National Transplant Guidelines

Quo Vadis?

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Quo Vadis
Whither goest thou?
Where the F#$% do we go next?
Overview

WAITING LIST ELIGIBILITY

ALLOCATION

• What have we got currently?
• Desirables for a good system.
• Major potential inputs:
  – Immunology
  – Waiting Time
  – Quality/Age Matching of Donors and Recipients
80%  5 Year Survival

• “Improve uniformity for wait list eligibility between the states”
• It is NOT perfect – but neither are previous thresholds
• It IS somewhat arbitrary – but so are previous thresholds
• At least it provides a uniform goal for all transplant units to try to approximate, and hence a greater similarity between units.
### ANZDATA – 5 yr outcomes

<table>
<thead>
<tr>
<th></th>
<th>Graft</th>
<th>Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>All DD1 transplants</td>
<td>79.8%</td>
<td>88%</td>
</tr>
<tr>
<td>Type II Diabetes</td>
<td>65.8%</td>
<td>74%</td>
</tr>
<tr>
<td>Any Vascular Disease</td>
<td>72.7%</td>
<td>77%</td>
</tr>
<tr>
<td>Diabetes + any Vascular</td>
<td>60.5%</td>
<td>69%</td>
</tr>
<tr>
<td>Diabetes but no Vascular</td>
<td>69.2%</td>
<td>77%</td>
</tr>
</tbody>
</table>
80% 5 Year Survival

• Almost any threshold we choose to use is arbitrary.
• EXCEPT – Anybody on dialysis who wants a kidney transplant.
• Regularly criticized (also widely supported)
• BUT no better proposal put forward.
• Any worthwhile suggestions appreciated!
NOMS

• Son of NKMS
• Built in 1999 because of Y2K
• Run by the Red Cross in Sydney
• A National Algorithm (Interstate Exchange)
• 5 State-Based Algorithms (slightly different to allow for pool sizes)
National Algorithm

• 7 Levels
• Aims to “assist” the highly sensitized (by Class 1, CDC PRA) to find a good match.
• Finds 0 MM kidneys
• Make up at lower levels to maintain Interstate Balances.
• A little under 20% of kidneys are shipped.
• Other kidneys allocated by state protocols
What do we want?

- Fair to patients who are waiting
- Achieves a good outcome for available kidneys
- Tries to assist “biologically disadvantaged” e.g. sensitized
- Avoids discriminating against groups, e.g. ethnic minorities
- Ideally meets public approval
Potential Inputs

- Waiting Time
- Immunology
  - Sensitization
  - HLA Matching
  - Donor Specific Antibodies
  - Graft Number
- Donor/Recipient “Quality Matching”
  - Age
  - Size
  - Comorbidities
Waiting Time

• Seems “fairest”
• Important for outcome
• Important for lifestyle
• Time to List v Time to Transplant
Marked Variation of the Association of ESRD Duration Before and After Wait Listing on Kidney Transplant Outcomes


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Figure 1. Adjusted hazard ratio for overall graft loss among deceased donor transplant recipients. Among patients with ESRD onset prior to placement on the waiting list; model adjusted for donor and recipient age, gender and race, primary diagnosis, panel reactive antibody level, body mass index, HLA-mismatches, educational attainment, donor history of hypertension and diabetes, donor cause of death and donor terminal creatinine and primary insurance.
HLA Matching

- Used to be very important
- Now less than it used to be
- Still plays a role, especially DR Matching
- More critical for regrafts and sensitized
- It is easier for some races to get a good match than others
- Matching helps some, possibly at the expense of others
- Important interaction with waiting time!
HLA Matching

Figure 22. Overall graft survival by mismatch at A locus

Figure 25. Overall graft survival by mismatch at B locus

Figure 28. Overall graft survival by mismatch at DR locus

Figure 31. Overall graft survival by HLA mismatch
Donor / Recipient Matching

• It is not good for a patient with a 40 year potential survival to get a kidney with a likely 3 year survival.

• It is potentially wasteful to put a kidney with a potential 30 year survival into a patient with a likely 5 year survival.

• Should we match in some way?
Figure 16. Overall graft survival by age mismatch

- **agemismatch = D+R<60**
- **agemismatch = D<60, R>=60**
- **agemismatch = D>=60, R<60**
- **agemismatch = D+R>=60**

*p* < 0.001
Figure 10. Overall graft survival by donor type

- *ecd60 = Non ECD*
- *ecd60 = ECD, aged <60*
- *ecd60 = ECD, aged >=60*

*p<0.001*
Figure 73. Effect of donor age on graft survival
Figure 74. Effect of recipient age on graft survival
Proposed Factors - US

- Kidney Donor Profile Index (KDPI)
  - Donor age
  - Race/ethnicity
  - Hypertension
  - Diabetes
  - Serum creatinine
  - COD CVA
  - Height
  - Weight
  - DCD
  - HCV

- Candidate Estimated Post-Transplant Survival (EPTS)
  - Candidate Age
  - Candidate Diabetes
  - Prior transplant
  - ESRD time
In three steps: How does this system work?

- It all starts with the estimated potential function of the kidney that is available for allocation...

  ...is the kidney one of the 20% longest potential functioning or not?

  
  
  KDPI \leq 20\% \quad \text{OR} \quad \text{KDPI} > 20\%
## Who gets priority for which kidneys?

<table>
<thead>
<tr>
<th>Kidney</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>KDPI (\leq 20%)</td>
<td>Candidates with longest 20% estimated post-transplant survival</td>
<td>Candidates with 21%-100% estimated post-transplant survival</td>
</tr>
<tr>
<td>KDPI (&gt; 20%)</td>
<td>Candidates within +/- 15 years of donor’s age</td>
<td>Candidates more than 15 years older/younger than the donor</td>
</tr>
</tbody>
</table>
Candidates With Priority if Age Within X Years of Donor Age Shifts Kidneys Away From Oldest Candidates

Restrictions to Access to Donors by Candidate Age and Rule (Candidate within X years of Donor Age)

% Donors Available to Candidates

# Newly listed at each year of age

Within 10
Within 15
Within 20
Distribution among newly listed in 2008
Quo Vadis?

- A Luminex-Based, Calculated PRA that incorporates both Class 1 and Class 2.
  - Effectively a transplantability index
- Acceptable Mismatches to assist sensitized patients (possibly regrafts?).
- Exclusion on basis of Class 2, as well as Class 1 DSAs
- Reconsideration of balance between HLA matching and Time Waited
Quo Vadis?

- Avoid offering “older” kidneys to “younger” recipients except on request.

- Avoid offering “younger” kidneys to “older” recipients, unless highly sensitized.

- Beginning to model these variables in Australia

- Greater reliance on age matching, especially for older recipients.
THE END
Sensitization

- Important for outcome
- Makes matching more critical
- More of an issue for women
- How to measure it?
- Currently Class 1, CDC PRA (except WA)
HLA Matching

- HLA Matching (esp. DR) still helps!
- BUT, how does it stack up against:
  - Time on dialysis
  - Quality of kidney
  - Perceptions of equity
- How long is it worth waiting, and how old a kidney is it worth accepting to get matching?
- How much longer should somebody else wait if you get offered a kidney early for matching?
A Potential Starting Point

1. Interstate Exchange based on Acceptable Mismatches if PRA > 50% or regrafts > 20%
2. Interstate Balance Make-up.
3. Last Ditch Make-up (Current Level 7).
4. State Based Priority Patients.
5. If the donor is over 60, then bump up recipients over 60 and others by request.
6. The normal part of the program for donors under 60 years old.
7. Older patients (over 60) relegated if more than 30 years older than the donor.
A Potential Starting Point

8. If the donor is over 60, then bump up recipients over 60 and others by request.

9. The normal part of the program for donors under 60 years old.

10. Older patients (over 60) relegated if more than 30 years older than the donor.

All could be run as National Override for other states’ recipients.
A Potential Starting Point

- If HLA Matching still helps significantly for the “general masses” it is probably mainly DR matching in the young recipient
- Issues as previously discussed

- ? Could have a graded advantage for full DR matches for young patients (<40), e.g. boost by 4 years waiting time if DR matched at 0 years old, reducing to 2 years benefit at 20 years old and nil at 40 years old.