

The American Society of Transplantation responded to the nine public comment proposals released for comment on January 25, 2016 as well as a request for comment on a concept paper related to transplant performance metrics. The responses below, with the exception of the concept paper feedback, were entered on the OPTN website. The concept paper response was submitted directly to OPTN/UNOS Membership & Professional Standards Committee staff after the close of the public comment period on March 25, 2016. Many thanks to the communities of practice that shared subject matter expertise to finalize these responses.

Improving post transplant communication of new donor information

The American Society of Transplantation is supportive of this proposal, but shares the following comments for consideration by the DTAC:

Regarding VCA, there are some extra concerns for donor-derived infections (DDIs). In addition to the common bacterial organisms seen with surgical site infections and SOT, there are some additional considerations in VCA. In skin-containing VCAs, DDI related to skin flora can include Staphylococcus, Streptococcus, dermatophytes, and others; in maxillofacial transplantation, sinus/respiratory flora (MSSA/MRSA and/or gram-negative infections) and oral organisms (such as Streptococcus, anaerobes, and Capnocytophaga) should be considered, and subungal/paronychia infections may become significant for hand transplants. Possible fungal DDIs in VCA include candidiasis (mucosal or invasive), dermatophytes, endemic mycoses (histoplasmosis, coccidioidomycosis, blastomycosis), cryptococcosis, and mold infections due to filamentous fungi (Aspergillus, Mucor species, Scedosporium). Donors with known or possible cutaneous infections should be carefully evaluated prior to VCA donation, and may require additional samples, via biopsy or other modality, for culture(s) and pathology. VCAs with large amounts of skeletal muscle, such as upper extremity transplants, have potential for toxoplasmosis encystation and transmission, such that we would recommend routine serologic screening of these donors by the OPO. As VCA is a new field, we would tend to err on the side of more communication regarding possible pathogen transmission, until we have a better feel as to what would be the best guidelines regarding transmission of information for VCA.

We believe that OPOs should be required to test heart donors for toxoplasmosis. Many healthcare systems are not set up to send specimens on donors who do not have registration at their hospitals, and can't enter the data under the recipient information. Lack of clarity of donor status can make post-transplant management complicated and potentially risky. Although trimethoprim-sulfamethoxazole is commonly used for prophylaxis, intolerance is not rare, and precise knowledge of donor status can become import in clinical decision-making regarding prophylaxis and diagnosis of infection. Lack of knowledge of donor status is particularly relevant with the recent increased cost of pyrimethamine ("Drug Goes From \$13.50 a Tablet to \$750 Overnight", <http://www.nytimes.com/2015/09...>, used as a second line agent. Furthermore, toxoplasmosis is sometimes seen outside of heart recipients, and this information should be available upon request for all organ transplant recipients (which it would not be if it were

embedded in the heart transplant recipient's data). Given that OPOs send all other required donor testing, we see no reason that this should be handled differently. Toxoplasmosis infection in solid-organ transplant recipients has been associated with increased risk of morbidity and mortality based on the literature. At a minimum, the society believes that the host OPO should complete toxoplasmosis screening for all donors where heart allocation is being considered. We request further evaluation on whether this should be expanded to test all donors for this parasite.

Adding HLA DQA1 unacceptable antigen equivalences table

The American Society of Transplantation supports this proposal as written.

Changes to HOPE Act open variance

The American Society of Transplantation supports the proposed "Modifications to the Open Variance for the Recovery and Transplantation of Organs from HIV Positive Donors" as written, and believe that it fulfills the important mission as outlined, including an end date. This proposal aims to fulfill the OPTN's requirement under the HOPE Act to review the results of the scientific research to determine whether the results warrant revision of the standards of quality. UNOS must work with HOPE Act researchers to monitor the safety of the transplants performed as part of the research studies. Therefore, this proposal includes a requirement for researchers to submit periodic data safety monitoring board reports to the OPTN. This will allow UNOS to identify issues or trends across multiple research studies and proactively address potential problems.

KAS clarifications

The American Society of Transplantation is supportive of a requirement for consent for multi-organ recipients receiving kidneys with KDPI >85%. Kidney dysfunction is associated with increased morbidity and mortality in general. Additional data may be required to determine if well-functioning kidney transplant is an important variable for reducing the morbidity of multiorgan transplant recipients. Without these data, we cannot say that kidneys with KDPI >85% will not impact the outcome of a multiorgan transplant recipient. At the present time, all kidney transplant alone candidates are required to sign informed consent prior to receiving offers for kidneys with a KDPI score greater than 85%. The AST agrees that the policy should be clarified for multiorgan transplant candidates. The Society favors a policy that would require written informed consent from all multi-organ candidates to receive offers with kidneys with KDPI>85%. This consent should be obtained prior to receiving offers as is the case for kidney alone candidates.

The AST is not supportive of the removal of mandatory sharing. Members cited anecdotal evidence regarding donors and local OPOs that are discordant and troublesome for their highly sensitized candidates. The AST believes that these highly sensitized candidates should not be disadvantaged because of their rank on the top of the list, but believes that OPOs must be held accountable to improve pre-donation planning in determining recipients to keep CIT down.

Simultaneous liver-kidney allocation 2016

The American Society of Transplantation is supportive of this concept, but concerned that the proposed criteria and documentation requirements are not aligned as proposed. The Society's specific concerns are noted below:

1. Criteria for SLK priority: Our primary concern with this is table 9.6 (the problematic portion is copied below):

Criteria Documentation

Chronic kidney disease (CKD) with a measured or calculated glomerular filtration rate (GFR) less than or equal to 60 mL/min for greater than 90 consecutive days At least one of the following:

- That the candidate has begun regularly administered dialysis as an end-stage renal disease (ESRD) patient in a hospital based, independent non-hospital based, or home setting.
- At the time of registration on the kidney waiting list, that the candidate's most recent measured or calculated creatinine clearance (CrCl) or GFR is less than or equal to 30 mL/min.
- On a date after registration on the kidney waiting list, that the candidate's measured or calculated CrCl or GFR is less than or equal to 30 mL/min.

The criteria and the documentation are not aligned. The criteria reads GFR less than 60 for 90 days, but the documentation calls for a GFR 30 or less either at time of registration on the kidney list or AFTER registration and no documentation of the 90 consecutive days (although records could be reviewed by a surveyor). The criteria and documentation should be aligned, and we would suggest either omitting the third option OR clarify it by specifying that the GFR must be 30 or less at the time that the patient is also registered for a liver and thus eligible for the SLK preference in allocation. The other criteria and documentation are much more straightforward.

2. Local, and regional allocation of livers and kidneys for patients listed for SLK: The proposal would make offering of both the liver and kidney only mandatory for patients listed as 1 A or MELD of 35 or greater. It would be optional for non-1A patients or those with MELDs less than 35. This greatly disadvantages patients for whom MELD does not accurately reflect severity of illness and nearly half of all those now receiving SLKs according the data presented (and

perhaps more as the cut point for the data was 30, not 35). The AST suggests that the SLK preference be preserved at least at the local level, regardless of MELD.

3. Safety net allocation preference for liver recipients: This provision would give liver recipients who did NOT receive a SLK and have GFRs less than 20 or on dialysis within one year of liver transplant to receive priority for kidneys with KDPIs >20. This provision in the proposal appears to be well thought out and reasonable. The AST is supportive of this section of the proposal.

Additionally, the AST requests that the following points be considered as it considers additional data collection or monitoring for implementation of this proposal:

- Examining renal function after SLK in both the transplanted and native kidneys—this will give the transplant community even better sense of renal transplants done in SLK context that were not needed. We recommend that centers collect and submit data at 6 and 12 months post SLK with Cr clearance, biopsies and functional scans (all or any would be helpful) to assess whether the SLK recipient has three functioning kidneys.
- Learning more on Cr weighted MELD (patients with chronic and ESRD) and early cirrhosis vs. other MELD matched cohorts re: survival pre- and post-transplant; outcomes pre- and post-transplant.
- Collecting data on the policy effect on patients wait-listed for kidneys – i.e. how many kidney candidates are passed over? What is the increase or decrease in wait time for kidney patients before and after policy implementation?
- Capping SLK patients' MELD is a reasonable proposal provided it is based on preliminary data of use so as not to inadvertently penalize patients' best interest for the sake of controlling resources (prospectively reviewing performance will provide a safety layer).

List covered body parts for VCA

The American Society of Transplantation is supportive of the proposal as written.

National liver review board

The American Society of Transplantation does not support this proposal in its current form. The policy seeks to address regional differences (well-documented) review/granting of MELD exceptions, suggesting that these differences lead to inequities for patients when compared region to region. To our knowledge, outcomes data to address this question are suboptimally studied and documented. We believe that a well-studied needs assessment with structured/fair governance and adequate resources will benefit this effort.

Specific areas of concern include:

- The proposal for a national board is premature. In this current era where the liver community is contemplating a nationalized sharing system, the AST cautions that it may be unwise to make this change before final plans related to redistricting are in place.
- While there are differences in granting of MELD exceptions, it is not clear that this has led to worse/better outcomes for any specific patient population. Regional differences in MELD exceptions may actually reflect differences in the patient population only known to providers in those regions. The AST requests data to support the proposed shift to a national system.
- The proposed NLRB would be comprised of 5 members. This model may pose a significant time commitment for those serving on the NLRB.
- Each region has different challenges and resources that are specific to its own. We anticipate that it will be challenging and time consuming to generate national standards agreed upon by the nation's liver community, especially in relation to HCC.
- A national board may potentially constitute an oversight board that reviews regional conflicts and performances and advises on possible changes to current practices.

Adult heart allocation changes 2016

The American Society of Transplantation's Thoracic and Critical Care Community of Practice considered this proposal in detail and offers the following for consideration. These comments from the AST membership were discussed at the Cutting Edge of Transplantation's heart symposium held on February 27, 2016.

Comments to specific concerns on the proposal:

1. Is there a preference for a heart allocation score (HAS)?

Overall, the AST membership is in favor of a heart allocation score. We realize that data limitations related to evolving technology postpone a reliable HAS score at this time. We look forward to the committee's efforts to assemble such a score in the future.

2. Should ECMO be prioritized in the highest status?

There were many concerns regarding ECMO in the highest status (Status 1). One concern is that the outcome of the patients post-transplant is not optimal and based on a very few patients. We believe that patients on ECMO should be stabilized and placed on a durable mechanical circulatory support device to allow them to become better candidates for heart transplantation. A suggestion was made to make them status 1 for a 14 day limit. Another concern was that there

would be a shift in therapeutic intervention with more patients undergoing ECMO to obtain a donor heart. A suggestion was made to mandate that ECMO flows be at full use (more than 4L/min) to prevent low flow ECMO use. Another suggestion was to place ECMO in Status 2 (see below #3).

3. Is there a concern regarding status 1 inclusion of non-dischargeable biventricular mechanical circulatory support device?

Of specific concern is that the proposal for status 1 includes those patients with a non-dischargeable biventricular mechanical circulatory support. Patients who have a dischargeable biventricular mechanical circulatory support device are listed in status 2. In most cases, the device implanted depends on the technical ability and/or available device in the transplant center. In the two patient examples above, these patients with biventricular heart failure on either device are of the same illness. Therefore, programs that only have the technical experience/device availability to place a non-dischargeable biventricular mechanical circulatory support device are being advantaged over those programs that do have the technical ability to place a dischargeable biventricular mechanical circulatory support device. Furthermore, Appendix A lists those devices (by company name) that are used for non-dischargeable and dischargeable biventricular mechanical circulatory support. Status 1 patient should not qualify for Status 1 listing by the device placed but rather it should be due to their severe biventricular heart failure physiology. Mentioning devices with company names may imply favoritism of one company over another as their device (non-dischargeable device) qualifies the patient for a higher listing status. We believe that all patients in biventricular heart failure that require biventricular mechanical circulatory support should all be placed into the same status. It was mentioned that these patients with both a non-dischargeable and dischargeable biventricular mechanical circulatory support devices should be placed into status 2. This would allow programs throughout the country to implant the appropriate device (within their program's means) for their patients with severe biventricular heart failure and they would all be listed in the same tier. ECMO could also be considered in this status 2 as it would allow the patient to become more stable with transition to a more durable biventricular device.

4. Should total artificial heart (TAH) be placed in Status 2?

As noted above, the TAH is being placed for severe biventricular heart failure. It is not a support device but an actual heart replacement. Up to 40% of these patients were InterMacs 1 category which placed them in the sickest heart failure group. The TAH patients are believed to require Status 2 listing as there is no backup to the TAH unlike the left ventricular assist devices which have the diseased heart as support if there is device malfunction. The TAH patient also requires 24/7 care-giver support and the incidence of stroke is greater than that of LVADs. Implanting and providing expert care for the TAH will limit its use which will continue to be in small numbers. As noted in question #3 above, severe biventricular heart disease requiring mechanical support (TAH in this case) should be in Status 2.

5. Is placement of an intra-aortic balloon pump (IABP) of concern?

It is noted that several heart transplant programs place an IABP (via subclavian or axillary approach) as first line therapy for their patients with decompensated heart failure instead of starting intravenous inotropes. In the above case, whether a decompensated heart failure patient receives an IABP or intravenous inotropes, the patient is of the same severity yet the patient with the IABP would be in a higher status (Status 2 versus Status 3 for intravenous inotropes). Therefore, we believe that the IABP should be placed in the same category as intravenous inotropes (status 3). There is concern that many programs would place IABPs prior to administering intravenous inotropes if it would upgrade the status of their patient.

6. How should the highly sensitized patient be listed?

The AST membership believes that the sensitized patient should have an upgrade in status. However there are several concerns. Antibody strength is not standardized and the antibody threshold to designate the corresponding antigen as an avoid is also not standardized. The Canadian system which provides a status upgrade to sensitized patients has many concerns. The antibody threshold to which corresponding antigens are avoided is very low at 2000. At this low level, compatible donor heart may be excluded. A consensus conference on circulating antibodies in heart transplant is planned for April 2016 prior to the ISHLT meeting. There is also an all organ antibody consensus conference that is being organized by the American Society of Transplantation which will convene in February 2017. Hopefully, more information and technology will help in the future to appropriately list the sensitized patient.

7. Should we extend or eliminate the 30 day elective ventricular assist device (VAD) times?

This issue was split among our membership. Proponents believe that this elective time allows stable VAD patients to have a chance to receive a heart transplant before experiencing a VAD complication which are common. Avoiding VAD complications would also save monies as hospitalization for these complications are costly. Against this proposal is that stable VAD patients have good outcome and should not have a temporary upgrade which would disadvantage other patients waiting in that higher tier.

8. Will the community agree with the selected physiological principles that qualify a patient for inotrope use?

Members of the AST believe that these doses of intravenous inotropes were arbitrarily selected. Many believe that doses should not be mandated as there are some patients who do respond to lower doses of inotropes. The stated low cardiac index was found to be appropriate. The issue of maintaining a Swan-Ganz (SG) catheter was questioned. It was suggested that perhaps the SG catheter can be replaced every 2 weeks to check hemodynamics while on intravenous inotropes, but patients that should qualify for this status (the use of inotropes and continuous monitoring of filling pressures and cardiac output) are those whose degree of illness (i.e.

physiology) requires continuous hemodynamic monitoring for patient management. If a patient only requires measurements every two weeks, this patient's degree of illness is not the same as a patient that requires continuous monitoring. If a patient doesn't require continuous monitoring info for patient care, the degree of illness is less and the patient shouldn't qualify for this status but a lower status.

9. Is it appropriate to lump congenital heart disease and restrictive cardiomyopathy?

The AST membership was supportive to combine these diseases into the same tier.

10. How will broader sharing be viewed by the public?

The AST membership was split on this topic. Against broader sharing was concern regarding increasing the cold ischemic time and increasing costs. In addition, it is feared that the close relationship between the OPO and the local heart transplant center would be disrupted. A suggestion was made to decrease Zone A to 250 miles or less so as to keep ischemic time to a safe level (which may also avoid excess competition between neighboring centers).

Standardize organ coding and tracking system

The American Society of Transplantation supports this proposal. Requiring OPOs to use TransNet is essential to it becoming consistently useful to transplant centers and ultimately requiring its use at centers as well. While this creates a burden on OPOs (and ultimately transplant centers), we believe this burden is justified because it will allow the implementation of simplified, standardized methods of verifying ABO, etc. The Society believes that the ultimate goal of TransNet must include standardizing an automated process for ABO, identity, compatibility, and serology verification within TransNet that can eliminate the need for paper or other alternative processes (and the resulting variation in interpretation by surveyors) by facilitating the verification through TransNet.

Performance Metrics Concept Paper

Please accept the following feedback from the AST regarding the MPSC's request for comment regarding its concept paper. The Society appreciates the extension to allow for Executive Committee review and approval, and shares the following comments:

The AST agrees that the metrics as currently implemented are inducing unintended consequences in the transplant community, but believes that the concept proposal outlines a nuanced revision that may impact pre-transplant decision-making but not the unmeasured factors on the recipient side that may be impacting access to transplant for some "high risk" candidates. In the short term, the AST suggests reducing the number of flags if this is impacting access to patient care.

We offer the following comments to the specific questions posed:

- 1. Would you support a specific exclusion of higher risk transplants from the data analysis used to identify programs for MPSC review of one year patient and graft survival?**
 - a) If so, should higher risk transplants be defined using only donor characteristics, only recipient characteristics or both?**
 - b) If so, explain whether you agree with the specific criteria identified in this concept paper.**

No, there is no evidence that specific exclusion of higher risk transplants would improve measurement of quality of transplant centers. A recent study by Snyder et al (AJT, 2016) demonstrated that exclusion of higher risk donors had no effect on flagging programs and almost all of the low performing centers had lower than expected outcomes in 'low risk' transplants. The issue is that "high risk" in this case is defined by characteristics in the model already and are therefore accounted for by risk adjustment. The more salient concern is that factors outside of the model influence performance evaluations and while these may ultimately be influential, there are by definition not available to test. Exclusion of higher risk transplants would reduce the statistical power to test performance, not reward centers that are proficient with these transplants and increase the effect of losses associated with lower risk transplants.

- 2. Would a system like this encourage you to use kidneys that are acceptable for transplant but that you may be unlikely to accept today?**

We believe that this is the open question. While there is no evidence to support the effect on measured performance, whether this proposal would influence behavior and specifically utilization of higher risk organs is a separate untested question. If indeed, utilization rates were increased as a product of the proposal, there could be some overall net benefit. This benefit could be attenuated however if the utilization of high risk organ/recipient combinations were taken to an extreme beyond typical selection criteria leading to significantly reduced graft survival in these transplants.

- 3. Are there other issues that the MPSC work group should consider?**

The overall net change in flagging associated with this proposal seems minimal. As such all the documented unintended consequences (reduced transplant rates, volume, etc.) associated with those centers that still receive flags would still be salient and not addressed by this proposal.