Paired Donor Kidney Transplantation in the UK

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Senior Statistician, NHSBT
Overview

• Introduction – NHSBT, Organ Donation and Transplantation
• Kidney transplantation
• Paired donation
• Matching algorithm
• Activity
• Further developments
• Future challenges
Introduction
NHSBT – Organ Donation and Transplantation

• NHS Blood and Transplant (NHSBT) is a Special Health Authority, dedicated to saving and improving lives through the wide range of services we provide to the National Health Service

• We match, allocate, audit and analyse organ donations across the whole of the UK

• Each year our donors give around two million donations of blood and 3,500 organs – saving and transforming countless lives
Kidney Transplantation
Why do people need a kidney transplant?

• Chronic kidney disease affects 1 in $10^1$ in the population (less common in young adults)

• For those patients where the disease progresses to kidney failure, dialysis or a transplant may be needed

• Around 7000$^2$ people start dialysis in the UK each year

• Transplantation is often seen as the best form of treatment for a patient with kidney failure

$^1$ Source: National Kidney Federation

$^2$ Source: UK Renal Registry
Kidney Transplantation

- There are currently over 5000 patients in need of a kidney transplant in the UK
- Around 3000 patients join the waiting list for a kidney each year
- Average waiting time for a transplant is over 3 years for a deceased donor kidney
- Currently expect over 2000 deceased donor kidney transplants each year
Living Donor Kidney Transplantation

• If a patient has a living kidney donor (relative, partner or friend) then this eliminates waiting time on the list

• Around 1000 living donor kidney transplants in the UK every year

• However, due to the patient being medically incompatible with the donor a transplant may not be able to go ahead
Living Donor Kidney Transplantation

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Living Donor Kidney Transplant Rates

Living donor kidney transplant rates for Europe and the USA, 2014

Source: Council of Europe – Transplant Newsletter
Paired Donation
Pairs registered for Matching Run

D1  P1  D7  P7  D4  P4  D6  P6  D2  P2  D8  P8  D5  P5  D3  P3
Patients Matched
Transplants Identified

2-way

3-way

Short Altruistic Donor Chains
Transplants Identified

2-way

3-way

Short Altruistic Donor Chains

Long Altruistic Donor Chains

From April 2015
Paired Donation

- Prior to 1 September 2006, transplants could only take place between those with a genetic or emotional connection

- Human Tissue Act 2004 and Human Tissue (Scotland) Act 2006:
  - legal framework created to allow transplants between strangers

- New possibilities for live-donor transplants:
  - *Paired kidney donation*: a patient with a willing but incompatible donor can swap their donor with that of another similar patient
  - *Altruistic* (non-directed) donors
UK National Paired Donation Scheme

- Started in April 2007
- ‘Matching runs’ take place every 3 months
- Includes all 24 UK kidney transplant centres
History of Paired Kidney Donation Programmes

- **KPD 1st suggested by Rapaport [4]** in 1985
- **Korea starts performing 3-way and 4-way exchanges**
- **1st exchange in Europe performed in Switzerland [6]** in 1995
- **Ohio Solid Organ Transplantation Consortium Living Donor Kidney Exchange Program established** in 1995
- **1st exchange performed in Korea by Park et al [5]**
- **1st exchanges performed in US in New England and Johns Hopkins [7]** in 2000
- **Paired Donation Network established**
- **New England Program for Kidney Exchange founded**
- **Dutch establish 1st national KPD program [8]** in 2005
- **Alliance for Paired Donation unites over 70 transplant centers in US into 1 KPD coalition**
- **UNOS announces plans to establish national KPD program in US in 2010 [75]**

**National KPD programmes**

- **Spain**
- **UK**
- **Italy**
- **Australia**

Matching Algorithm
Identifying Optimal Combination of Transplants

- Over 200 pairs every ‘matching run’
- This results in 2000-5000 arcs (donor-recipient matches)
- Arcs are weighted to give preference to patients who are more difficult to match
- Need to maximise the number of transplants according to criteria developed with transplant community

Acknowledgement: Tommy Muggleton
## Identifying Optimal Combination of Transplants

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<thead>
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<tbody>
<tr>
<td>1</td>
<td>Maximise 2-way exchanges (inc embedded in 3-way)</td>
</tr>
<tr>
<td>2</td>
<td>Maximise number of transplants</td>
</tr>
<tr>
<td>3</td>
<td>Minimise 3-way exchanges</td>
</tr>
<tr>
<td>4</td>
<td>Maximise 3-ways with embedded 2-ways</td>
</tr>
<tr>
<td>5</td>
<td>Maximise ‘score’ of set of transplants</td>
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</tbody>
</table>

**Score based on**

- Previous matching runs of patient (50 points per unsuccessful run)
- Sensitisation of patient (0-50 points for 0-100% sensitised)
- HLA mismatch of identified transplant (0–15 points for levels 4 to 1)
- Donor-donor age difference (3 points if <=20 years)

Matching software implemented by colleagues at University of Glasgow, School of Computing Science
Integer Programming Model

• Builds on the so-called cycle formulation
  • first formulated by Roth, Sönmez and Ünver, 2007
  • investigated computationally by Abraham, Blum and Sandholm, 2007
  • Running time of under 2 seconds for all data sets to date

Matching software implemented by colleagues at University of Glasgow, School of Computing Science
Paired Donation Activity
Number of Patients in Quarterly Matching Runs

- Jan 2016: 223 patients
- Apr 2007: 9 patients
Summary of Registered Patients

Total of 1438 patients (1586 pairs) enrolled

- 44% spouse/partner pairs, 56% female patients
- Mean age at first matching run 46 years (range 2-78 yrs)
- 35% ABO incompatible, 47% HLA incompatible,
  15% ABOi + HLAi, 3% compatible
- 44% patients with high level of antibodies
## Overall Activity

<table>
<thead>
<tr>
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</tbody>
</table>

- **Long Chain**: 2-way, 3-way
- **Short Chain**: 2-way
- **2-way**
- **3-way**
# Overall Activity

Jan 2012-Jan 2016
(146 transplants not proceeding, 38% of identified)

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- **Antibody reaction**
- **Donor or Recipient withdrew**
- **Donor or Recipient unfit**
- **Other**
Summary of Transplanted Patients

Total of 563 patients transplanted

- Median of 2 runs to get a match
- 28% patients with high level of antibodies
- 562 adult, 1 paediatric
UK Living Donor Kidney Transplants
Further Developments
Further Developments

- Simulation work utilising the matching algorithm has also helped shape the scheme
  - Used to develop a tool to help patients understand their chance of transplant
  - Different policies within the scheme have been simulated to inform changes
Simulations

New Pairs

One-Way Matches

Pairs Registered

No Match

Transplants Identified

Match

Transplant

Drop Out

Non-proceeding Transplants
Helping Patients Understand Their Chance of Transplant

• The nature of the paired donation scheme, means that chances of transplant depend on patient and donor characteristics.

• Previous to this work, there was limited information available to patients regarding how long they can expect to wait for a transplant.

• The availability of the matching algorithm allowed us to use resampled data and simulate 3 years in the scheme to estimate chance of transplant, based on patient and donor characteristics.
Helping Patients Understand Their Chance of Transplant

- Data from the simulations includes patients that enter the scheme for a few matching runs and then drop out without transplant
- Censored data – Cox proportional hazards models
- Factors included in the model that are relevant in waiting time
  - Recipient Blood Group
  - Donor Blood Group
  - Level of patient antibodies
Helping Patients Understand Their Chance of Transplant

Incompatible Pairs Living Donor Kidney Application

<table>
<thead>
<tr>
<th>Variable</th>
<th>Select</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipient Blood Group</td>
<td>A</td>
</tr>
<tr>
<td>Calculated Reaction Frequency</td>
<td>55-94</td>
</tr>
<tr>
<td>Donor Blood Group</td>
<td></td>
</tr>
<tr>
<td>ABOi TX with willing Donor†</td>
<td>Select</td>
</tr>
<tr>
<td>HLAi TX with willing Donor†</td>
<td>Select</td>
</tr>
<tr>
<td>Recipient Age</td>
<td></td>
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Estimated Chance of Transplant

<table>
<thead>
<tr>
<th></th>
<th>Deceased Donor</th>
<th>NLDKSS</th>
<th>ABOi</th>
<th>HLAi</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 Months</td>
<td>&lt;10%</td>
<td>41-50%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1 Year</td>
<td>11-20%</td>
<td>71-80%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3 Years</td>
<td>41-50%</td>
<td>&gt;90%</td>
<td>-</td>
<td>-</td>
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</tbody>
</table>

Transplant Survival Rates

<table>
<thead>
<tr>
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<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3 Years</td>
<td>-</td>
<td>-</td>
<td>-</td>
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</tbody>
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Disclaimer: The information is provided for guidance only.
†Low titre/Low DSA means acceptable for incompatible transplant. High titre/High DSA means unacceptable for incompatible transplant.
Note: NLDKSS chance of transplant is based on paired donation including short altruistic donor chains. Chances of transplant through the NLDKSS could be increased by considering an antibody incompatible transplant within the scheme.

For a more accurate estimate of waiting time for a deceased donor transplant based on more variables, please visit http://www.odt.nhs.uk/doc/chance_of_transplant.xls

Available at: http://www.odt.nhs.uk/transplantation/guidance-policies/tools/
The availability of the matching algorithm also allows us to investigate the effect of making changes to the scheme using simulations:

- The addition of long altruistic donor chains
- Non-simultaneous long donor chains
- Changing the frequency of matching runs
- Matching altruistic donors as soon as they register
Informing Changes to the Scheme

• Results have shown the benefit of the introduction of long altruistic donor chains. This led to them being introduced in April 2015

• No conclusive evidence under current system that there is a strong benefit of increasing the frequency of matching runs

<table>
<thead>
<tr>
<th>Policy</th>
<th>Transplants over 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current scheme policy</td>
<td>+/- 0%</td>
</tr>
<tr>
<td>Matching runs every 2 months</td>
<td>+0.7%</td>
</tr>
<tr>
<td>Matching Altruistic donors every week</td>
<td>-1.5%</td>
</tr>
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</table>
Future Challenges
Future Challenges

• Addressing the rate of non-proceeding transplants
• Keeping up with expectations of the clinical community
• Centres wanting local flexibility
• Large increase in the number of pairs in the scheme
Summary

• The UK paired donation scheme helps difficult to match patients with a willing live donor to get a transplant

• Matching algorithm is vital to optimise transplants and maximise patient benefit

• The availability of the matching algorithm allows us to investigate the effect of making changes to the scheme, and to give more information to patients
Acknowledgements

- University of Glasgow
  - David Manlove, Gregg O’Malley, James Trimble

- NHSBT
  - Rachel Johnson, Lisa Burnapp, Iain Harrison, Lin Shelper, Debbie West, Information Services

“To match world class performance in living donor kidney transplantation”

www.nhsbt.nhs.uk
www.odt.nhs.uk