ASTS Responses to OPTN Proposals Open for Public Comment

March 2022

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1. OPTN Proposal - Pediatric Candidate Pre-Transplant HIV, HBV, and HCV Testing

The American Society of Transplant Surgeons (ASTS) supports the proposal as written. This proposal removes an unnecessary timeframe from policy while still ensuring pediatric candidates safety prior to transplant. Even with the removal of the time requirement, pediatric candidates who are 10 years old or younger will still have a baseline test result, since it is already common practice to perform the HIV, HBV, and HCV tests during the candidate evaluation process. Within this cohort of pediatric candidates, the risk of HIV, HBV, and HCV transmission is significantly low while the risk of adverse medical outcomes from overdrawing blood is high; thus, this proposal aims to limit infectious disease transmission while addressing patient safety concerns.

2. Reinstatement of Updates to Candidate Data During the COVID-19 Emergency

The American Society of Transplant Surgeons (ASTS) supports the retroactive approval of the OPTN policy 1.*4.F: Updates to Candidate Data During the COVID-19 Emergency* regarding data submission during the COVID-19 pandemic.

3. Modify Graft Failure Definition for VCA

The American Society of Transplant Surgeons (ASTS) opposes this OPTN proposal with the following comments.

1. Does the proposed definition appropriately distinguish between graft failure and planned removal of a VCA graft following a successful transplant?

The proposed definition does not appropriately distinguish between graft failure and planned removal. Currently, the only VCA type with the intent of a temporary transplant is uterus. The definition of successful uterus transplantation is the birth of a healthy baby. Thus, even if the uterus transplant is planned to be removed, if the uterus is removed before the birth of a child, it will be considered graft failure. Reproductive failures unrelated to graft function (i.e. failure to carry successful pregnancy) in the absence of technical (vascular) or immunologic etiologies would not represent VCA graft failure. There may also be benefit, especially for the potential target audience, to report separately on failures to complete a successful pregnancy (miscarriage) as a relevant outcome.

Other VCA have not been performed with the intent as temporary transplants. Specifically, musculoskeletal transplants have not been reported and due to the risks of immunosuppression,

indications are considered for permanent correction of a defect. A designation of planned removal for other VCA would result in under-reporting of VCA that are designated as quality-of-life transplants.

2. **Is the definition of "planned removal of a VCA graft" clear?**

The definition is not clear. Recommendation would be to limit the application of planned removal designation only for uterus transplantation. As stated, reproductive failures unrelated to technical or immunologic graft failure should be identified separately from VCA graft failure. Under-reporting of graft failures for other VCA would be a potential consequence of a planned removal designation.

3. **Are the proposed modifications to data collection regarding uterus transplant outcomes sufficient to capture data on various circumstances (e.g. rejection of uterus graft following live birth, uterus graft removal due to contraindications to pregnancy, etc.)?**

The proposed modifications do not allow for capture of specific data on the various circumstances of non-graft failure outcomes as noted above.

4. Establish OPTN Requirement for Race Neutral Estimated Glomerular Filtration Rate (eGFR) Calculations

The American Society of Transplant Surgeons (ASTS) strongly supports the OPTN policy proposal in the recommendation to eliminate the use of race in the calculation of eGFR and re-submit our previous statement as follows. We know that the use of race in such a way is a vestige of misguided and archaic beliefs in a supposed biological difference between Black people and people of other races. However, as our understanding of human biology has evolved over the years, so should our use of these common clinical metrics.

It is important to begin by noting some overarching clinical truisms about race and transplantation. First, race is a social construct that is often used in clinical decision making and research as a surrogate for specific (and increasingly identifiable) biological processes. As noted by several NIH leaders in 2018, "imprecise use of race and ethnicity data as population descriptors in genomics research has the potential to miscommunicate the complex relationships among an individual's social identity, ancestry, socioeconomic status, and health, while also perpetuating misguided notions that discrete genetic groups exist."[1] More precise biologic markers are now available or potentially discoverable that have the potential to more accurately reflect genetic variants (e.g., APOL1 testing) to guide the design of clinical tools in our field and others. As we continue to make progress in the identification of biologic markers, it is our expectation that the imprecise and potentially harmful[2] use of race as a surrogate for biologic markers or genetic ancestry in clinical tools will discontinue. We are buoyed by recent medical advances that will replace race with more precise biologic markers.

By systematically reporting both an eGFR for Black patients and an eGFR for all other patients, we are perpetuating the notion that there is a fundamental difference in organ function between these two populations. We are encouraging healthcare providers to see these two groups as different. We are allowing a subset of the population to be "othered" in a way that could have a profound impact on everything from antibiotic dosing to kidney transplantation. The over 30 million patients with

ESRD in this country deserve an equal opportunity for kidney transplantation. We know that an eGFR less than 20 ml/min is a key lab value that allows patients to be eligible for a transplant. The fact that two clinically identical individuals could have different eGFR calculations and therefore different transplant eligibility is not a reality that we can continue to accept. This is particularly important given the disproportionately high number of Black patients who have ESRD and the fact that Black people are given a higher eGFR based on the same serum creatinine in the current system.

ASTS believes a few centers have already eliminated the use of the eGFR tool or have replaced it with a race neutral mechanism, while other centers are waiting for an OPTN policy change to formally remove it from their practice. We anticipate the use of a race neutral eGFR would increase listing, improve access, encourage earlier evaluations, and reduce wait times for black and minority patients. With the implementation of a race-neutral eGFR, transplant centers will only need to educate their coordinators and nephrology staff on listing referrals; otherwise the transition would be straightforward. ASTS recommends the OPTN establish standards by which centers provide educational resources for their staff and related health care professionals.

Transparency during implementation is key for patients and families. During this phase, we are concerned that variations in centers' abilities to openly allow patients' access to the listing process, may impact referral/care patterns and cause staffing and outreach challenges or create delays in waitlisting. Another unintended consequence is that we may have fewer data points to help us distinguish disparities in access because we are not taking race into consideration. Finally, medical formulas should be race neutral, as race is not a biological factor.

The field of medicine is not perfect. It has been shaped by the knowledge and understanding of individuals who are not immune to social systems such as racism and prejudice. But as we continue to identify areas within medicine that contain remnants of misguided race-based assumptions, it is our role as providers to eliminate them from clinical practice. The ASTS supports this change.

References:

1. Bonham VL, Green ED, Pérez-Stable EJ. Examining How Race, Ethnicity, and Ancestry Data Are Used in Biomedical Research. JAMA. 2018 Oct 16;320(15):1533-1534. doi: 10.1001/jama.2018.13609. PMID: 30264136; PMCID: PMC6640836.
2. Vyas DA, Eisenstein LG, Jones DS. Hidden in Plain Sight - Reconsidering the Use of Race Correction in Clinical Algorithms. N Engl J Med. 2020 Aug 27;383(9):874-882. doi: 10.1056/NEJMms2004740. Epub 2020 Jun 17. PMID: 32853499.

5. Proposal to Revise the OPTN Charter

The American Society of Transplant Surgeons (ASTS) strongly supports this OPTN proposal and thanks the Executive Committee for aligning language in the OPTN charter with the Final Rule.

6. Ongoing Review of National Liver Review Board (NLRB) Diagnoses

The American Society of Transplant Surgeons (ASTS) supports this policy proposal as written and provides the following responses to the OPTN Liver & Intestinal Organ Transplantation Committee's request for feedback:

1) Changes to HCC guidance: Specifically, are there candidates who would be able to bypass the six-month waiting period that shouldn't be able to? Or are there candidates who should be able to bypass the six-month waiting period but are not able to? No. The policy is well-conceived, and evidence based. ASTS does not advocate for additional candidates to bypass the waiting period and believes candidate classifications that would be able to bypass the six-month waiting period are appropriate as well. We also do not recommend changes to the proposed HCC guidance language.

2) Changes to IC guidance and PLD guidance: The proposed IC and PLD guidance are appropriate and we do not recommend changes to this proposed policy.

7. Change Calculated Panel Reactive Antibody (CPRA) Calculation

The American Society of Transplant Surgeons (ASTS) will abstain from supporting this proposal until the following issues are addressed.

On its face the proposal is relatively simple, to add sensitization to HLA-DQA, -DPB, and/or -DPA to the CPRA calculation. Aside from the merits of doing that, multiple changes are being made to CPRA in order to get to this goal. These include: 1) changing the underlying CPRA calculation, 2) including provisions for allele specific antibodies in the CPRA calculation, and 3) outsourcing the data set used to provide the frequencies underlying the calculation. That's a lot of changes in light of the fact that "current CPRA is relatively predictive of access to transplant."

The key data appear in figures 4 and 5. Figure 4 suggests that using the modified calculation, in the aggregate, there is minimal change from 'old' CPRA irrespective of whether looking at UA for which there are known frequencies (A,B,C,DR,DR51,52,53,DQB) or for UA without frequencies (DQA, DPB, DPA). However, looking at the tails of that distribution for modeled candidates with UA of known frequencies (Fig 5, lines 1&2), a few candidates had as much as 15% decrease in their CPRA value while a few had as much as 11% increase in their CPRA value. This means for a few candidates, the new CPRA calculation is quite different; why is that?

A possible explanation comes from a footnote and from information on page 8. The OPTN data set has multiple limitations, but the NMDP donor registry data set is also not without limitations. Per the proposal, 37 alleles which could have been reported as individual UA nonetheless were reported as equivalent in NMDP data. This is because NMDP considers any two alleles that are identical in primary sequence within the so-called antigen recognition domain (ARD) to be the same, even though they may have substantial differences outside the ARD that may well contribute to their antigenicity. This flaw in the NMDP dataset would have affected "over 5% of the kidney waitlist" and would have "skewed candidate CPRA up to 44 points." And yet footnote 21 states the data for Figures 4 & 5 are "based on ARD- equivalent frequency data." Is there supporting data from a dataset that is not considered to be flawed i.e. the one "typed from 2015 onward?"

Turning to the section, "Addition of DQA1, DPA1 and DPB1 loci and Allele-level Antibody Values to Calculation, it is unclear as to what the proposal asserts would happen if CPRA calculation changed. Figures 11 and 12 show the obvious. If you include sensitization for DQA1, DPA1 and DPB1 (fig.11) and if you include allelic UA (fig.12), then CPRA values will be higher, i.e. candidates will be

pushed into higher allocation categories. Technically, this increases access to transplant in the respect that candidates are awarded more allocation points. But does this mean that it will result in more transplants because every increase in CPRA value also restricts the size of the donor pool? This could be modeled, as was done when the original CPRA was implemented. The UNOS HLA committee modeled the effect of CPRA adoption on actual transplant volumes. Why isn't the current committee doing the same?

Finally, ASTS notes that much of the benefit gained by including allele-level antibody frequencies in the CPRA algorithm is contingent on increasing the level of resolution of HLA typing for deceased donors. The OPTN does not have allele frequency data for calculating allelic CPRA expressly because the allocation process does not permit deceased donors to be high-resolution HLA typed. This isn't a situation that will be changed by policy proposal. Until the typing requirements for deceased donor are changed to require allele-level typing, this proposal is before its time. And HLA typing methods have not advanced to permit both rapid and high-resolution HLA typing of deceased donors at present.

ASTS provides the following feedback to the OPTN Histocompatibility Committee's request for information.

1. Does the proposed transition time of one week for programs to view candidates' updated CPRA calculations prior to implementation allow sufficient time for kidney programs to obtain necessary documentation for allocation priority for CPRA 99-100% candidates?

   The time period of 1 week is insufficient to verify and correct all PRAs for a center. It should at least be a month. The few added weeks will not impact greatly on the overall intended outcome and may improve the quality by allowing more time for the centers to enter accurate data.

2. Would transplant programs find it beneficial in waitlist management for CPRA to be viewable for all candidates, or only candidates for organs that use CPRA in allocation?

   We do not see any benefit in having CPRA displayed in wait list management screens for organs that do not utilize CPRA for allocation.

8. Establish Minimum Kidney Donor Criteria to Require Biopsy

The American Society of Transplant Surgeons (ASTS) thanks the OPTN Kidney Transplantation Committee for the opportunity to respond to the policy on "Establishing Minimum Kidney Donor Criteria to Require Biopsy" and supports this proposal with the following recommendations.

Overall, ASTS believes providing standard donor kidney biopsy criteria will facilitate timely organ placement and minimize cold ischemia time, once the new kidney allocation system is fully implemented.

Question #1: Are these criteria globally agreeable? Are there any criteria that should be removed or added? Proposed Criteria are globally agreeable but we recommend adding the following criteria:

- Persistently elevate donor serum creatinine (any age or co-morbidities). Terminal creatinine >1.8. https://doi.org/10.1111/ctr.13990.

- Donors with DIC (any age or co-morbidities).
- Donation after Cardiac Death (DCD).

Although the OPTN committee didn't feel that donation after cardiac death (DCD) alone is a strong indicator, one could argue against that. The current criteria cannot account for potential micro thrombi development during the recovery process. Kidney biopsy is the only way to determine that. DCD status is already captured in the KDPI calculation but kidney biopsy is not an element included in that calculation.

Question #2: Are the timeframes and thresholds specified for anuria and renal replacement therapy suitable and reasonable? ASTS agrees that timeframes and thresholds for anuria and renal replacement therapy are suitable and reasonable.

Question #3: Will there be unintended consequences or impacts for OPOs? For transplant centers? Although some unintended consequences are invariably unavoidable, ASTS does not think this will have major unintended consequences or impacts for OPOs or Transplant Centers.

Finally, ASTS recommends the OPTN Kidney Transplantation Committee should standardize A1C testing criteria in donors, since the OPTN Committee included, "history of diabetes, including hemoglobin A1c (HbA 1c) of 6.5 or greater during donor evaluation or management" in the list of criteria. As mentioned in the proposal, "onset of diabetes can predate diagnosis by years," therefore it becomes imperative to obtain HbA1c in donors which have risk factors for diabetes e.g. family history, obesity, and insulin requirement (continuous or intermittent) during that hospital admission etc.

9. Standardize Kidney Biopsy Reporting and Data Collection

Overall, the American Society of Transplant Surgeons (ASTS) supports the OPTN proposal "Standardize Kidney Biopsy Reporting and Data Collection" with one caveat. The ASTS believes that standardization will reduce inconsistency in reporting and should, therefore, increase allocation efficiency. However, prior to full support for this proposal, the ASTS recommends inclusion of **arteriolar** disease as a distinct data field from **arterial** disease.

ASTS proposes the addition of **arteriolar hyalinosis** as a discrete data field with value choices of: 1**. None, 2. Focal, or 3. transmural or circumferential**. Diabetes and hypertension, common concerns for potential kidney donors, affect arterioles to a greater degree than arteries. Additionally, large arteries are more likely to be missed in sampling, further limiting usefulness. While mild arteriolar disease may be difficult to ascertain on some frozen sections, the relevant, severe arteriolar sclerosis can be recognized. Literature does support use of arteriolar disease (arteriolar hyalinosis) as a predictor of recipient outcomes [see PMID: 27333454 (Banff Preimplantation Kidney Biopsies) and PMID: 34584213]. Surgeons evaluating kidney offers frequently utilize this information as part of the decision making process; when evaluating a marginal kidney, if vascular disease data is missing (due to lack of artery sampled and no arteriolar data provided), kidneys may be discarded for insufficient reassuring data.

The ASTS supports the use of nodular mesangial glomerulosclerosis as an appropriate parameter but suggests quantifying may be helpful. The other response data field categories are sufficiently granular and should provide adequate, reliable information. The proposed form is understandable and sufficiently usable. Aligning data collection in the DDR with updates in DonorNet is sensible. There will likely be a short learning curve and teaching required for OPO staff. Of note, some pathologists may be reluctant to completely fill out the pathology form, which may lead to increased work for OPOs. The provision of a PDF sample should ease implementation.

10. Establish Eligibility Criteria and Safety Net for Heart-Kidney and Lung-Kidney Allocation

The American Society of Transplant Surgeons (ASTS) strongly supports this OPTN policy proposal with additional consideration to the following.

What is the racial make-up of the waitlist for heart and lung vs kidney?
ASTS supports this policy because our initial impression is that the proposed changes would not disproportionately impact minorities. However, the OPTN/UNOS should evaluate and establish a baseline as well as conduct a follow-up evaluation for any potential changes or unintended consequences over time. It is our hope that the proposed changes may help to standardize decisions across centers, OPOs, etc. vs. more subjective decision-making. However, we are concerned about any policies that may disadvantage underserved patient populations.

In addition, ASTS provides feedback on the OPTN Ad Hoc Multi-Organ Transplantation Committee questions:

1. Is it appropriate to use eligibility criteria for the heart-kidney and lung-kidney allocation similar to the criteria used for simultaneous liver-kidney allocation? ASTS strongly supports this concept.
2. For heart-kidney candidates diagnosed with chronic kidney disease, is less than or equal to 30 mL/min the appropriate eGFR threshold to be eligible for simultaneous heart-kidney transplantation? ASTS strongly supports this approach.
3. Should adult status 4 heart candidates who are on dialysis be included with adult heart status 1, 2, and 3 candidates as part of the simultaneous heart-kidney eligibility criteria? ASTS favors including status 4 candidates within the proposal for simultaneous heart-kidney eligibility.
4. Is the use of 500NM from the donor hospital an appropriate eligibility criteria for simultaneous heart-kidney allocation? Why or why not? ASTS strongly supports this approach as we support wider distribution in general.
5. Should the metabolic disease diagnosis in the eligibility criteria for simultaneous liver-kidney allocation also be included in the eligibility criteria for simultaneous heart-kidney and/or lung-kidney allocation? ASTS does not think the metabolic disease diagnosis needs to be included in the eligibility criteria for simultaneous heart-kidney or lung-kidney allocation.

11. Improving Liver Allocation: MELD, PELD, Status 1A and Status 1B

The American Society of Transplant Surgeons (ASTS) overall supports this proposal which seems reasonable and may improve liver allocation for children. The changes to improve liver allocation for children are overdue. The PELD/MELD score does not accurately reflect the severity of liver disease as evidenced by the majority of programs applying for exception points for their pediatric

candidates. ASTS thanks for the OPTN Liver and Intestinal Organ Transplantation Committee for their work and provides the following feedback for consideration:

1. the use of creatinine rather than eGFR. *ASTS prefers race neutral eGFR which may better represent the renal function especially with muscle wasting.*
2. the use of sex-based variable in MELD 3.0. *This may not be relevant to children, perhaps more for adults.*
3. the use of MELD 3.0 rather than SRTR-derived MELD models. *This sounds reasonable*.
4. the inclusion of albumin in the proposed MELD 3.0 model*. ASTS agrees with this addition.*
5. proposed data collection changes. *ASTS agrees with these changes.*
6. which score should be used for adolescent candidates? *We agree with MELD 1.33 points for adolescent candidates.*
7. PELD Cr? *Yes.*
8. the inclusion of additional PELD points? *Yes.*
9. proposed changed to Status 1A policy for pediatric candidates? *We agree with the proposed changes.*
10. the removal of the MELD/PELD threshold for candidates with chronic liver disease? *We agree.*
11. the updated GI bleeding threshold and the GI bleeding extension criterion? *We agree.*
12. the removal of these criteria from Status 1B policy? *We agree.*
13. proposed policy for sorting Status 1B candidates? *We agree.*
14. proposed change to liver-intestine points? *We agree with removing the MELD/PELD 25 points threshold.*
15. the proposed changes to pediatric NLRB guidance? *We agree with both proposed changes.*

12. Modify Living Donor Exclusion Criteria

The American Society of Transplant Surgeons (ASTS) supports the OPTN 14.4.E: Living Donor Exclusion Criteria policy proposal with recommendations. ASTS appreciates the opportunity to comment on this important proposal that seeks to further protect living donors, increase access to living donation, and preserve the autonomy of living donor transplant programs.

With regard to living donor exclusion criteria, the previous stipulations outlined in OPTN policy 14.4E and subsequent modifications are well-established, and the current proposal represents the OPTN Living Donor Committee effort to update them.

We comment on the proposal based on each section:

“Active malignancy or incompletely treated malignancy”

Overall, the language in the proposal fits with current modern clinical practice in living donation. We applaud the OPTN for allowing program autonomy in making clinical judgments in these cases as well, as it is difficult for the OPTN to provide specific exclusions for specific cancers that may be challenging to judge in individual circumstances. The ASTS supports the exclusion criteria as described, and agree that specific stipulations to allow for living donation in the setting of low-grade malignancy undergoing surveillance in accordance with the best clinical judgment of the living donor program. The ASTS also agrees that active malignancies such as non-melanomatous skin cancers that may have lower transmission potential should be treated in advance of living donation as well.

“High suspicion of donor coercion”

We agree with the change in language to the policy to include an exclusion of living donor candidates who are highly suspected to be under donor inducement, coercion, or undue pressure. These suspicions need to be carefully vetted by the program.

"High suspicion of illegal financial exchange between donor and recipient"

The proposed language states that the policy will be changed to the exclusion of living donors with "high suspicion of knowingly acquiring, receiving, or otherwise transferring anything of value in exchange for any human organ." The ASTS wholeheartedly agrees with the current legal precedent established by the National Organ Transplant Act of 1984 (NOTA) that prohibits donors from receiving "valuable consideration" in exchange for donation. However, the language change, as stated, leaves some subjectivity to interpretation. Under NOTA and Organ Donation and Recovery Improvement Act of 2004 (ODRIA), it is permissible for transplant recipients to support the reimbursement of costs associated with living donation to living donors, including for lost wages, child/dependent care, and travel/subsistence costs. Having recipients cover these costs for donors constitutes reimbursement and is not considered profiteering by donors through the act of donation. The National Living Donor Assistance Center, which is supported by the ASTS, is based legally on the reimbursable nature of these expenses that intrinsically are of value to those in need, and are specifically allowed to be reimbursed by recipients. The language as stated may create ambiguity for transplant programs, specifically social workers, financial counselors, and ILDAs, in advising donors and recipients on what is allowable and often much-needed reimbursement of out-of-pocket expenses. Access to this reimbursement is associated with greater access to living donor transplantation, particularly in racial/ethnic minorities and other vulnerable populations. We encourage the OPTN Living Donor Committee to modify the language of the proposal to include "high suspicion of knowingly acquiring, receiving, or otherwise transferring anything of value in exchange for any human organ. Reimbursement of living donor out-of-pocket expenses by recipients is allowable as stated in the Organ Donation and Recovery Improvement Act of 2004."

The inclusion of this final statement in our proposed addendum serves two purposes. First, the inclusion of this statement ensures that the public is aware of this language in federal statute and it continues to be a relevant and acknowledged stipulation of law that should extend beyond its presence in the verbiage of a legal act and be enlivened part of OPTN policy that guides the everyday care of living donors and recipients. Further, this statement provides clarity to living donor transplant programs so they can properly advise their patients without conflating the concepts of donor reimbursement (making a donor financially whole or financially neutral) and financial or other gains through donation (if a donor profits from donation).

"Diabetes"

We applaud the language of the exclusion policy in allowing more program autonomy in evaluating living donor candidates with pre-diabetes and diabetes. We encourage the OPTN Living Donor Committee to change the language in the policy from "Type I" and "Type II" to a more modern terminology of "insulin dependence." Insulin dependence fits more in modern endocrinology practice, and we support the notion that insulin dependent individuals should be prohibited from being kidney donors, as is currently outlined in the section of "Type I Diabetes." For the section entitled "Type II Diabetes," we believe this language should change to "Non-insulin dependent diabetes." Consideration of non-insulin dependent diabetics as living kidney donors is a clinically

nuanced decision, and is appropriate in highly selected individuals. We encourage the committee to consider the following language to exclude living donor candidates: "individuals with insulin-dependent diabetes" and "individuals with non-insulin dependent diabetes who have undergone individualized assessment of donor demographics and comorbidities and have evidence of end organ damage or a lifetime risk of complications."

"Is both less than 18 years old and mentally incapable of making an informed decision"

We had considerable debate and discussion about the potential of "mature minors" to serve as pediatric living donors. While there is considerable variation in the attitudes toward mature minor living donation, we agree with the OPTN Living Donor Committee in their approach to not be too proscriptive in written policy in this area, especially when there have not been any pediatric living donors in the US in the last decade aside from domino donors.

With regard to the language in the following sections: "Uncontrollable hypertension or history of hypertension with evidence of end organ damage," liver donor candidates with "HCV RNA positive," "HBsAg positive," "Donors with ZZ, Z-null, null-null and S-null alpha 1-antitrypsin phenotypes and untype-able phenotypes," "expected donor remnant volume less than 30% of native liver volume," and "Prior living liver donor," the ASTS Living Donor Committee supported the language proposed.

We applaud the OPTN Living Donor Committee for their work on the consideration of incarcerated individuals as living donors. A thorough study of these scenarios is warranted and it is best for living donor programs to consider these on a case-by-case basis. We appreciate the opportunity to provide feedback to the OPTN on this policy proposal.

13. Redesign Map of OPTN Regions

The American Society of Transplant Surgeons (ASTS) overall supports the portion of the proposal suggesting redesign involving 11 contiguous regions, however we oppose proposed changes to the governance structures. ASTS provides the following feedback to the OPTN Executive Committee's questions:

Which regional redesign map would best serve the OPTN or should the current map be maintained? Why?
The ASTS commends UNOS for working to balance discrepancies among the various UNOS regions in several important metrics. The Committee has offered several well thought out redesign maps for consideration. The advantages and disadvantages of lesser regions are presented as well. The ASTS believes the number of regions should remain the same at 11, and these regions should remain largely contiguous. This maintains the diversity and constancy of regional representation, and makes it less cumbersome for attending regional meetings by keeping the regions smaller. Among the redesign maps that have been presented, Figure 3(a) appears to hit the average on almost all important metrics.

Which metric(s) should the OPTN consider for reconfiguring regional boundaries?
Agree with the proposal to consider the number of transplant hospitals and number of transplant patients (both waitlist and recipients) as the metrics of choice in determining the boundaries. We would also prefer that state lines be used to determine boundaries, to factor in local state practices of the OPO and transplant centers.

Should the OPTN use one consistent regional design for governance, structure, and data reporting functions or select specialized regional designs for each? Why?
The ASTS believes that the OPTN should use one consistent design for governance, structure, and data reporting functions of regions. Considering that there is impetus to remove discrepancies between regions with the redesign map, there should be less impetus to govern them differently. The transplant community is relatively small, and well connected with each other. Implementing differences in governance and regulation between regions will only serve to create rifts in the community. With the newly implemented allocation changes, the "silos" of regions no longer exists as organs frequently cross regional boundaries at this time.

Vendor Report Archetype Designs
The ASTS appreciates the extent of detail that has gone into the preparation of the vendors report. However, the ASTS sees issues with each of the 3 archetypes described. The ASTS also understands and supports the need to trim the size of the board, but we remain insistent that each region have a voting member that should be a transplant professional due to the specialized content of the proposals.

In the vendors report, each of the archetypes have their risks and challenges described. These include creating silos, reducing diversity, and reducing Board representation, all of which are counterintuitive to our common goal. Once again, it seems reasonable to consider redesigning the regions as mentioned above first, with appropriate follow up assessment, before implementing such radical governance redesigns.

What alternative improvement initiatives will improve the regional governance model, regardless of final decisions around structure, responsibility, and governance?

- Raise awareness about the OPTN to increase national interest in participation in OPTN policy development processes, particularly among patients, donor families, and junior members of the transplant community.
- Encourage committees to share draft proposals with other committees to gather initial input/feedback, rather than obtaining such initial feedback through the public comment process.
- Clarify committee nomination and appointment processes, removing barriers to entry for new volunteers to participate.
- Ensure that all meetings conducted under the auspices of the OPTN dedicate time to best-practice sharing and collaboration in meetings, either through standardized collaborative sessions or through designated agenda topics.

14. Update on Continuous Distribution of Kidneys and Pancreata

The American Society of Transplant Surgeons (ASTS) remains supportive of increased organ distribution and system transparency. We stand neutral regarding several of the proposals made in this concept paper without more scientific evidence and with the understanding that many variables beyond geography will play an important role in our journey to establish as fair and equitable a system as possible.

With regard to how these concepts will impact patients and the community, ASTS asks what are the major shortfalls with the newly implemented 250NM circle distribution system?

Without reviewing the data / results from this system over a couple of years after the country reaches a new equilibrium, it is unclear which issues need addressing. It is also difficult to currently weigh variables based strictly on value judgments without solid data from a system in equilibrium.

For example, when considering geography and that the population is not evenly distributed, we believe a distance variable may impact rural people more severely than urban people. We believe the OPTN should weigh other critical concerns such as: population density, how many hospitals and recovery centers serve a given area, the number of transplant centers and their size; and, a combination of variables that are integral to improving health disparities and improving equity in the system. Perhaps the OPTN should consider different size circles in different parts of the country as both a more equitable and efficient distribution system that may be much more easily implemented than a continuous distribution system.

We offer the following feedback requested by the OPTN Kidney & Pancreas Transplantation Committeeon shapes of rating scales for each attribute (ex. linear, non-linear, binary) and on how each attribute should be weighted in the composite allocation score.

Medical Urgency

What other factors should be incorporated into the allocation of kidneys and pancreata within acontinuous distribution framework?

1. Do you agree with the medical urgency definition rating scale recommendation for kidney? Binary – yes. The OPTN may consider lowering the Medical Urgency allocation sequence to below99% CPRA candidates.

2. How should the medical urgency definition attribute be weighted in the composite allocation score?You can weigh medical urgency to allow for these candidates to have good access below CPRA 99%candidates that are within the 250NM area of donor hospital. They should not have priority access to Sequence A: 0-20% KDPI organs unless they are in the Top 20% EPTS. Do we know about short- and long-term outcome for medically urgent candidates to ensure these transplants are providing significant benefit? It is possible that in more rural areas of the country, these candidates may require a 500NM sharing circle for rapid transplantation.

Post-Transplant Survival

3. Do you agree with the HLA matching rating scale recommendation for kidney?
   a. DR matching is appropriate as long as data show no significant effects on various populations, asstated in the document. ASTS would like to see the data that suggests no priority should be given to 0-ABDR matched combinations, as this is not present in the figure.
   b. The committee should determine if 0-ABDR(BQ) mismatching may be a benefit in outcome for highly sensitized individuals (CPRA >= 99%) due to unmeasured minor antigens. ASTS feels that 0-ABDR matching is likely to increase the graft survival of these well matched transplant events and that some priority should be given to these well matched transplant events.

4. How should the HLA matching attribute be weighted in the composite allocation score?

HLA DR Matching appears to significantly increase the longevity of the allograft transplanted and decrease future sensitization, so this should continue to have weight that is at least equal toits current weight of 1 point per DR match equivalent to 1 year waiting time. If the committee wants to prioritize longevity of transplants, then DR matching should receive more weight.

5. How would prioritizing DR antigen matching affect different populations? From past information shown to the OPTN Kidney Committee, there was little variation in DR due to race. This needs to beverified and data analysis is needed on the past 10 years of US deceased donors vs. candidates.

6. How should HLA matching be considered for pancreata? It should add prioritization points as abovein kidney transplantation for the same reason of prolonging graft survival and limiting sensitization for subsequent transplants.

7. Should the initial implementation of kidney continuous distribution mirror current approach to longevity matching, by awarding points to EPTS Top 20 percent candidates for KDPI Top 20 percent kidneys? Or should a more sophisticated approach be considered?
   Continuous points for combinations EPTS and KPDI as described in the proposal document should beinvestigated as was proposed in the LYFT concept during KAS development. These scales are likely robust enough to allow for reasonable matching of potential organ function with patient need. There is an urgent need to recalculate KDPI for HCV positive donor organs as the long term function of these organs may be greatly improved with the ready available treatments for HCV. KDPI may also be restudied in regard to using the Cr at the time of offer versus the best donor Cr or average of Cr values, etc.

   How should EPTS be used in the new allocation framework? Although the proposal discusses fourEPTS variables currently used, the LYFT concept employed a more accurate EPTS value based on many more variables, including interactive terms with the particular donor allograft. This could incorporate HLA Matching and distance if desired. The current four variable EPTS was found to be accurate to describe the 'Top 20%' candidates and thus was employed for the current KAS that onlyneeds to differentiate the Top 20% from the total candidate pool. Therefore, we would support theoriginal EPTS definition and an interaction with the specific donor / KDPI to more accurately align the need of the recipient with the potential function of the allograft as was proposed in the originalLife-Years-From-Transplant (LYFT) proposal.

8. What are some measures of post-transplant survival for pancreata that should be considered? Exogenous Insulin free time post-transplant, or insulin as long as it is less than ½ unit per kg bodyweight per day. Oral hypoglycemics allowed.

Candidate Biology

9. Do you agree with the rating scale recommendations for CPRA? We favor a steep, non-linear scale and agree with over-prioritization for CPRA over 99.9% (99/95%) in the future system. We encourage the OPTN to recalculate CRPA based on actual access for the last couple of years and should not round up as it currently does. By current access to transplant, the most

highly-sensitized patient is rated over 99.9%, not just 99.51% which currently rounds to CPRA 100%.

In general, having a steep increase in CPRA points to the most highly sensitized is correct. High CPRA points need to be moved up to the most highly sensitized; CPRA over 99.9% or 99.95%, not just 99.51%. There are multiple publications showing those 99.51 to 99.8 have greater access to national organ offers than they should. The CPRA points needs to be recalculated based on the new 250NM sharing circles so appropriate access, not greater access, is given to sensitized patients.

10. How should the CPRA attribute be weighted in the composite allocation score? In current allocationsystem, candidates with CPRA 99.51 to around 99.8 have greater access to organs, i.e., are usually transplanted much more quickly than the average unsensitized candidate in that area. We need to more carefully balance access of high CPRA patients so that their access is fair, but not overly advantaged. The fact that many of these patients have already had multiple prior kidney transplants needs to be weighed in the overall consideration of fair and equal access to each candidate's first transplant opportunity. That is, it may be appropriate for patients who have had multiple deceased donor transplants not be prioritized over patients who have had less opportunity for kidney transplantation.

11. How should different blood types be prioritized against each other in the new system? Should non- A1/non-A1B donor kidneys be prioritized for other blood groups? If so, which blood groups? Non-A1 / non-A1B should be allocated to A and B candidates. However, the B candidates should have equal access as the A candidates, not preferred access as occurs in the current KAS. The current KAS incorrectly interpreted the non-A1 allocation intention of the original KAS committees. Currently, B candidates exist in a category above the A candidates, so a B candidate with 1 month of waiting time can get a non-A1 kidney aboveA candidates with multiple years of waiting time. This is an error in the current KAS that has yet to be corrected. The B candidates should be intermixed with the A candidates and be ranked based ontheir other variables (CPRA points, waiting time, DR matching, distance from donor hospital, etc.). This intermixing of blood types currently does occur properly in liver transplant match runs.

Patient Access

12. Do you agree with the rating scale recommendations for Prior Living Donor Candidates? Binaryscale, yes.

13. How should the prior living donor attribute be weighted in the composite allocation score? Living donors should always be weighted near the very top of the allocation list. Only in rare events, suchas a 0-ABDR mismatch in a CPRA > 99.9% candidate, should a candidate be able to come above a prior living donor.

14. What other factors should be considered in the prioritization of these candidates? DR matched organs in low KDPI donors (<35%) should be offered to prior Living Donors from longer distancesthan general allocation if the candidates are interested.

15. Do you agree with the rating scale recommendations for pediatric candidates? Giving

pediatric patients high priority for donors with KDPI <35% is very appropriate. The arguments that pediatric patients will have more rapid transplantation from higher KDPI donors is not realistic. The youngest pediatric candidates have many organ refusals before transplantation. They get many organ offers but have very low acceptance rates. We do not believe that using small pediatric donors in pediatricrecipients is a solid strategy based on literature showing improved long-term graft function in children with normal sized organs, not very small organs.

16. How should the pediatric attribute be weighted in the composite allocation score? What other factors should be considered in the prioritization of these candidates? Points for pediatric candidates based on the three age ranges mentioned should be reasonable. The allocation points tothe children can be high enough to guarantee access to these children over all but prior living donors and the most highly sensitized adults.

17. What are your thoughts on the options for waiting time outlined above? Are there other options that should be considered? Keeping waiting time as 1 point per year in linear fashion seems to be very understandable to patients and fair for allocation. There are very few patients at extremes ofwaiting times, so adjustment is just not necessary.

18. Should there be a difference in points for those candidates on or off dialysis? No. Being referred prior to dialysis for early listing helps encourage early referrals by the community nephrologists. It is also a major advantage for older candidates who may decline rapidly on dialysis.

19. Do you agree with the rating scale recommendation for kidney-after-liver safety net candidates?ASTS agrees. We would suggest that these safety net candidates have access to Sequence A, KDPI 0 to 20% donor organs only if the candidates EPTS score is in the Top 20%. Otherwise, they should all have access to Sequences B, C, and D. The Heart-Kidney and Lung-Kidney safety nets are proposed to be identical to the Liver-Kidney safety net. We would suggest the same access to KDPI sequences to all safety net candidates: all have access to Sequences B, C and D, and only those with abbreviated EPTS in the Top 20% of candidates have access to Sequence A.

20. Do you agree with maintaining the existing KDPI threshold? ASTS agrees as noted in Sequences B, C,and D. Candidates need to be in Top 20% EPTS to have access to Sequence A (KDPI 0 to 20) organs.

21. Do you have additional input on the criteria to qualify for kidney-after-liver safety net priority?Appears appropriate as it currently is except for Sequence A qualification as above.

Placement Efficiency

22. Do you agree with the Workgroup's approach to placement efficiency? The recent move to 250NM sharing circles has greatly increased the difficulty / work / expense of performing deceased donor kidney transplantation in most areas of the country. It has not increased the work for those in geographically low population density areas as those centers had already been flying in many of their deceased donor kidneys. We should evaluate how well the change in

geographic distribution of organs with the 250NM sharing circles has equated patient access before we force even broader routine sharing for deceased donor kidneys. Kidneys are not routinely flown by charter, so distance means more challenging transportation than with chartered flights for non-renal organs. We do believe that encouraging local use of difficult to place organs could decrease discards of these donated organs. This local system would need to be more friendly to the local transplant centers in many ways, including regulatory scrutiny, to encourage a meaningful improvement in organ utilization. The ASTS recommends the OPTN determine if UPS, FedEx, and chartered airlines could be contracted to address issues associated with the transport of organs, or if the major airlines could be convinced totreat organs differently than normal freight and allow loading of these closer to the time of departure to reduce ischemia times.

23. When considering placement efficiency, what donor factors should be weighted differently? KDPI > 85, anatomical injury, any complex procurement issue in DCD donation such as long WIT, poor flush,inability to pump or biopsy, etc.

24. What should the distance for the “inner plateau” be? (Figure 19) The ASTS is unclear on the value ofthe “inner plateau” and requests more information on the usefulness of this concept.

25. How steep or shallow should the driving/flying uncertainty zone be? The driving distance should beas flat as possible for 250NM.

26. How should placement efficiency for kidneys and pancreata be weighted differently in the totalcomposite allocation score? No major differences required.

27. What are some other measures of the efficient management of organ placement that should be taken into account in a points-based framework? For KDPI organs over 80, give all patients with EPTS over 80 a number of bonus points (such as 10 in the current system) to encourage their utilization into these patients before they become more ill on the waiting list. For organs that are declined by a given number of centers, the allocation system should change to maximize utilizationof that organ. This can be done in several ways, such as allocating the organ as an open offer to transplant centers.

28. How could the Workgroup account for administrative burden of organ placement? OPOs should bestrongly encouraged to offer organs during standard work-day hours. After hour organ offers are becoming the norm with the 250NM circle sharing zones.

    For predefined “difficult to place organs, “consider offering the organ(s) to one center on rotation for any patient on their list to maximize the utilization of that organ. Centers will be on rotation, soeach has equal opportunity to have open offers over the year.

29. What other methodologies should be considered for predicting ischemic time? Estimated time whena kidney is ready for transport with the availability of commercial flights, etc., but this is likely to be very complex. The OPTN could simply add 6 to 8 hours of cold time to any kidney procured after 10:00pm at night that needs to be flown by commercial jet. We should also try to work with the commercial airlines to allow organs to be flown more easily—reducing the time

window that they need to be at the airport, or see if partnering with Fed-Ex or other commercial transport services can be possible.

30. Do you agree with the en bloc rating scale recommendation for kidney? Forcing an en bloc kidney into Sequence A, KDPI 0 to 20, unfairly requires a good outcome by the transplant center. Also, centers may not wish to place their Top 20% EPTS candidates under this surgical risk, thus decreasing organ placement efficiency (Page 27 of 36). 'Masking' the true KDPI of the organs is nottransparent and should not be allowed in the US transplant system. Transplant centers were encouraged to use these organs when the en-bloc kidneys had a higher known KDPI as there was some perceived forgiveness for their increased risk of vascular thrombosis. If you allocate these organs to the standard recipient pool, KDPI over 20%, you are much more likely to improve allocation efficiency as centers are more likely to find an appropriate size recipient in this larger candidate group.

    Kidneys should be separated based on their size as is the routine practice. The OPTN should decideon a given size, for example 7cm, at which kidneys must be offered as single organs.

31. How should dual kidneys, en bloc kidneys, and islets be operationalized in the new continuous distribution framework?
    The workgroup's findings on the age and BMI when donors are not utilized for organ pancreas, and thus would be islet donors, appears reasonable (40yo and BMI >30) (Page 28 of 36). There are rare centers using allogeneic islet donors now due to FDA regulations and extreme expense. The only option for allogeneic islets in the future may be through a commercial company.

    Dual kidneys should be offered more quickly in the allocation process when more than five (or eight) unique transplant centers have declined a donor for standard adult allocation patients on the matchrun.