Kidney Allocation Concepts

Request for Information

Issued by: The OPTN/UNOS Kidney Transplantation Committee

The Organ Procurement and Transplantation Network (OPTN) is seeking comments regarding the use of three concepts in the allocation of deceased donor kidneys.

Circulated for Consideration September 24, 2008 through December 18, 2008

Table of Contents

Request for Information (RFI) Instructions

Key Dates

Release Date: September 24, 2008
Responses Due By: December 18, 2008 by 11:59pm (PCT)

Issued by

United Network for Organ Sharing (UNOS) as the organization designated as the Organ Procurement and Transplantation Network (OPTN) by contract with the Health Resources and Services Administration (HRSA)

Purpose and Background

Purpose

UNOS is requesting input on concepts for possible incorporation into the allocation system for deceased donor kidneys. The targeted questions asked are intended to reveal gaps and highlight specific opportunities for action that will improve kidney allocation in the United States.

Background

The current kidney allocation system has been in place for more than 20 years. During this time, some changes have been made, but the system cannot keep up with current trends in medicine. As waiting times for kidney transplant increase throughout the United States, the need for review of the current system and discussion of possible revisions is great. This RFI is the next step in a series of events (including public hearings and a public forum) designed to gather public feedback and promote dialogue on allocation concepts.

The OPTN/UNOS Kidney Transplantation Committee (the Committee) has considered many concepts and approaches to allocation over the past four years. Throughout its review, the Committee has been including concepts that meet the requirements of the OPTN Final Rule and the *UNOS Statement of Principles and Objectives of Equitable Organ Allocation.* The Committee is now considering the following three concepts that would work together to determine a candidate Kidney Allocation Score (KAS):

- *Life Years from Transplant (LYFT):* determines the estimated survival a recipient of a specific donor kidney may expect to receive versus remaining on dialysis. LYFT is primarily a measure of utility.

- *Dialysis Time (DT):* Time spent on dialysis allows candidates to gain priority based upon the length of time they have been receiving this treatment, adding the essential element of justice into the allocation system.

- *Donor Profile Index (DPI):* provides a continuous measure of organ quality based on clinical information. DPI increases individual autonomy by providing a metric for deciding which organs are appropriate for which candidates.

LYFT, DPI, and DT are incorporated so that kidneys are matched to candidates based on the expected survival of both the kidney and the recipient.

Information Requested

UNOS welcomes your comments on all aspects of the document; however, your feedback as a transplant professional, candidate, recipient, donor family member, or member of the public on how to improve the kidney allocation system is most particularly desired. Responses to the following questions are of the most interest to the Committee:

1. **Life Years from Transplant (LYFT)**
   Please describe any limitations to the use of LYFT in an allocation system. Equally, are there any benefits you see to incorporating LYFT? If so, please concisely describe them.

2. **Donor Profile Index (DPI)**
   Please describe any limitations to the use of DPI in an allocation system. Are there any benefits you see to incorporating DPI? If so, please concisely describe them.

3. **Dialysis Time (DT)**
   Please describe any limitations to the use of DT in an allocation system. Alternately, what benefits do you see to incorporating DT? Please concisely describe them.

4. **Solutions to Limitations**
   Please concisely describe specific approaches or concepts that would address any of the above limitations.

How to Submit a Response

Responses will be accepted until December 18, 2008. They may be submitted electronically by e-mail to kidneypolicy@unos.org. Attachments are permitted in the following formats: .pdf, .doc, .txt.

Please note, e-mail addresses will not be shared with reviewers, only information contained in the subject line and body of the e-mail will be shared. If you do not wish to be identified by your response, do not include identifying information in the e-mail subject line, body or attachments.

For those without internet access, responses may be faxed to 804-782-7896 (attention: Kidney RFI Coordinator), or mailed to:

Attention: Kidney RFI Coordinator
United Network for Organ Sharing
700 N 4th Street
Richmond, VA 23219

The collected information may appear in reports. Although UNOS will try to protect against the release of identifying information, there can be no guarantee of confidentiality.

A summary of the results obtained from the responses to this RFI will be available to the public on the following websites: www.unos.org and www.optn.org.

How to use this document

This RFI is broken into sections for your review. Like an encyclopedia, sections start with very basic information and increase in complexity. Those who have an interest in methods and statistics will find such information at the end of the sections or in attachments to this document. Specific questions appear throughout the document in blue boxes.

RFI Question #1: Example

Please describe any limitations to the use of LYFT in an allocation system. Equally, are there any benefits you see to incorporating LYFT? If so, please concisely describe them.

Executive Summary

The OPTN/UNOS Kidney Transplantation Committee believes that the concepts presented in this document will most effectively improve kidney allocation for the now almost 79,000 candidates currently awaiting kidney transplantation. The supply of deceased donor organs is limited, and the demand is great. When combined into an approach for allocation, the concepts described below are designed to provide equitable access to kidney transplantation for all candidates, while improving the outcomes achievable from the transplantation of the limited supply of precious organs.

The OPTN/UNOS Kidney Transplantation Committee conducted an extensive, three-year long review of kidney transplantation. From these deliberations, the Committee found that the current allocation system has several limitations. First, the current kidney allocation system is heavily reliant upon the length of time a candidate has been on the OPTN Waiting List. Unlike the liver and lung allocation systems, kidney allocation is not based on a number of other available objective medical criteria. Secondly, the current system does not match donors and recipients well. The result is that kidneys with long projected post-transplant survival commonly are allocated to candidates with expected short post-transplant survival. Partly as the result of this allocation, death with a functioning graft is now the most common cause of kidney graft failure. Finally, unlike the allocation systems for livers and lungs, the Committee found that the current kidney allocation system has no agreed upon central goal such as reducing waitlist mortality or improving post-transplant survival.

The Committee concluded that the current system could be improved by the inclusion of several new allocation concepts including:

- Ranking candidates based upon objective medical criteria using survival with transplant compared to survival with dialysis, termed Life Years from Transplant (LYFT).
- Classifying of donor kidneys with a continuous measure called a donor profile index (DPI).
- Changing waiting time from time since being added to the OPTN Waiting List to the time from the start of dialysis (DT) regardless of when the candidate was listed.

These three major concepts could be combined in a novel way so that candidates have equitable access to deceased donor kidneys, and those donor kidneys are matched more appropriately with potential recipients. In this system, kidneys with longer potential for survival would be allocated primarily to candidates with longer expected survival. This approach should result in fewer re-transplants and lower rates of death with a functioning graft.

The Committee also concluded that the following other important changes to kidney allocation could improve the system when combined with the three major concepts described above:

- Maintaining priority for pediatric candidates and for candidates who were prior living organ donors.

- Changing prioritization rules for sensitized candidates in order to provide increasing priority based on the degree of sensitization, thus improving access for moderately sensitized candidates.

- Eliminating the absolute priority for zero-antigen mismatches to unsensitized candidates while still providing access for highly sensitized adult candidates and pediatric candidates. The kidney payback system also would be eliminated.

- Allocating kidneys to simultaneous pancreas-kidney (SPK) candidates similarly to the way in which kidneys are allocated to liver-kidney and heart-kidney candidates. The pancreas allocation algorithm would determine placement for SPK transplantation.

- Allowing blood group B candidates to be offered blood group A_2 or A_2B donor kidneys when clinically appropriate.

Compared to the current system, the concepts described here are expected to increase the overall number of life years gained from the kidney allocation system by over 3,000 years in its first year of operation. Additionally, transplantation rates for minority candidates, as well as highly and moderately sensitized candidates would be expected to improve. Additionally, when combined into an allocation system, these concepts would be expected to provide transplant professionals and candidates with individualized information regarding survival benefit from transplantation.

Background and Significance

In 2004, the OPTN/UNOS Board of Directors charged its Kidney Transplantation Committee[1] with conducting a comprehensive review of the national kidney allocation system. In response, the Kidney Allocation Review Subcommittee (KARS) was formed and was tasked first with reviewing the system from multiple perspectives and then analyzing ways of improving kidney allocation in the United States. Throughout this process, KARS and the Kidney Transplantation Committee have sought and obtained feedback from members of the transplant community including: transplant professionals, candidates, recipients and donor families. This feedback has been essential to the development of the following concepts.

Review of Regulatory Requirements and System Performance

The review process began in early 2005 with a review of the National Organ Transplant Act (NOTA) of 1984 and the OPTN Final Rule, which set forth the requirements for organ allocation policies.[2,3] NOTA requires the Secretary of the Department of Health and Human Services (HHS) "by contract [to] provide for the establishment and operation of an Organ Procurement and Transplantation Network which meets the requirements of subsection (b) of this section." Under NOTA, as amended, the OPTN is required to:

- "establish . . . medical criteria for allocating organs and provide to members of the public an opportunity to comment with respect to such criteria,
- assist organ procurement organizations in the nationwide distribution of organs equitably among transplant recipients,
- recognize the differences in health and in organ transplantation issues between children and adults throughout the system and adopt criteria, policies, and procedures that address the unique health care needs of children, and
- carry out studies and demonstration projects for the purpose of improving procedures for organ donation, procurement and allocation."

In 2000, HHS promulgated the OPTN Final Rule, which is a set of federal regulations for the operation of the OPTN. Pursuant to the OPTN Final Rule, the Board of Directors of the OPTN shall develop policies "for the equitable allocation of cadaveric organs among potential recipients." In addition to being "equitable," the OPTN Final Rule directs that policies shall:

- "be based on sound medical judgment,"
- "seek to achieve the best use of donated organs,"

[1] In 2004, the Committee was the OPTN/UNOS Kidney and Pancreas Transplantation Committee. In 2005, a separate committee to examine pancreas allocation issues was established.
[2] Final Rule
[3] NOTA

- "be specific for each organ type," and
- "be designed to avoid wasting organs, to avoid futile transplants, to promote patient access to transplantation, and to promote the efficient management of organ placement."

The UNOS Statement of Principles and Objectives of Equitable Organ Allocation provides additional historical guidance for allocation policies and stipulates that organs should be allocated "based upon medical criteria, striving to give equal consideration to medical utility (i.e., net medical benefit to all transplant patients as a group) and justice (i.e., equity in distribution of the benefits and burdens among all transplant patients)."

Limitations of the Current Allocation System

The architecture of the current deceased donor kidney allocation system was developed in the 1980's and 1990's based upon the best information and practices available at the time. New medical insights and experience with the allocation of deceased donor livers and lungs suggest that improvements in patient and allograft survival could be achieved in kidney allocation. Advances in transplant medicine (including immunosuppression, histocompatibility assessment, and preservation of donated kidneys) have outpaced changes in the allocation system. To assess the limitations of the current allocation system, KARS held a series of focused public hearings in 2005 (Appendix 1). These hearings, which were publicized and open to the public, helped the Committee understand the scope of the issues associated with the current system. A broad range of transplant professionals, patients and the general public participated in these hearings. The major topics for the public hearings included:

- Review of Current Allocation System,
- Scope of End Stage Renal Disease (ESRD),
- Ethical Issues,
- Barriers to Access Issues,
- OPO Issues,
- Introduction to New Allocation Systems,
- Histocompatibility Issues,
- Patient Issues,
- Minority Issues,
- Specific Biologic Issues Such as Those of Diabetes,
- Net Benefit Model, and
- Transplantation in Other Countries.

These public hearings helped the Committee identify the following limitations of the current allocation system:

- the general inefficiency of procedures for placing kidneys from expanded criteria donors (ECD), which lead to high discard rates of otherwise transplantable kidneys,
- the lack of predictability of kidney allocation, which makes maintenance of current medical workups for candidates on the list difficult,

- the great variability in access to transplantation by blood group and geographic location for otherwise clinically similar candidates,
- the inefficiency of current methods of identifying and allocating kidneys to sensitized candidates, and
- the mismatch between expected graft and patient survival resulting in death with a functioning graft in many patients and an increase in the need for retransplantation for many other patients.

Even with additional priority given to sensitized candidates, highly matched kidneys, and children, the current system (which has evolved over time into being primarily based on waiting time), does not adequately balance utility and justice factors. The current allocation system utilizes few of the specific objective medical criteria that are now available to rank candidates.

In addition to the above described limitations of the current system, the changing demographics of the waiting list have introduced additional challenges for kidney allocation. In 2005, as reported by the United States Renal Data System, the prevalence of end stage renal disease (ESRD) in the U.S. was 341,000.[4] At the time of this RFI, there were 76,502 candidates registered for kidney transplantation and 2,278 registered for kidney-pancreas transplantation.[5] In contrast, in 1996 there were 28,757 candidates awaiting kidney transplantation and 1,194 awaiting kidney-pancreas transplantation.[6]

The gap between the number of kidneys available for transplant and the number of candidates on the waiting list is large and expanding. While the number of deceased kidney donors rose 33% between 1996 and 2005 (from 5,037 to 6,700), the increase was not enough to keep pace with the new additions to the waiting list. In addition to the growth of the waiting list over the past decade, demographics of the candidates on the waiting list have changed, most profoundly with a large increase in the listing of older candidates. It is important to note that the age of donors, candidates, and recipients is easily available and is always recorded, but that age in and of itself is not the determining factor in the current or proposed kidney allocation system for adults (pediatric age candidates are afforded a preference by NOTA). In determining health status, age is used as a factor along with numerous other factors such as diabetes or hypertension. Health status is always the factor that is being measured. However, age is a commonly used point of reference in roughly estimating the effects of organ allocation policies. As shown in Figure 1, the waiting list has aged disproportionately over the past decade. The number of candidates in the 50-64 and 65+ age categories has increased substantially, while the number of candidates under the age of 35 has remained stable.

---

[4] U.S. Renal Data System, USRDS 2007 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2007.

[5] OPTN Data, accessed August 12, 2008. http://www.optn.org/data/.

[6] USTransplant.org accessed February 2, 2008. http://www.ustransplant.org/annual_reports/current/801a_age_kp.htm .

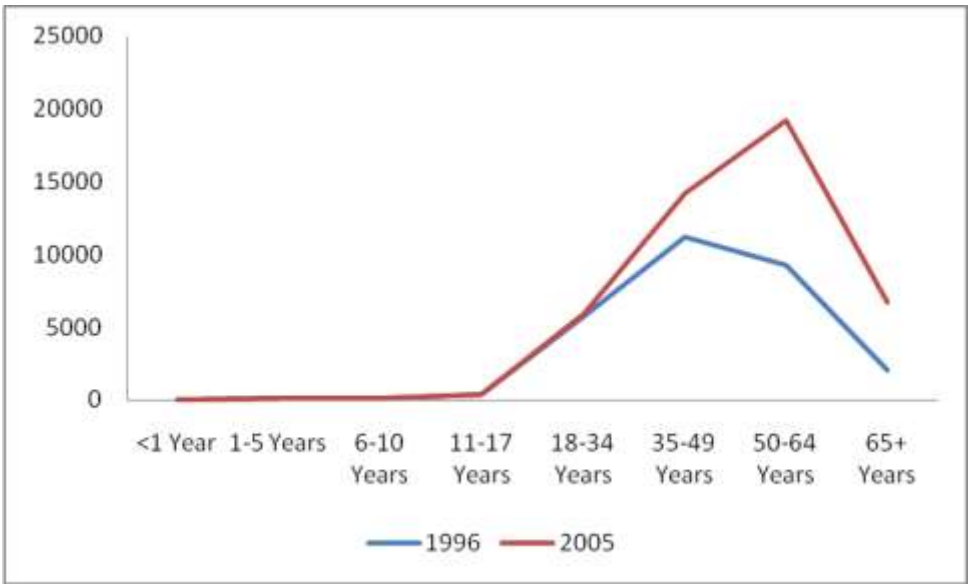


Figure 1: Number of active candidates on the kidney transplantation waiting list by age category (www.ustransplant.org)

In parallel to this increase, the number of older donor kidneys available, has increased. Unfortunately, discard rates of such kidneys (termed expanded criteria donor [ECD] kidneys) are high, possibly due to inefficient allocation. The expanding waiting list is leading to longer waiting times for kidney transplantation for all candidates (Figure 2). Due to increasing waiting times, candidates with longer estimated post-transplant survival may opt to receive ECD kidneys under the current system, potentially increasing the need for retransplants. These changing demographics, the increasing demand for kidney transplants, and the advances in the field of transplantation, necessitated a thorough review and reconsideration of the kidney allocation system including its objectives.

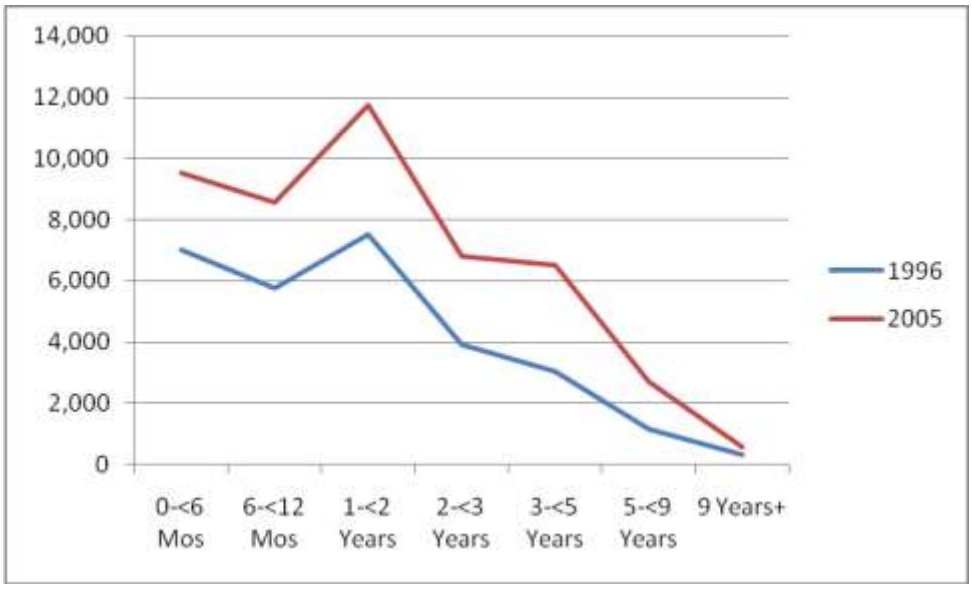


Figure 2: Time waiting by number of active candidates on the kidney transplantation waiting list (www.ustransplant.org)

Allocation systems are limited in the objectives that they can achieve. Some issues, such as the shortage of available kidneys or the lack of access for underinsured populations can only be minimally addressed through allocation policy. While the approach described in this proposal will not solve all of the limitations of the current kidney allocation system (e.g., differences in waiting times due to a candidate's geographic location), it does provide a tool for an objective, quantitative analysis of geographic differences. This analysis could inform future policy development to reduce geographic disparities.

Improvements to the kidney allocation system could be defined and achieved in a number of ways. For example, allocation that prioritizes only the candidates with the greatest survival benefit would improve the overall survival rates for those receiving a transplant. However, such an approach would not provide acceptable access to transplant for many candidates. The Committee did investigate such a system and determined that survival improvements must be tempered to ensure that all candidates have equitable access to transplant opportunities. As such, the concepts presented here incorporate a measure of survival benefit (LYFT) with time on dialysis (DT). These elements are combined based on donor characteristics to rank-order candidates.

Summary

Based on the requirements of NOTA and the Final Rule, the objective analysis of the current system and of several potential alternative systems and public input, the Committee undertook a process to investigate several different approaches to better achieve equitable kidney allocation. This process involved examination of the current system to determine areas for improvement, establishing goals and objectives for the allocation of kidneys, and simulation modeling to test the effects of several possible approaches to kidney allocation. The concepts presented here represent the approach that the Committee believes would best improve kidney allocation by increasing the longevity of kidney transplant recipients, by increasing the number of years that donated kidneys function, and by maintaining access to kidneys from both deceased donors and living donors for individuals with ESRD in the United States. The purpose of this RFI is to obtain feedback for the committee as to whether the Committee's beliefs in that regard are correct and to solicit advice regarding improvement of the kidney allocation system.

Chosen Allocation Concepts

Objectives for Kidney Allocation

Early in the review process the Committee recognized that kidney allocation policy must be based upon very different considerations than the newly updated liver and lung allocation policies. The OPTN Final Rule recognizes that kidney transplantation is unique as a treatment option due to the availability of dialysis for candidates suffering from renal failure. The OPTN Final Rule provides that "rankings shall be ordered from most to least medically urgent (taking into account, in accordance with paragraph (a) of this section, and in particular in accordance with sound medical judgment, that life sustaining technology allows alternative approaches to setting priority ranking for patients)."

The liver allocation policy was recently modified with the central goal of reducing the number of deaths of candidates who are on the waiting list. The lung allocation system was also recently modified with the goal of reducing deaths of candidates who are on the waiting list and improving recipient survival during the first year following transplant. While these goals are appropriate for the allocation of livers and lungs, any goal for allocating kidneys is affected by the availability of life-saving therapy (i.e., dialysis) that is not available to candidates in organ failure for livers, hearts, and lungs. The goal of reducing deaths of candidates who are on the waiting list may not be appropriate for kidney allocation because such deaths are not necessarily due to lack of a kidney transplant but may be due to co-morbid conditions such as heart disease, diabetes, and dialysis related complications. Furthermore, for kidney allocation the goal of reducing deaths of candidates who are on the waiting list would mean that candidates who could initially benefit greatly from a kidney transplant must remain on dialysis *longer* until they deteriorate to the point where their projected waitlist mortality has sufficiently increased to receive a transplant.

Due to the availability of other treatment options for ESRD patients, the Committee decided that the goals for other organ allocation policies of reducing waiting list mortality should not be applied to kidney allocation. Instead, the kidney allocation policy should have the goal of providing equitable access for kidney transplant candidates to deceased donor kidneys for transplantation while improving the outcomes of recipients of such kidneys. . Ultimately, these goals should drive improvements in reducing geographic differences in transplant rates, addressing the needs of candidate populations that face unique biologic challenges, decreasing discard rates, improving predictability of candidate priority on the waiting list, and allowing for the use of medical judgment.

Components of the Kidney Allocation Score (KAS)

The KAS is calculated based upon years on dialysis, termed time on dialysis (DT); expected life years from transplant (LYFT); a measure of organ donor quality, called the Donor Profile Index (DPI); and calculated panel reactive antibody (CPRA) through the formula shown below. The following is a description of each of the components of the KAS. For ease of reference, the following acronyms are frequently used:

- LYFT, life years from transplant,

- DPI, donor profile index
- DT, dialysis time
- CPRA, calculated panel reactive antibody (a measure of candidate sensitization)
- KAS, kidney allocation score

Previously, many in the transplant community understood quality of life as the primary benefit of kidney transplant. However, research on survival following dialysis and kidney transplantation indicates that nearly all candidates with ESRD are predicted to live longer with kidney transplant than on dialysis.[7] The number of additional survival years following transplantation varies based on candidate and donor factors, and some recipients live substantially longer with transplant than others. Therefore, a metric that rank-orders candidates according to the difference between their expected survival on dialysis and expected survival with a functioning kidney graft would prioritize candidates with higher medical urgency *and* those with longer post-transplant survival. The OPTN Final Rule provides for a measure of evaluating allocation policies that involves measuring life-years of benefit. For each organ-specific allocation policy, the OPTN is to provide data to assess organ allocation including "risk-adjusted total life-years pre- and post-transplant."[8] Thus, evaluation of the effectiveness of organ allocation policies based on the concept of life-years is specifically contemplated by the OPTN Final Rule. Incorporation of net benefit into the kidney allocation system is appropriate as a measure of utility, to be balanced with measures of justice. The metric the Committee is considering has been termed "life years from transplant" and given the acronym "LYFT."

LYFT accounts for two important outcomes in kidney allocation: estimated survival on dialysis and estimated survival following transplant. However, *no single metric* can achieve the above stated goals for allocation. As such, LYFT is only one concept under consideration. Other elements to account for, among other things, candidate sensitization level, candidate time on dialysis and the differences in deceased donor kidneys are also being considered. The combination of these elements results in a kidney allocation score (KAS) for each candidate.

Since LYFT is a utility-based metric, it must be balanced by a metric that is created to represent justice in the kidney allocation system. For this reason, a candidate's time on dialysis (DT) will be factored into the calculation of the KAS. The weights applied to a candidate's LYFT score and time on dialysis will be determined each time that a kidney from a deceased donor becomes available based on the DPI score. The formula for determining KAS is provided below.

[7] Wolfe, Robert A., Ph.D., Valarie B. Ashby, M.A., Edgar L. Milford, M.D., Akinlolu O. Ojo, M.D., Ph.D.,Robert E. Ettenger, M.D., Lawrence Y. C. Agodoa, M.D., Philip J. Held, Ph.D., and Friedrich K. Port, M.D. "Comparison of Mortality in All Patients on Dialysis, Patients on Dialysis Awaiting Transplantation, and Recipients of a First Cadaveric Transplant." N Engl J Med 1999; 341:1725-30.

[8] 42 C.F.R

Kidney Allocation Score (KAS) Formula

(KAS) = LYFT * 0.8 * (1-DPI) + DT * (0.8*DPI + 0.2) + (CPRA*4/100)

How is the LYFT score calculated?

LYFT is defined as the difference between a candidate's post transplant survival (the candidate's projected lifespan following a transplant) minus waitlist survival (the projected survival for that candidate while remaining on dialysis without ever receiving a transplant). Waitlist survival is made up entirely of time on dialysis, while post-transplant survival includes survival with a functioning transplant and survival on dialysis after any failure of that allograft. The dialysis survival component of LYFT (both on dialysis and after any graft failure) is adjusted by a factor of 0.8 to account for the diminished quality of life (QoL) reported by candidates on dialysis. The factor of 0.8 was selected based on studies of candidates on the kidney transplant waiting list as reported in the peer-reviewed literature. [9,10] The LYFT formula is provided below. A working paper on the methods for calculating LYFT is included as Attachment A.

Life Years From Transplant (LYFT) Formula

LYFT= (estimated survival with transplant from available donor) – (estimated survival on dialysis)

Please note that estimated survival on dialysis is adjusted for quality of life by a factor of 0.8. Additionally, graft failure after transplant is accounted for in the equation and is also adjusted for quality of life by a factor of 0.8.

LYFT is calculated based on clinical factors for both the candidate and the donor. The calculation was developed based on data from actual transplant candidates who were active on the waiting list on January 1, 1988, 1990, 1994, 1998, and 2002 and recipients during the period 1997 – 2006.[11] As described below, the factors used in the LYFT calculation were selected based on their objectivity, statistical significance, clinical importance, and quality of available data.

- **Objectivity**
  NOTA and the OPTN Final Rule require that allocation systems be equitable and based upon objective medical criteria. Therefore, the data elements selected need to be consistent and reproducible across transplant centers. For example, the calculation for body mass index (BMI) can be replicated reliably for all transplant candidates. Factors such as the determination of candidate

[9] Laupacis A, Keown P, Pus N, Krueger H, Ferguson B, Wong C, Muirhead N. A study of the quality of life and cost-utility of renal transplantation. Kidney Int. 1996 Jul;50(1):235-42.
[10] Hornberger JC, Best JH, Garrison LP Jr.Cost-effectiveness of repeat medical procedures: kidney transplantation as an example. Med Decis Making. 1997 Oct-Dec;17(4):363-72.
[11] A detailed paper of the methods used to calculate LYFT may be accessed at www.optn.org/kars.asp

race or ethnicity, however, may not be able to be replicated reliably for all transplant candidates and as such are not utilized in the current proposal.

- **Data Quality**
  Since the analyses rely on actual data collected from 1988-2006 on kidney transplant candidates and recipients, data elements selected for LYFT had to be available during this time period in order to be utilized. Data elements that were discontinued were also eliminated from the calculation, as these cannot be used for allocation in the future. Data elements added to UNet[sm] too recently to assess their relationship with outcomes (patient and graft survival) were also not included in the LYFT calculation.[12] Additionally, many of the data elements in UNet[sm] are optional, meaning that the amount of data may be too limited to be of use. The Committee excluded those data elements where the data quality or completeness was compromised. In the future, data elements could be added to improve the predictability of the LYFT calculation.

- **Statistical Significance or Clinical Importance**
  Each data element was assessed to determine if it had a statistically significant effect on the LYFT calculation; elements not found to be significant were excluded. Data elements which were not found to be clinically important (e.g., type of dialysis treatment) were also excluded.

The following variables are included in the LYFT calculation:

- Candidate age at offer
- Zero antigen mismatch
- Degree of mismatch at the HLA-DR loci
- Candidate and donor located in same donor service area
- Donor after cardiac death
- Donor age
- Donor cause of death
- Donor CMV serology
- Donor hypertension
- Donor weight
- Candidate years on dialysis at offer
- Candidate BMI
- Candidate albumin
- Candidate diabetes status
- Candidate previous transplant
- Candidate CPRA
- Candidate diagnosis of polycystic disease

While there are some donor factors included in the LYFT calculation, these factors will not affect the relative ranking of candidates, only the value of candidate LYFT scores. These factors are included because donor characteristics affect the post-transplant graft and recipient survival. Some data

[12] UNet[SM] is the web-based electronic utility used by the OPTN contractor to conduct the business of the OPTN. UNet[SM] comprises the Match System, all software, applications and security architecture needed for the collection, modification, validation, reporting, management and redundancy of data associated with the tasks and activities of the OPTN.

elements were considered and then excluded from the LYFT calculation because they did not meet one or more of the above criteria for objectivity, statistical significance, clinical importance, or data quality. These data elements included candidate angina noted, candidate cerebrovascular disease, candidate peripheral vascular disease, candidate previous malignancy, candidate gender, candidate insurance status, candidate drug-treated hypertension, type of dialysis, candidate race/ethnicity, HLA-A and HLA-B loci, and candidate diagnosis of glomerular nephritis or hypertension

Methods for estimating patient and graft survival

In order to estimate the patient and graft survivals necessary for the LYFT calculation, median survival was used. Median survival is the point at which half of the candidates in the cohort are alive. As shown in Figure 3, there are three survival curves: a curve for the candidates on the waiting list, and curves for recipients of average SCD and ECD kidneys. Median survival is determined on each curve. The advantages of median survival are that it is statistically stable and can be estimated based on available data. Figure 4 provides an example of how median survival is used in the LYFT calculation.

An alternative approach to estimating survival would be to truncate survival for all candidates at an arbitrary point (e.g., after five or ten years). The Committee reviewed time horizons of 10, 15, 20, 25, and 30 years of life with and without kidney transplantation in several iterations of the analytic model. The time horizon selected was found to impact allocation priorities. For example, shorter time horizons favored patients with relatively worse waitlist survival, while longer time horizons appear to favor patients with greater opportunity for life post-transplant. The Committee also considered the HHS Program Goal to increase the average number of life years gained in the first five years after transplantation for deceased kidney/kidney-pancreas transplants by 0.003 life-years annually, until the goal of 0.436 life-years gained per transplant is achieved in 2013.[13] However, the Committee did not consider the five year time frame to be a recommendation for a time horizon in the analyses. The Committee determined that the truncated survival approach was inappropriate because kidney transplant recipients experience relatively long post-transplant lifetimes.

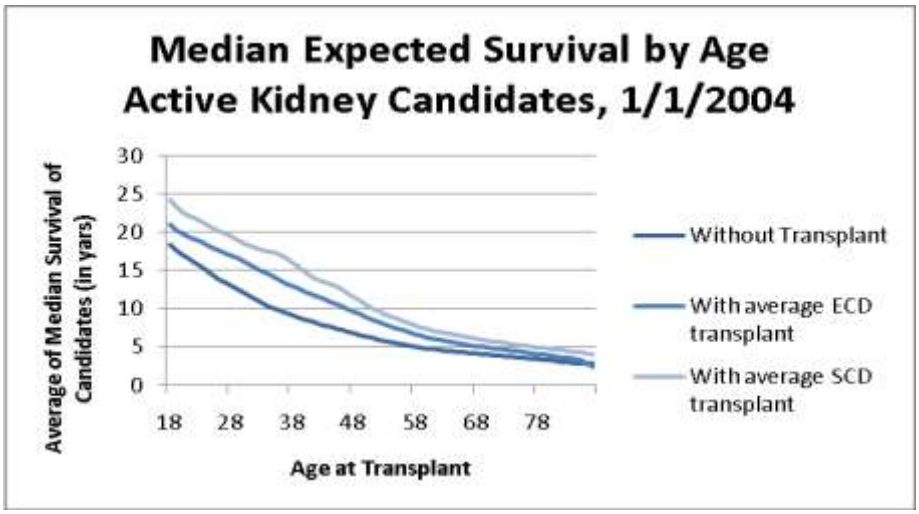


Figure 3: Median expected survival by age (based on active candidates from January 1, 2004)

[13] http://www.hrsa.gov/about/budgetjustification07/HealthCareSystemsPerformanceAnalysis.htm

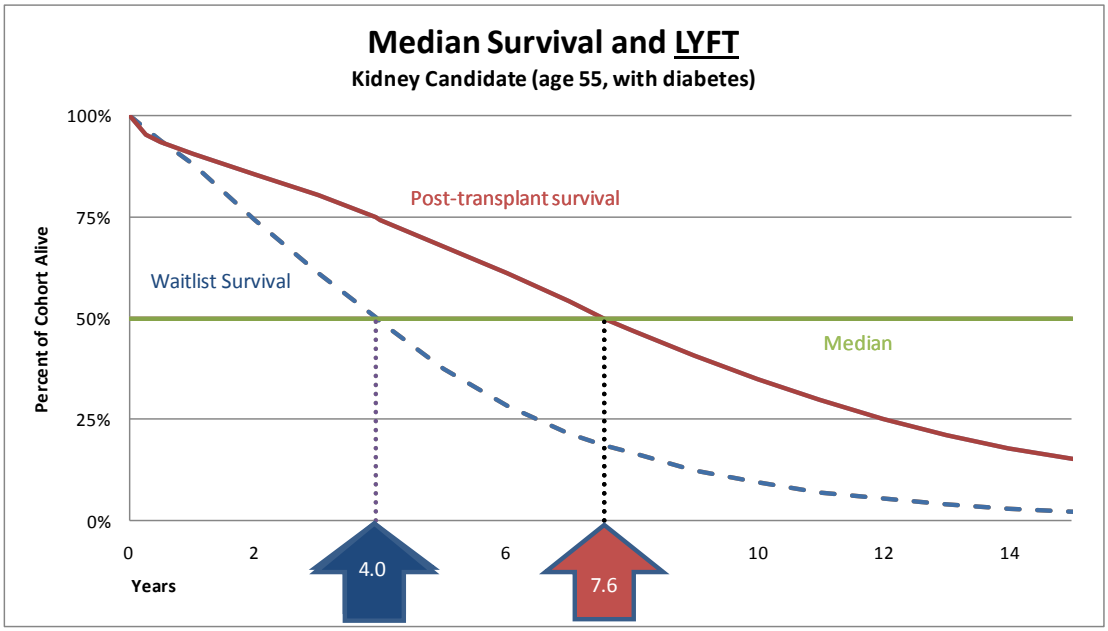


Figure 4: Example of how median survival is used in the calculation of LYFT. In this example, the 4.0 years of median waitlist survival are subtracted from the 7.6 median years of post transplant survival for a LYFT score of 3.6

Accounting for Quality of Life

Within the LYFT calculation, factors can be weighted to emphasize or de-emphasize their effect. For example, the Committee decided to give more weight to the post-transplant time during which the patient has a functioning kidney to account for the improvement in quality of life (QoL) achieved with a transplant. In order to determine an appropriate weight for QoL, peer-reviewed literature was consulted. Findings from this review indicate that there is remarkable agreement regarding QoL values reported for candidates on the kidney waiting list.[14,15] These studies report that QoL is lower on dialysis than with a functioning transplant. To approximate the difference in QoL, the Committee agreed to apply an adjustment factor of 0.8 to each year that a candidate is expected to survive on dialysis (either on the waiting list or following failure of a kidney transplant).

RFI Question #1: Life Years from Transplant (LYFT)

Please describe any benefits to the use of LYFT in an allocation system. Conversely, what limitations do you see to incorporating LYFT?

What is Donor Profile Index (DPI) and how is it calculated?

Currently, deceased donors are designated as either standard criteria donors (SCD), or expanded criteria donors (ECD), based on the medical characteristics of the donor. ECD kidneys are defined as having a relative risk of graft failure of more than 1.7 when compared to a reference group of nonhypertensive

[14] Laupacis A, Keown P, Pus N, Krueger H, Ferguson B, Wong C, Muirhead N. A study of the quality of life and cost-utility of renal transplantation. Kidney Int. 1996 Jul;50(1):235-42.

[15] Hornberger JC, Best JH, Garrison LP Jr.Cost-effectiveness of repeat medical procedures: kidney transplantation as an example. Med Decis Making. 1997 Oct-Dec;17(4):363-72.

deceased donors, between the ages of 10 and 39 years, whose cause of death was not a cerebral vascular accident, and whose terminal creatinine was ≤ 1.5 mg/dl.[16]

Many transplant professionals expressed that the categories of SCD and ECD did not adequately reflect the recipient outcomes from receiving these organs. Some reported that ECD kidneys are less likely to be accepted both by transplant professionals and candidates due to the perception that they are inferior to SCD kidneys when, actually, the risk of graft failure for SCD and ECD kidneys overlaps, as shown in Figure 5. This means that the rate of graft failure for some SCD kidneys exceeds that of some ECD kidneys. The Committee determined that the current categories of SCD and ECD kidneys are no longer adequate, and a continuous measure of donor quality is needed. This concept was strongly supported at a public forum held in Dallas, Texas in February 2007.

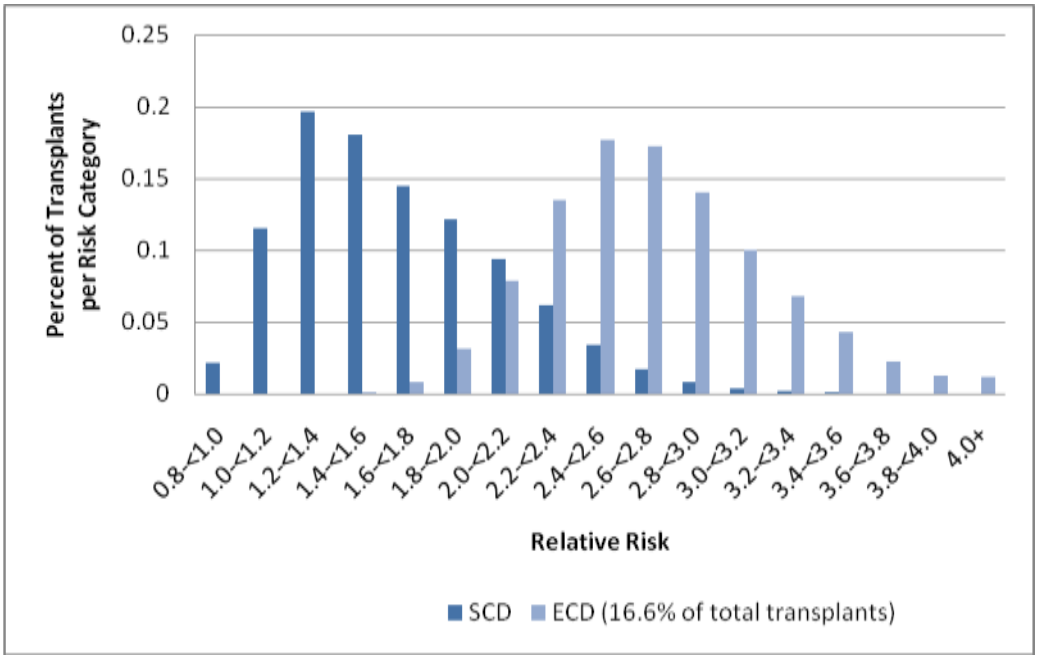


Figure 5: Relative risk of graft failure for SCD and ECD kidneys

The Committee investigated the use of a donor profile index (DPI) score to provide transplant professionals and candidates with a continuous measure of organ quality. DPI is based on the donor criteria listed below and the equation is calculated from actual outcomes of adult kidney-alone transplants used for deceased donor transplantation from 1995 to 2005.

[16] OPTN/UNOS Policy 3.5.1 (Definition of Expanded Criteria Donor and Standard Donor). www.unos.org. Accessed November 8, 2007.

- Age,
- Gender,
- Race,
- Height,
- Weight,
- Creatinine ,
- History of smoking,
- Donor after cardiac death,
- Current ECD definition,
- Hepatitis C virus,
- History of hypertension,
- History of diabetes, and
- Cause of death (i.e., anoxia, stroke, central nervous system tumor, other)

A continuous measure (DPI) would replace the current categories of ECD and SCD. The organs with the longest survival potential are assigned a DPI score of zero. The organs with the shortest survival potential are assigned a DPI score of one. The Committee believes that this approach will provide more useful information for assessing the appropriateness of a kidney offer for specific candidates on the waiting list than the current SCD/ECD designations. The Committee also believes that use of DPI will reduce the discard of ECD kidneys that may have similar outcomes to SCD kidneys. DPI provides the information that transplant professionals and individual patients need in order to make acceptance decisions, even prior to the time of an organ offer. Better clinical information about donor kidneys should increase efficiency of allocation and decrease kidney discard rates, ideally leading to more transplant opportunities across the national candidate pool.

RFI Question #2: Donor Profile Index (DPI)
Please describe any limitations to the use of DPI in an allocation system. Are there any benefits you see to incorporating DPI? If so, please concisely describe them.

How is time on dialysis incorporated into the proposed system?

During the development of this proposal, the Committee heard from many stakeholders that any proposed kidney allocation system should include a mechanism for candidates to gain priority over time. Some reported that without a way to improve the kidney allocation score over time, candidates (especially those with lower LYFT scores) may lose hope that they could receive a transplant, resulting in negative health-related consequences or the discontinuation of dialysis. To ensure that the kidney allocation policy results in equitable allocation, the policy must achieve justice (fairness) while maximizing utility (medical results), which requires balance between the two ideals. Inclusion of an ability to gain priority over time provides a mechanism for achieving a component of justice within the policy.

The current kidney allocation system gives considerable priority based on waiting time for adult candidates. Waiting time in the current system is defined as the amount of time since the candidate was placed on the OPTN Waiting List. When a candidate is added to the OPTN Waiting List necessarily affects how much waiting time a candidate can accumulate. Therefore, a candidate's waiting time in the current system may be affected by many factors including: geographic region, blood type, referral

patterns, geographic location (e.g., urban versus rural), and proximity to a transplant center.[17] Initiation of dialysis, however, is determined based on candidate medical factors.

The intent of including dialysis time in the allocation system is to provide hope to candidates that their opportunity for a transplant can improve with time. The intent is also to ensure that the allocation system is based on objective medical criteria, as required by NOTA and the OPTN Final Rule.

RFI Question #3: Dialysis Time (DT)

Please describe any limitations to the use of dialysis time in an allocation system. Alternately, what benefits do you see to incorporating dialysis time? Please concisely describe them.

Priority for sensitized candidates

Several recent policy changes have been made with the intention of improving the identification of candidate sensitization levels, by requiring the use of a calculated panel reactive antibody (CPRA). CPRA is the calculated percentage of donors having one or more human leukocyte antigens (HLA) that would be considered as incompatible with, or contraindicated for, a given transplant candidate. The policies for identifying CPRA would remain unchanged with a proposal for a new kidney allocation policy. Each transplant center would continue to define its criteria for unacceptable antigens that are considered as contraindications for transplantation. Unacceptable antigens that are defined by laboratory detection of HLA specific antibodies must be determined using at least one solid phase immunoassay employing purified HLA molecules. It would continue to be the prerogative of the transplant center to establish criteria for additional unacceptable antigens, such as repeat transplant mismatches. The CPRA would be calculated automatically when the unacceptable antigens are listed initially or when updated on the waiting list. The CPRA would be derived from HLA antigen/allele group and haplotype frequencies for the different racial/ethnic groups in proportion to their representation in the national deceased kidney donor population.[18, 19] This CPRA system was designed by the OPTN/UNOS Histocompatibility Committee and is currently being implemented.

Any changes to the kidney allocation policy would not change the requirements for identifying candidate sensitization levels, but would change the allocation priority given to sensitized candidates. In the current national allocation system:

- highly sensitized candidates (those with a CPRA $\geq$ 80% and at least one unacceptable antigen listed) have an additional four points in their allocation scores; and
- moderately sensitized candidates (those with a CPRA 21% to 79%) do not receive any additional priority.

The Kidney Transplantation Committee found that in addition to highly sensitized candidates, moderately sensitized candidates (those with a PRA between 21% and 79%) also experience barriers to transplant. Rather than continuing the current priority of four points for candidates with a CPRA $\geq$ 80%,

[17] Ashby VB, Lin M, Kalbfleisch JD, Port FK, Wolfe RA, Leichtman AB. Geographic Variability in Access to Kidney Transplantation in the United States, 1996-2005. Am J Transplant 7(5):1412-1423, 2007.

[18] For additional information on calculated panel reactive antibody (CPRA) including a calculator for determining CPRA values based on unacceptable antigens, please visit: http://www.optn.org/resources/professionalResources.asp?index=10

[19] Leffell MS, Cherikh W, Land G, Zachary AA, Improved definition of human leukocyte antigen frequencies among minorities and applicability to estimates of transplant compatibility. Transplantation, 2007; 83: 964-72.

a new system could use a sliding scale of priority based on CPRA. The formula for determining the priority is (4*CPRA/100). With this formula, the additional priority given to sensitized candidates would be assigned based upon CPRA value across the entire PRA spectrum and not subject to an artificial cut-off point (currently 80%)(Figure 6).

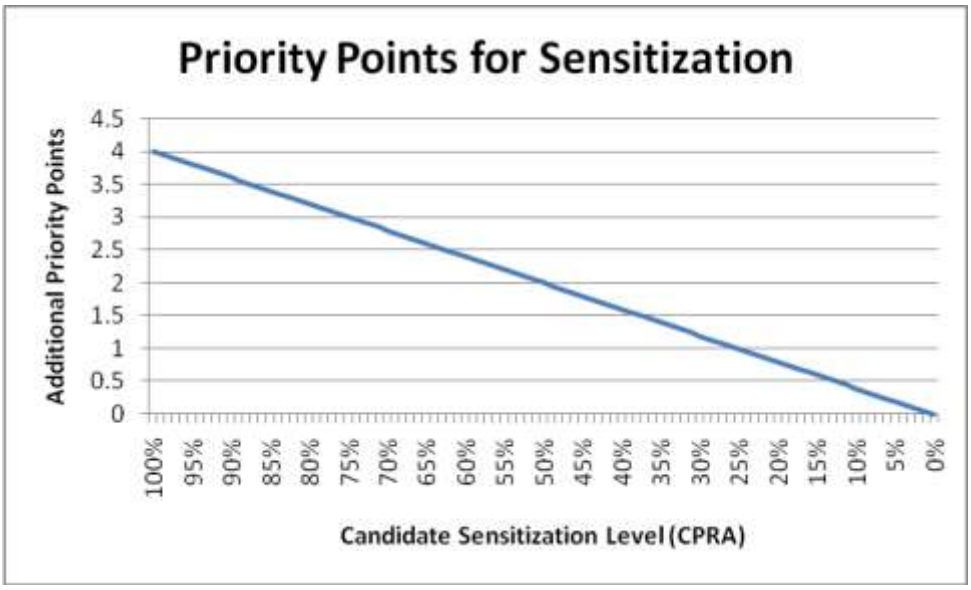


Figure 6: Priority points for sensitization (as defined by CPRA)

Determining the Kidney Allocation Score

In the calculation of a Kidney Allocation Score (KAS) for a particular deceased donor kidney, Figure 7 and 8 illustrate the proportional and relative impact of a candidate's LYFT score and the candidate's time on dialysis based on the DPI for that kidney. Each candidate would receive a kidney allocation score (KAS) that includes the LYFT calculation (the solid line) and time on dialysis (the dashed line). For the purposes of this illustration, these examples assume that the candidate has a sensitization level of 0%. As a donor kidney becomes available, it would receive a donor profile index (DPI) score. Each candidate would then receive a KAS based on a combination of his or her LYFT score and time on dialysis. The proportion of LYFT and dialysis time is determined by the DPI score.

For example, when a donor kidney from the 39th DPI percentile becomes available, each candidate would receive an allocation weight comprised of 50% LYFT score, and 50% time on dialysis. For a donor kidney from the 20% percentile, each candidate would receive an allocation weight of 36% of time on dialysis and 64% of LYFT. For sensitized candidates, the appropriate points for sensitization would be added into the KAS.

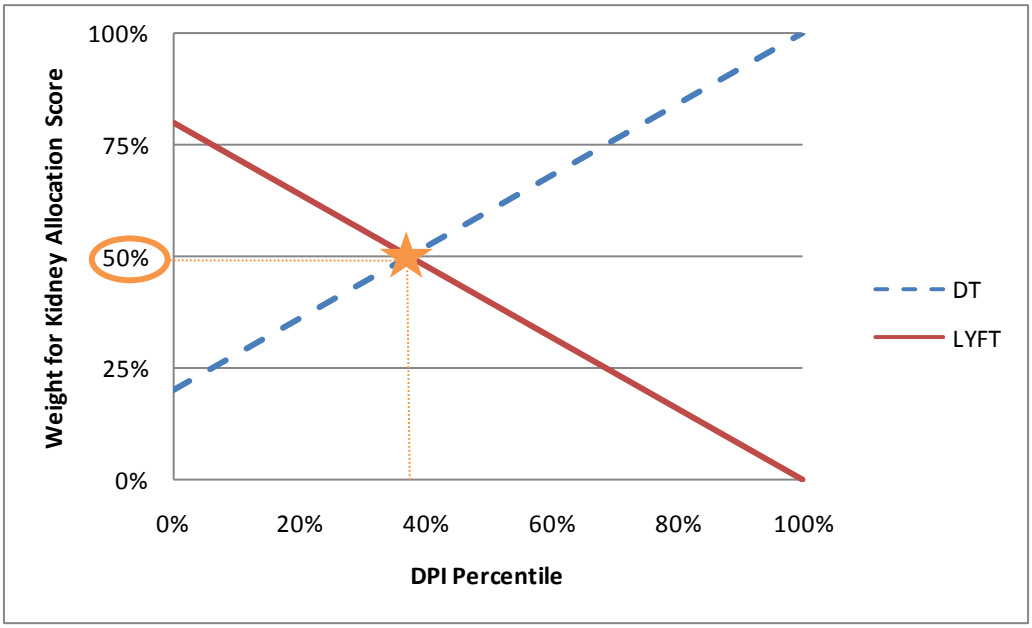


Figure 7: Interaction between time on dialysis (DT), life years from transplant (LYFT), and donor profile index (DPI) in the kidney allocation score (KAS). In this example, a donor from the 37.5th percentile is available. Candidate KAS scores will be comprised of 50% LYFT and 50% time on dialysis.

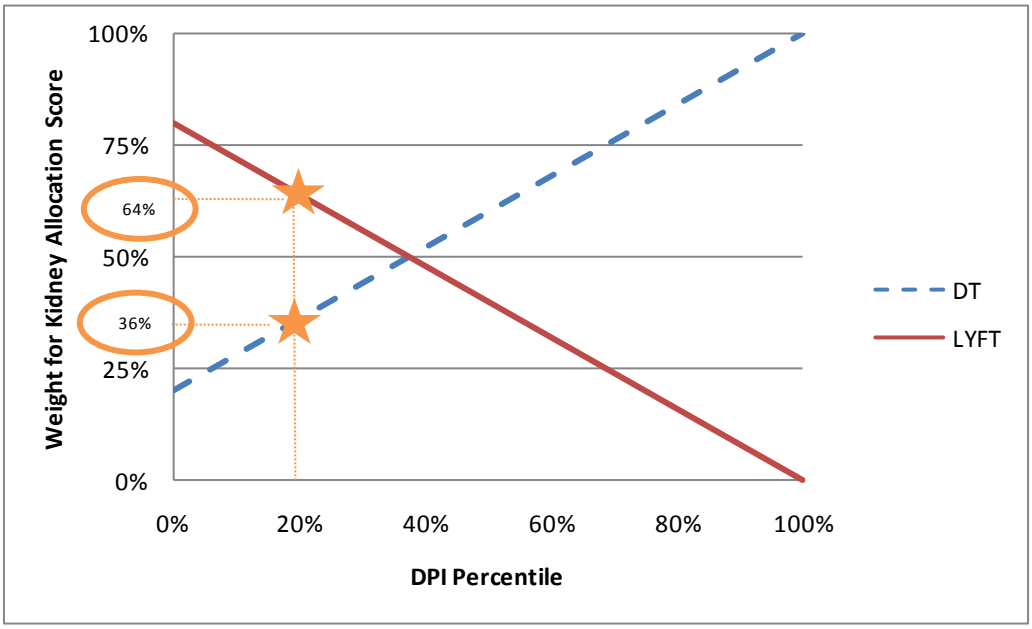


Figure 8: Interaction between time on dialysis (DT), life years from transplant (LYFT), and donor profile index (DPI) in the kidney allocation score (KAS) In this example, a donor from the 20th percentile is available. Candidate KAS scores will be comprised of 64% LYFT and 36% time on dialysis.

During the policy development process, the Committee received inquiries regarding possible unintended consequences of a new allocation system on living donation rates. Data on kidney transplants from living donors have shown that, in most cases, graft and patient survival are better for recipients who receive kidneys from living donors than from deceased donors.[20] However, if an allocation system provides immediate access to kidney transplant for very high-LYFT candidates who do not have any time on dialysis, this system may inadvertently provide disincentives for these candidates to pursue a living donor. The Committee reviewed data that validated this concern. Following implementation of the current policy to give additional priority to pediatric candidates for donors <35 years of age, living donor transplant rates fell among pediatric candidates.

Some options for addressing this unintended consequence in the new allocation system included mandating a certain period of waiting time for all candidates, but determining a length of time was not possible due to a lack of evidence for the period of time on dialysis that would be necessary to motivate pursuing a living donor. Instead, the Committee decided that the contribution of LYFT to the KAS should be capped at 80%. This means, that even for the highest quality kidneys, that 20% of the KAS would be candidate time on dialysis. This approach does not deny candidates access to a deceased donor transplant for an arbitrary period of time. The Committee investigated the effect that this 80% cap would have on post-transplant outcomes and found that it would not substantially reduce the average lifetime, graft lifetime, or extra years of life experienced by transplant recipients.

RFI Question #4: Solutions to Limitations

Please concisely describe specific approaches or concepts that would address any of the above limitations.

[20] OPTN data as of February 1, 2008. www.optn.org,

Description of Other Possible Components

In addition to the Kidney Allocation Score (KAS), there are a number of additional components and priorities that could be included in a new allocation system. In this section, each component or priority is described along with an explanation of how it differs from the current kidney allocation system. Among these, priority for pediatric candidates, prior living organ donors, zero-antigen mismatches, and multi-organ transplants are described. Possible modifications to the kidney payback system, alternative allocation systems, and incorporation of transplants from blood type A_2 and A_2B donors into blood type B recipients, are also described in this section.

Priority for Pediatric Candidates

Allocation for pediatric candidates would remain largely the same as it is under the current system, where children receive priority for kidneys from donors less than 35 years old.[21] Since the KAS was developed based on data from adult candidates and recipients, it could not be applied to pediatric candidates. Additionally, pediatric candidates would continue to be ranked primarily according to waiting time (defined as time from listing) instead of time on dialysis. Pediatric candidates would also continue to receive points for matching at the HLA-DR loci and for sensitization.

The OPTN has always assigned preference in kidney allocation to pediatric transplant candidates in an effort to expedite their access to deceased donor kidneys. This is appropriate because young children and adolescents experience unique problems associated with dialysis and disruption to expected growth and developmental processes due to renal failure.

Early reversals of renal failure through transplantation can avoid the problems of dialysis and minimize or prevent many of the adverse effects of end stage renal disease which confront pediatric patients. Rapid treatment provides the best opportunity for reversing the growth and developmental deficits and preventing lifelong adverse consequences. The unique needs of children awaiting an organ transplant are also acknowledged by the Children's Health Act of 2000, Public Law 106-310. The transplantation portion of the Act was incorporated as an amendment to the National Organ Transplant Act (NOTA). The Children's Health Act recognizes the differences in health and organ transplant issues between children and adults and specifies the adoption of criteria, policies, and procedures addressing the special health care needs of children.

In the proposed system and in the current system pediatric candidates are defined as candidates listed before turning 18 years old. In the current allocation system, pediatric candidates:

- receive priority for mismatched kidneys from donors < 35 years old, and
- are ranked along with adult candidates for donors >= 35 years old.

The proposed allocation system would:

[21] OPTN/UNOS Policy 3.5.11.5 (Pediatric Kidney Transplant Candidates).

- continue to give priority to candidates <18 at listing for non zero-mismatched kidneys from donors < 35 years old,
- continue to give priority to candidates who are <18 at the age of listing for zero-antigen mismatched kidneys,
- eliminate organ offers to candidates who are <18 at time of offer for mismatched kidneys from donors >=35 years old, and
- separate pediatric and adult candidates for allocation purposes. Pediatric candidates will be ranked ahead of adult candidates at the local, regional, and national levels for donors <35.

Candidate Age at Listing	Candidate Age at Offer	Receives Priority for	Receives offers for kidneys from Mismatched donors >35
<18	<18	--Zero antigen mismatches --Non-zero antigen mismatches from donors <35	No
<18	≥18	--Zero antigen mismatches --Non-zero antigen mismatches from donors <35	Yes, organ is allocated by KAS.

Table 1: Description of pediatric allocation used for simulation modeling.

In the two years following the implementation of pediatric priority policy, only 30 patients listed before age 18 have received a kidney from a donor ≥ 35. These 30 transplants represent only 2% of all pediatric transplants during the two years following policy implementation. Therefore, restricting pediatric candidates from offers of kidneys from these donors is expected to improve allocation efficiency without adversely limiting the donor pool for sensitized pediatric candidates. The Kidney Transplantation Committee will work with the OPTN/UNOS Pediatric Transplantation Committee to verify that access for pediatric candidates is satisfactorily maintained in the proposed system.

Priority for Prior Living Organ Donors

Currently, kidney transplant candidates who previously donated a vital organ or segment of a vital organ (i.e., kidney, liver segment, lung segment, partial pancreas, or small bowel segment) to a recipient within the United States receive additional allocation priority. This policy is intended to recognize the sacrifice that living organ donors make for others and would be maintained in any proposed system.

Priority for Zero-Antigen Mismatches

With few exceptions, current policy requires mandatory sharing of kidneys that have zero antigen mismatches, regardless of other donor or candidate characteristics.[22] The receiving organ procurement organization (OPO) then incurs an obligation to pay back a kidney.

The original policy for mandatory sharing zero antigen mismatch kidneys was based on the superior graft survival outcomes observed in the recipients. Improvements in immunosuppression and other advances in organ transplantation have narrowed the gap between graft survival of recipients of perfectly matched kidneys (i.e., zero antigen mismatched kidneys) and recipients of less well-matched kidneys. In 1995, the OPTN/UNOS Board of Directors eliminated the allocation points assigned for candidates and donors who matched at the HLA-A locus. In 2003, the Board eliminated the allocation points assigned for candidates and donors who matched at the HLA-B locus. Currently, allocation priority for HLA matching only exists for candidates and donors who:

- are not mismatched at the HLA A, B, and DR loci (i.e. zero-antigen mismatches); and
- have zero or one mismatch at the HLA-DR locus.

In a proposed system, the inefficiencies of the current system could be addressed to provide access to zero antigen mismatch kidneys for pediatric candidates and highly sensitized adult candidates. To accomplish this, a proposed system could modify the allocation of zero antigen mismatch kidneys. Rather than providing categorical priority for highly sensitized adult candidates, adult candidates with a CPRA $\geq$ 80%, who have a zero antigen mismatch with a donor, would be included on every local waiting list. These highly sensitized adult candidates would be ranked by their KAS on these local waiting lists. Sharing of an organ to a highly sensitized candidate outside of the local unit would not generate a payback.

There are currently 50 distinct allocation categories for zero-antigen mismatch offers. Within each category, candidates are ranked according to their allocation points (e.g., waiting time points, sensitization points, prior living donor points). The zero-antigen mismatch categories are determined based on:

- Geographic proximity of the donor to the candidate (i.e., local, then regional, then national),
- Age of the candidate at time of listing (i.e., pediatric or adult),
- Sensitization level (i.e., PRA $\geq$80%, PRA 21%-79%, PRA 0%-20%),
- Blood type (i.e., identical or compatible to the donor), and
- Whether or not the kidney is offered as a payback.

In a proposed system, the categories for zero-antigen mismatch could be reduced by:

[22] In June 2008, the OPTN/UNOS Board of Directors passed a policy change to only require sharing of zero antigen mismatches for adult candidates with CPRA>20% and pediatric candidates (regardless of sensitization level).

- Placing all regional/national highly sensitized adult zero antigen mismatched candidates in the category of local adult candidates, and
- Eliminating the kidney payback category.
- Allowing for sharing of zero-antigen mismatch nationally for any pediatric candidate listed before 18 years of age.

Within each category, adult candidates would be ranked by their KAS and by current allocation points for pediatric candidates. As predicted by simulation modeling, these changes would result in a decline in zero-antigen mismatches from 11% in the current system to less than 2%.

Elimination of the Kidney Payback System

Current policy states that when an OPO accepts a zero-antigen mismatch offer from another OPO, it is required to "pay back" the kidney with a kidney from the same blood group after at least two debts have been accrued. Kidneys are offered as paybacks after being offered to zero-antigen mismatch candidates, prior living organ donors, highly sensitized candidates who are listed in the same donation service area (DSA) as the donor, and children (if the kidney is from a donor younger than 35 years old). The current payback policies were instituted as a mechanism to address the imbalances created by the zero antigen mismatch sharing policies. Since zero-antigen mismatches are more frequent among those with common antigens, the payback policy was intended to rebalance the allocation system so that no patient population benefited from the zero antigen mismatch sharing rules to the harm of any other patient population.

Some OPOs have reported difficulty in placing payback kidneys for several reasons including the fact that transplant centers are not required to accept payback kidneys. Therefore, a transplant center may choose to turn down several payback offers, and wait for a kidney from a donor with specific characteristics to be offered, before accepting a payback offer. Since the pediatric priority policy for donors under the age of 35 went into effect in 2005, some OPOs have observed a decrease in the percent of kidneys from donors <35 available for payback offers. The Kidney Transplantation Committee has reviewed acceptance rates for kidneys offered as paybacks and has found that few of the kidneys offered for paybacks are actually accepted, and acceptance rates vary widely based on OPO.

The penalties for exceeding the stated payback debt levels have not served as an effective governor for the zero-antigen mismatch and payback policies. One penalty reprioritizes unsensitized candidates from OPOs with payback debt levels greater than 9 to the bottom of the match run category for zero-antigen mismatches. Additionally, when a donor service area (DSA) reaches a debt level of 9 kidneys across all blood groups, it may no longer retain a kidney for local simultaneous pancreas-kidney (SPK) transplantation. Instead, the kidney must be offered as a payback. The result has been a decrease in SPK transplantation in some of OPOs with consistently moderate to high debt levels. In 2006 and 2007, the Pancreas Transplantation Committee reviewed reports from several pancreas transplant programs that were unable to perform SPK transplants due to kidney payback debt levels. Thus, SPK patients within the DSA are penalized. Informed by the actual data on this issue, the Kidney Transplantation

Committee and Pancreas Transplantation Committee both believe that this situation is disproportionately affecting candidates listed for kidney-pancreas transplantation.

Given these problems, the kidney payback system will be eliminated in the proposed system. Eliminating the kidney payback system, while still ensuring equitable access for highly sensitized candidates to zero-antigen mismatched kidneys, is expected to improve the efficiency of the kidney allocation system.

Due to the complexities associated with the payback accounting system, all existing payback debts and credits need to be settled prior to implementation of a new kidney allocation system. Any debts/credits remaining at the time of implementation would be eliminated. Considering that repayment of debt and fulfillment of credits may take some time, organ procurement organizations with either high debt or credit levels should now consider ways to reduce these levels.

Multiorgan Transplants

Currently, policy 3.9.3 (Organ Allocation to Multiple Organ Transplant Candidates) requires that candidates who are listed for a kidney, *and* who are also listed for a liver, heart, or lung, must receive an offer of a kidney with an offer for the liver, heart, or lung from a donor who is in the same DSA as the candidate. Current policy, however, does not require that candidates who are listed for a kidney and pancreas, and receive an offer for the pancreas, also receive the offer for the kidney (except in cases of highly sensitized candidates who receive zero-antigen mismatch offers).

Most candidates who are listed for SPK transplantation have Type I diabetes and tend to have high LYFT scores. Rather than include these patients within the proposed kidney allocation system, it could be proposed that the multiorgan policy be altered to include patients who are listed for SPK transplantation. Essentially, this policy would require that candidates who are listed for a pancreas but who are also in need of a kidney would be offered the kidney with the pancreas. This modification is expected to improve the efficiency of the kidney (and pancreas) allocation systems, increase the number of organs transplanted per donor, and increase the life years from transplantation for SPK candidates.

The Kidney Transplantation Committee is currently discussing with the OPTN/UNOS Liver and Intestinal Organ Committee the creation of "minimal listing criteria" for kidney-liver candidates. These criteria would help maximize proper use of the donated kidney across all candidates who qualify for transplantation. Any criteria would be circulated for public comment prior to Board consideration.

Blood Group A_2/A_2B Kidneys for Blood Group B Recipients

In 2001, the OPTN/UNOS Board of Directors passed a Committee-sponsored alternative allocation system to allow the transplantation of kidneys across certain blood groups. The primary goal of this system was to increase the rate of transplantation in blood group B candidates by allocating A_2 or A_2B deceased donor kidneys into blood group B candidates without negatively impacting the post-transplant outcomes. Since the majority of blood group B candidates are minorities, this system was expected to also decrease an important barrier to access to transplantation for minorities.

As a committee-sponsored system, OPOs could elect to participate, but the system was not applied as national policy. This approach allowed for the study of the effects of the system before national application was considered. Since the system was implemented, 55 blood type B candidates have received kidneys from blood type A_2 or A_2B donors as of February 1, 2008. Nearly three quarters of these recipients were non-white. Additionally, publications on the results of this system have indicated that access to transplant for blood type B candidates has improved, and outcomes of recipients of A_2 or A_2B transplants have been comparable to outcomes of recipients who received blood type B or O kidneys.[23,24,25,26] Due to the improved access for minority candidates and comparable clinical outcomes observed from this system, the requirements for participating would become mandatory in the proposed national system. Briefly, those requirements are as follows.

- Anti-A titers must be performed at least every three months on each candidate before transplantation. At least two anti-A titers must be entered into UNet[sm] before a candidate is eligible to receive a kidney from an A_2 or A_2B donor. A longer history of up to one year of anti-A titer testing is recommended to assure the patient's titer is consistently low.[27] One way the anti-A titer history for B candidates on a waiting list can be obtained quickly would be to perform the test on serum samples from that candidate that the HLA laboratory has stored away for crossmatching. The anti-A titer must be < 1:8 for a blood type B candidate to be listed for a blood type A_2 or A_2B kidney.

- Anti-A titer testing must only be performed by technologists who are licensed to perform such tests according to local, federal and/or state laws. Each technologist performing such tests must take part in a recognized proficiency program if it exists, or must take part in regular parallel testings with other laboratories whose OPO is taking part in the variance.

- All A_2 or A_2B donors must have their ABO confirmed since A_2 and A_2B is defined based on negative reactivity of the donor red blood cells (RBC's) with an A lectin, which may come from various companies and in different lots. It is also critical that the determination of A_2 or A_2B blood group must be done on pre-transfusion donor blood, since any transfusion(s) would likely

[23] Nelson PW, Shield CF 3rd, Muruve NA, Murillo D, Warady BA, Aeder MI, Bryan CF. Increased access to transplantation for blood group B cadaveric waiting list candidates by using A2 kidneys: time for a new national system? Am J Transplant. 2002 Jan;2(1):94-9.

[24] Bryan CF, Shield CF 3rd, Nelson PW, Pierce GE, Ross G, Luger AM, Warady BA, Helling TS, Aeder MI, Martinez J, Hughes TM, Beck ML, Harrell KM. Transplantation rate of the blood group B waiting list is increased by using A2 and A2B kidneys. Transplantation. 1998 Dec 27;66(12):1714-7.

[25] Williams WW, Cherikh WS, Young CJ, Distant DA, Bryan CF. First Report on the OPTN/UNOS National Voluntary Variance to Allocate A_2/A_2B Deceased Donor (DD) Kidneys to Blood Group B Candidates. Am. J. Transplant, 5(Suppl 11):282, 2005

[26] Williams WW, Cherikh WS, Young CJ, Distant DA, Bryan CF. Updated Report on the OPTN/UNOS National Voluntary Variance to Allocate A_2/A_2B Deceased Donor Kidneys to Blood Group B Candidates. Am. J. Transplant, 6(Suppl 2):1058, August 2006.

[27] UNet[SM] is the web-based electronic utility used by the OPTN contractor to conduct the business of the OPTN. UNet[SM] comprises the Match System, all software, applications and security architecture needed for the collection, modification, validation, reporting, management and redundancy of data associated with the tasks and activities of the OPTN.

be with blood from A_1 donors. Transfusion of A_1 blood into an A_2 donor would likely cause the donor's type to falsely appear to be A_1 or A-intermediate. Any reactivity of the RBC's with A lectin should be interpreted as not being a blood group A_2 or A_2B and the kidneys should not be allocated as an A_2 kidney. Confirmation of the A_2 or A_2B type of the donor should be done by another laboratory prior to transplantation.

Alternative Allocation Systems/Alternative Local Units

Currently, the majority of OPOs have at least one alternative allocation system (AAS) in place. These systems generally have different allocation points or priority categories than the national system. Since these systems were designed to address limitations of the current kidney allocation system, they would be eliminated upon implementation of a new kidney allocation system. After a pre-determined period (e.g., six months) of operation for a new system, the Kidney Transplantation Committee will review applications for new alternative allocation systems. The intent is to gain experience with a single, national allocation system and to address issues that arise on a national level rather than devising a number of local or regional modifications. Any applications for alternative allocation systems requested after the implementation period would need to conform to the variance requirements of the OPTN Final Rule (i.e., include a research design, data collection and analysis plans; all variances will be time limited).[28]

The Committee will review Alternative Local Units (ALUs) during its March 2008 meeting. Since a number of these ALUs are designed to increase sharing, it may be appropriate to continue these units in the new system. Recommendations on whether to continue or discontinue each ALU will be included in the public comment proposal.

[28] OPTN Final Rule

Supporting Evidence

The Committee reviewed the results of simulations of more than 30 different allocation models as performed by the Scientific Registry of Transplant Recipients (SRTR) using the Kidney Pancreas Simulated Allocation Model (KPSAM). The following is a description of the results of the simulations from the presented approach as compared to the current system. Also included are descriptions of five of the major alternative allocation approaches reviewed by the Committee and reasons why those approaches were not selected. Complete data analyses and a description of the methods used may be found at www.optn.org/kars.asp.

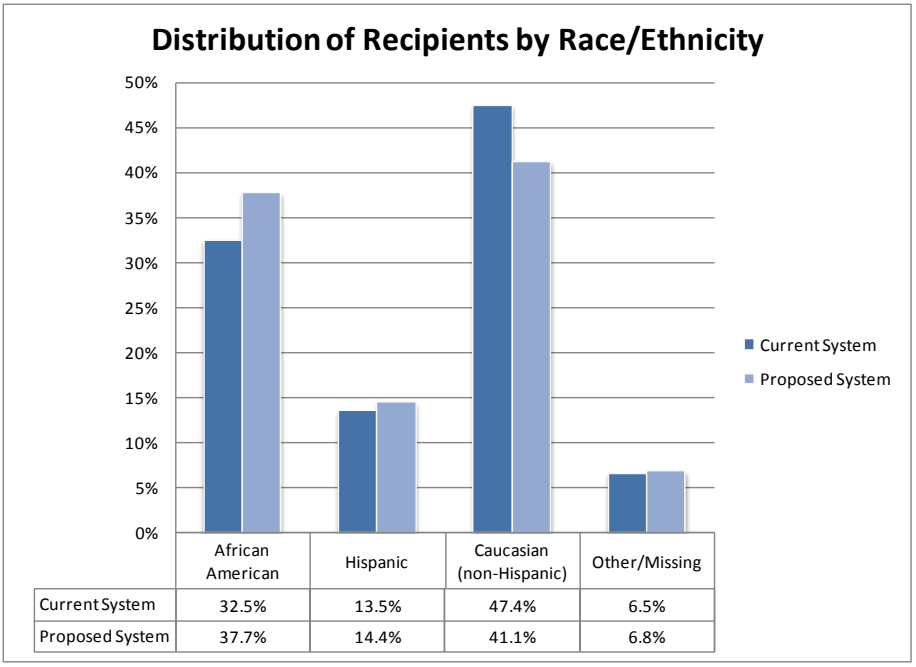
When compared to the current system, the approach presented is projected to obtain an additional 3,402 life years over the current system. This overall gain is based on a 1.3 year gain in the average post-transplant lifetime and a much smaller loss in average waitlist lifetime. Comparison of the expected outcomes of the current system to the proposed system is provided in Table 2.

	Current System	Approach Presented
Life years after transplant	107,865	118,133
Total graft years	72,814	73,772
Total extra life years	48,187	51,589
Average post-transplant lifetime (in years)	11.8	13.1
Average graft lifetime (in years)	8.0	8.2
Average extra years of life	5.3	5.7
Change in years after transplant		10,268
Change in graft years		958
Change in total extra life years		3,402

Table 2: Years of life expected with current kidney allocation system and the approach presented

As with any allocation system, it is important to understand if candidates with particular characteristics are more or less likely to receive a transplant due to policy changes. The approach presented was evaluated on a number of levels to ensure that no one group of candidates benefitted at another group's expense. Figure 9 through Figure 14 provide the distribution of kidney recipients for the approach as compared to the current system. These distributions are provided by race/ethnicity, blood type, sensitization level, diagnosis category and age. Please note that small percentage increases or decreases may not be statistically significant.

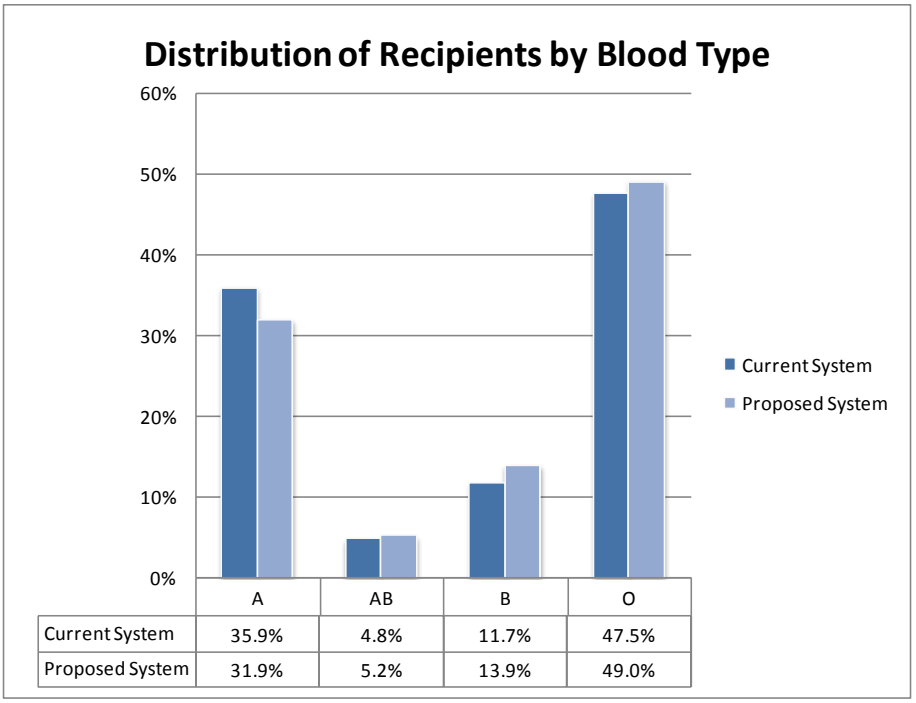
As shown in Figure 9, transplants for racial/ethnic minorities are projected to increase with the approach presented. This increase was the highest of all of the systems considered and was one of the determining reasons for the selection of this approach.



	African American	Hispanic	Caucasian (non-Hispanic)	Other/Missing
Current System	32.5%	13.5%	47.4%	6.5%
Proposed System	37.7%	14.4%	41.1%	6.8%

Figure 9: Distribution of recipients by race/ethnicity

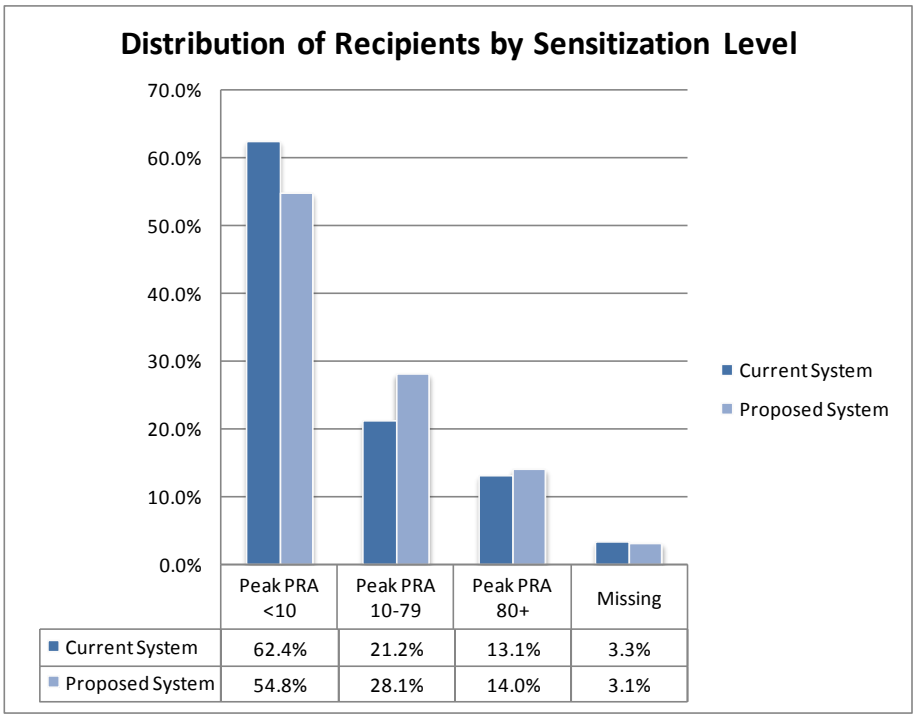
As shown in Figure 10, the percentage of transplants by blood group is not expected to change dramatically under the presented approach. Due to the incorporation of the system to transplant blood type A_2/A_2B kidney into B candidates with low anti-A titers, transplants for blood group B candidates are expected to increase slightly from 11.7% under the current system to 13.9% under the presented approach.



	A	AB	B	O
Current System	35.9%	4.8%	11.7%	47.5%
Proposed System	31.9%	5.2%	13.9%	49.0%

Figure 10: Distribution of recipients by blood type

As shown in Figure 11, the percentage of transplants for moderately and highly sensitized candidates is expected to increase under the proposed approach as compared to the current system. As sensitized candidates experience increased barriers to transplantation due to immunologic response to a larger portion of donors than unsensitized candidates, an improvement in transplantation rates among moderately and highly sensitized candidates was a determining reason for selection of the proposed approach.

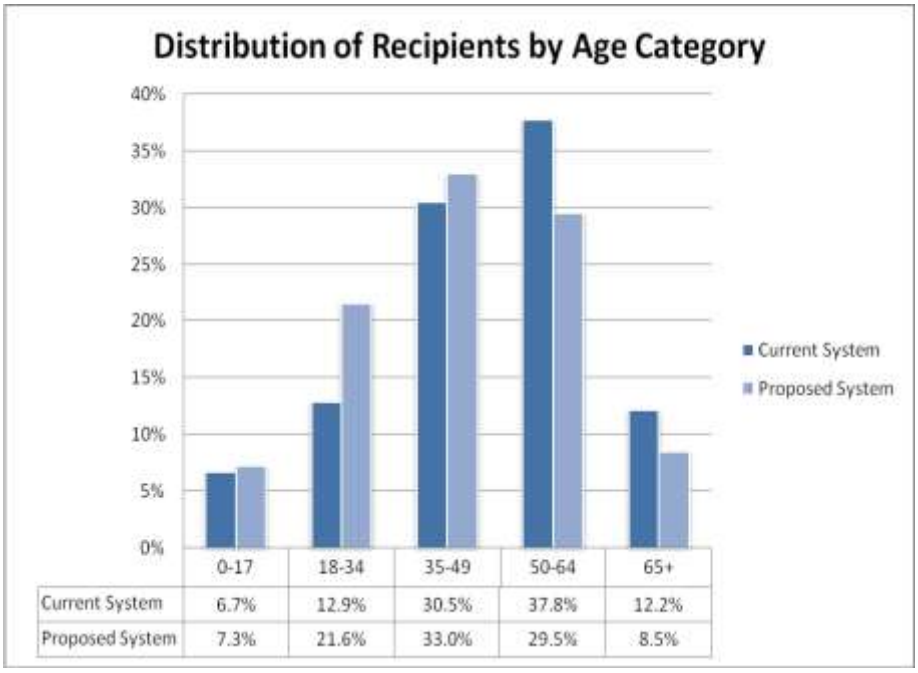


	Peak PRA <10	Peak PRA 10-79	Peak PRA 80+	Missing
Current System	62.4%	21.2%	13.1%	3.3%
Proposed System	54.8%	28.1%	14.0%	3.1%

Figure 11: Distribution of recipients by sensitization level

As shown in Figure 12, the percentage of transplants among candidates of different age groups is expected to change markedly under the proposed approach. Younger candidates, shown here as 18-34, are expected to receive 21.6% of all kidneys as opposed to the 12.9% received under the current system. As a note, this age group received 13.5% of SCD kidney transplants in 2005.[29] The percentage of transplants for candidates ages 50-64 is expected to be 29.5% in the proposed approach versus 37.8% in the current system. This percentage was among the highest in this age group of all of the systems reviewed that used LYFT and time on dialysis to allocate kidneys. The percentage of transplants for candidates over the age of 65 is expected to be 8.5% under the proposed approach versus 12.2% in the current system. Again, this percentage is among the highest in this age group of all of the LYFT/time on dialysis systems reviewed. As a note, these graphs provide a way of looking at groups of candidates; the graphs do not imply that candidates who are 49 years old will have significantly different kidney allocation scores than candidates who are 50 years old.

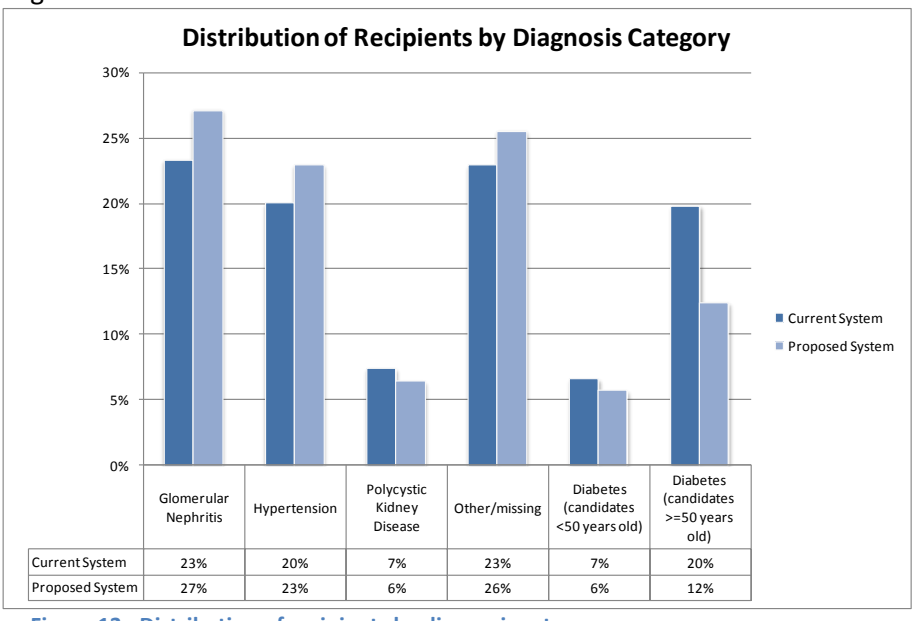
[29] Table 5.4a Transplant Recipient Characteristics, 1996 to 2005 Recipients of Deceased Donor non-ECD Kidneys. www.ustransplant.org.



	0-17	18-34	35-49	50-64	65+
Current System	6.7%	12.9%	30.5%	37.8%	12.2%
Proposed System	7.3%	21.6%	33.0%	29.5%	8.5%

Figure 12: Distribution of recipients by age category

The number of transplants by category of disease is also expected to change for candidates with diabetes, however, the impact on candidates with diabetes is expected to be different for older candidates than younger candidates. Younger candidates with type 1 diabetes tend to do very well with a SPK transplant and rather poorly on dialysis. Therefore, they are expected to have high LYFT scores and consequently, higher kidney allocation scores. The absolute priority proposed for SPK transplantation is expected to continue to provide transplant opportunities for these candidates with type 1 diabetes. The diagnosis category for diabetes has been divided in Figure 13 to show the effect for candidates younger than 50 years of age with diabetes versus those candidates with diabetes who are 50 years of age or older.



	Glomerular Nephritis	Hypertension	Polycystic Kidney Disease	Other/missing	Diabetes (candidates <50 years old)	Diabetes (candidates >=50 years old)
Current System	23%	20%	7%	23%	7%	20%
Proposed System	27%	23%	6%	26%	6%	12%

Figure 13: Distribution of recipients by diagnosis category

Finally, as shown in Figure 14, the percentage of transplants among the 11 OPTN/UNOS regions is not expected to change substantially from the current system. The number of kidneys transplanted in the same DSA in which they are procured is expected to increase (due to the reduction of zero-antigen mismatch sharing and the payback system), but this effect is expected to be fairly uniform across the regions.

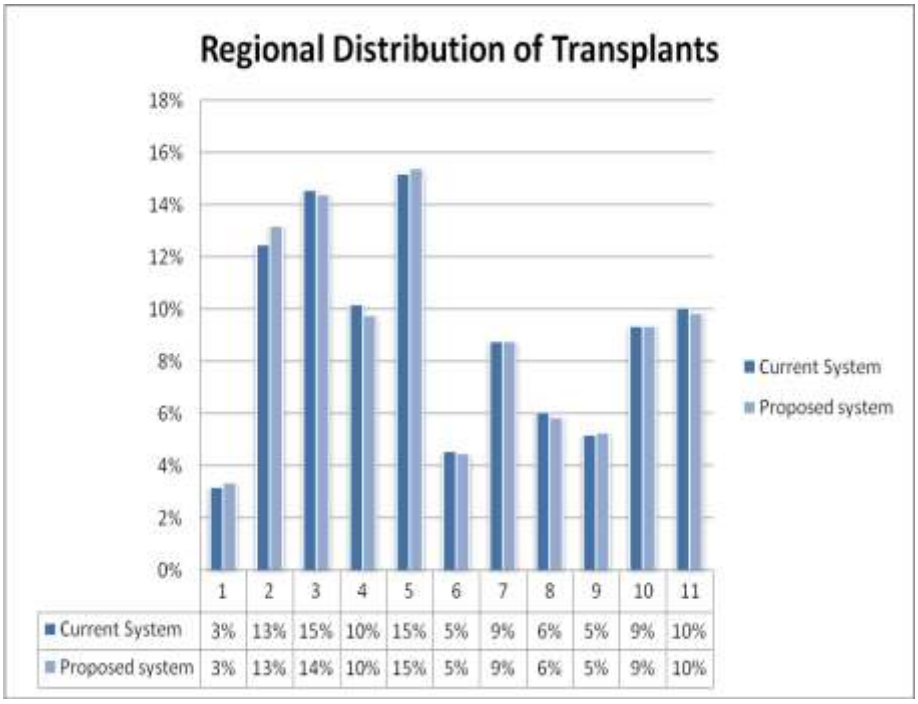


Figure 14: Regional distribution of transplants

Alternative Allocation Approaches Reviewed

As a required step in the policy development process, the Committee reviewed more than 30 different iterations of alternative allocation approaches. Its intent in this review of alternative approaches was to determine that the proposed approach achieved the best possible outcomes in relation to the stated objectives of the system. These iterations can be categorized into 4 distinct categories, each of which are described in detail below. The Committee compared the outcomes of each alternative approach to the outcomes of the current national allocation system.

The four categories of alternative allocation approaches reviewed by the Committee were allocation based on:

- age matching of donors and potential recipients
- LYFT primarily
- post-transplant survival, and
- categorizing candidates by LYFT and donors by DPI.

Each of these approaches was considered based on whether or not they achieved the Committee's objectives for allocation and the projected outcomes. Each approach was also evaluated based on the following metrics:

- average post transplant lifetime,
- average graft lifetime,
- average extra years of life,
- total extra years of life,
- correlation between donor and recipient age
- number and percentage of transplants by degree of HLA mismatch, and
- number and percentage of transplants to candidates by,
  - degree of HLA mismatch,
  - race/ethnicity,
  - blood type,
  - age,
  - diagnosis category, and
  - sensitization level (as defined by PRA).

Detailed results for each iteration of the simulation modeling may be found at www.optn.org/kars.asp.

Allocation Based on Age Matching of Donors and Potential Recipients

The Committee reviewed a system that matched donors and potential recipients based only on age. In this system, candidates were ranked according to the proximity of their birth dates to the donor's birth date. Due to the composition of the donor population, the system resulted in a substantial gain in life years from transplant (mostly due to the transplantation of younger recipients who were matched with younger donors). Due to the emphasis on matching donor and recipient age in this system, the donor/recipient age correlation was 66%, the highest of all of the systems reviewed.

While this system was simple to explain, it did not meet the requirements of the OPTN Final Rule that allocation should be based on objective medical criteria. Basing allocation only on age fails to recognize the effect that comorbid conditions such as diabetes can have on survival. Additionally, since the donor population tends to be younger than the candidate population, older candidates were found to have fewer opportunities for transplant based solely on age. Due to these limitations, this system was not found to be suitable for national kidney allocation.

Allocation Based Primarily on LYFT

In February 2007, the Committee requested feedback on an allocation system that was based primarily on life years from transplant (LYFT). For kidneys from standard criteria donor kidneys, this system would rank order candidates by the number of extra life years that he or she was expected to gain from transplant. Expanded criteria donor kidneys would continue to be allocated primarily by waiting time. While this system was found to provide the most life years gained from transplant of any system reviewed, it also resulted in a substantial decrease in the number of transplants for older candidates. When presented publicly, the feedback received indicated that candidates wanted a way to increase their allocation priority over time, through incorporation of time on dialysis. Additionally, many in the transplant community expressed that the current SCD/ECD designations were not adequate for

describing the actual risk of graft failure for donor kidneys. The Committee investigated different weights for time on dialysis to see what effect incorporating this factor would have on the life years gained from this system.

Ultimately, this system was not found to provide the necessary balance of medical benefit (utility) and fairness (justice) that is necessary for any organ allocation system. Additionally, the Committee determined that the current designations for SCD and ECD kidneys are no longer adequate for determining the relative risk for graft loss and that the kidney allocation system should employ a continuous measure such as DPI.

Allocation Based on Categorizing Candidates by LYFT and Donors by DPI

In this system, five categories (referred to as quintiles) were developed based on the LYFT scores of recipients during the previous year. The recipients were divided into five categories, each with an equal number of individuals. Candidates were then categorized into quintiles based on their LYFT scores. Similarly, donor kidneys were categorized into quintiles based on their DPI.

Within the candidate quintiles, candidates were rank-ordered according to their time on dialysis. The candidates' LYFT scores were fixed at the time of listing and would not diminish with increasing age or time on dialysis. Figure 15 depicts how candidates and donors were separated into categories and matched.

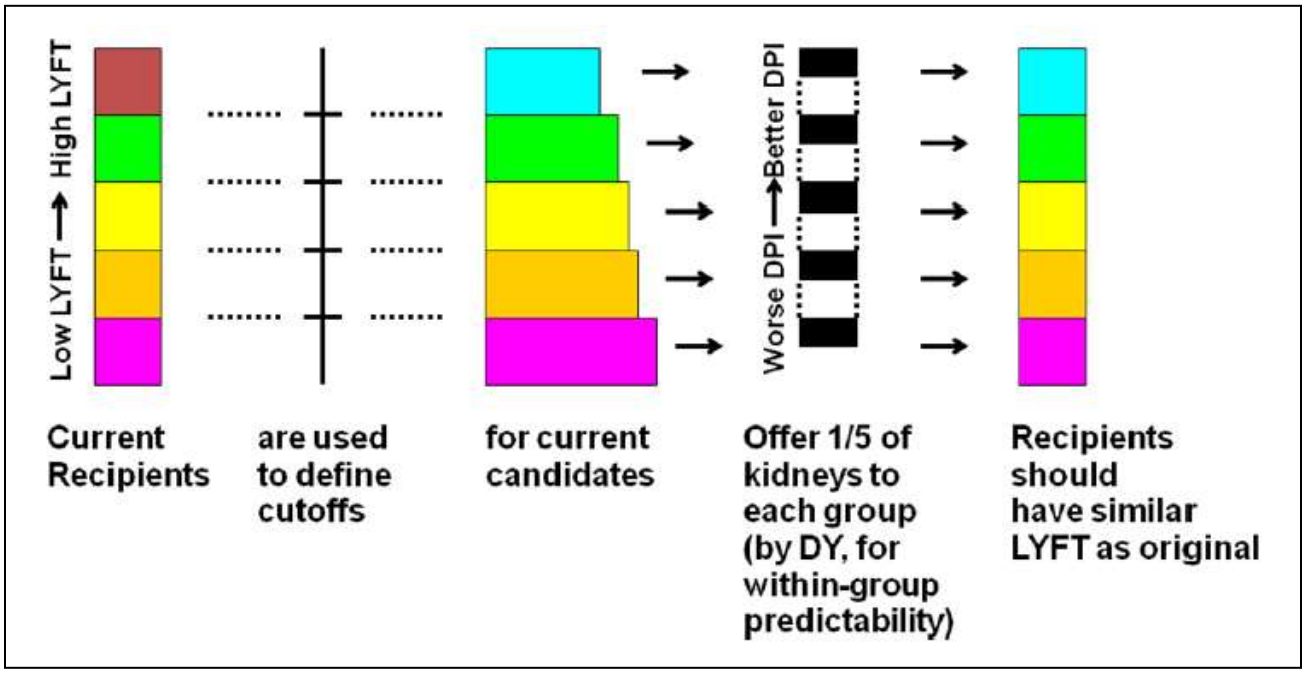


Figure 15: Method for defining donor and candidate quintiles

There was concern that candidates may miss the next highest quintile by fractions of a point, a difference that may not be clinically relevant but would preclude those candidates from the opportunity for a kidney from a donor with a better DPI. When compared to the current system, allocation based on quintiles resulted in fewer life years gained. Since this system underperformed the current system on this important metric, it was not selected for the national allocation system.

Allocation Based on Post-transplant Survival

This allocation approach is similar to the allocation approach described above where candidates are categorized according to LYFT and donors are categorized according to DPI. Rather than utilizing a LYFT score, however, this system would categorize candidates based on their post-transplant survival. By not taking into account candidate survival on dialysis (which is a component of the LYFT score), this system would not account for medical urgency. For example, candidates who may have excellent post-transplant survival but very limited survival on dialysis would not receive any additional allocation priority. As an example, candidates with Type I diabetes tend to have excellent post-transplant survival but relatively poor survival on dialysis. Without a metric to account for expected survival on dialysis, these candidates are less likely to survive to receive a transplant. Additionally, when compared to the current system, this system did not result in added years of post-transplant survival.

Opportunities to Provide Feedback

The Kidney Transplantation Committee is committed to communicating the progress of its work to the transplant community and general public. Beginning in 2005, the Committee held a series of public hearings to assess the limitations of the current kidney allocation system. In 2007, the Committee held a public forum to present some of the allocation concepts under consideration and to solicit feedback. The Committee took the feedback gained from each of these public events and incorporated it into the development of this allocation approach.

In addition to the traditional OPTN public comment process, the Committee will offer additional opportunities to engage the transplant community and general public in the policy development process. The feedback gained during this process will be considered by the Committee. Once the Committee has assessed the feedback provided, it will make any necessary modifications to its approach and circulate for public comment. The public comment proposal will contain the policy language for the proposed kidney allocation system. Due to the potential impact of this proposal, the Committee and the Board of Directors wants to ensure that all parties have had an opportunity to provide feedback.

In 2009, the Committee will host a public forum to discuss the response to this RFI. All members of the transplant community and general public are encouraged to participate in this forum. For those who are unable to attend in person, a teleconference option will be provided. Please visit www.optn.org/kars.asp for additional information.

Alerts for additional communication and education opportunities will be posted to the OPTN website (www.optn.org/kars.asp). You may also request to receive alerts for opportunities by sending an e-mail to kidneypolicy@unos.org.

Glossary of Abbreviations and Acronyms

A2	blood type
A2/A2B to B	A and AB blood types compatible with B blood type
A2B	blood type
ALU	alternative local unit
BMI	body mass index
CPRA	calculated panel reactive antibody
DPI	donor profile index
DR	antigen used in matching
DSA	donation service area
ECD	expanded criteria donor
ESRD	end-stage renal disease
HHS	Department of Health and Human Services
HLA	human leukocyte antigen
HLA MM	human leukocyte antigen - mismatch
HLA-DR	specific human leukocyte antigen - DR
HRSA	Health Resources and Services Administration, an agency of the Department of Health and Human Services
HTN	hypertension or high blood pressure
KARS	Kidney Allocation Review Subcommittee of the OPTN/UNOS Kidney Transplantation Committee
KAS	kidney allocation score
KPSAM	Kidney-Pancreas Simulated Allocation Model
LYFT	life years from transplant
OPO	organ procurement organization

OPTN	Organ Procurement and Transplantation Network
PRA	panel reactive antibody
QOL	quality of life
SCD	standard criteria donor
SPK	simultaneous pancreas-kidney transplant
SRTR	Scientific Registry of Transplant Recipients
UNOS	United Network for Organ Sharing