

CANADIAN COUNCIL FOR
DONATION AND TRANSPLANTATION



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Deceased Donor Kidney Allocation in the US, Europe, Australia, and New Zealand

October, 2006

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**A paper prepared for the
Canadian Council for Donation and Transplantation**

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October, 2006

As the demand for kidney transplantation increases, the onus is on policymakers to review deceased donor kidney allocation strategies in an effort to strike the right balance between medical efficacy and social equity. The present document reviews current kidney allocation algorithms in the United States, Europe, Australia and New Zealand. For each jurisdiction, the factors that enter into the attribution of deceased donor kidneys are listed in order of their importance. Unique differences among organizations are highlighted.

Introduction

Fueled by the growing patient waiting lists and relative lack of donors, the allocation of deceased donor kidneys is a subject of much current debate. In the early years of kidney transplantation, the prevailing opinion in the transplantation community was that HLA matching was of prime importance, and most allocation schemes were heavily weighted toward close matching. With the passage of time and the introduction of better immunosuppression, other factors are being considered and given greater importance. All the recipient and donor characteristics relevant for kidney allocation are listed in Table 1. Other issues that may be considered include logistic factors such as cold ischemia time and the balance between organ supply and demand in a given area.

Table 1: Factors Taken into Consideration when Allocating Kidneys

RECIPIENT CHARACTERISTICS	DONOR CHARACTERISTICS
HLA Blood Group Age Medical Urgency Need for combined transplant Previous live organ donor Degree of prior sensitization Likelihood of an offer from the donor pool Waiting time	HLA Blood Group Age Donor type: <ul style="list-style-type: none"> • Standard donor (SD) • Expanded criteria donor (ECD) • Donor after cardiac death (DCD)

Depending on the jurisdiction, allocation criteria may differ and/or the weight given to a particular factor may vary. In addition, the rules for local, regional, national or international distribution are specific to each organ allocation body.

National and international organizations with deceased donor kidney allocation algorithms

The principal organizations with well-defined kidney allocation algorithms that will be considered in this document are:

United Network for Organ Sharing (UNOS)

United States

UK Transplant (UKT)

United Kingdom (excluding Ireland)

Transplantation Society of Australia and New Zealand (AUS)

Australia, New Zealand

Eurotransplant (ET)

Austria, Belgium, Germany, Luxembourg, The Netherlands, Slovenia

Etablissement français des Greffes (EfG)*

**Agence de la Biomédecine since May 2005*

France

Organizacion Nacional de Trasplantes (ONT)

Spain

Scandiatransplant (ST)

Denmark, Finland, Norway, Sweden, Iceland

Web links and/or relevant publications are listed in the appended references. These documents can be consulted for the details of the specific allocation algorithms. The present document will focus on the general structure of the allocation systems, highlighting in particular the weight given to various factors in the attribution process and any unique characteristics of each of these allocation policies.

HLA Typing, Crossmatching and Blood Groups

HLA typing of potential kidney recipients and blood group determination are prerequisites for wait listing in all jurisdictions.

In addition, the degree of sensitization must be specified as % panel reactive antibodies (PRA). PRA can be determined using a variety of tests, and the minimum requirements for testing are specified by each organization. Special provisions for highly sensitized patients are included in virtually all kidney allocation schemes (see below).

All deceased organ donors are HLA-typed to permit some degree of HLA matching. The only exception is the ET Seniors Program that allocates kidneys from donors over 65 years

of age to recipients of the same age group who are not sensitized and have a negative crossmatch with their potential donor. HLA matching is not taken into consideration in order to reduce cold ischemia time, and donor HLA typing is therefore not a requirement prior to transplantation.

Kidney offers in all jurisdictions are made *only if donor and recipient are shown to be crossmatch negative* using a standard test specified by the allocation organization. *Donors and recipients must be blood group compatible at a strict minimum*, and some organizations require that kidneys from O donors be reserved for O recipients unless there is no suitable O recipient or an exceptional circumstance exists giving priority to another recipient. Table 2 lists all the blood group regulations currently in effect.

Table 2: Allocation of Kidneys by Blood Group

ORGANIZATION	ALLOCATION RULE
UNOS	O → O, B → B
UKT	O → O or B
AUS	O → O, B → B
ET	Must be blood group compatible If no HLA mismatches, O → O or B If 1 or more mismatches, O → O
EfG	ABO identical takes precedence over ABO compatible
ONT	?
ST	O → O, B → B

HLA Considerations

All jurisdictions currently give priority to zero HLA mismatched kidney recipient-standard donor pairs. Patients with only one antigen identified at an HLA locus are considered to be homozygous at that locus. Mandatory kidney sharing is implemented for zero-mismatched pairs with some differences among organizations as to local versus regional or national attribution.

Certain organizations have special provisions for zero HLA mismatched recipient-donor allocation if the kidney is from an ECD or DCD donor (e.g., UNOS). These kidneys are offered to patients who have given prior informed consent, and local/regional attribution will be attempted before national attribution in an effort to reduce cold ischemia time.

The zero mismatch priority is linked in most jurisdictions to other considerations such as recipient age, degree of sensitization, and payback requirements.

When there is any degree of HLA mismatching, the weight given to the discrepancy varies based on the HLA locus involved. Table 3 summarizes the degree of importance that each organization currently gives to HLA mismatches. The specific point systems are available on the appended web sites and/or in the attached references.

Table 3: Relative Importance of HLA Mismatching

ORGANIZATION	HLA LOCI
UNOS	Only DR taken into consideration since 2003
UKT	DR > A or B
AUS	DR > A or B
ET	DR, A and B mismatches given equal weight
EfG	DR > B > A
ONT	?
ST	DR, A and B mismatches given equal weight

The least stringent current requirement is that of UNOS (only DR mismatches taken into consideration). This change to the allocation scheme was adopted in an effort to direct more deceased donor kidneys to minority groups in the US. Population heterogeneity has been less of an issue in countries outside of the US, but this is now recognized as an increasing problem by organizations such as UKT, AUS, ET and EfG. Although they have not changed their HLA requirements, special consideration is given to patients with rare HLA phenotypes.

In general, the various allocation algorithms give priority to “least mismatching” over waiting time, but the latter enters into the attribution process as a tie-breaker if necessary.

Recipient Age

Pediatric recipients are given special consideration in all allocation systems as indicated in Table 4. The intent is to favor transplantation for children unless other priorities trump pediatric allocation for a given donor. Within the pediatric age group, sensitized recipients are also given priority over non-sensitized patients.

Table 4: Pediatric Allocation Systems

ORGANIZATION	ALLOCATION OF KIDNEYS TO CHILDREN
UNOS	For zero HLA antigen mismatches, extra points given to children < 18 yrs of age (4 pts if under 11, 3 pts if 11-18); Kidneys from donors < 35 yrs of age preferentially offered to candidates < 18 yrs of age.
UKT	<i>Kidneys from adult donors:</i> For zero HLA antigen mismatches, children < 18 yrs have priority over adults; for favourable matches (no DR mismatch and no more than one A and/or B mismatch), children < 18 yrs have priority. <i>Kidneys from donors under 18 yrs:</i> Offered preferentially to pediatric candidates. Only kidneys from donors ≤ 50 yrs of age are offered to children unless an exceptional situation arises.
AUS	Bonus points added for children <18 yrs who started dialysis when <15 yrs of age and who have been on dialysis for over 1 yr.
ET	Pediatric patients up to age 16 receive additional waiting time points based on the age at first dialysis; children also get double points for HLA matching.
EfG	National priority for children < 16 yrs when the kidney donor is < 16 yrs of age; inter-regional priority for children < 16 yrs when the kidney donor is over 16 yrs but under age 30; in both cases, only up to 2 HLA mismatches are tolerated, only one can be a DR mismatch.
ONT	Priority for candidates < 15 yrs of age, specific algorithms vary by region.
ST	Priority for candidates < 16 yrs for kidneys from donors < 40 yrs of age as long as there is DR compatibility and no more than 2 HLA A or B mismatches.

Age considerations are prominent in the UKT allocation algorithm. Wait listed patients are stratified into age bands, and more points are allotted to younger kidney transplant candidates (i.e., 10 points for 18 – 30 year old patients versus 1 point for those 66 years and over). Donor/recipient age difference is also taken into consideration by allotting 10 points for an age difference of up to two years, but only 1 point if the age difference is 30 years or more. In France, certain regions such as Ile-de-France (Paris and environs) have also incorporated age differential into their allocation algorithm since 2004.

Donor Age and Type

Given the progressive increase in donor mean age over time and the declining quality of many donor kidneys, many allocation systems have special provisions for the use of older donor kidneys.

UNOS has defined the concept of the “expanded criteria donor” (ECD) as a donor ≥ 60 years of age or aged 50 – 59 years with any two of the following characteristics: cerebrovascular accident as the cause of death, preexisting hypertension, or final serum creatinine > 1.5 mg/dl (130 μ moles/l). Transplantation of ECD kidneys is associated with an estimated adjusted risk of graft failure $\geq 70\%$ (RR ≥ 1.7) compared to standard donor kidneys (SD). Patient survival is 5% lower at 1 year following transplantation and 8-12% lower at 3-5 years for ECD kidney recipients. Adjusted graft survival for ECD kidneys is 8% lower at 1 year and 15-20% lower at 3-5 years after transplantation compared to SD kidneys. These differences are considered acceptable for certain categories of wait-listed patients given the current shortage of deceased donor kidneys.

In recognition of the fragility of ECD kidneys, UNOS has a distinct point system for their allocation to candidates who have previously agreed to accept such kidneys. The point system is based on waiting time alone, and every effort is made to minimize cold ischemia time by favoring local and regional over national allocation. This is also true for kidneys from donors after cardiac death (DCD).

Although the UNOS definition of ECD donors is not used by other allocation organizations, older donor kidneys are directed to older recipients in those systems that take donor/recipient age differences into account (see above).

ET has a Seniors Program (ESP) that also directs kidneys from donors over 65 years of age to suitable recipients of the same age group without taking HLA matching into consideration.

In contrast to UNOS, ET allocates DCD kidneys through the standard kidney attribution system. Only Germany is excluded where DCD kidney transplantation is prohibited by law.

Most organizations have provisions for the transplantation of two kidneys from a marginal donor to a single consenting recipient (double kidney allocation). In general, these kidneys are from older donors with low estimated creatinine clearances.

Medical Urgency

The concept of medical urgency is part of all allocation algorithms. When a local center identifies a patient with an urgent need for kidney transplantation (often but not always because of dialysis access failure), there is a procedure that can be followed to obtain an allocation priority. Special committees within the allocation organization generally consider these requests on a case per case basis.

Combined Organ Transplantation

When a patient is deemed to require a vital organ transplant (heart, lung or liver) in combination with a kidney, most allocation organizations will give priority to the combined transplant over other kidney allocation considerations.

Previous Live Organ Donor

UNOS has a specific policy concerning previous live organ donors who are waiting for a kidney transplant. An extra 4 points are given to such individuals in the calculation of their overall score.

Degree of Sensitization

It is well-recognized that patients with pre-formed anti-HLA antibodies are difficult to match with potential donors, and that waiting time on the kidney list is longer in all jurisdictions for sensitized versus non-sensitized patients.

In an effort to facilitate transplantation of sensitized patients, all allocation organizations give some degree of priority to patients with elevated PRA (panel reactive antibody). The PRA cutoff and whether or not peak and/or current serum results are important vary among the different organizations. The weight attributed to high PRA is also variable.

Certain organizations have special programs intended to address the issue of sensitization. ET has an Acceptable Mismatch Program for patients with historical or current PRA \geq 85%. Laboratory testing is performed to define the HLA antigens to which a highly sensitized patient has never formed antibodies. This permits attribution of blood group compatible and minimally matched kidneys to such patients on a priority basis. Minimal matching is defined as the sharing of one HLA B and one HLA DR antigen or 2 HLA DR antigens.

Likelihood of an Offer from the Donor Pool

Some allocation organizations have created a database of their donor characteristics in order to predict what the likelihood of a kidney match is for a given kidney transplant candidate. If a patient has a rare HLA phenotype and/or blood group (particularly if highly sensitized), the likelihood of a kidney offer is slim. This is taken into account and some degree of priority is given to these patients by UKT, ET, and EfG.

Waiting Time

Patients waiting for a kidney transplant are given points for accrued waiting time in most allocation algorithms. Waiting time is calculated either from the time of wait listing or from the time of first dialysis depending on the regulations of the allocation organization. Patients can be listed for pre-emptive transplantation; however, they do not automatically get points for waiting time in every allocation scheme. The importance given to waiting time

differs among the various organizations, and no existing algorithm for the attribution of SD kidneys gives more importance to waiting time over the other factors discussed above. In general, waiting time becomes decisive only when two kidney transplant candidates have identical scores in a given allocation scheme. Under these circumstances, the patient waiting the longest will get the kidney offer.

Kidney-Pancreas Allocation

Diabetics who are waiting for kidney-pancreas transplantation are usually given some degree of priority for the simultaneous allocation of the two organs if no other priorities prevail. The attribution of a kidney-pancreas combination is often linked to a payback requirement.

Within UNOS, combined organ allocation on a local level is encouraged unless trumped by another priority. Blood type O kidneys are reserved for blood type O recipients. Length of waiting time is taken into consideration for purposes of allocation. A specific payback policy applies. [Median times to simultaneous pancreas-kidney (SPK) transplantation have decreased in the US from a peak of 542 days for patients listed in the year 2000 to 457 days for those listed in 2003].

UKT specifies that local combined kidney and pancreas transplants may be performed with the kidney counted as a locally retained kidney. The other kidney is allocated through the National Sharing Scheme for zero and favorably mismatched recipients. Balance of exchange is taken into account.

In France, kidney-pancreas candidates ≤ 45 years of age are given priority for combined organ allocation if their PRA is $< 5\%$ and it is a first transplant. Other kidney-pancreas candidates are considered for simultaneous allocation of the two organs, but this is not mandatory.

Tracking and Reporting Systems and Monitoring of Compliance

All organizations track donation and transplantation activity closely, and some monitor for compliance with existing allocation algorithms. A discussion of these practices is beyond the scope of this document, but details are available by consulting the web sites listed in the appended reference section.

Simulation of Allocation Strategies

Several organizations have developed simulation strategies in an effort to predict the results of proposed changes in allocation scoring systems. UNOS, UKT and EfG are particularly active in this regard. After sufficient time has elapsed, these organizations also study the outcome of an allocation change in order to validate their predictive models.

As an example, UNOS eliminated HLA-B matching from deceased donor kidney allocation in 2002-2003. The predicted effect was to decrease the number of transplantations for Caucasians by 4% over a one year period while increasing the number among non-

Caucasians by 6.3%. This change was not expected to significantly affect the acute rejection or graft loss rate. In a recent analysis, the actual effect of the policy change was similar to the predicted effect insofar as the rate of kidney transplantation in Caucasians decreased by 5%, while it increased by 4.9% in all other ethnic groups combined. This was achieved at the expense of less stringent HLA-DR matching in the entire population while improving the transplantation rate for patients with elevated PRA and long waiting times. No difference in graft survival was noted when the pre-policy period was compared to the post-policy period.

In France, simulation software has been developed that allows the Agence de la Biomédecine to study regional donation and transplantation trends, and to predict the effects of policy changes. Individual patients who are waiting for a kidney are given a composite score when a donor becomes available based on the existing allocation algorithm. Each factor entering into the score is given a certain weight based on regional needs. The relative importance of each factor can be varied by region and over time in response to changing donation and transplantation trends, in keeping with an overall allocation strategy that balances efficacy and equity. This type of analysis allows for rapid “fine tuning” of the scoring system. Major changes in allocation practice are not allowed to occur precipitously, and skewing attribution of kidneys to any one patient subgroup is not permitted indefinitely.

Waiting Time Statistics

All jurisdictions are reporting a progressive increase in demand for kidneys which cannot be met by current supply. The waiting time for a deceased donor kidney continues to lengthen, and the overall median time to transplant for new patients added to the waiting list in the US cannot be calculated beyond 2001 when it was 1176 days. This is true despite an unprecedented 11% increase in donation between 2003 and 2004 in the US, attributed, at least in part, to the US Organ Donation Breakthrough Collaborative.

In general, current allocation systems favor early transplantation for children, but other patient sub-groups must wait for several years especially those who are sensitized or who have rare HLA phenotypes. Blood group O patients are disadvantaged with respect to all other blood groups. Distinct regional disparities also exist, especially in the US.

The demand for deceased donor kidneys has been partially met by expansion of the donor pool. More kidneys from ECD and DCD donors are being transplanted every year. In 2004, 15% of transplanted kidneys in the US were from ECD donors. Between 2003 and 2004, DCD donors increased by 39% (although the absolute numbers of these transplants remains small). The rise in ECD and DCD donation has prompted many organizations to consider some type of age-matching in kidney allocation.

Waiting time before kidney transplantation is calculated in a variety of different ways depending on the organization. Current waiting times and calculation methods are reported annually by most organ procurement organizations and can be accessed online.

Summary

This paper reviews deceased donor kidney allocation in the US, Europe, Australia and New Zealand. Although all countries consider similar key donor and recipient characteristics when developing allocation algorithms, the importance allotted to each of these factors varies by jurisdiction. Most existing systems try to strike a balance between medical efficacy and equity. In order to optimize kidney allocation, careful analysis of donation and transplantation trends is an integral part of the activity of all the organizations reviewed, and some have developed powerful tools that can help to identify problems and to simulate the impact of proposed solutions. As waiting lists and waiting times lengthen, allocation practices are coming under greater scrutiny to ensure that a scarce resource is used appropriately. This comparison among various countries underlines that certain problems are shared by all jurisdictions and call for similar solutions, whereas some issues are unique and must be dealt with nationally or regionally. It is clear that policymakers are increasingly preoccupied with the issue of kidney allocation, and that a concerted effort is being made in many countries to analyze and improve existing systems to ensure the best possible outcomes.

Acknowledgement

The author would like to thank Ivan Shaw PhD for his assistance in collecting the country-specific data on kidney allocation for this paper.

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Websites

UNOS/OPTN

www.unos.org

UK Transplant

www.uktransplant.org

Transplantation Society of Australia and New Zealand

www.racp.edu.au/tsanz/

Eurotransplant

www.eurotransplant.org

Agence de la Biomedecine (France)

www.agence-biomedecine.fr

Organizacion Nacional de Trasplantes (Spain)

<http://donacion.organos.ua.es/ont/>

Scandiatransplant

www.scandiatransplant.org