Institution: University of Glasgow (UofG)

Unit of Assessment: UoA11 Computer Science and Informatics

Title of case study: Algorithms for Paired Kidney Donation: Increasing Living Kidney Transplantation in the UK

Period when the underpinning research was undertaken: 2007–2013

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
(1) Prof David Manlove	(1) Lecturer; Senior Lecturer; Professor	(1) 2000–2009; 2009–2018; 2018–present
(2) Dr Péter Biró	(2) Research Assistant	(2) 2007–2010
(3) Dr Gregg O'Malley	(3) Research Assistant	(3) 2008–2009 and 2010–2011; 2011–2013
(4) Dr William Pettersson	(4) Research Associate	(4) 2017–2020
(5) Mr James Trimble	(5) Research Assistant	(5) 2015–2016

Period when the claimed impact occurred: 2008–present

Is this case study continued from a case study submitted in 2014? Yes

1. Summary of the impact

Bespoke algorithms developed at UofG have increased the number of kidney transplants arranged through the UK Living Kidney Sharing Scheme (UKLKSS). Since August 2013, 316 additional transplants have taken place, a 44% increase over the number of transplants that would have been identified using previous algorithms. These algorithms, optimised to the unique requirements of the UKLKSS, allow NHS Blood and Transplant to match recipients requiring a kidney transplant, who have a willing but incompatible donor, with the donor of another recipient in a similar position. The improved functionality of the algorithms has increased transplant numbers and freed many more kidney patients and their families from the burden of long-term dialysis. This has saved the NHS a minimum of GBP76.2 million between 2013–2030 based on current transplant numbers.

2. Underpinning research

In 2007 NHS Blood and Transplant (NHSBT) established what is now called the UK Living Kidney Sharing Scheme (UKLKSS), to increase opportunities for living kidney donation. This scheme identified *paired kidney exchanges* (PKEs; groups of two or more recipients who can swap their willing but incompatible donors with one another to obtain a compatible kidney). It has grown to become the largest kidney exchange programme (KEP) in Europe in terms of the number of transplants achieved and the proportion of registered patients receiving a transplant through the scheme. It is recognised as an exemplar in terms of innovation and complexity [5.9]

The original NHSBT matching algorithm identified optimal sets of PKEs, but its computational requirements restricted it to PKEs involving only two donor-recipient pairs (*pairwise exchanges*) with datasets of ~100 potential transplants.

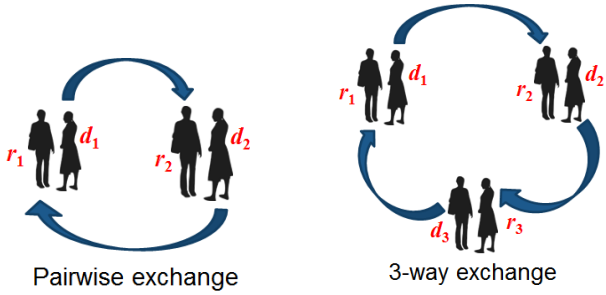

Figure 1: Schematics of pairwise and 3-way exchanges: r=recipient; d=donor for r

In May 2007, UofG researchers, Prof Manlove and Dr Péter Biró, developed a novel approach to enable both pairwise and *three-way exchanges* (involving three donor-recipient pairs; see Figure 1)

to be analysed [3.1], using graph-matching algorithms. Simulations run by the UofG team in early 2008 demonstrated that this new algorithm could accommodate datasets of up to 3,000 potential transplants and highlighted that the inclusion of three-way exchanges could increase transplant numbers.

From July 2008, NHSBT used the UofG algorithm to find optimal solutions from UKLKSS matching runs, including three-way exchanges. These quarterly matching runs apply the algorithm to the current pool of donors and recipients to find an optimal set of PKEs.

Between 2010 and 2013 Prof. Manlove, with Dr O'Malley, developed a novel algorithm using integer programming techniques to address both scalability issues with the 2007 algorithm and UKLKSS-specific optimality criteria [3.2]. Moreover, this bespoke solution enabled the search for *altruistic donor chains* (ADCs) – chains of transplants triggered by altruistic donors. In the case of a *short chain*, an altruistic donor donates a kidney to a recipient who has a willing but incompatible donor, in exchange for that donor donating a kidney to a recipient on the deceased donor waiting list (DDWL). *Long chain*s are similar but involve one additional donor-recipient pair (see Figure 2).

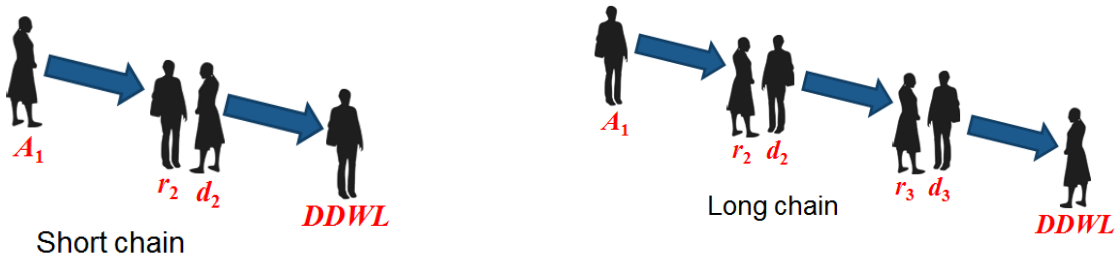

Figure 2: Schematics of short and long chains: A=altruistic donor, r=recipient; d=donor for r, DDWL=deceased donor waiting list.

In 2011, NHSBT deployed a version of the software by Prof Manlove and Dr O'Malley as part of an NHSBT-funded project [3.4], ahead of ADCs being introduced as part of the UKLKSS in January 2012. NHSBT opted to deploy its functionality in stages to ensure that other parts of the transplant system (e.g. operating theatres, histocompatibility laboratories) could accommodate the increased number of transplant matches produced by larger datasets containing more altruistic donors. Until January 2015, only short chains were permitted at each matching run, and in April 2015, long chains were introduced.

Subsequently Prof Manlove and his team have developed improved algorithms [3.3,3.5] capable of both identifying longer ADCs (in readiness their future introduction to the UKLKSS) and handling larger datasets [3.3, 3.5] such as those arising from transnational European collaboration through the European Network for Collaboration on Kidney Exchange Programmes (ENCKEP) chaired by Prof Manlove [3.6].

Since April 2018, following a change in policy, more altruistic donors are participating in the UKLKSS. In October 2018, NHSBT deployed a more advanced version of the UofG software to efficiently accommodate larger datasets including increased numbers of altruistic donors (recent datasets have involved over 6,000 potential transplants and up to 29 altruistic donors). This code was originally written as part of a previous NHSBT-funded project [3.7].

This UofG algorithm design is thus a prime example of high-quality fundamental research [3.1–3.3] that has advanced the work of NHSBT in matching kidneys to transplant recipients, improving and saving lives, and reducing long-term treatment costs. The research quality was recognised in

the 2019 award of the Royal Society of Edinburgh Lord Kelvin Medal to Prof Manlove "for his outstanding contribution to computing science; his pioneering work in matching algorithms and software has enabled a significant increase in living kidney transplants, thereby improving public health".

3. References to the research

3.1 Paper in refereed journal: P. Biró, D.F. Manlove and R. Rizzi, Maximum weight cycle packing in directed graphs, with application to kidney exchange programs, Discrete Mathematics, Algorithms and Applications, 1 (4) :499–517, 2009. doi:10.1142/S1793830909000373.

3.2 Paper in refereed journal: D.F. Manlove and G. O'Malley, Paired and altruistic kidney donation in the UK: Algorithms and experimentation, ACM Journal of Experimental Algorithmics, vol. 19, no. 2, article 2.6, 21 pp, 2014. doi:10.1145/2670129 *

3.3 Paper in refereed conference proceedings: J.P. Dickerson, D.F. Manlove, B. Plaut., T. Sandholm and J. Trimble, Position-Indexed Edge Formulations for Kidney Exchange, in Proceedings of EC 2016: the 17th ACM Conference on Economics and Computation, pp. 25–42, ACM, 2016. doi:10.1145/2940716.2940759. *

Externally-funded research projects:

3.4 Software for the National Matching Scheme for Paired Donation. Duration: 1 April 2010–30 June 2011. Amount: GBP108,000. Funder: NHS Blood and Transplant. Principal Investigator: Prof David Manlove. Research Assistant: Dr Gregg O'Malley.

3.5 IP-MATCH: Integer Programming for Large and Complex Matching Problems. Duration: 1 November 2017–31 October 2020. Amount: GBP353,000. Funder: EPSRC (grant EP/P028306/1). Principal Investigator: Prof David Manlove. Research Associate: Dr William Pettersson. Joint project with the University of Edinburgh.

3.6 ENCKEP: European Network for Collaboration on Kidney Exchange Programmes. Duration: 2 September 2016–1 September 2020. Budget approx. GBP120,000 per annum. Funder: EU Cooperation in Science and Technology (Action CA15210). Chair: Prof David Manlove.

3.7 Optimising options and strategies for living donor kidney transplantation for incompatible donor-recipient pairs. Duration: 1 January 2012–30 June 2013. Amount: GBP151,000. Funder: NHS Blood and Transplant. Co-Investigator: Prof David Manlove. Research Associate: Dr Gregg O'Malley.

* = best indicators of research quality

4. Details of the impact

Each year, 64,000 UK patients are treated for end-stage renal failure, 30,000 of whom are on dialysis, with kidney failure having a devastating impact on patients' lives. Transplantation is the most effective treatment for end-stage renal failure; the life expectancy of transplant recipients is doubled or tripled compared to those remaining on dialysis. Globally, the demand for available kidneys has consistently exceeded supply. Increasing kidney availability is critical for improving the outcomes of prospective and current renal transplant candidates. As of 29 February 2020 [5.1], 4,960 patients were on the UK's kidney transplant list. However, only 3,448 kidney transplants took place between April 2019–March 2020, of which 2,466 were from deceased and 982 from living donors. During this period, 246 people died whilst awaiting a kidney transplant. NHSBT estimates the median waiting time on the kidney transplant list at 633 days for adults and 291 days for children.

Increasing the number of potential donor-recipient kidney matches

UofG researchers have shown how to model a complex, hierarchical set of criteria that define an optimal set of kidney exchanges. Their algorithms have enabled the UKLKSS to optimise the number of potential donor-recipient matches by including three-way exchanges from July 2008; short chains from January 2012; and long chains from April 2015. In 2018, a change in NHSBT policy, which lead to chain donation becoming the default option for altruistic donors [5.2], resulted in refined algorithms being used [3.7] which further increased matching rates.

Between 1 August 2013–31 December 2020,1,652 potential transplants have been identified by these algorithms (1,420 of which stem from three-way exchanges and ADCs), from which 1,031 transplants were performed. Had NHSBT continued to use their previous algorithm from 2007, we estimate that only 715 transplants would have taken place (from a total of 1,146 identified matches, using the same conversion rate). This represents an increase of 316 transplants (or 44%) in this period, compared to the estimated number had the earlier NHBST algorithm continued to be used. The Assistant Director of Statistics and Clinical Studies at NHSBT says: *"The collaboration between NHSBT and the University of Glasgow in developing the UKLKSS has continued to progress over the last seven years. Most recently it has enabled the algorithm for living kidney exchanges to include 'long altruistic donor chains'… an important new development, allowing 273 additional kidney transplants to date (Dec 2020), with many more expected in future years. Within the scheme, long chains now represent about 25% of transplant activity and enable many recipients who are very difficult to match (highly sensitised) to get a transplant. The possibilities afforded by the scheme are life changing for the many recipients who benefit"* [5.3].

Improving recipients' quality of life

For recipients, the benefits of this research are numerous. Transplanted kidneys obtained from living donors last on average 25% longer than those from deceased donors (15 years compared to 12) so increasing the number of these types of exchanges translates into more patients living for longer with a healthy kidney and resuming normal, working lives. By comparison, the life expectancy of patients on dialysis is around 5 years. Such quality-of-life benefits for UKLKSS recipients have been described in NHSBT recipient stories [5.4] and in three television documentaries [5.5]. [5.6] is associated with the first of these; the second and third feature Prof. Manlove's work. A recipient from one 3-way exchange noted that, post-transplant, *"You could start to have these moments again… feeling great and being able to do normal family things and going for a meal with family and spending more time because I'm not in hospital 3 nights a week…believing that you're going to be well in the future"* [5.7]. Transplants facilitated by the UofG algorithm also improve the quality of life of those who donate to the UKLKSS. As one grateful donor noted, it enables her family to *"just forget, because it is just normal and life's great, and I do think that we are happier"* [5.7].

Financial benefits for the NHS

In addition to improving donors' and recipients' quality of life, the work of Prof. Manlove and colleagues also provides economic benefits to the NHS. Each kidney transplant saves the NHS GBP241,000 over 10 years (the median graft survival time, compared to the cost of dialysis over that time period, and taking into account the cost of the operation itself) [5.8]. Thus, by enabling 316 more kidney transplants from 2013–2020, the UofG researchers have potentially saved the NHS around GBP76.2 million in total from 2013–2030, with additional savings to come with each new matching run.

Overall, as stated in the Living Donor Kidney Transplantation (LDKT) Position Paper from August 2017: "*The UK has developed the largest living kidney sharing scheme (UKLKSS) in Europe [5.2] in terms of the number of transplants achieved and the proportion of registered recipients receiving a transplant through the scheme. It is recognised as an exemplar in terms of innovation and complexity. The scheme particularly benefits long-waiting recipients with immunological complexity and recipients from Black and Asian communities. The effectiveness of the UKLKSS is significantly enhanced by the inclusion of non-directed altruistic kidney donors, who are willing to donate to anyone in need of a transplant and can initiate a chain of up to three transplants by a single donation. The UKLKSS currently contributes up to 20% of total LDKT (Living Donor Kidney Transplantation) activity"* [5.9].

Impact on transnational kidney exchange programmes

The ENCKEP project, funded by the EU COST framework, brings together policy-makers, clinicians, economists, social scientists and optimisation experts from across Europe to share best practice in the establishment of national and transnational KEPs. Chaired by Prof. Manlove, it has resulted in a series of handbooks and strategy papers addressing policy, clinical practice and evidence, and optimisation criteria critical for improving the quality of life of a growing European patient population with end-stage renal disease. Corroborating details outlining how the outputs of UofG research, contributing to the ENCKEP COST Action, have helped to shape transnational KEPs including STEP (the ScandiaTransplant Exchange Programme (STEP) can be obtained from [5.10].

5. Sources to corroborate the impact

5.1. NHSBT Annual Activity Report for 2019–2020, https://bit.ly/2CodLDz
5.2. NHSBT policy POL274/1 on Living Donor Kidney Transplantation: https://bit.ly/2tF4RiC
5.3. Testimonial, Assistant Director, Statistics and Clinical Studies, NHSBT
5.4. NHSBT Living Donation Stories: https://www.organdonation.nhs.uk/helping-you-to-decide/real-life-stories/living-donation-stories/
5.5. BBC documentary output includes: Hospital, Series 1, Episode 6, https://bbc.in/2OTRwsj; The Secret Rules of Modern Living: Algorithms, https://bbc.in/2Djnex4; Royal Institution Christmas Lectures 2019: Secrets & Lies – The Hidden Power of Maths: 2. How to Bend the Rules, https://bbc.in/2N9n52x
5.6. Imperial College Healthcare Trust blog: How UK Living Kidney Sharing Schemes mean more recipients can receive life-changing transplants, https://bit.ly/2RwxzJ1
5.7. Transcript from donor/recipient participants of 3-way exchange.
5.8. NHSBT Factsheet: Cost-effectiveness of transplantation, https://bit.ly/36doz3f
5.9. Living Donor Kidney Transplantation: Position Paper August 2017, https://bit.ly/2N6wMz4
5.10. Corroborating testimony can be obtained from ScandiaTransplant Exchange Programme, contact details on request.