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# Kidney transplantation of highly sensitized recipients under the new kidney allocation system: A reflection from five different transplant centers across the United States

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ABSTRACT

Deceased donor kidney allocation was reorganized in the United States to address several problems, including the highly sensitized patients disadvantaged with large, diverse repertoires of antibodies. Here, five transplant surgeons review their center's experience with the new allocation changes: highlighting areas of accomplishment, opportunities for improvement and, in some cases, stark differences in practice. Across these five centers the highly sensitized patients (CPRA ⩾98%) range from 5.5 to 9.2% of the 12,364 candidates on their collective waitlist. All centers reported greater rates of kidney transplantations in highly sensitized patients (12.4–27%). Three of the programs (Emory, UCSF, UW) relied upon the virtual crossmatch prior to organ acceptance in a majority of cases (70–86%)—the mere presence of antibody on HLA antibody screen was sufficient to exclude the donor in most cases at Emory and UCSF. Penn and UAB relied upon the physical flow crossmatch in almost all cases prior to proceeding with transplantation. Current or historical donor-specific antibody was occasionally crossed in certain cases at UW and UAB necessitating IVIG/plasmapheresis and/or B cell depletion perioperatively. Some authors raised concerns for cost efficiency given the increased need for organ/specimen transportation, and extensive use of hospital resources and ancillary services. In general, we found that the new allocation system has successfully achieved one of its primary goals—increased kidney transplantation in the disadvantaged, highly sensitized patients; the long-term outcomes in all patients and the cost ramifications of these changes will require continued reassessment and clarification.


## 1. Introduction

On December 4, 2014, the US kidney allocation algorithm changed significantly, as the new Kidney Allocation System (KAS) was implemented. KAS was designed to improve access to kidney transplantation for ethnic minorities and highly sensitized candidates (increase equity), as well as ensure that the highest quality kidneys were preferentially transplanted in the youngest, most healthy candidates (enhance utility) [1,2]. Specifically, dialysis time prior to listing was credited to transplant candidates as accumulated waiting time, the best kidneys as defined by kidney donor profile index (KDPI) <20% were preferentially allocated to the healthiest 20% of candidates, defined by Estimated Post Transplant Survival (EPTS) score, and candidates with calculated panel reactive antibody (cPRA) ⩾98% were given increased priority [3]. However, changes to allocation policy can have unintended consequences and may vary significantly by transplant center and donor service area. Potential KAS consequences that warrant further attention include impact on: cold ischemic time, delayed graft function rates, zero antigen mismatch transplant rate, pediatric transplant access, logistical complexity, and rate of organ discard [4]. Important graft and patient survival data are still under collection and will be scrutinized closely over time – reporting this at 1–2 years after policy implementation may not give a fair or final view of the impact of the policy change on post-transplant survival. The financial implications for the KAS remain unclear—

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for example the increased costs associated with organ transportation across larger distances, and the transplantation of patients with greater complexity.

Overall, we find that while the revised KAS increased organ equity (dramatically, for highly sensitized patients, see Table 1), it introduced short-term challenges and unmet objectives that create uncertainty about long-term outcomes. The United Network for Organ Sharing (UNOS) Kidney Transplantation Committee and national transplantation societies are actively engaged in clarifications and improvements to the KAS through public discussions and negotiation. As an adjunct to that effort we present five institutional experiences after the change in allocation and provide feedback to foster future dialogue toward even better kidney allocation.

## 2. University of Alabama, Birmingham

Approximately 4.8 million people live in the state of Alabama, comprising only 1.5% of the US population [5]; yet, Alabama has the highest incident and prevalent cases of ESRD [6]. Not surprisingly, the need for kidney transplantation among Alabamians is great, and as a result, UAB has the third largest kidney transplant waiting list in the US. Approximately 3000 candidates are listed at UAB, 9.2% of waitlist candidates have a cPRA $\geqslant$98% and 74.8% are considered an ethnic minority. Given the waitlist demographics at UAB, implementation of KAS has impacted our center in several significant ways: 1) surge in organ offers; 2) changes in donor kidney origin; and 3) changes in recipient risk profile.

We have experienced a 2.29-fold increase in the number of organ offers since implementation of KAS (1 yr pre-KAS: 322 vs. 1 yr post-KAS: 738). Prior to implementation of KAS, list maintenance required approximately 200 waitlist candidates to be transplant-ready at any given time. Since implementation of KAS, this number has risen to more than 580, and has placed strain on the evaluation and re-evaluation process. To account for workflow issues, we have implemented rapid inpatient evaluations and hired physician extenders to increase throughput in our outpatient clinics. These changes have added cost in terms of provider time and hospital resources (testing, ancillary services), yet our kidney transplant volumes pre and post KAS have remained static.

Prior to implementation of KAS, 92.7% of deceased donor kidneys came from donors within our local donor service area; post-KAS 78.7% of deceased donor kidneys come from our local donor service area ($p < 0.0001$). This represents a 15% decline in kidneys from local donors, and has increased logistical complexity due to the increase in imported kidneys. Despite increased utilization of deceased donor kidneys outside our donor service area, compared to the year prior to KAS implementation cold ischemia time (CIT) has only increased 2 h in the post-KAS era, and in fact, rates of delayed graft function (DGF) have significantly declined likely related to more stringent selection criteria for import kidneys.

Median waitlist time has decreased across all blood groups in the post-KAS era. Moreover, blood group B recipients, of which minorities represent a larger proportion, have a median waiting time 3.2 years less in the post-KAS era compared to the year prior to KAS implementation (4.0 yrs vs. 7.3 yrs, $p = 0.01$). The mechanism for this decreased waiting time among blood group B candidate remains unclear, but likely reflects a bolus effect from transplanting highly sensitized patients as we have performed few A2-to-B kidney transplants. Highly sensitized patients (cPRA $\geqslant$98%) have also been transplanted at a higher rate after implementation of KAS (11.0% vs. 2.7%, $p = 0.01$), and while not statistically significant the proportion of recipients with a history of previous transplant increased post-KAS (11.6% vs. 10.3%). Given the abrupt change in recipient risk profile, particularly the significant increase in volume of transplants among highly sensitized patients, we have implemented additional processes designed to identify allograft dysfunction early to afford the opportunity for swift intervention and preservation of function. Specifically, our algorithm for highly sensitized recipients involves: 1) avoidance of repeat mismatches with prior donors; 2) pre-treatment with rituximab in the setting of a past positive, current negative crossmatch(XM) and history of prior transplant; 3) donor specific antibody (DSA) surveillance on post-operative days 3, 7, 14, 21 and 30; 4) protocol biopsies at reperfusion, 1 month, 6 months, 1 year; 5) pre-transplant initiation of tacrolimus and mycophenolate mofetil for DSA+/XM negative transplants; and 6) avoidance of positive flow and cytotoxic XM transplants.

## 3. Emory University

At the Emory Transplant Center (ETC) our experience with the new kidney allocation system (KAS) has, with a few notable exceptions, mirrored the national experience [7]. To date the KAS has had a tremendously positive impact on our highly sensitized candidates (HSC, defined here as cPRA 98–100%) as our ability to successfully transplant these patients has increased dramatically.

Prior to the implementation of the KAS, the HSC constituted approximately 14% of our active waitlist (vs. $\sim$8% nationally) as our waitlist has a large demographic of patients who have developed HLA antigen reactivity (most commonly multiparous, African American women). Our listing approach for the HSC was the same before KAS implementation as after. Prior to the KAS, the ETC transplantation rate for the HSC approximated the infrequent national levels of 2–3% [7]. The KAS "out of the gate" reports demonstrate an initial "bolus effect" of almost 18% of all transplants to HSC nationally, which then receded down to 12.6% by July of 2015 [8]. We are transplanting HSC at a rate of $\sim$32% [9].

Our success with transplanting HSC is multifactorial but begins and ends with ability of our HLA laboratory to perform vXM upon donor hospital typing information. We define a negative vXM as the absence of DSA, as determined by single antigen bead testing (One Lambda, Inc.), from a serum sample collected within 30 days of transplantation. We typically hold a cutoff MFI for our vXM less than 2000 for HLA A, B, DR, DQ, DP and less than 5000 for the C locus. For all vXM cases, a physical XM is performed using flow cytometry. HLA antibody assessment and a vXM using a serum collected within the past 30 days (monthly serum samples are routinely collected on patients with cPRA $\geqslant$98%) has permitted our team to confidently accept organ offers and proceed directly to transplantation without a prospective physical XM.

A few factors unique to the ETC are important to mention with regard to our success under the KAS. First, our general approach to the HSC is to avoid desensitization with medical therapy. We encourage all of our HSC to seek live donation. For the HSC with a living donor we will aggressively pursue paired donor exchange via the National Kidney Registry. For HSC who have exhausted their live donation options we will accept deceased donor kidneys that fit within our criteria for HLA compatibility. Second, at the ETC important logistical tasks for managing organ offers after implementation of the KAS have been instituted to maximize our ability to transplant the HSC. We make every effort to communicate clearly with the donor hospital prior to organ offer acceptance. In cases where possible DSA is present and pre-operative donor material is not available before organ acceptance and no local back up is permitted then we would typically decline the offer.

With the increased number of organ offers to HSC with multiple HLA antibodies the KAS has undoubtedly generated greater workloads for our HLA lab, stressing the limits of our system. Our HLA lab has been able to rise to the challenge. Since the KAS implemen-