.3

As expected, this percentage is approximately an increasing function of τ, varying not too much w.r.t. the considered parameters (Tab. 2 (left)). The fact that this percentage is almost independent of the duration of the transient period ensures that this kind of policies does not suffer from the point of view of the accumulation effect due to the underdemanded pairs. If we look only at the percentage of transplanted patients, the most advantageous policy is the one performing the exchanges only once a year. On the other hand, in the evaluation of a given policy, also the average time that a pair spends in the system is relevant. The average waiting time of those receiving a transplant is considerably different from type to type, and the results agree with the ones regarding the average number of pairs in the system reported in Fig. 1. It turns out that the average waiting time for underdemanded pairs is very long, no matter which policy is adopted, while the average waiting time for the remaining pairs slightly increases as τ grows. As a paradigmatic example we consider pairs of type 2 and 5.

Furthermore, as can be seen from Tab. 2 (right), the situation of underdemanded pairs further deteriorates if the transient period is longer, due to the accumulation effect, as it has been observed in [10], where the results of a 3-year simulation of policy π_1 have been discussed.

Comparing our results with the ones obtained in [1] is not straightforward, since in that paper the average waiting time is not considered, and different policies are compared only on the base of the total number of performed exchanges. In our case maximizing this quantity would imply the use of a policy organizing the exchanges on the last month of the simulation, which is not a viable solution from a practical point of view.

4 Conclusion

In this paper we discussed the results of realistic simulations of several matching policies obtained thanks to a tool, available upon request to the authors. We highlighted that such simulations suggest that KEPs must address *in primis* the problem of underdemanded patients accumulating in the pool without receiving a transplant. Moreover we showed how the timing between a matching and the subsequent one affects the number of performed transplants and the average waiting time w.r.t. pairs characteristics.

The present model can be modified in order to deal with more general situations in which there are more pair types, based also on other genetic or physical characteristics; using a compatibility matrix whose entries can assume real non-negative values enables to model policies that favor the exchanges involving underdemanded pairs, thanks to a (very) small increasing of their *revenues*. Exploiting the flexibility of the tool, further improvements may be in the direction of allowing exchanges involving more than two pairs, via a cyclic series of transplants.

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