Allocation of deceased donor kidneys: A review of international practices

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SUMMARY AT A GLANCE
This paper summarizes organ allocation for deceased donor kidneys across the globe. It presents a contemporary view of a fairly fast moving field relevant to any nephrologist caring for patients with end stage renal disease.

ABSTRACT:
The demand for kidney transplantation continues to exceed the availability of deceased donor kidneys. Balancing the overarching principles of the optimal use of (utility) and equal access to (equity) this scarce resource requires a sophisticated allocation system. This review will examine how various factors are addressed in allocation systems around the world to strike a balance between utility and equity.

The number of patients awaiting a kidney transplant exceeds the number of kidneys available from deceased donors. Therefore, a system is required to determine how to allocate this scarce resource. The ethical principles guiding allocation are equity (or fairness) and utility.1 Equity requires fair and equal access for all while utility promotes allocation to achieve the greatest benefit. Allocation protocols have been devised predominantly by transplant clinicians; however, some have called for broader community involvement recognizing that donor organs are a public resource.1 Reassuringly, community attitudes from a recent study also supported balancing equity and utility.2 Because these principles are commonly in competition, a compromise must be met. Waiting time generally represents equity principles with those waiting the longest being prioritized, while to meet utility principles, younger recipients and those with greater human leukocyte antigen (HLA) matching are prioritized to achieve the best outcomes (Fig. 1).

A priority point system exists in the backbone of most allocation systems where points are awarded for factors based on their perceived importance. For instance, in the new kidney allocation system (KAS) in the United States (US) implemented in December 2014, four points are awarded for patients who have developed kidney failure after previously serving as a living donor (equity), two points for a zero HLA-DR mismatched donor (utility) and one point for each year spent on dialysis (equity).3 A prior living donor will therefore be allocated a kidney ahead of a zero HLA-DR mismatched recipient who has recently
commenced on dialysis, but not one on dialysis for 5 years. In addition to the priority point system, a proportion of donor kidneys are preferentially allocated to a subgroup of waitlisted patients considered best suited. An example is to prioritize allocation of kidneys with the best-predicted graft survival to recipients with the best-predicted patient survival to maximize utility.

This review discusses factors considered and approaches taken in allocation systems globally attempting to balance utility and equity, summarized in Table 1. Relevant articles and documents were obtained by searching the PubMed electronic database using the search term ‘deceased donor kidney allocation’. In addition, we examined allocation policies of multiple jurisdictions available from their official websites.

**UTILITY**

**Longevity matching**

There is a clear survival benefit from transplantation compared with dialysis which extends to older recipients with medical comorbidities. However, older recipients are more likely to die with a functioning graft. Therefore, unrestricted allocation of kidneys from younger donors (with longer predicted graft survival) to older recipients would result in unrealized graft life-years. Conversely, transplanting kidneys from older donors (with shorter predicted graft survival) to younger recipients will not derive the maximum benefit, with the recipient returning to the waiting list sooner for re-transplantation, placing further demand on the donor pool. Avoidance of transplanting younger donor kidneys into older recipients has been modelled to increase overall graft life years and cost savings. Various allocation policies internationally have implemented ‘longevity matching’ strategies which seek to optimize graft life-years by matching the life expectancy of donor organs with that of recipients. In general, kidneys from younger donors are prioritized to younger recipients or are restricted from being allocated to older recipients.

**Facilitating ‘young-to-young’ and avoiding ‘young-to-old’**

In addition to the paediatric bonus (discussed later), some jurisdictions preferentially allocate younger kidneys to younger recipients. In the United Kingdom (UK), this is achieved by deducting points from pairings with a large donor–recipient age difference. Although variations exist in different provinces of Canada, British Columbia preferentially allocates kidneys from younger donors (≤35 years) to recipients under 55 years to prevent allocation to older recipients.

**Facilitating ‘old-to-old’**

The Eurotransplant program is an international collaboration between Germany, the Netherlands, Austria, Belgium, Luxembourg, Slovenia, Croatia and Hungary. In addition to the conventional allocation system, non-sensitized patients aged ≥65 years are eligible for the Eurotransplant Senior Program to receive kidneys from donors aged ≥65 years to facilitate a reduction in waiting times (3.55 vs. 4.64 years) while achieving comparable 1 year patient survival (86% vs 90%). Although older recipients receiving kidney transplants from older donors have a higher mortality risk, they still benefit compared with waitlisted patients, especially if this facilitates earlier transplantation. However, a recent review in the Netherlands concluded that older recipients may not benefit from receiving kidneys from older donors, compared with waitlisted patients. In fact, mortality was increased from older donation after circulatory death.
donors. Therefore, while allocation of older donor kidneys to older recipients increases utility, it might pose additional risks to this susceptible group.

**Kidney donor profile index and estimated post-transplant survival**

The most significant and novel change in the US Kidney Allocation System (KAS) was longevity matching, based on continuous scores of predicted post-transplant patient survival and graft survival by estimated post-transplant survival (EPTS)\(^{12}\) and kidney donor profile index (KDPI),\(^{13}\) respectively. The scores are based on 4 recipient and 10 donor characteristics, respectively (Table 2). Although this approach replaces dichotomous stratification by recipient and donor age, the EPTS and KDPI scores remain heavily influenced by age. In the new KAS, the top 20% of waitlisted patients with the longest predicted patient survival (EPTS ≤20%) are prioritized for the top 20% of kidneys with the longest predicted graft survival (KDPI ≤20%). As a result, younger donor kidneys are prioritized to younger recipients. In Australia, there is no longevity matching in the current allocation system, but some form of approach is planned. Modelling of this strategy predicts improved overall graft-years (utility) but prolonged waiting times (reduced equity) for recipients aged ≥60 years.\(^{14}\)

Unlike the Eurotransplant Senior Program, higher KDPI kidneys are not preferentially allocated to older patients with higher EPTS in the US. An opt-in system exists for accepting extended criteria donors (with KDPI >85%). Accepting these kidneys may benefit older patients compared with waiting for a lower EPTS kidneys. Prior to the KAS changes, older patients (>50 years) who accepted higher KDPI (71–100%) donor kidneys experienced better long-term survival compared to those waiting for a lower KDPI kidney.\(^{15}\) In addition, a different study demonstrated that older recipients (>60 years) experienced a lower mortality risk beyond the first post-transplant year when accepting kidneys with a KDPI >85%.\(^{16}\)

It is worth noting that KDPI and EPTS scores do not predict graft and patient outcomes with certainty. C-statistic measures how well a score predicts the actual outcome. A c-statistic of 0.5 is equivalent to flipping a coin while 1.0 predicts the outcome perfectly. For KDPI, the average c-statistic is 0.62, representing modest predictive power. It improves to 0.78 (considered good discriminatory power) when comparing donors with the highest and lowest 20%

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**Table 1** Factors considered in deceased donor kidney allocation internationally

<table>
<thead>
<tr>
<th></th>
<th>United States</th>
<th>United Kingdom</th>
<th>Eurotransplant</th>
<th>Australia</th>
<th>Canada</th>
</tr>
</thead>
<tbody>
<tr>
<td>Longevity matching</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>– (To be implemented)</td>
<td>+ (varies amongst provinces)</td>
</tr>
<tr>
<td>Young to young: Low KDPI to low EPTS</td>
<td>+ (Scoring to minimize donor-recipient age difference)</td>
<td>+ (Except in ESP)</td>
<td>–</td>
<td>– (in most provinces)</td>
<td></td>
</tr>
<tr>
<td>HLA mismatch</td>
<td>+</td>
<td>+ (Especially in young recipients)</td>
<td>+</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>A/B/DR importance</td>
<td>DR only</td>
<td>DR &gt; B</td>
<td>DR = B = A</td>
<td>Varies amongst states</td>
<td>–</td>
</tr>
<tr>
<td>Zero mismatch</td>
<td>+</td>
<td>+</td>
<td>Graded</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Waiting time on dialysis</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Highly sensitized</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>cPRA criteria</td>
<td>≥99%</td>
<td>≥85%</td>
<td>&gt;85% (Acceptable Mismatch program)</td>
<td>&gt;80% (1/6 or 2/6 HLA MM) ≥50% (0/6 HLA MM)</td>
<td>≥95%</td>
</tr>
<tr>
<td>Recipient is a prior living kidney donor</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Varies amongst states</td>
<td>+</td>
</tr>
<tr>
<td>Racial minority:</td>
<td>A2 and A2B donor prioritization</td>
<td>O donors allocated</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Blood group B</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Paediatric priority</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Medical urgency</td>
<td>+</td>
<td>Paediatric patients only</td>
<td>+</td>
<td>Varies amongst states</td>
<td>+</td>
</tr>
</tbody>
</table>

C-PRA, calculated panel reactive antigen; EPTS, estimated post-transplant survival; ESP, Eurotransplant senior program; HLA, human leukocyte antigen; KDPI, kidney donor profile index. Recent change in 2018 – from the time of wait listing to the time of dialysis commencement (personal communication).

**Table 2** Factors consider in kidney donor performance index and estimated post transplant survival

<table>
<thead>
<tr>
<th>KDPI</th>
<th>EPTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Age</td>
</tr>
<tr>
<td>Height</td>
<td>Dialysis time</td>
</tr>
<tr>
<td>Weight</td>
<td>Prior organ transplant status</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Diabetes status</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
</tr>
<tr>
<td>Cause of death</td>
<td></td>
</tr>
<tr>
<td>Serum creatinine</td>
<td></td>
</tr>
<tr>
<td>Hepatitis C status</td>
<td></td>
</tr>
<tr>
<td>Donation after circulatory death</td>
<td></td>
</tr>
</tbody>
</table>

KDPI, kidney donor profile index; EPTS, estimated post-transplant survival.
estimated graft survival, supporting these categories of stratification for allocation.\textsuperscript{17} There is, however, a concern that labelling kidneys, ‘high KDPI’ will increase non-utilization rates and compromise overall utility.\textsuperscript{18,19} Similarly, the c-statistic for EPTS is 0.69,\textsuperscript{12} which has been externally validated in Australia and New Zealand.\textsuperscript{20} This suggests that although longevity matching may not be precise for each individual donor-recipient pair, the use of EPTS and KDPI should improve overall utility.

**HLA matching**

Even with contemporary immunosuppression, each additional HLA-A, -B or DR mismatch is associated with a decrease in graft survival.\textsuperscript{21} The median graft survival is substantially superior from a deceased donor kidney with 0 versus 6 mismatches (18.4 and 12.9 years, respectively), although there is no difference between 3 and 4 mismatches (Fig. 2a). Therefore, incorporating HLA matching in allocation algorithms to maximize utility seems sensible. However, its emphasis varies in different jurisdictions as it commonly competes with preferring those who have waited longer on dialysis (equity).

Eurotransplant places most emphasis on HLA matching, awarding points for the absence of each HLA-A, -B or DR mismatch. In contrast, HLA matching is not considered in most Canadian provinces. Most jurisdictions prioritize national sharing of zero-mismatched kidneys across regional borders including the UK, the US and Australia. Globally, there is a trend to place less emphasis on HLA matching. Apart from zero HLA-A + B + DR mismatch, points are only awarded for HLA-DR matching in the US.\textsuperscript{3} In the UK, HLA-DR matching is ranked higher than HLA-B matching while HLA-A matching is no longer considered.\textsuperscript{8}

Certain patients are disadvantaged in allocation systems that favour HLA matching. Ethnic minorities have less common HLA while HLA-homozygous individuals have a reduced probability of receiving a lower HLA-mismatched kidney. To address this, points are awarded for HLA-B and HLA-DR homozygosity in the UK.\textsuperscript{8} To counterbalance their emphasis on HLA matching, the Eurotransplant awards points for patients with rare HLA.\textsuperscript{22}

**EQUITY**

**Waiting time**

Waiting time is the most widely accepted factor for equity and fairness in kidney allocation. To avoid inequalities for those with reduced access to the waiting list, since 2014, the US recently changed by awarding points from the time at wait listing to dialysis commencement\textsuperscript{3} while the UK has also adopted a similar amendment in 2018 (personal communication). Pre-transplant dialysis duration is a strong predictor for post-transplant mortality.\textsuperscript{23} Furthermore, while 13 501 patients received a deceased donor kidney transplant in the US in 2016, 4830 patients died on the waiting list, and a further 4411 patients became too sick and were removed from the list.\textsuperscript{24} Therefore, a fair allocation system minimizes dialysis duration to prevent the development of complications which could prevent patients achieving transplantation.

**Sensitization**

Sensitization to HLA can be induced by previous transplantation, pregnancy and blood transfusion. Some patients develop anti-HLA antibodies against a high proportion of potential donors expressed as the calculated panel reactive antibody (cPRA). Various jurisdictions use different levels of cPRA to define highly sensitized patients (HSP) (Table 1). HSP have reduced access to transplantation and without
prioritization, may miss a rare opportunity to receive a transplant from an immunologically compatible donor. Regional and/or national sharing of organs is commonly required to increase their donor pool. Most programs prioritize kidney allocation to avoid unacceptable antigens (where patients have pre-formed antibodies against donor HLA). In contrast, the Eurotransplant Acceptable Mismatch program prioritizes allocation of compatible kidneys with acceptably mismatched HLA that patients have no antibodies against. Compared with their conventional program, this approach resulted in superior 10 years death-censored graft survival (72.8% vs 62.4%), only marginally inferior to non-sensitized patients (74.8%).25

Unlike the Eurotransplant Acceptable Mismatch program, most registries, including the Collaborative Transplant Study, show inferior graft survival for HSP,26 many of whom had previous transplants (Fig. 2b). Therefore, equity for HSP competes with the principle of utility. Furthermore, some argue that prioritization of HSP for re-transplantation ahead of those who have not yet received their first transplant also conflicts with equity.27 This poses an ethical dilemma for HSP in balancing prioritization with a potential reduction in graft-years.

Prior living kidney donors

Living kidney donors facilitate timely (often pre-emptive) transplantation and superior patient and graft survival over deceased donors. They also alleviate the demand for deceased donor organs.28 Despite its relative safety, there is a small increased risk of kidney failure compared with healthy non-donors.29,30 It seems fair therefore, that many allocation policies incorporate prioritization for prior living kidney donors (Table 1).

Blood group

In most jurisdictions, kidneys are allocated to blood group identical (rather than compatible) waitlisted recipients, with the exceptions of prioritization for HLA sensitization and zero HLA-A + B + DR mismatch. This is to avoid longer waiting times for O recipients that would result if the universally compatible blood group O donor kidneys were allocated to non-O recipients.31 Allocation of kidneys by identical blood group; however, contributes to ethnic minorities being disadvantaged. This is because blood group B, which has the longest waiting time, is more prevalent in ethnic minorities living in Western countries.32 To address this, blood group B (but not A or AB) candidates are eligible to receive O donor kidneys in the UK. Given the long-term success of transplanting A2 and A2B kidneys into blood group B recipients (who often have low anti-A titres),32 A2 and A2B donor kidneys are prioritized to pre-consented B candidates in the US.

Medical urgency and needs

Inadequate dialysis

For patients unable to achieve adequate dialysis and with no further dialysis access options, kidney transplantation becomes an urgent lifesaving treatment. Most allocation policies allow urgent prioritization for such patients. Defining medical urgency eligible for prioritization can however be challenging. In the US, where multiple transplant programs may exist in the same donor service area, the candidate’s transplant physician must receive agreement from other programs.33 For the Eurotransplant program, a ‘Kidney High Urgency’ form needs to be completed. Each application is then evaluated by two members of the Advisory Committee, and in the case of a split decision, a third member will be consulted for a final judgement.34 Similarly, in the state of Victoria in Australia, the candidate’s transplant nephrologist is required to submit a written request for consideration by the Victorian and Tasmanian Kidney Transplant Advisory Committee to reach a consensus.

Paediatric bonus

Children are prioritized in most allocation policies due to the detrimental impact of dialysis and unique benefits of transplantation for growth and development.35 Donor kidneys of higher quality are often coupled with the paediatric bonus to improve graft longevity and delay the need for future re-transplantation (utility). Share-35 was an initiative implemented in 2005 in the US to preferentially allocate young deceased donors (<35 years old) to paediatric patients (<18 years old). Although it doubled the number of transplants from young deceased donors, the majority had 5 or 6 HLA A + B + DR mismatches. In addition, the proportion of paediatric kidney transplants from living donors decreased from 55% to 35%, an unintended consequence.36

Paediatric patients usually require re-transplantation. To minimize HLA-sensitization from poorly HLA-matched kidneys, different strategies have been employed. In the new KAS, paediatric patients receive 1 point if the donor has a KDPI <35% and 3–4 points for a zero HLA mismatched donor kidney.3 In the UK, zero mismatched and well-matched (no DR mismatches) kidneys are prioritized to paediatric recipients.8 Alternatively, rather than promoting HLA matching in a minority of paediatric recipients, the Royal Children’s Hospital in Melbourne, Australia established prospective exclusions of donors with HLA associated with high eplet mismatches for each individual patient. This approach significantly lowered class 2 eplet mismatches while a paediatric point bonus still allowed timely access to transplantation.37
**CASE STUDY: CHANGES TO THE KIDNEY ALLOCATION SYSTEM IN THE US**

In December 2014, the US implemented several amendments to the KAS to optimize the utilization of organs and improve equity for disadvantaged subpopulations. The key changes are outlined in Table 3. These included: (i) longevity matching by preferentially allocating lower KDPI kidneys to lower EPTS patients; (ii) broader regional and/or national sharing of kidneys for highly sensitized patients; (iii) awarding points for waiting time from dialysis initiation to compensate patients with reduced access to the waiting list; (iv) allocation of blood group A2 and A2B kidneys to the B candidates with prolonged waiting times and (v) broader sharing of high KDPI kidneys to reduce the non-utilization rate.3 Some of the goals were achieved, including reducing donor-recipient age mismatch and increasing transplant rates for highly sensitized patients and those with long dialysis waiting times, with a bolus effect.38 While the transplant rate for younger recipients increased, it fell modestly for those aged ≥65 years (who would benefit most from early transplantation). No increase in transplant rates for blood group B recipients was observed due to the low uptake of A2 and A2B kidneys, especially in ethnic minorities for which this initiative was targeted.39 There was also a marginal increase in the non-utilization rate.

Due to broader sharing of organs, cold ischaemic time increased. Delayed graft function also increased from 24.4% to 29.2% across all ischaemic times, suggesting that the issue may relate to transplanting patients with longer dialysis duration. Although the 6 months graft survival has remained similar, longer follow-up is required to ensure that the changes have not resulted in reduced overall graft-years. Some argue that these changes may not have achieved the desired goals and led to unintended consequences.27

**SPECIAL CONSIDERATIONS IN ASIA PACIFIC**

There is wide variation in socioeconomic status in the Asia Pacific region which may impact on universal access to transplantation and the sophistication of deceased donor programs.40 Traditional cultural beliefs might also play a role in low deceased donor rates. For a large economy such as Japan, the deceased donor rate was only 0.72 per million population (PMP) in 2015, in contrast to 9.96 PMP in South Korea and 28.5 PMP in the US.41 To promote organ donation in Japan, organs from deceased donors are preferentially allocated to the donor’s first-degree relatives if they require transplantation. This initially prompted debate regarding the fairness of directed donation disadvantaging other waitlisted patients. Nevertheless, this was ultimately considered acceptable to the Japanese community.42

Precise information regarding allocation policies in most Asian jurisdictions is lacking from the public domain. Most, including China, South Korea, Japan and Hong Kong, report medical urgency, waiting time, HLA matching and sensitization as factors considered in their allocation algorithms.

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**Table 3** Key changes, goals and consequences in the Kidney Allocation System in the United States

<table>
<thead>
<tr>
<th>Key changes</th>
<th>Goals</th>
<th>Consequences</th>
</tr>
</thead>
</table>
| Low KDPI (≤20%) donor kidneys preferentially allocated to low EPTS (≤20%) candidates | Longevity matching to avoid wasted graft years (utility) | • Donor-recipient age mismatch >30 years decreased from 21.1% to 16.3%  
• Recipients aged ≥65 receiving KDPI 0–20% kidneys decreased from 3.2% to 1.1%  
• Recipients aged ≤40 receiving KDPI 0–20% kidneys increased from 7.1% to 12.8%  
• Recipients aged 18–34 increased from 8.8% to 12.8%  
• Recipients aged ≥65 decreased from 22.9% to 18.1%  
• Recipients with cPRA ≥99% increased by 4-fold from 2.4% to 13.4% (after bolus effect; from peak of 14.8% to 12.1%)  
• Recipients with ≤10 years of dialysis vintage increased from 4.3% to 10.9% (after bolus effect; from peak of 13.1% to 7.9%)  
• A2/A2B donor kidneys to B recipients increased from 0.2% to 1.0%  
• No increase in blood group B recipients  
• No decrease in blood group A recipients  
• No increase in use of kidneys with KDPI ≥85%  
• Marginal increase in non-utilization rate from 18.5% to 19.4% |
| Broader sharing of kidneys to highly sensitized candidates with cPRA ≥99% | To increase access to transplantation for highly sensitized patients (equity and fairness) |  
| Stepwise priority points for cPRA ≥20% | To avoid disadvantaging patients with reduced access to early referral for transplantation (equity and fairness) |  
| Points for waiting time from dialysis initiation rather than activation on waiting list | To reduce waiting time for blood group B candidates with longer waiting time than blood group A candidates (equity and fairness) |  
| Blood group A2 and A2B kidneys preferentially allocated to blood group B candidates |  |  
| Broader sharing of kidneys with high KDPI (≥85%) | To reduce discard rate of high KDPI kidneys which may still benefit some recipients (utility) |  

cPRA, calculated panel reactive antigen; EPTS, estimated post-transplant survival; KDPI, kidney donor profile index.
Given low deceased donor rates in Asia, median waiting times are often prolonged, for instance, over 9 years in Singapore. Consequently, kidney transplantation relies heavily on living donors, with access to the deceased donor waiting list restricted to those aged <60 years without comorbidities. Predictably, this is associated with superior waiting list restricted to those aged <60 years without comorbidities. Predictably, this is associated with superior longevity matching is unlikely to achieve significant gains in utility while it seems fair to prioritize dialysis waiting time (equity) in such allocation systems.

In conclusion, with the ongoing shortage of organ donors, striking a balance between utility and equity in the allocation of deceased donor kidneys is challenging. The significant changes to the US KAS were made to address their deficiencies and they have fulfilled some of their goals. Their experience might help other jurisdictions contemplating amendments to their allocation systems. Modelling the impact of potential changes based on local circumstances may help individualize each allocation system to its needs. Achieving an allocation system acceptable to all is challenging and will vary by region and nation and be dependent on available resources. It should consider population factors and be founded on expert opinion but also broader community values and beliefs.

REFERENCES


