Simulations for measuring efficiency of international kidney exchange programmes

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Abstract: In this paper we present simulations for international kidney exchange programmes (KEPs). KEPs are organised in more than ten countries in Europe, the largest ones in the UK, in the Netherland and Spain, to facilitate the exchanges of immunologically incompatible donors. The matching runs are typically conducted in every three months for finding optimal exchanges using hierarchical optimisation with integer programming techniques. In recent years several European countries have started to collaborate to organise international exchanges using different collaboration policies. In this paper we conduct simulations for estimating the benefits of such collaborations with a simulator developed in a European COST Action project, called ENCKEP.

Keywords: kidney exchange, integer programming, hierarchical optimisation

1 INTRODUCTION

Patients with end-stage renal disease can be treated by dialysis, but their quality of life is poor and their life expectation is short. The only long-term solution according to our knowledge is transplantation. One can get a kidney from a deceased donor, but the demand is very high and waiting lists are long even in the developed world (over 100,000 patients are on the US waiting list, with an average waiting time of 8-10 years). Therefore living donation became a common practice, also due to the longer graft survival rates. However, if someone has a willing, but immunologically incompatible donor then transplantation is not possible. To resolve this issue, kidney exchange programmes (KEP) have been established in many countries to facilitate the exchanges of the donors. Due to the simultaneity of the exchanges the length of the exchange cycles is limited. For example, only 2- and 3-way exchanges are allowed in the UK and Spain, whilst four-way exchanges are also possible in the Netherlands. The goal of the KEPs is to find and arrange optimal exchanges for the pool of registered patient-donor pairs in the regular matching runs. The European practices have been surveyed in [1] and the optimisation aspects of the European KEPs were described in [2], as the results of a COST Action called European Network for Collaboration on Kidney Exchange Programmes (ENCKEP).

International kidney exchanges have been conducted first in between Vienna and Prague in 2016 [3], followed by the collaboration of Spain, Portugal and Italy. In the recent Handbook [6] of Working Group 3 and 4 of the ENCKEP COST Action has studied the practice of international KEPs, the modelling possibilities including results from [5] and [7], and the description of a simulation and evaluation tool developed by these working groups. In this paper we will illustrate the usage of the simulator tool by a case study with generated data for three countries, UK, Netherlands and Spain.

Optimisation policies used in the European Kidney Exchange Programmes (KEPs) consist of multiple optimisation criteria, which they use for finding the optimal solution in each matching run. These policies specify a priority order for the criteria, which is called the lexicographic order. Using this means, that there will be an optimisation run for each level of the order, and each lower level will get a constraint for the objective value of all the criteria above.

At the lowest level of the priority order, often there are multiple criteria used for weighted optimisation in practice. The weights are given according to the settings of the criteria, either on the cycle-level (e.g. maximisation of the number of cycles selected) or on the transplant-level (e.g. prioritisation of highly sensitised recipients). For a recent paper on sophisticated integer programming techniques for hierarchical optimisation for KEPs see [4].

2 COMPUTER SIMULATIONS

To simulate the operation of national and international KEPs, we used the ENCKEP Simulator tool [6]. This simulator is based on a standard technique of generating historical dataset for a period of time (e.g. five years) and conducting matching runs in regular time intervals (e.g. in every three months). For a survey on KEP simulators, see [8].

In order to conduct a simulation with this software, we have to provide input files, which will contain data about the pool, virtual compatibility graph, arc and pair failures, as well as the collaboration and optimisation policies we would like to use.

After the simulation has finished, the tool produces detailed output data about the simulation in 4 output files for further analysis. These files contain information about the cycles selected, matching runs, pool of donors and recipients, and the implemented arcs subject to the simulation. In the following chapters, we present the results of analysing these output files.

2.1 Simulations for individual countries

In the first part we will describe simulation results for national KEPs, namely for the UK, the Netherlands and Spain.

2.1.1 UK

In the KEP of the UK, they conduct matching runs every 3 months, and set the length upper bounds for both exchange cycles and chains to 3. We used the same settings, and allowed internal recourse in the simulation in order to search for embedded cycles to implement in cycles with either arc or node failure. As for the optimisation policy, we used the following set of criteria (see [6] for details).

Lexicographic:

1. Maximise the number of effective 2-cycles
2. Maximise the size of solution
3. Maximise the number of cycles selected
4. Maximise the number of back-arcs

Weighted:

- Priority for waiting time in KEP (linear function with score 50)
- Priority for highly sensitised recipients (linear function with score 50)
- Minimise the donor-donor age differences (threshold function with score 3 and threshold 20 years)

This optimisation policy is almost identical to the one used in real practice, but since we cannot generate HLA-data yet, we did not use the maximisation of HLA-matching optimisation criterion. However, the software is capable of using this as well, provided the HLA-data is available (e.g. in case of real historical datasets). The scores given for the weighted optimisation criteria during the simulation are depicted in Figure 1.

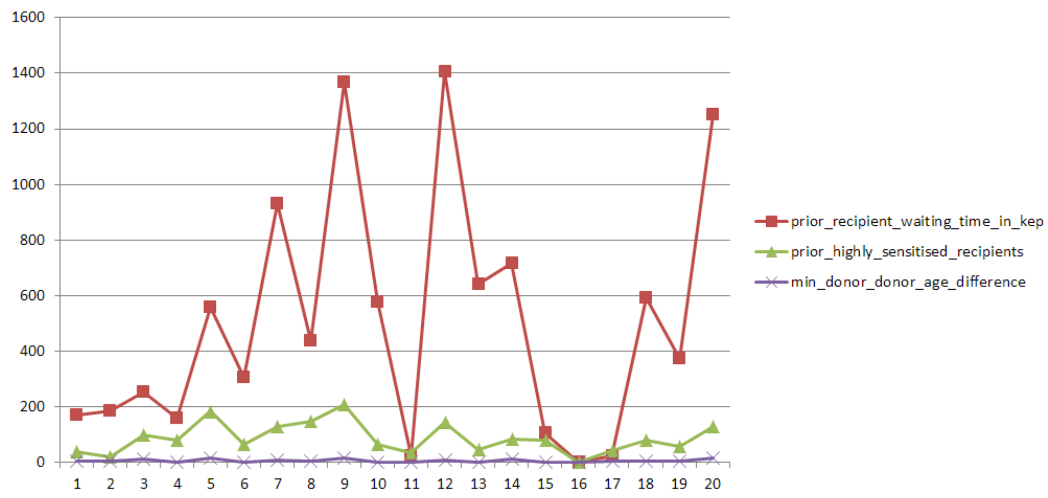

Figure 1: Weights given for the weighted criteria in each matching run for UK

The figure shows that in every matching run, the most influential weighted criterion was the prioritisation of waiting time in KEP. This was to be expected, since for this criterion, the UK policy gives 50 points for each matching run based on the waiting time of the recipient.

2.1.2 Spain

The KEP operating in Spain, sets the limit for maximum length of exchange cycles to 3. They do not use length constraint on chains, but since we have to set an upper bound for this in the simulation, which should be reasonable to limit run-time, we used 4. Also, we allowed internal recourse in the simulation. The optimisation policy we used consists of the following set of criteria (see [6] for details).

Lexicographic:

1. Maximise the size of solution
2. Maximise the number of cycles selected
3. Maximise the number of back-arcs
4. Priority for highly sensitised recipients (reciprocal function with score 5)

Weighted:

- Minimise the age-differences between donors and recipients (threshold function with score 15 and threshold 10 years)
- Priority for recipients with low matching probability (linear function with score 30)
- Priority for waiting time in KEP (threshold function with score 30 and threshold 1 year)
- Priority for same blood-group transplants (30 points)

This is very similar to the real policy, the difference is that we left out three criteria from the weighted optimisation. Priority for paediatric recipients was not used, because the generated pool contained only adult patients. Priority for time on dialysis and priority for donor-patients in the same region were left out also. Scores given for each weighted optimisation criteria are depicted on Figure 2.

To mimic practice, we tried to use realistic relative pool sizes, which meant that the Spanish pool was set to be smaller than the pool of the UK. As shown on the Figures 1 and 2, this

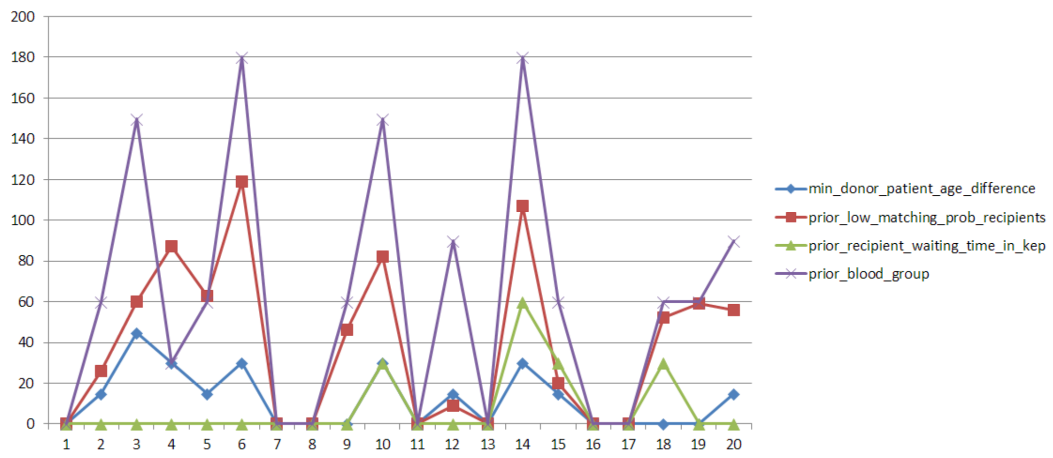

Figure 2: Weights given for the weighted criteria in each matching run for Spain

resulted in an increased number of matching runs where there were no available cycles in the virtual compatibility graph. In case of the UK, there was only one such matching run, while we had six in the Spanish simulation.

2.1.3 Netherlands

In the Netherlands, they use 4 as upper length limit for both exchange cycles and chains. Internal recourse was enabled here as well. The optimisation policy we used in the simulation was the following (see [6] for details).

Lexicographic:

1. Maximise the size of solution
2. Priority for same blood-group transplants
3. Priority for recipients with low matching probability (using reciprocal function with score 5)
4. Minimise the lengths of cycles selected

In practice, they only use lexicographically ordered criteria, so we did the same in the simulations. The policy is similar to the real one, the difference is that we left out the 5th and 6th criteria, which are the maximisation of the number of transplant centres in long cycles and priority for time on dialysis respectively. Since only lexicographic order is used here, it might be important to know that which levels of the hierarchy are usually not considered to find the final solution. To study this, we analysed the number of matching runs that stopped on the given priority level, because a unique solution was reached. The result is shown on Figure 3.

The pool size was approximately the same as the one used in the Spanish KEP simulation, but here were only had 2 matching runs, where no cycles were detected. The solution became final on the last (4th) level 6 times, and this number applies to the 3rd and 2nd levels as well.

2.2 Simulations for international exchanges

The software can simulate three different collaboration policies.

- Individual policy: Each participating pool will have its own matching run separately.

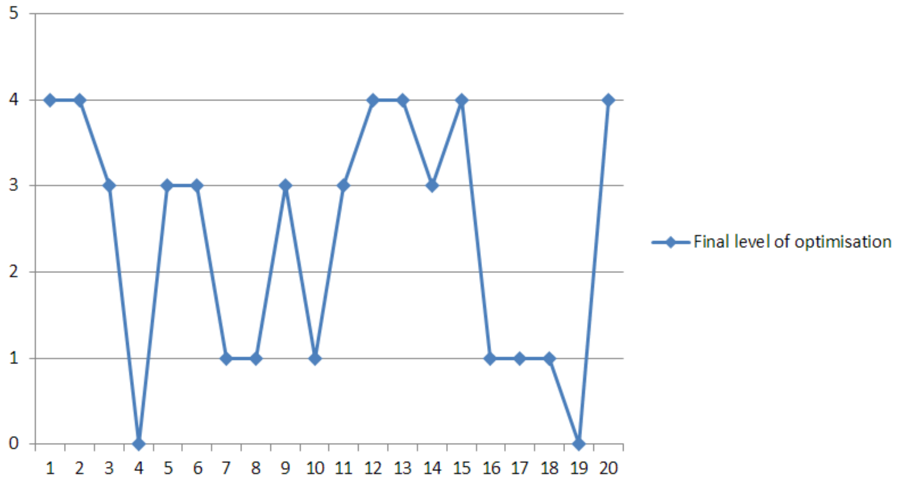

Figure 3: Level on which the solution became unique in each matching run for Netherland

- Consecutive policy: First, in each matching run, there will be an optimisation run for every pool separately. Then, the pairs who are still in the pools after that, will be merged into one joint pool, and there will be an optimisation run for this as well.
- Joint policy: All the participating pools will be merged into one pool, this will be used in the matching runs.

Each pool can have a different optimisation policy in the simulations for separate pools, just as in practice, so we used the corresponding settings. For the merged pools, we used the optimisation policy of the UK. The results are depicted on Figure 4.

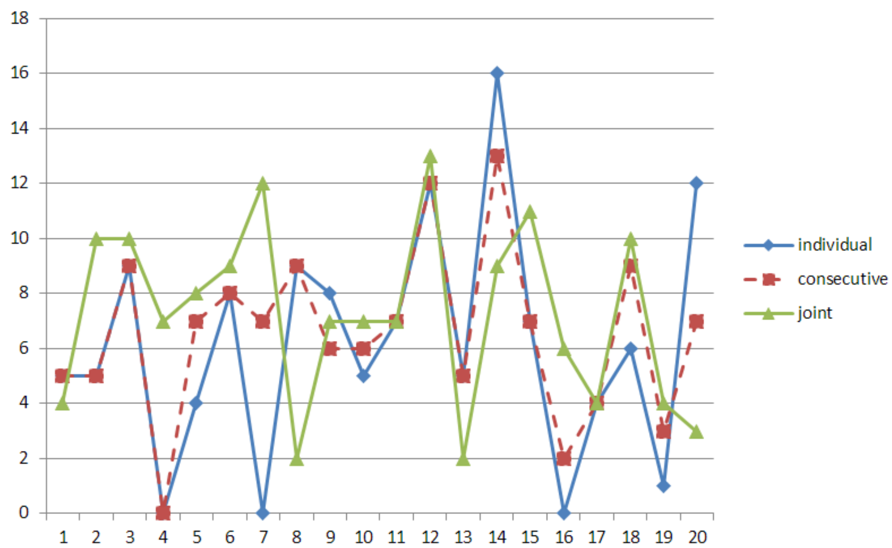

Figure 4: Number of transplants in each matching run with different collaboration policies

In some matching runs, the joint policy resulted in less transplantation than the individual policy, which should not happen in general. But it is reasonable here, because we set the upper bound for cycle and chain lengths to 3 for the joint pools, and we left them at 4 for the Netherlands to mimic real practice. Also, in these cases, often many of the selected cycles were cancelled in the joint collaboration, and with no embedded cycles to implement with internal recourse, these were cancelled completely.

	individual	consecutive	joint	total
UK	52	53	57	162
ES	23	28	40	91
NL	48	50	48	146
total	123	131	145	399

Figure 5: Number of total transplants by pools and collaboration policies

As depicted on Figure 5 the total number of transplants for the individual, consecutive and joint collaboration policies were 123, 131, 145 respectively. According to our simulation result, the total number of transplants can be increased by initiating a collaboration between the countries, where the joint policy seems to be the best approach.

Acknowledgements

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