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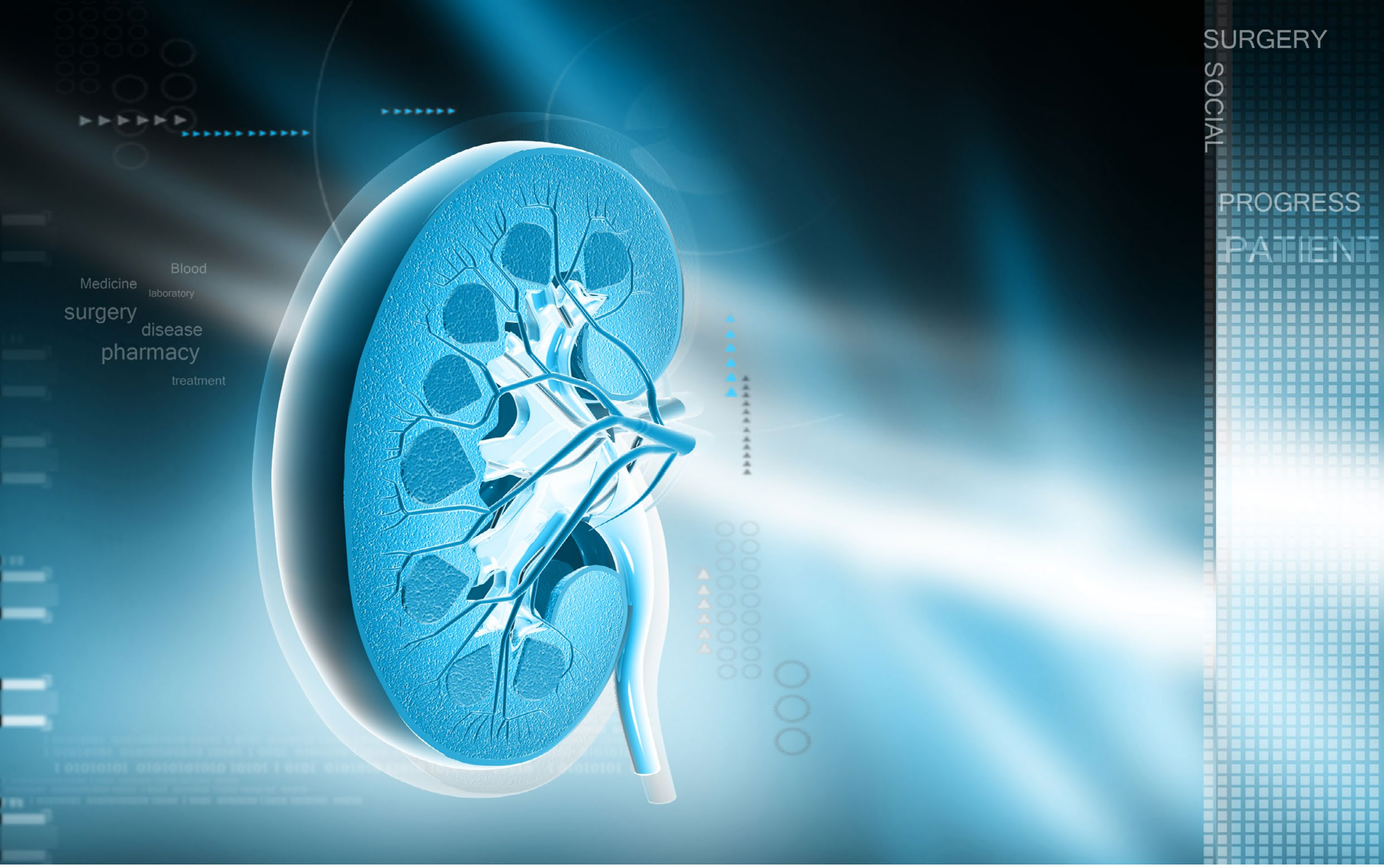

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HOW OPERATIONAL RESEARCH HELPS KIDNEY PATIENTS IN THE UK

DAVID MANLOVE

ALGORITHMS DEVELOPED BY UNIVERSITY OF GLASGOW RESEARCHERS led to over 200 more kidney transplants taking place between 2008 and 2017 than is estimated to have been the case had a previous algorithm continued to be used. This potentially saved the NHS around £52M over a 10-year period.

KIDNEY EXCHANGE

Kidney failure has a devastating impact on patients' lives, and long-term survival rates after transplantation demonstrate a doubled or tripled life expectancy compared to dialysis. NHS Blood and Transplant (NHSBT) estimates that over 37,500 people in the UK have end-stage renal failure; nearly 21,000 are on dialysis. As of 31 March 2017, there were 5233 patients on the transplant list for a donor kidney. The number of kidney transplants carried out each year is much less than this number: 3347 transplants took place between 1 April 2016 and 31 March 2017, of which 1009 were from living donors.

A patient may have a willing donor who is blood-type or tissue-type incompatible with them. In the past, typically that would have meant that the donor would have been unable to help their loved one. However, following the introduction of the Human Tissue Act in 2006, there is now the legal framework to allow transplants between strangers, thus opening up new possibilities for living donor transplants. For example, through a *paired kidney exchange* (*PKE*), a group of two or more kidney patients can swap their willing but incompatible donors with one another in a cyclic fashion, so that each patient can receive a compatible kidney.

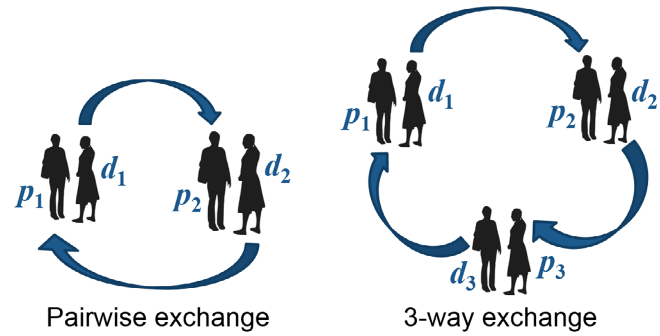

FIGURE 1 HOW THE KIDNEY EXCHANGES WORK. IN EACH PKE, p REPRESENTS A PATIENT AND d REPRESENTS A DONOR. IN THE CASE OF THE PAIRWISE EXCHANGE, FOR EXAMPLE, d_1 DONATES A KIDNEY TO p_2 IN EXCHANGE FOR d_2 DONATING A KIDNEY TO p_1

In a number of countries, centralised programmes (also known as kidney exchange matching schemes) have been introduced to help optimise the search for PKEs. These countries include the UK, USA, the Netherlands, Australia, South Korea and many others around the world

Most commonly, PKEs involve either two or three patients, in which case they are called *pairwise exchanges* and *3-way exchanges* respectively (see Figure 1 for illustrations of these types of PKEs). In a number of countries, centralised programmes (also known as kidney exchange matching schemes) have been introduced to help optimise the search for PKEs. These countries include the UK, USA, the Netherlands, Australia, South Korea and many others around the world.

In general, it is logistically challenging to carry out the transplants involved in a PKE when the number of pairs involved in a single such exchange is large. This is mainly because all operations have to be performed simultaneously due to the risk of a donor reneging on his/her commitment to donate a kidney after their loved one has received a kidney. But also, longer PKEs involve more participants, and therefore carry a higher risk that the whole cycle will break down if one of the donors or patients involved becomes ill. Mainly for these reasons, most centralised programmes only allow PKEs to involve pairwise and 3-way exchanges. Even 3-way exchanges, for example, require substantial coordination, involving six operating theatres and surgical teams scheduled on a single day (for three nephrectomies and three transplants).

COLLABORATION

In early 2007, NHSBT (formerly UK Transplant) set up the UK's national kidney exchange matching scheme, now known as the *UK Living Kidney Sharing Schemes* (UKLKSS), to identify optimal sets of PKEs from among the patient and donor data on the NHSBT database. The algorithm that they developed was only capable of finding pairwise exchanges and could only handle datasets of up to 100 potential transplants.

In May 2007, the author and Dr Péter Biró (both of the University of Glasgow) developed a novel approach involving graph matching algorithms which enabled optimal sets of PKEs, involving pairwise and 3-way exchanges, to be identified. They also significantly increased the capacity of the algorithm to deal with larger datasets of up to 3000 potential transplants. Simulations that they ran using their implemented algorithms indicated the likely benefit, in terms of numbers of additional transplants, of allowing PKEs to involve 3-way exchanges in addition to pairwise exchanges. Following this initial research, NHSBT took the decision in April 2008 to allow PKEs to include 3-way exchanges. The introduction of these exchanges meant that finding an optimal set of PKEs had become a provably hard problem (known technically as an *NP-hard* problem), making it challenging to solve efficiently. This software was used at quarterly matching runs of the UKLKSS between July 2008 and October 2011 to find optimal sets of kidney exchanges.

Between 2010 and 2011, an improved version of the Glasgow software was written in collaboration with Dr Gregg O'Malley (also of the

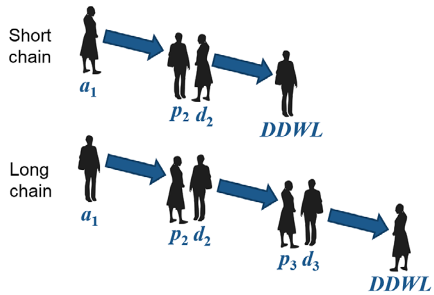

FIGURE 2 DOMINO PAIRED DONATION (DPD) CHAINS. IN EACH CHAIN, a_1 IS AN ALTRUISTIC DONOR, WHO DONATES A KIDNEY TO p_2, IN EXCHANGE FOR d_2 DONATING A KIDNEY, ETC., WITH THE FINAL DONOR IN EACH CHAIN DONATING A KIDNEY TO A PATIENT ON THE DECEASED DONOR WAITING LIST (DDWL)

University of Glasgow), using integer programming, a technique often used in Operational Research. This also addressed some changes in the established criteria for matches, which are described in more detail below. Moreover, the software was extended to deal with *domino paired donation* (*DPD*) *chains*. Such chains are triggered by altruistic donors, who wish to donate a kidney but do not have a specific patient in mind, together with incompatible donor-patient pairs, with the final donor donating to the deceased donor waiting list (see Figure 2 for illustrations of DPD chains). DPD chains have featured in the matching scheme since January 2012. Drs Manlove and O'Malley developed an in-house version of the software for NHSBT, allowing them to conduct the searches themselves and speed up response times. This software was delivered to NHSBT in June 2011, and has been used to find optimal solutions for quarterly matching runs of the UKLKSS since January 2012.

THE OPTIMISATION PROBLEM

The algorithm developed by the University of Glasgow researchers for the UKLKSS currently has to solve a complex optimisation problem involving five optimality criteria that are optimised in a hierarchical fashion. These criteria involve maximising the overall number of transplants, mitigating the risk associated with 3-way exchanges and long chains (by minimising their use where possible), and maximising the overall score of the identified PKEs and chains. The score of a potential solution is calculated by a scoring function used by NHSBT, which takes into account factors such as waiting time (based on the number of previous matching runs that a participant has been unsuccessfully involved in), sensitisation (which roughly corresponds to how difficult to match a patient is), HLA mismatch levels between a donor and patient (which relate to levels of tissue-type incompatibility) and points relating to the difference in ages between donors. (See the article by Manlove and O'Malley referenced at the end for a more detailed description of the optimisation problem and the algorithm used to solve it.)

As indicated previously, the algorithm is based on integer programming. It is implemented in C++ and uses the COIN-CBC solver. Figure 3 gives an illustration of the optimisation problem, together with an optimal solution found by the algorithm for the July 2015 data-set. The diagram shows a representation of the problem as a *directed graph*, consisting of *vertices* (depicted by circles, representing donor-patient pairs and altruistic donors) and *arcs* (depicted by arrows, representing compatibilities between donors and patients). An optimal solution found by the algorithm is highlighted using solid arcs, comprising seven pairwise exchanges, five 3-way exchanges and six long chains. To date, the algorithm has

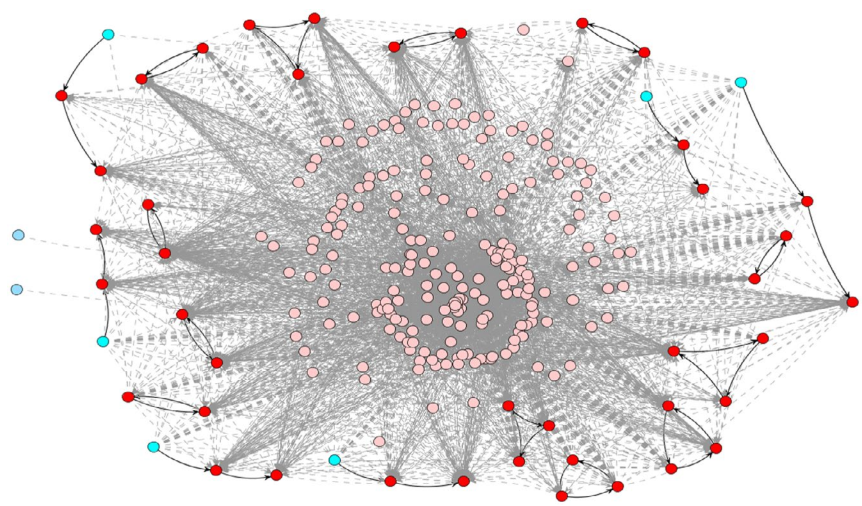

FIGURE 3 THE UNDERLYING DIRECTED GRAPH CORRESPONDING TO THE JULY 2015 DATA-SET, TOGETHER WITH AN OPTIMAL SOLUTION. TURQUOISE AND BLUE VERTICES ARE ALTRUISTIC DONORS (THE FORMER TRIGGER LONG CHAINS WHILST THE LATTER ARE UNMATCHED). TURQUOISE AND RED VERTICES BELONG TO PKES AND CHAINS, WHILST PINK VERTICES REPRESENT UNMATCHED DONORS AND PATIENTS

found optimal solutions for the datasets arising from all quarterly matching runs within 7 seconds.

Since delivering the software containing the optimal matching algorithm to NHSBT, subsequent work has involved carrying out simulations to measure the effectiveness of the current optimality criteria, and has also led to improved integer programming formulations combined with column generation techniques to handle larger datasets and longer DPD chains. A key aim of this scalability work is to ensure that the matching algorithms are capable of anticipating future challenges that may emerge from larger pool sizes and more complex optimality criteria.

OUTCOMES

By optimising these PKEs and DPD chains, the algorithms have led to 752 actual transplants taking place between 2008 and 2017. Had NHSBT continued to use their pre-existing algorithm, which was only capable of identifying pairwise exchanges, it is estimated that 534 transplants would have gone ahead. Thus the 752 transplants that took place represents an increase of 218, or 41%, compared to the estimated number that would have occurred if the status quo techniques had continued to be used.

According to NHSBT, each kidney transplant saves the NHS £240K over 10 years (based on a comparison with the cost of dialysis over that time period, and taking into account the cost of the operation itself). This means that by enabling an increase of 218 new kidney transplants, the research has potentially saved the NHS around £52M over a 10-year period.

In 2010, Rachel Johnson, the Head of Organ Donation and Transplantation Studies, NHS Blood and Transplant stated 'Since July 2008, we have been collaborating with Dr. David Manlove and Dr. Péter Biró in relation to the NMSPD [National Matching Scheme for Paired Donation, now the UK Living Kidney Sharing Schemes]. Their matching algorithms have been used in order to construct optimal solutions to the datasets that we provide. Some of these datasets have encoded particularly challenging underlying problems, and the task of producing an optimal solution would have been highly complex without the assistance of these matching algorithms. We anticipate that this will be a growing issue as the number of people in the database increases over time.'

Transnational European collaboration (in which countries pool their datasets in order to obtain more transplants and better quality matches) will require the algorithms to be extended to ensure that they can cope with larger and more complex datasets

FUTURE WORK

Transnational European collaboration (in which countries pool their datasets in order to obtain more transplants and better quality matches) will require the algorithms to be extended to ensure that they can cope with larger and more complex datasets. Work is ongoing to put in place the infrastructure to support these collaborations as part of the EU COST Action entitled 'ENCKEP' (European Network for Collaboration on Kidney Exchange Programmes), running from September 2016 to 2020, for which the author is Vice-Chair.

The algorithmic objectives are also supported by the £800K EPSRC funded project entitled 'IP-MATCH' (Integer Programming for Large and Complex Matching Problems), joint with the University of Edinburgh, running from November 2017 to October 2020, for which Dr Manlove is the University of Glasgow Principal Investigator.

David Manlove is a Senior Lecturer in Computing Science at the University of Glasgow. The work described above was an impact case study for the School of Computing Science's REF 2014 submission. It has also been featured on the EPSRC website and as part of a BBC4 documentary on algorithms.

FOR FURTHER READING

Biró, P., D.F. Manlove and R. Rizzi (2009). Maximum weight cycle packing in directed graphs, with application to kidney exchange programs. *Discrete Mathematics, Algorithms and Applications* **1**: 499–517.

Dickerson, J.P., D.F. Manlove, B. Plaut, T. Sandholm and J. Trimble (2016). Position-indexed formulations for kidney exchange. In *Proceedings of EC 2016: the 17th ACM Conference on Economics and Computation*, 25–42, ACM.

Manlove, D.F. and G. O'Malley (2014). Paired and altruistic kidney donation in the UK: Algorithms and experimentation. *ACM Journal of Experimental Algorithmics* **19**(2): article 2.6.