U.S. changes in Kidney Allocation

- Match kidneys with longest survival to patients with longest survival
  - No parallel matching for kidneys with lower survival potential

- Decrease discard of kidneys with lower survival potential
  - Increased sharing ...different from Eurotransplant

- Increase transplantation for highly sensitized patients
  - Some kidneys with long projected survival allocated to high risk patients
    (sensitized with long dialysis exposure)

- Backdated patients to dialysis start date
  - Improved access for ethnic minorities/low SES patients
  - Transplanting patients with long dialysis exposure – where survival benefit of
    transplantation compared to treatment with dialysis is less certain
Kidney Allocation in the UK: Did the Last System Work? What will the next one look like?

Chris Watson
University of Cambridge, UK
Conflict of Interest Disclosure

- I have no relevant financial relationships to disclose.
- I will not discuss off label drug use
- I chair the Kidney Advisory Group of NHSBT
  = Kidney committee of UNOS
UK & USA: two nations divided by a common language ... and an oval ball

You pass forwards to score a touchdown

We pass backwards to go forwards to score a touchdown
UK Renal Replacement

Oversight: NHS BT

UK population
60 million
↓
71 Local Dialysis Centers
↓
23 Regional Transplant Centers

$ UK National Health Service pays for all costs for life
Access to the waiting list

- 52% of patients undergoing renal replacement therapy have a transplant
- Of those on dialysis 48% are listed for transplant

UK Renal Registry 2014
UK kidney allocation: Outline

- How we did we get here?
- Oversight in the UK
- Where are we going next?
1989 scheme: Beneficial matching

- Beneficial HLA match:
  - 000, 100, 010 mm
- One kidney shared
  - Preference for child / local patient
- One kidney kept locally

Gilks et al. Transplantation 1987;43:669
Analysis of 2282 kidney Tx in UK, 1979-84
Why not share both kidneys?

- Poorer outcomes of shared kidneys
  - 1.2 RR of graft failure
- Balance of exchange
  - North of England donate more kidneys
  - South of England list more recipients
1998 scheme: Favorable matching

- Favorable mismatch 100, 010, 110
- Both kidneys offered for 000 or favorable
  - One kidney for non-favorable
- Priority
  - Highly sensitised
  - Children
  - Local vs. national patient

Morris et al. Lancet 1999;354:1147

Analysis of 6338 Tx in UK, 1986-93
Effect of favorable offering: better matching

- Pre-scheme year: 7% non-favorable, 50% favorable
- Year 1: 13% non-favorable, 38% favorable
- Year 2: 13% non-favorable, 52% favorable
- Year 3: 16% non-favorable, 51% favorable
- Year 4: 15% non-favorable, 54% favorable
- Year 5: 19% non-favorable, 45% favorable

Legend:
- Non favorable
- Favorable (100,010, 110)
- "000"
Problems with favorable matching

- Blood group B waited longer
  - And so ethnic minorities waited longer

- Bias against HLA DR homozygotes
Minimising HLA-DR mismatches penalises HLA-DR homozygotes

Heterozygote: A1, A10, B8, B27, DR17, DR5

1-1-1 mismatch

0-0-0 mismatch

A1, -
B8, -
DR17, -

Homozygote
Homozygotes waited longer

- 59% Not Homozygous
- 20% B
- 21% A & B

Median waiting time (days)

- A: 570
- B: 672
- A & B: 723
- DR: 785
- A & DR: 785
- B & DR: 863
- A & P: 888

14% of donors were HLA-DR Homozygous
2006 scheme aims

- Remove concept of ownership
  - Share both kidneys nationally
- Re-evaluate role of HLA
  - Match younger patients better than older
- Address existing inequalities
  - Long waiting patients
  - Ethnicity / Blood group
  - homozygosity
- Reduce cold ischaemic times
Default rare HLA types to related common type

- Rare HLA types are difficult to transplant
- Rare HLA types defaulted to more common ones based on
  - serological cross reaction
  - Sequence information
- **Consequence**
  - Improved access to first transplant
  - May result in sensitisation and longer wait for subsequent Tx

<table>
<thead>
<tr>
<th>Rare specificity</th>
<th>Related specificity</th>
<th>% of donor pool</th>
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</thead>
<tbody>
<tr>
<td>A36, A80</td>
<td>A1</td>
<td>18</td>
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<tr>
<td>A43</td>
<td>A10</td>
<td>4</td>
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<tr>
<td>B53</td>
<td>B5</td>
<td>5</td>
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<tr>
<td>B42, B73, B81</td>
<td>B7</td>
<td>15</td>
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<td>B59</td>
<td>B8</td>
<td>13</td>
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<td>B82, B83</td>
<td>B12</td>
<td>18</td>
</tr>
<tr>
<td>B46</td>
<td>B15</td>
<td>7</td>
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<td>B67</td>
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<td>B41, B48</td>
<td>B40</td>
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<tr>
<td>DR101, DR10</td>
<td>DR1</td>
<td>10</td>
</tr>
<tr>
<td>DR9</td>
<td>DR4</td>
<td>20</td>
</tr>
<tr>
<td>DR11, DR12</td>
<td>DR5</td>
<td>8</td>
</tr>
</tbody>
</table>

Johnson et al. Transplantation 2010; 89: 387
2006 scheme

• Points based scheme
  – Waiting time: 1 point for each day on list
  – HLA mismatch level & recipient age: maximum 3500
HLA mismatch and transplant survival

4 levels of mismatch

• 000 mismatch
• 0DR & 0/1 B mm
• 0DR & 2B mm or 1 DR & 0/1 B mm
• Others

Johnson et al. Transplantation 2010; 89: 379
HLA mismatch / age relation

- Part of a points based allocation
- Age & HLA mismatch
  - More points for better matched kidney in young patient

Johnson et al. Transplantation 2010; 89: 379
2006 scheme

• Other elements of scheme
  – Donor recipient age difference: \(-0.5 \times (\text{don} - \text{recip age})^2\)
  – Location of donor (minimise ischaemic time):
    • 900 if same centre (23 centres, 3m population)
    • 750 if same region (3 regions, 20m population)
  – HLA B homozygous: 100
  – HLA DR homozygous: 500
Effect of current scheme on HLA matching by age group

Proportion of Txs

Age group

<18 18-29 30-39 40-49 50-59 60-69 >70

0% 20% 40% 60% 80% 100%

0DR & 2B or 1DR & 0/1B
0DR & 0/1B mm
000 mismatch

Other
Transplants for ethnic minorities

- “Black” patients
  - Transplants
  - Transplant List

- “Asian” patients

- White patients
  - Transplants
  - Transplant List

Year

Percent
Reduction in proportion of long waiting patients

- <1 yr: 35% (31-Dec-05), 38% (31-Mar-14)
- 1-3 yrs: 35% (31-Dec-05), 37% (31-Mar-14)
- 3-5 yrs: 14% (31-Dec-05), 14% (31-Mar-14)
- 5-7 yrs: 8% (31-Dec-05), 5% (31-Mar-14)
- ≥7 yrs: 8% (31-Dec-05), 6% (31-Mar-14)
Cold ischaemic times since 2006

- Q1
- Median
- Q3

1998 scheme 2006 scheme
Problems with current scheme

1. Excess of highly sensitised (cPRA* >85%) patients

- New Listing: 9.9
- Waiting list: 26.7
- Transplants: 16.4

*cPRA is termed calculated reaction frequency in UK, based on reactivity to 10000 UK donors
Problems with current scheme

2: Donor & Recipient factors not accounted for

Proportion of “poorer quality” kidneys increasing

Problems with current scheme:

3: It doesn’t integrate DCD kidney offering


37% are DCD
Discard rates for kidneys from deceased donors, 2014

% of retrieved kidneys not transplanted

- Spain: 24
- US: 19
- UK: 10

Source: ONT – Spain data, OPTN - US data, NHSBT - UK data
Discard rates for kidneys from deceased donors, 2014, by donor age

Source: ONT – Spain data, OPTN – US data, NHSBT - UK data
Oversight: CUSUM monitoring

- 3 month reports
- Triggers for graft loss & death
  - Baseline is that center’s own past performance
- Letter from NHSBT to explain trigger
  - Response reviewed by
    - NHSBT medical director
    - Kidney committee chair
    - NHS Commissioner

Liver Transplantation 2010;16:1119
Oversight: Publication of center specific data

- Waiting list
  - Demographics
  - Waiting time
  - Pre-emptive listing rate
- Transplants
  - Demographics (DRI; DCD/DBD; LD)
  - Cold ischaemic time
  - Graft and patient survival

http://www.odt.nhs.uk/uk-transplant-registry/organ-specific-reports/
Survival from listing

- 5 year patient survival
  - From listing: 87% (84 – 92%)
  - From transplant: 89% (81 – 95%)
The future: beyond HLA matching

- Reduce sensitisation by improved matching
- HLA epitope
  - Not whole antigen
- Electrostatic charge minimisation

AJT 2013; 13: 3114
Hum Immunol 2011;72:1049
Future: Reduce offer decline rate
Each offer should be the best offer for that patient
ATTOM study

- Access to renal Transplantation and Transplant Outcome Measures study

- Sample (n=6862):
  - All incident dialysis patients in the UK in a year
  - All new kidney & Kidney/pancreas transplants
    - Plus matched controls
ATTOM Analyses

• Quality of life and quality of health
  – Including in depth interviews with subset
• Clinical data on co-morbidity
  – e.g. cardiac status
• Survival
• Health economics
• Analysis of unit differences in protocols and practice
The future: smarter offering

<table>
<thead>
<tr>
<th>Recipient factors</th>
<th>Donor factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Age</td>
<td>• DBD and DCD</td>
</tr>
<tr>
<td>– Child vs. old adult</td>
<td>• Ischaemic time</td>
</tr>
<tr>
<td>• Life expectancy</td>
<td>– Tissue matching</td>
</tr>
<tr>
<td>– On dialysis</td>
<td>– HLA / Epitope / electrostatic</td>
</tr>
<tr>
<td>– Post transplant</td>
<td>• Donor kidney quality</td>
</tr>
<tr>
<td>• Waiting time</td>
<td>– e.g. KDPI</td>
</tr>
<tr>
<td>– From dialysis start</td>
<td>• Donor disease risk</td>
</tr>
<tr>
<td>• Sensitization</td>
<td>• Others, e.g. cost effectiveness</td>
</tr>
<tr>
<td>• Quality of life</td>
<td></td>
</tr>
</tbody>
</table>
Summary

UK allocation schemes have been developed using evidence-based modeling.

- evolved from simply matching for HLA
- Take some recipient & donor factors into account
- evolved from offering one kidney for a beneficial match, to both kidneys going into the national pool
- All schemes have losers and winners.
  - regular review and adjustment has been necessary to ensure fairness.
- The next scheme will further personalize offering.