Update on the Development of a New U.S. Kidney Transplant Allocation System

Silas P. Norman, MD

The author is with the University of Michigan in Ann Arbor.

A substantial revision of the adult kidney allocation system in the U.S. is currently underway. The proposed revised system combines the new concepts of life years from transplant (LYFT), the donor profile index (DPI), and dialysis time (DT) into an overall kidney allocation score (KAS). The KAS for the first time integrates a measure of medical utility into kidney allocation. A KAS-based system holds the promise of improved efficiency, increased waitlist access and a gain in the number of life-years achieved from transplantation. This article discusses the rationale for the development of a new system, the state of the KAS proposal, and the challenges that remain to implementation of a new kidney allocation system.

The current deceased-donor kidney allocation system in the U.S. has been in existence for more than 20 years. Over the last 4 years there has been a dedicated effort toward the development of a new system of transplant allocation. The development of a new kidney allocation system has been driven by the competing goals of improving the utility of kidney transplantation and enhancing the equity of the system. A number of trends in kidney transplantation informed the framers of the new allocation system proposal. The average age of waitlisted candidates has increased (Figure 1), resulting in the transplantation of older candidates with multiple cardiovascular comorbidities. Consequently, there has been a marked increase in recipients dying with otherwise functional allografts[1] and a simultaneous decline in estimated post-transplant survival (Figure 2). In addition, much of the work on the system revision has been driven by an interest in eliminating extreme mismatches between donor kidney and recipient survivals. This article reviews the history of the development of the new allocation system proposal, discusses the expected outcomes if such a proposal is adopted, and discusses the progress to date toward implementation of a new kidney allocation system.

Revision of the Allocation System

The first steps toward revision of the allocation system began in 2004 when the Organ Procurement Transplant Network (OPTN) Board of Directors charged the Kidney Transplantation Committee (KTC) with performing a comprehensive review of the current allocation algorithm. The subsequent kidney allocation review subcommittee (KARS) report concluded that the allocation system was inequitable, lacked predictability, and did not effectively utilize the potential life years available from donor kidneys.[2] The current system was also shown to be no longer consistent with sections of the National Organ Transplant Act (NOTA) of 1984[3] or the OPTN Final Rule,[4] the 2 directives that guide organ

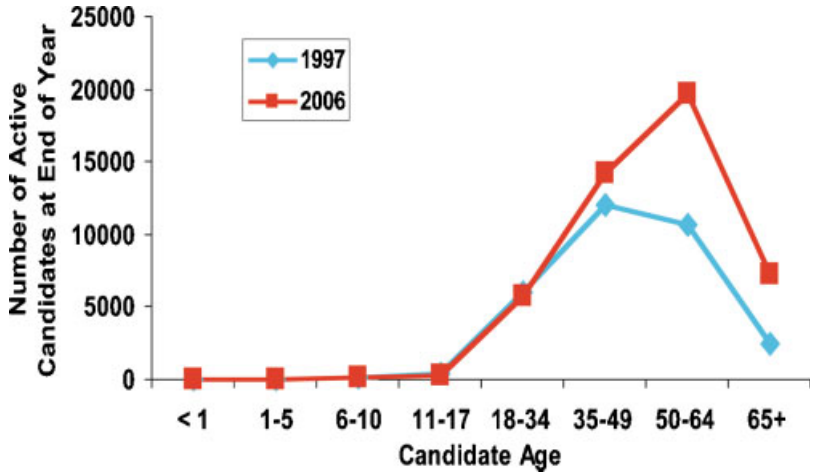

FIGURE 1. *Age of waitlist candidates by age category, 1997 and 2006.*
Source: 2007 OPTN/SRTR Annual Report, Transplant Data 1997-2006: Table 5.1a. Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation, Rockville, MD

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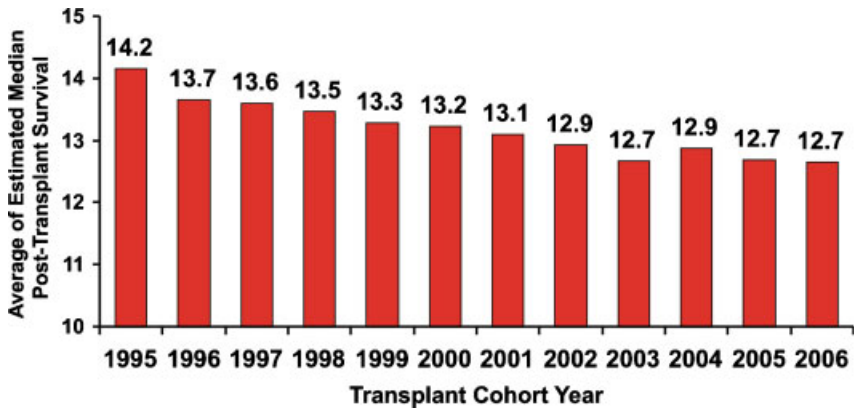

FIGURE 2. *Average of estimated median post-transplant survival by year of transplant. An estimated survival curve was generated for each recipient and the median survival in years was determined. The average was taken of the median survival for all recipients in each given year of transplant. Source: Mccullough Kp, Leichtman Ab, Port Fk, Wolfe Ra. Trends In Kidney Recipient Age And Survival Benefit Due To Transplant By Year.* Am J Transplant. *2007;7(suppl 2):231.*

TABLE I. Comparison of the current allocation system and the KAS system.

	Current	KAS
Medical Criteria	HLA	LYFT
Waiting Time	Active waitlist	DT
Sensitization	4 points for % PRA > or = 80%	4 x % PRA/100
Donor	SCD/EC	Donor profile

Abbreviations: KAS, kidney allocation score; HLA, human leukocyte antigen; LYFT, life years from transplant; DT, dialysis time; PRA, panel reactive antibody; SCD, standard criteria donor; ECD, extended criteria donor; DPI, donor profile index.

TABLE II. Covariates in the life years from transplant calculation.

Recipient Factors	Donor Factors
Age	Age
Transplant type (K or SPK)	DSA relation to recipient
Recipient diagnosis	Cause of death
Previous transplant	Deceased after cardiac death
Peak panel reactive antibodies	Human leukocyte antigens (A, B, DR)
Albumin	Cytomegalovirus status
Years on dialysis	Hypertension
Body mass index	Weight

Abbreviations: K or SPK, kidney or simultaneous kidney-pancreas; DSA, donor service area

allocation in the U.S. Specifically, NOTA directs that the allocation system be based on established medical criteria and function to increase transplantation among populations with special needs, including ethnic minority groups and sensitized candidates; the OPTN Final Rule instructs that allocation policy be based on sound medical judgment; seek to achieve the best use of donated organs; be designed to avoid wasting organs; and to promote the efficient management of organ placement.

The KTC recognized that the current system, with its emphasis on waiting time, non-biologic point scores for matching and sensitization, and a limited definition of donor quality did not adequately achieve the allocation directives. The KTC was instructed to address the limitations identified by their review through revision of the adult kidney transplant allocation system. The KTC began to explore integrating a measure of medical benefit into a new allocation system. The result has been the development of a new national allocation system proposal that would transplant waitlisted candidates on the basis of a kidney allocation score (KAS).

Components of the Kidney Allocation Score

Life Years from Transplant

The underlying considerations in the KAS are very similar to those of the current allocation system (*Table I*). Both systems contain medical criteria, recognition of waiting time and sensitization, along with measures of donor quality. In the current allocation system, the major medical criterion for allocation is human leukocyte antigen (HLA) matching. The use of HLA functions to maximize allograft survival and currently priority is based on the number of HLA-DR matches between donor and recipient. In the KAS-based system, the major medical consideration becomes life years from transplant (LYFT). The LYFT calculation describes the difference between the life expectancy of a candidate with a deceased-donor transplant from a specific donor compared to the candidates expected survival if they were not transplanted.[5] In contrast to HLA matching, LYFT seeks to optimize recipient survival and introduces for the first time a patient-centered utility measure into kidney allocation. The LYFT calculation takes into account a number of measurable factors that are known to affect long-term recipient survival including HLA matching, where HLA is assigned a weight based on its biologic effect on post-transplant survival (*Table II*). In addition, there is a quality of life (QoL) adjustment to the LYFT calculation, with the recognition that life with a functioning transplant is superior to that experienced on the waitlist or after graft failure. All candidate and recipient life years without a functioning transplant are discounted to 80% of the value of a ➲

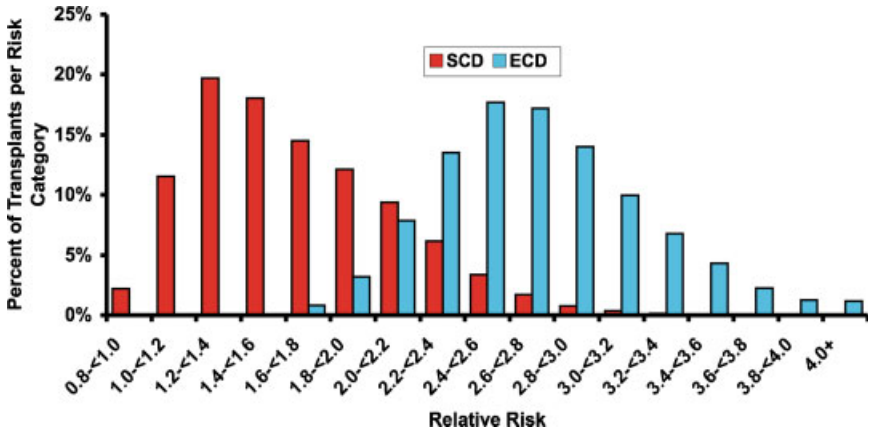

FIGURE 3. *Distribution of relative risk for graft failure among standard criteria (SCD) and extended criteria donor (ECD) organs.*
Source: Modified From Data Contained in Rao PS, et al. Comprehensive Risk Quantification Score For Deceased-Donor Kidneys: The Kidney Donor Risk Index. Transplantation. *2009;88(2):231-236 And Presentations To The KTC in 2009.*

$$KAS = LYFT \times 0.8 \times (1\text{-}DPI) + DT \times (0.8 \times DPI + 0.2) + CPRA \times 4/100$$

FIGURE 4. *Kidney Allocation Score Calculation. Source: Kidney Allocation Concepts, Request for Information. Issued by: The OPTN/UNOS Kidney Transplantation Committee. Circulated for Consideration September 24, 2008 through December 18, 2008. http://www.optn.transplant.hrsa.gov/SharedContentDocuments/KidneyAllocationSystem-RequestForInormation.pdf. Accessed July 26, 2009.*

transplanted year of life, resulting in QoL adjusted LYFT which is used in the KAS.

Dialysis Time

In a KAS-based system, waiting time is calculated from the date of first maintenance dialysis (expressed as dialysis time [DT]) in contrast to the current practice of using the date of first active waitlisting. Because the majority of candidates have initiated maintenance dialysis before the date of transplant evaluation, the waiting time often has little relation to the onset of end-stage kidney disease (ESRD). Minority candidates in particular tend to be listed after longer periods of time on dialysis than their majority counterparts and are disadvantaged by current waitlisting practice. Use of DT instead of waitlist time helps equalize access to transplant opportunities among candidates and has been in use in the states of Michigan, California, and Iowa as part of the Kidney Dialysis Wait Time Study.[6] In addition to DT, there has been broad support for preserving the opportunity for waitlisting prior to dialysis in order to maintain the possibility of pre-emptive transplantation.

Donor Profile Index

Deceased-donor kidneys are currently characterized as either standard criteria (SCD) or extended criteria donor (ECD) organs. The ECD definition identifies a group of kidneys with a higher risk for allograft failure than that of SCD organs.[7] Extended criteria donor organs are recognized to have a higher discard rate than SCD organs, presumably on the basis of physician concerns for organ quality.[8] As it happens, however, there is substantial overlap in the distribution of allograft survivals seen among SCD and ECD organs (*Figure 3*). In the KAS proposal, the Donor Profile Index (DPI) replaces the current SCD/ECD differentiation.[9] In contrast to the SCD/ECD dichotomy, the DPI provides a continuous measure of donor quality. Donor quality is evaluated as the expected risk of long-term allograft failure. The DPI is expressed numerically as a value ranging from 0 (the longest-lived kidneys) to 1 (the shortest expected graft survivals). The DPI provides transplant professionals with very specific information that can be used to consider each offer relative to the intended recipient. The DPI holds the promise of improved efficiency in the utilization of marginal kidneys by allowing physicians to more confidently match different quality donor kidneys to the appropriate candidates who could benefit from them.

Sensitization

One more consideration that has been integrated into the KAS proposal has been to redefine how candidate sensitization is prioritized. In the current allocation system, candidates with panel reactive antibodies (PRA) $\geq$80% are given the equivalent of 4 years of waiting time to prioritize them on the waiting list if a crossmatch negative organ becomes available. Candidates with PRA <80% receive no priority and are relatively disadvantaged. In addition, there is an incentive for transplant centers to report the highest PRA obtained from a candidate in order to gain priority points, even if the antigens identified would not preclude transplantation at that center. More consistent with the disadvantage of increasing PRA is to introduce a sliding scale of allocation consideration such that candidates receive priority points on a 4 times PRA divided by 100 (PRA $\times$ 4/100) scale for continuous accounting of sensitization. As the histocompatibility community has moved increasingly toward using calculated PRA (CPRA),[10,11] that is, the likelihood of a positive crossmatch given a candidate's antigens and his local donor pool, CPRA is used in the KAS proposal.

The concepts of LYFT, DT, DPI, and CPRA have been integrated into a kidney allocation score (*Figure 4*). The KAS is calculated for each candidate when a particular donor kidney (with its specific DPI) becomes available. The mathematical expression of the KAS shows that for a given candidate, as the expected survival of the donor organ decreases, the fraction

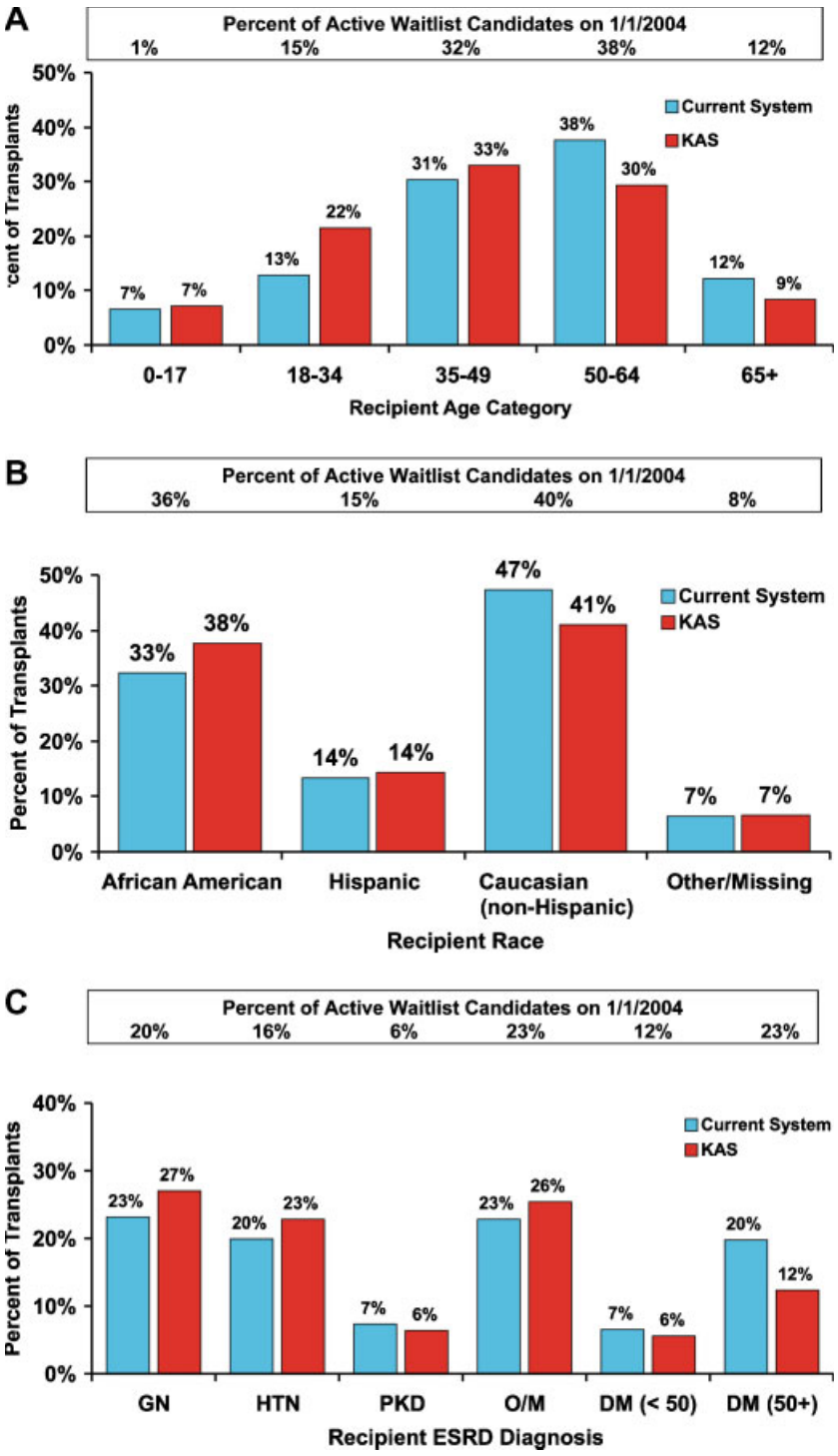

FIGURE 5. *Model of outcomes in the current system and KAS: A. By recipient age category; B. By recipient race; C. By recipient ESRD diagnosis. For each figure, the header represents the percent of active waitlist candidates that have each characteristic considered for outcome. Source: Kidney Allocation Concepts, Request for Information. Issued by: The OPTN/UNOS Kidney Transplantation Committee. Circulated 9-24-2008 through 12-18-2008. Available at: optn.transplant.hrsa.gov/SharedContentDocuments/KidneyAllocationSystem—RequestForInformation.pdf. Accessed August 13, 2009.*

of the LYFT score considered in the KAS decreases and the fraction of DT considered in the score increases. For candidates competing for very long-lived organs, consideration of the projected survival of the candidate (LYFT) is very important to maximize potential allograft years. For kidneys with shorter projected survival, DT becomes more important such that sicker candidates with lower LYFT scores and long dialysis histories can still be competitive for kidneys that may improve their lives. Similar to candidates in the current system with little waitlist time, candidates in the KAS system with both poor LYFT scores and little DT will not be competitive for organs.

Expected Outcomes From KAS-Based Allocation

Compared to the current system, an allocation system utilizing the KAS as proposed is projected to achieve an additional 3,400 years of life for patients for each year of deceased-donor allocation.[12] The additional life years are largely achieved by shifting long and moderately lived kidneys into younger candidates. Because younger candidates transplanted with better kidneys are likely to realize the full allograft survival, substantial life years are gained over the current system by KAS-based allocation. In addition, using the KAS, the number of transplants is expected to improve for African Americans, candidates with ESRD from glomerulonephritis and hypertension (*Figure 5*), and moderately sensitized individuals (not shown). The main patient groups with lower transplantation rates under the KAS compared to the current system are expected to be candidates over the age of 50 years, particularly those with diabetes mellitus (DM).

Progress to Date

In the last 4 years there has been significant effort to develop a new allocation system based on the KAS. More than 28 sets of allocation algorithms were considered prior to arriving at the current proposal.[2] A number of them, particularly the pure LYFT-based systems achieved substantially more life-years from transplant, but at a cost of decreased equity in the system. Currently, the use of DPI, DT, and PRA in allocation has been widely embraced by the ➲

transplant community. In addition, most stakeholders support the concept of better matching of recipient and allograft survivals even when LYFT itself has not been specifically supported. Although the KAS proposal improves on the current allocation system substantially, there are a number of issues to be considered by the transplant community prior to implementation. These include discussion of patient groups likely to have decreased access to transplants, questions about the accuracy of the survival estimates used in the LYFT calculation, and the complexity and predictability of the KAS-based system.

Unlike the current system where waitlist mortality is shared across all patient groups, it is clear that under the KAS system, older candidates and diabetics above age 50 will have less access to transplantation. Clearly, increasing age and the presence of diabetes decrease expectations for long-term survival. Also clear is that the shift of organs to younger candidates results in a net gain in total recipient life years. However, the fairness to decreasing access to a transplant on the basis of the biologic effects of age and DM and whether all DM should be considered equally (type 1, type 2, ESRD from DM, ESRD with DM) are issues still to be resolved. The use of age in the allocation system has been examined by the Department of Health and Human Services Office of Civil Rights (OCR) to determine if there was any issue of age discrimination. The OCR has decided to reserve judgment until a revised system is approved.

There are 2 categories of questions about the LYFT calculation. The first has to do with the relatively limited data from which the Scientific Registry of Transplant Recipients (SRTR) had available to make estimates of long-term recipient survival. Most prominently discussed is the absence of a specific measure of cardiovascular disease burden and how that might affect the accuracy of survival estimates. A subcommittee of the KTC is being formed to examine this issue. The second surrounds the accuracy with which LYFT can differentiate the survival of pairs of candidates on the waiting list. The accuracy with which LYFT can correctly order the survival of candidate pairs has been assessed by looking at the index of covariance or C-statistic of the model. A model with a C-statistic of 0.5 has a 50-50 chance of correctly ranking the survival of 2 candidates. The overall C-statistics for the components of LYFT range from 0.61 to 0.68.[13] However, this underestimates the value of the LYFT calculation. For candidates who are medically similar, LYFT provides estimates of survival that are very similar, but for candidate pairs who are medically dissimilar, the accuracy of LYFT for ordering survival increases substantially (C-statistic ~0.9). Comparison with other models used for allocation show LYFT is comparable or better than the C-statistics for waitlist survival in the liver allocation model for end-stage liver disease (MELD; 0.64) and post-transplant survival in the lung allocation score (LAS; 0.59). In the case of both MELD and the LAS there is agreement that these systems work well, serve the patient interests, and are significant improvements from their respective previous allocation systems.

Building community consensus has been as much a part of the KAS proposal as development of the score itself. There is always inertia to remain with the status quo in the face of such a large change, even if the current system is inferior to the proposed revision. The KAS proposal describes a system that is clearly more predictable than the current system but at the same time, somewhat more complex. Truthfully, the complexity is in the calculations themselves, not the concepts, but concern over patient perception has been a prominent part of system development discussion. All parties agree on the importance that patients perceive the allocation system to be fair. As such, the level of complexity that can be introduced in the name of system improvement versus the transparency necessary for patient trust will be a critical issue.[14]

There have been two public forums, a formal request for information (RFI) from the KTC along with deliberate engagement of more than 20 transplant and nontransplant organizations with a stake in the outcome of a revised kidney allocation system.[12] Based on feedback to the RFI and comments from the forums, the next steps in proposal development will likely involve modeling of alternatives to LYFT. Most alternatives to date have involved systems that were less equitable (direct age matching), imposed arbitrary cutoffs for candidate priority (donors <35 years old being offered to candidates <35 years old),[15] or have suggested allocation of only some candidates by LYFT and the remainder by waiting time.[16] Many additional alternatives will likely follow in the near future.

In the OPTN Board of Directors meeting, June 23, 2009 and a recent article, the outgoing Chairman of the KTC presented the progress to date on allocation system revision and outlined a suggested path forward for a system emphasizing dialysis time, estimated post-transplant recipient survival, and a suggestion to limit the best quality kidneys to the candidates with the highest estimated survivals.[17,18] The system would likely involve the phasing in of DT and DPI in the near future and integration of the utility measure at a later date once it was refined. Integral to the Chairman's suggestions were the preservation of patient choice in accepting kidneys and flexibility for transplant centers to focus on individual patient needs by specifying acceptable HLA matches. Each of the recent suggestions still needs to be modeled and compared with the current and KAS systems before any new allocation system proposal can be finalized.

Conclusions

The most substantial revision of the adult kidney transplant allocation system since its inception is underway. More than 4 years of effort have gone into the development of the current KAS proposal. The KAS incorporates, for the first time, a measure of medical benefit into an allocation algorithm. As simulated, the KAS holds the promise of better resource utilization, improved predictability, and significant improvement in the life years available to recipients following transplantation. The proposal still faces several challenges to approval and implementation, not the least of which is patient and provider readiness to move to a new system. At the end of the process, however, there is hope for a new deceased-donor allocation system that functions to transplant candidates efficiently and equitably, using medically-based criteria. D&T

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