The American Society of Transplantation (AST) responded to 15 items that the OPTN posted for feedback during the July 27 – September 19, 2023, public comment period. This includes the proposal "Modify Lung Allocation by Blood Type" posted August 24 – September 7, 2023, during a special public comment period. The responses submitted to the OPTN during this public comment cycle are below, and derived from the AST's communities of practice, OPTN/UNOS Policy Committee, and Board of Directors input.

1. Modify Lung Allocation by Blood Type

The American Society of Transplantation (AST) is supportive of the proposal, "Modify Lung Allocation by Blood Type."

2. Efficiency and Utilization in Kidney and Pancreas Continuous Distribution

The American Society of Transplantation (AST) is generally supportive of what is outlined in the request for feedback, "Efficiency and Utilization in Kidney and Pancreas Continuous Distribution," and offers the following comments for consideration:

- Placement efficiency is of high importance for released organs to make sure that they are transplanted. OPOs should be allowed to place these organs in similar fashion as hard to place kidneys/pancreata to minimize cold time. The AST suggests that the OPTN require OPOs to run a released organ match run based around the previously accepting transplant program and supports carrying over previous refusals as outlined.
- The Committee has done a lot of background work to calculate percentage and sequence run data for appropriate use of kidney minimum acceptance criteria (KiMAC) in continuous distribution. The AST believes there should be further research into clearly defining "hard to place" kidneys to improve the allocation, placement, and utilization of such organs using KiMAC. The goal of increasing efficiency would be best met by immediately applying KiMAC to the entire match run, with a longer-term goal that transplant centers use the offer filters appropriately, the role of KiMAC will decrease, and the match run can be simplified with a combination of KiMAC and offer filters. Until then, we support KiMAC being run at 8% with the mentioned exclusions.
- The AST supports a dual kidney match run that carries over the qualifying refusals to minimize allocation time. As dual kidney allocations essentially include hard to place kidneys and time is of essence, the AST supports the placement efficiency attribute for this allocation. The AST also recognizes the existing complexities OPOs are required to manage and the lack of clarity around how to prioritize the variety of match runs that exist. If the OPTN determines a second, dual kidney match is not advisable, the AST recommends the creation of clearly defined donor eligibility criteria for dual kidney allocation and a modification to the current match run similar to the appearance of the mandatory kidney share indicator. This would provide OPOs the option to allocate kidneys meeting the aforementioned donor eligibility criteria as either single or dual as they work down the match run.
- If a separate match run on the same donor is generated (either for dual kidney or for released organs) it will be important for both the offer notification and the information in DonorNet to make this clear (including the reason for a separate match run and offer notification) so that centers recognize when they are re-reviewing a donor and can efficiently generate a response.
- The AST recommends that programs obtain patient consent prior to opting candidates into receiving dual kidney offers. Dual kidney transplants carry separate risks perioperatively that ought to be discussed prior to being listed on a dual kidney match run. In addition, without

prior consent, the efficiency of placement of dual kidneys may be compromised if the intended recipient declines the offer simply for being a dual kidney offer because they had not previously been consented to opt in for the separate dual kidney match run.

- For dual kidney offers, the AST recommends the donor meet at least two of the following criteria:
  - Cold time > 6 hours
  - Terminal creatinine >1.5, cerebrovascular accident, and age >60
  - Hypertension> 10 years
  - Diabetes mellitus
  - Kidney donor profile index (KDPI) >60% - glomerulosclerosis (GS) >10%; KDPI 35-59% - GS >20%
  - Vascular disease and >10% fibrin thrombi
  - Anuria

- The AST recommends the OPTN creates a unique field for donors to capture dialysis/ continuous renal replacement therapy.
- The AST recommends waiting for 6% or Sequence >500 as a pre-procurement threshold for offering dual organs (given the organs match certain criteria mentioned above).
- The AST supports the recommendations for *en bloc* kidney allocation. Using the *en bloc* coefficient within the KDRI calculation to assign *en bloc* kidneys a KDPI score in continuous distribution is reasonable.
- The AST supports maintaining the 250NM distance for applying facilitated pancreas bypasses and the proposed qualifying criteria. The qualifying criteria should be applied for six months and reassessed on an annual basis. Regarding the proposed qualifying criteria from two to four pancreas transplants from donors > 250 NM in the previous two years- what percentage of pancreas transplants that are performed using grafts >250 NM from the donor are facilitated pancreas offers? With the current two transplants in two years threshold, 46 of 118 (39%) of programs are eligible for facilitated pancreas allocation. Raising the requirement to four transplants in years will reduce this percentage. If a center is no longer eligible for facilitated pancreas offers with this new proposal, and facilitated pancreas allocation is a major factor for how that center obtain pancreas grafts >250NM away, how would the program manage to regain the opportunity for facilitated pancreas offers in the future?
- The AST supports exception-based medical urgency for pancreas based on documented hypoglycemia unawareness.
- The AST wants to underscore the need to capture nuances in the point-based framework which may impact pediatric kidney and pancreas transplant recipients such as size discrepancy, or post-transplant survival, so that attributes which will impact organ access for pediatric patients get adequate weightage or priority.

3. <u>Update Guidance on Optimizing VCA Recovery</u>

The American Society of Transplantation (AST) supports the proposal, “Update Guidance on Optimizing VCA Recovery.”

4. Remove CPRA 99-100% Form for Highly Sensitized Candidates

The American Society of Transplantation (AST) generally supports the proposal, "Remove CPRA 99-100% Form for Highly Sensitized Candidates," and offers the following comments for consideration:

- While the AST appreciates the Committee's diligence in initially crafting policy requirements which promote compliance, we agree that in the absence of abuse this form is no longer necessary and should be abolished promptly considering the evidence the process may inadvertently delay candidates receiving offers.
- The AST believes maintaining the requirement that laboratories review and verify OPTN waiting list HLA data, including the unacceptable antigens listed for a candidate and retaining source documents (testing results) in accordance with applicable federal and state law, is sufficient. If there is a need to ensure compliance and accuracy of CPRA, this could be added as an additional data element that is reviewed during routine triennial surveys.
- Regarding other barriers highly sensitized patients may face, listing of allele-specific unacceptable antigens for highly sensitized candidates remains problematic. Because most donor typing is at the serologic antigen level, the match run often makes incompatible offers to these candidates. Highly sensitized patients are disadvantaged when centers choose to list antigen-level unacceptables to manage this issue, when only allele-specific unacceptables are justified by the antibody screening data. Thus, the burden on transplant centers of HLA-incompatible offers that must be refused through virtual crossmatch analysis remains a barrier to listing.
- The AST recommends continued monitoring and revisiting of data six months after implementation to assure that there isn't an impact in access or equity.

5. Modify Organ Offer Acceptance Limit

The American Society of Transplantation (AST) generally supports the proposal, "Modify Organ Offer Acceptance Limit." This proposal is an important first step towards aligning the allocation system with the goal of increased efficiency and improved organ utilization. The AST offers the following comments for consideration:

- In addition to the allocation inefficiencies outlined in the proposal that result from late declines, these inefficiencies also prompt equity concerns as deviating from the match is sometimes necessary to avoid discarding a transplantable organ.
- For additional context, consider that within Eurotransplant there is a policy that a recipient, who accepted an offer, will not receive any new offers unless the organ is turned down by the center after it was initially accepted.
- The AST suggests reconsidering the appropriateness of incorporating exceptions to this policy:
    - Adding exceptions will increase the risk of non-utilization which is counter to the goal of this proposal. If thoracic-specific and liver-specific exceptions for DCD donors can be crafted in a way that doesn't limit reduction of non-utilization, then AST would support those approaches.
    - The AST believes exceptions for patients of the highest medical urgency where delay in organ acceptance may risk patient death, e.g., high priority pediatric patients, would be reasonable. The proposed policy would be strengthened if there was a pathway to facilitate multiple acceptances in these scenarios to circumvent considerations about policy noncompliance.

- If feedback indicates this proposal is not supported, an alternative would be to set a time limit “prior to procurement time” (e.g., within six hours of the donor OR time) for which a program must “choose” between the two offers.

6. Require Reporting of Patient Safety Events

The American Society of Transplantation (AST) generally supports the proposal, “Require Reporting of Patient Safety Events,” and provides the following comments for consideration:

- The AST agrees with the proposed expanded patient safety event reporting requirements. Having a broader safety event reporting structure will help guide policy making in the future and improve patient outcomes.
- The AST requests that the OPTN address the ambiguity of the proposed requirement that members report “Any sanction is taken by a state medical board or other professional body against a transplant professional working for an OPTN member” absent clear definitions of “sanction” and “other professional body.” A sanction could be broadly interpreted to mean any action- investigation, hearings, suspension, probation, dismissal (or denial of reappointment), public reprimand, fines, remediation, revocation of licensure, etc. Likewise, a professional body could be assumed to include even an institution’s internal medical staffing and performance committees.

  Appendix D.10 of the OPTN Bylaws, Investigation of Transplant Personnel, states, “The hospital’s investigation must use the hospital’s standard medical peer review process for conducting inquiries of potential professional misconduct and conclude with appropriate action consistent with this process.” While we recognize the importance of transparency and the need to ameliorate threats to patient safety within the transplant community, we are concerned that if the MPSC’s intention is to incorporate the broader definitions, this may deny providers a fair internal peer review process and unnecessarily put the program and or institution at risk for claims of defamation, particularly if any ongoing investigation finds the provider acted reasonably and within the standard of care. On the contrary, if the MPSC’s intent is to limit the definitions and scope to include for example, revocation of license, we would have some concerns regarding the timing of such events as medical boards often deliberate for great lengths of time and may not move forward such a recommendation for a more than a year following the event prompting review. In scenarios involving these delayed recommendations, it is entirely plausible that the provider in question departs the institution at which the initial event occurred. What then is the institution’s obligation to monitor the outcome of such investigations and subsequently report any sanctions handed down?
- There are concerns with prescriptively defining “near miss” events as proposed. Heterogeneity in center practices may lead the same occurrence to be classified as a “near miss” at one center and not another (e.g., based on the center’s workflow of when recipients are brought to the OR holding area or the timing of verifications). The proposed definitions also prompt concerns that occurrences involving appropriate leveraging of safety processes will be inappropriately classified as a near miss. The AST suggests "near miss" events that rise to the level of alerting the OPTN/HRSA would be those in which an error was caught by chance after making it through all the check points and safety measures already in place (or perhaps caught at the last routine check point), suggesting that additional precautions may be needed to reliably prevent the error.
- Currently, the OPTN is not required to report transportation issues to HRSA. Therefore, the rationale for including these events with events the OPTN is required to report to HRSA is

unclear. If collection of information focused on the non-use of organs as a safety event is an OPTN priority, AST suggests excluding transportation issues from this proposal and addressing transportation issues – including clearer definitions focused on member preventable causes – with a separate proposal. In that case, reporting requirements for non-use of organs intended for transplant should be broadened to include other, more common causes, for example- surgical recovery errors.

7. <u>Deceased Donor Support Therapy Data Collection</u>

The American Society of Transplantation (AST) generally supports the proposal, "Deceased Donor Support Therapy Data Collection," and offers the following comments for consideration:

- Transitioning this data collection from narrative form to discreet quantitative elements will improve organ allocation efficiency by providing clear and concise data, that can be found in UNet in a consistent location. Additionally, collecting this information in a discreet field will be useful for evaluating post-transplant outcomes for recipients of organs from donors supported by these therapies and may improve research opportunities.
- Consider adding an additional field for reason intervention discontinued (e.g., "organ procurement", "withdrawal of care", "logistics", or "patient improved"). The inclusion of an additional field to collect discontinued intervention data would be important for centers evaluating the donor, potential future use for filters, and for retrospective data reviews.
- Start and end times can reasonably replace the current field requesting "duration."
- Recognizing the added data burden of recording this information, and the potential this data burden leads to inaccurate data, an alternative that may be useful is a field for indication to initiate therapy, particularly for renal replacement therapy (e.g., specific organ failure, clearance of toxins, volume management).
- Regarding other donor support interventions not mentioned, consider intra-aortic balloon pump, left ventricle assist devices (LVAD), peritoneal dialysis (used in critical care settings during COVID-19 Epidemic), and other renal replacement therapies.
- Regarding additional data elements related to this effort that could be added or eliminated, consider patients on continuous renal replacement therapy/continuous veno-venous hemodialysis/hemodialysis/peritoneal dialysis/etc., there should be an indicator field for pre-existing chronic kidney disease/end-stage renal disease versus acute kidney injury versus both. Additionally, with the inclusion of dialysis start and stop dates, consider accommodating multiple start and stop dates for a given modality.
- Anticoagulation therapy (heparin drip, bivalirudin, etc.) which is often implemented during ECMO and mechanical circulatory devices remains controversial and different among the institutions. However, their impacts on donor organs' quality, management, and transplant outcomes are so understudied that the collected data will be very important so that they should help move forward this project. We'd strongly suggest these data be proactively collected as well.

8. <u>Concepts for a Collaborative Approach to Living Donor Data Collection</u>

The American Society of Transplantation (AST) is generally supportive of what is outlined in the concept paper, “Concepts for a Collaborative Approach to Living Donor Data Collection,” and offers the following comments for consideration:

- The AST applauds this effort, and believes it is relevant to highlight an American Journal of Transplantation paper by Dr. Sanjay Kulkarni *et al*. regarding how the healthcare system and community engagement can be leveraged for long term donor follow-up (Am J Transplant. 2016;16(12):3385-3391).
- The AST believes it is reasonable to shift donor follow up from the OPTN to the Living Donor Collective (LDC).
- There are significant concerns that implementing some version of this concept will pose an increased burden on transplant hospital staff, as well as the donors who may not want to be contacted for an indefinite period. Either of these factors could negatively affect completeness of data collection, particularly at longer time points, and dampen the goals of the initiative. IT solutions to automate data transfer to LDC would help alleviate this additional burden and improve compliance.
- Due to concerns around increased staff and donor burden, a lack of adequate resources for reporting, and varied definitions for the beginning of a living donor evaluation, the AST believes it is essential to make participation in this program voluntary for each transplant hospital and each individual living donor candidate.
- Living donor candidates will have to consent to participate and provide this information. Transplant programs may not be the appropriate collector of these data as the donor’s decision, to donate or not to donate, is confidential. It may be more effective if a non-affiliated entity allowed donors to provide this information securely, independently, and confidentially.
- To make meaningful improvements in rates of living donation, it will be important to clearly define the beginning of the living donor evaluation, and use consistent nomenclature to support this definition, i.e., living donor candidate versus potential living donor (the AST suggests that “living donor candidate” is the most appropriate term). The living donor evaluation process is heterogenous among programs based on volume, geography, and patient characteristics. The AST believes it is reasonable to consider any living donor candidate who was educated, consented, and underwent any of the consultations or testing defined in OPTN Policy 14 to have begun the evaluation process whether they physically presented to the program or not.
- It will also be important to capture reasons why donors who have expressed interest (e.g., by submitting a health history questionnaire) are not selected for evaluation.
- The AST recommends that the OPTN also include the collection of pre-donation cystatin C, urine albumin to creatinine ratio, and psychosocial outcomes after donation.

9. Recognizing Seasonal and Geographically Endemic Infections in Organ Donors: Considerations during Deceased and Living Donor Evaluation

The American Society of Transplantation (AST) generally supports the proposed guidance document, "Recognizing Seasonal and Geographically Endemic Infections in Organ Donors: Considerations during Deceased and Living Donor Evaluation," and offers the following comments for consideration:

- Revisions to aspects of the section addressing histoplasma are recommended:
  - Donor screening for active histoplasmosis should use urine histoplasma antigen, rather than histoplasma antibodies by complement fixation. Serology may detect prior infection, which is common in endemic areas but does not confirm active or transmissible infection.
  - The recommendation to screen donors with a history of pneumonia of unknown type in the past two years is overly broad and will likely capture many potential donors who do not have histoplasma. The AST recommends clarifying what is meant by "unknown," as most pneumonias do not receive a microbiologic diagnosis. Additionally, the AST recommends changing the arbitrary two-year time frame, as potential donors who have recovered from illness (particularly if infected months to years prior to donation) are unlikely to transmit histoplasma.
- The AST recommends incorporating other endemic infectious diseases, e.g., babesiosis, yellow fever, in this guidance document or in future versions.
- A deceased donor's cause of death must also be considered when assessing a donor's risk of transmissible infection. For example, deceased donors who had seizures or febrile coma at time of death should be tested for viral encephalitis prior to donation.
- Frequent and effective communication between the transplant center and the OPO about infectious disease risks is critical. The OPTN should consider a standardized form for communicating this information to help transplant centers collect the necessary information and report it in a timely fashion. Periodic review of these forms should also be planned to account for changes in the prevalence of endemic diseases, reporting requirements, and transplant centers' ability to comply. Another suggestion to assist with communication is the addition of optional fields in UNet that would allow for transplant hospitals and OPOs to communicate and exchange information about potential endemic infectious disease risks.
- Communication between patients and transplant centers regarding the testing for endemic diseases is also critical and should be accomplished through consent forms that specify the endemic disease screening that will occur.
- Specifically for living donors, the AST believes consent forms should be updated to inform potential donors about the disclosure of these test results to the recipient for full transparency. Transplant centers should also be encouraged to develop workflows for communicating these test results.

10. Update on Continuous Distribution of Livers and Intestines

The American Society of Transplantation (AST) is generally supportive of what is outlined in the committee update, "Update on Continuous Distribution of Livers and Intestines," and offers the following comments for consideration:

- The proposed continuous distribution system incorporates both removal of hard geographic limits from prioritization and simultaneous implementation of a major overhaul in the prioritization scheme for patients to include several prioritization metrics that have not been validated with regards to alterations in waitlist and post-transplant outcomes. The impact of these factors should be carefully modeled and should not just be implemented and reassessed in real-time. While the system has potential to improve allocation, there is a real risk of unforeseen adverse impact on certain patient populations.
- Concern was raised regarding the difficulty of reallocation of organs, such as in the OR, with this system. Some inherent flexibility should be maintained for intraoperative reallocation so as not to inadvertently decrease utilization of transplantable organs.
- There are concerns about the continuous distribution implementation timeline. Liver allocation has only recently moved towards MELD 3.0, and several in the community were reluctant to see additional changes implemented in the absence of data regarding the effect of these most recent allocation changes, including extensive modeling of a new proposed system. There is precedence for continuous distribution, with the UK currently implementing a Net Benefit model for organ allocation; however, this system did not result in improvements in post-transplant outcomes when applied to external populations in New Zealand.
- It is stated that the committee will not include post-transplant outcomes in the initial iteration of continuous distribution. While avoidance of liver transplant futility is one of the principles defined in the Final Rule, current pre-transplant indices have not been shown to reliably identify patients at high risk for post-transplant mortality. The current population of liver transplant recipients is evolving, and historic indices may not reflect risks of the current population. Nonetheless, calculated risk for post-transplant mortality is continuously assessed by the SRTR in evaluation of center-level transplant outcomes. The Committee should explain why these models cannot serve as a starting point for a post-transplant score component.
- Although frailty metrics have been proposed as a mechanism to predict post-transplant outcome, current metrics are subject to reporter bias and manipulation. The AST recommends collecting data to assess the impact of frailty on both pre- and post-transplant mortality so that validated frailty factors can be incorporated in these models. Similar consideration should also be given to particularly vulnerable populations, such as pediatrics, re-transplant, ACLF, ALF, and geographically and socioeconomically disadvantaged groups.
- There is a need to address utilization of DCD organs and implementation of machine perfusion technology in the design of any algorithm, as these have the potential to affect center practice and future organ utilization. Especially in the case of machine perfusion technology, existing data is too preliminary to determine long-term implications.
- The proposed algorithm denotes a major alteration in liver and intestinal organ allocation. OPTN data regarding the prioritization of continuous distribution demonstrates differing opinion of the various stakeholders regarding the importance of distribution components. In contrast, medical urgency (as measured by MELD and its derivatives) is identified by the final rule as one of the main dictates for waitlist prioritization, and it must continue to be weighted as such.

- Clarification is necessary regarding how the risk for increased waitlist mortality for patients with MELD exceptions will be accommodated so as to not disadvantage these patients.
- The local impact on candidates residing in/near poorly performing OPOs should be considered, and OPO performance standards should be created and adhered to.
- While incorporation of body surface area may improve inequity for short stature patients, concerns were raised that these metrics may be artificially altered through modulation of volume status.
- Prioritization should be considered for patients able to receive organs via ground transportation, given its ability to make transplant more accessible and reduce transportation costs.
- The AST agrees with the committee's decision to table discussions on MELD/PELD and OPOM/POPOM until they can assess the results of each medical urgency score in the mathematical optimization analysis.
- It is unclear how incorporating a "population density" or "geographic equity" score component will improve patient-centered equity goals of continuous distribution. It is critical that the new liver allocation system solely focus on candidate access, not transplant hospital access.
- While proximity was not a prominent attribute in the values prioritization exercise (VPE), it may play a relevant role in the acceptance and utilization of potential donor livers. Proximity may not need to be heavily weighted for the continuous distribution model but for efficiency in allocation or placement, two options include:
    - Facilitated placement with centers known to aggressively accept open offer/intraoperative offers at a certain rate if the liver has not been placed by some time period prior to organ recovery.
    - Designation of a primary local backup as the first choice backup if there is an intraoperative refusal.
- Regarding attributes in Table 1, all attributes are independently discussed in the proposal and/or a part of the VPE except for travel efficiency. Given that there will be emphasis on geographic equity and proximity efficiency, we wonder whether travel efficiency has to be included in the model to further improve utility, access, or equity.
- Particularly given advancements in organ perfusion and preservation, we agree that candidates at similar MELD scores should receive similar access to liver offers regardless of the location of their transplant program, however this argument does not acknowledge the complex operational realities of the overall healthcare system in which transplant is a simple component. These technologies and travel, especially by air are incredibly expensive – not every program has the means or resources to support such practices. We must be mindful of the potential unintended consequences on an already fiscally strained system.
- The implementation of kidney organ offer filter tools has been helpful and the AST would urge the OPTN to prioritize developing similar tools for liver offers.

11. Clarification of OPO and Living Donor Recovery Hospital Requirements for Donors with Positive HIV Test Results

The American Society of Transplantation (AST) is generally supportive of what is outlined in the concept paper, "Clarification of OPO and Living Donor Recovery Hospital Requirements for Donors with Positive HIV Test Results," and offers the following comments for consideration:

- The AST applauds this effort, which must begin with detailed data-gathering. What is the absolute number and proportion of potential donors with any positive test for HIV that are ultimately confirmed to be a false positive, or cannot be confirmed to be a true positive? If this, the broadest example, is very rare, then it may not be efficient to establish a complex protocol and associated safety features for further interrogating this issue.
- The above findings can be considered separately for pediatric and adult donors because of differences in HIV prevalence, pre-test probability of HIV infection, and false-positive rates. There would be a low threshold to expand a protocol and associated safety features created for pediatric donors to also include the adult donors- if the OPTN creates an algorithm to address this issue, it should be put to maximal use.
- An additional study on those donors that test positive for HIV, and whether there are any distinguishing factors for those believed to be false positives, would be welcomed.
- Regarding utilization, the OPTN should also account for hearts and lungs from these donors, i.e., if abdominal organs were used for HOPE transplants but HIV results are ultimately thought to be false positive, could the heart and lungs from these donors also have been transplanted?
- This effort should include the OPTN Ethics Committee and input from other bioethicists to address the ethical implications of having or not having a zero-tolerance policy.

12. Continuous Distribution of Hearts

The American Society of Transplantation (AST) is generally supportive of what is outlined in the concept paper, "Continuous Distribution of Hearts Concept Paper," and offers the following comments for consideration:

- The AST commends the careful deliberation about the benefits and potential harms of including post-transplant survival as an attribute. The OPTN Heart Transplantation Committee (Committee) raised reasonable questions about the appropriateness of including this metric without a well-validated model. However, it is not clear from the concept paper why current SRTR performance models are sufficient for assessing heart program performance, but insufficient to serve as a post-transplant survival component of the heart composite allocation score.
- Regardless, AST supports the Committee's suggestion that the framework under development can be modified eventually to consider inclusion of a well-established and validated metric, and that such an approach would be preferable to including post-transplant survival in the initial policy proposal without robust support for the metric itself.
- The AST recommends in addition to waiting time accrued with an implanted VAD or LVAD, the Committee consider including a pathway for candidates with demonstrated complications or intolerance to the implanted device.

- The AST strongly supports incorporating in the initial version of the heart continuous distribution policies the congenital heart disease and hypertrophic and restrictive cardiomyopathy recommendations in the current guidance document for heart status exception requests. The AST urges the Committee to consider other opportunities to move away from the current exception dependent practice.
- With regards to placement efficiency, maintaining some semblance to the current system which considers distance between the donor and transplant hospital seems reasonable.
- The AST wants to underscore the need to capture nuances in the point-based framework which may impact pediatric heart transplant recipients such as size discrepancy, or post-transplant survival, so that attributes which will impact organ access for pediatric patients get adequate weightage or priority.
- In response to the specific questions included in the proposal:

Are the attributes the Committee has identified for inclusion in the first version of the continuous distribution of heart allocation framework appropriate? Do you agree with the Committee's decision to include each attribute in the first version of Heart CD? Why or why not?

- The AST believes that attributes created (medical urgency, post-transplant survival, reducing biological disadvantages, patient access and placement efficiency) are appropriate, albeit with anticipated challenges. Some anticipated challenges include the following:
    - Medical urgency – programs may ask for more exceptions as this is a major driver of where the patient ends up on the allocation list. As a result, exception requests may be used to increase priority of candidates with lower degree of medical urgency.[1] Furthermore with 95% approval rate of exception requests, without further monitoring and optimization of exception request process, the CD model may be further manipulated.[2] To incentivize durable LVADs, waitlist time with durable LVAD should be included in the composite allocation score as outlined in the concept paper. We would also emphasize that choosing variables that are truly reflective of medical urgency (Cr, disease entity, bilirubin, etc.) rather than just method of support will help further risk stratify and reduce gaming. This validated method is currently included in the new French Allocation system.[3]
    - Post-transplant survival – see below
    - Reducing biological disadvantages- While there is a need to help those at a disadvantage, heart transplant centers vary on their definition of sensitization and may not use the same lab for cPRA calculation. Highly sensitized also varies in definition with cPRA anywhere between 20-80%, depending on the transplant hospital or study. In order to add this, the AST agrees the proposed method of listing unacceptable antigens to obtain points for desensitization is likely the best approach for this particular component.
    - Patient access – agree with this component
    - Placement efficiency – agree with this component

Should the Committee create an attribute for post-transplant survival for inclusion in the first version of the continuous distribution of heart allocation framework? Why or why not? What, if any, predictive models should the Committee consider for use?

- The AST believes that post-transplant survival is an appropriate attribute to consider; however, as stated above, it should not be included in the first version of heart continuous distribution allocation policies. Post-transplant survival is variable based on patient co-morbidities, in hospital status 1-3, single vs multi-organ transplants, and the transplant

program's level of expertise (e.g., certain centers may do more congenital cases that others or simply high volume vs low volume transplant centers). As such, there should be a guidance document first advising which components would be included in the incorporation of a post-transplant survival score and then integrate the component in a follow up version.

- The new French Allocation System accounts for donor and recipient variables, rendering a Transplant Risk Score (TRS) which factors into their allocation to assess for post-transplant survival (the score has been prospectively validated). The TRS includes seven recipient factors: age, indication for transplantation, previous cardiac surgery, diabetes mellitus, mechanical ventilation, GFR, and total bilirubin level and two donor factors: age and gender.[3] Perhaps premature, but incorporation of more donor and recipient variables should be considered to help optimize patient outcomes.

Considering the individual attributes, what information should the Heart Committee use to evaluate success toward the outcome of that specific attribute?

- Medical Urgency: death on waitlist, increase in status requiring upgrades or additional tMCS, removal of waitlist for further deterioration requiring durable MCS or palliation.
- Post-transplant survival: not in this version until more data is available.
- Reducing biological disadvantages: rate of highly sensitized patient time to transplant or time on waitlist, modification of listed unacceptable antigens based on waitlist time.
- Patient access: assess each transplant rate of socioeconomic barriers (race, ethnicity, insurance status, etc.) Beyond the medical urgencies which are obvious are transplant centers offering care to patients of all socioeconomic challenges or are some centers better than others?[4]
- Placement Efficiency: Assess why hearts are turned down – if centers frequently turn down offers primarily due to distance and worry for post-transplant outcomes – is more research and technology optimization that allows broader sharing necessary?

From the patient, donor, family perspective, what do you consider to be the most important factors for allocating donor hearts?

- Allocation of the right heart at the right time without manipulation of medical urgency; including more rigorous review and selective approval of medical exception requests.

References:

1. Johnson DY, Ahn D, Lazenby K, et al. Association of high-priority exceptions with waitlist mortality among heart transplant candidates. *J Heart Lung Transplant*. 2023;42(9):1175-1182. doi:10.1016/j.healun.2023.05.009
2. Alam A, Hall S. Navigating the rough seas of heart allocation. *J Heart Lung Transplant*. 2023;42(9):1183-1184. doi:10.1016/j.healun.2023.05.021
3. Dorent R, Jasseron C, Audry B, et al. New French heart allocation system: Comparison with Eurotransplant and US allocation systems. *Am J Transplant*. 2020;20(5):1236-1243. doi:10.1111/ajt.15816
4. Chouairi F, Fuery M, Clark KA, et al. Evaluation of Racial and Ethnic Disparities in Cardiac Transplantation. *J Am Heart Assoc*. 2021;10(17):e021067. doi:10.1161/JAHA.120.021067

13. Amend Adult Heart Status 2 Mechanical Device Requirements

The American Society of Transplantation (AST) generally supports the proposal, "Amend Adult Heart Status 2 Mechanical Device Requirements," and offers the following comments for consideration:

- The AST agrees the policy should be modified to better prioritize the most critically ill patients. Members commented their experience also supports that heart candidates with an intra-aortic balloon pump (IABP) or percutaneous endovascular mechanical circulatory support device (MCSD), when stabilized using these therapies, largely do not demonstrate the same level of severity of illness as other Status 2 candidates. The use of inotrope support should be pursued before the use of IABP or MCSD. Heart candidates with an IABP or MCSD should be required to demonstrate failed inotropic support to qualify for adult heart status 2; otherwise, these heart candidates should qualify for adult heart status 3.
- There is overall agreement in the inotropic levels (high dose single inotrope versus at least two lower dose inotropes); however, it remains unclear how to define the duration of inotropic therapy before it is considered a failure. The duration of time to define inotropic therapy failure is highly debatable and depends on several variables, including patient acuity and hemodynamics. Recognizing that this aspect of the proposal is consistent with requirements in status 3 *OPTN Policy 6.1.C.ii Multiple Inotropes or a Single High Dose Inotrope Hemodynamic Monitoring,* did the Committee consider including other criteria – including duration of inotropic support – to demonstrate that the patient's condition did not improve with inotropic support?
- The proposal does not clearly address situations where patients can't tolerate high-dose inotropes prior to MCSD support (e.g., ventricular tachycardia). The AST believes it is important to create a mechanism for these candidates to qualify as Status 2, either through policy or specific exception guidelines.
- Did the Committee consider whether the heart status 2 timing should be limited to less than 14 days, as well as shortening the time for future extensions? Potential pros to reducing these time frames include better timing and careful device choice; potential cons are an increased number of exception requests and a more tedious process.
- The AST agrees that if a patient's condition improves on inotropes, then weaning off an IABP or MCSD should follow and correspond with adult heart status 3.
- The AST agrees with the proposed transition plan in which, following implementation, a candidate would remain at their assigned status until the expiration of their last justification form, then requiring a new justification form guided by the new policy.

14. Update Human Leukocyte Antigen (HLA) Equivalency Tables, 2023

The American Society of Transplantation (AST) supports the proposal, "Update Human Leukocyte Antigen (HLA) Equivalency Tables, 2023."

15. Ethical Analysis of Normothermic Regional Perfusion (NRP)

The American Society of Transplantation (AST) generally supports the proposal, "Ethical Analysis of Normothermic Regional Perfusion (NRP)" as it aligns with our position statement on NRP: https://www.myast.org/sites/default/files/AST%20KEY%20POSITION%20STATEMENT%20ON%20NORMOTHERMIC%20REGIONAL%20PERFUSION_final.pdf. The AST offers the following comments for consideration:

- The white paper could better differentiate between A-NRP and TA-NRP and the differences in ethical considerations between the two. For example, the committee may wish to include a comment to the effect of “it is important to note the procedural and thus potential ethical differences between A-NRP and TA-NRP” with some further elucidation of what those ethical differences are.
- Did the committee consider including discussion of the unified brain-based concept of death? This is the idea that the permanent absence of circulation to the brain is what ultimately defines death as an irreversible state. Using this definition as a principle could resolve much of the ethical concern related to NRP in terms of ensuring the dead donor rule is respected (it does not resolve remaining potential legal misalignments with the Uniform Determination of Death Act). Referencing this concept and the published papers supporting brain-based concept of declaring death based on circulatory criteria might be a useful addition to the white paper.
- The committee may wish to clarify the initial description in the background section that NRP is “aimed at improving organ quality by reducing cold ischemic time.” NRP is not focused on reducing cold ischemic time. NRP allows for warm perfusion of the organs shortly after the declaration of death. This process leads to a more rapid recovery from warm ischemic damage and allows the recovery team to assess the function and viability of the organs for transplant. After a period of assessment and dissection, the organs are then flushed with cold preservation solution and removed in a standard fashion. Cold ischemic time ensues until implantation into the recipients.
- The committee used the following terminology to describe NRP: recirculation, restoration of circulatory blood flow, and circulatory restoration. Utilization of these terms interchangeably can be confusing to the reader. The committee may wish to edit the document for more clarity in definition and consistent use of terminology.
- The committee may wish to clarify the comparison of TA- and A-NRP in the table on page 18. For TA-NRP it says that warm perfusion and circulation of oxygenated blood are initiated with an ECMO or bypass machine. In A-NRP, it says normothermic perfusion to the abdominal organs is initiated. However, in both cases, oxygenated blood perfuses the organs with the assistance of an ECMO or bypass machine. In TA-NRP, the donor is reintubated and the lungs are ventilated for gas exchange. Reintubation and ventilation are also used with all rapid recovery lung procedures. It is not, however, used in abdominal-only NRP donor procedures.
- In the table on page 18 under A-NRP the committee may wish to consider the following modification: “A laparotomy and sternotomy are performed, the iliac artery and vein and the suprahepatic abdominal aorta and the inferior vena cava are occluded (preventing blood flow through the thoracic aorta), the aorta is cannulated, normothermic perfusion to the abdominal organs is initiated.” (replace “or” with “and” after “iliac artery and vein”).
- On page 20, the authors note that “spontaneous reversal of asystole has been observed in TA-NRP when cardio-pulmonary bypass was used.” Seeing that asystole is reversed with the intervention of cardio-pulmonary bypass, this reversal is not ‘spontaneous.’ Therefore, we recommend removing ‘spontaneous’ from this sentence.
- On page 29, the paper notes that donors may be moved to an OPO recovery center. Unless the donor care unit is within a licensed hospital, at the current time this is not possible with DCD donation as only deceased individuals can be transferred to recovery centers, and DCD donors are not dead at the time of withdrawal of life-sustaining treatments. For clarity around this point, the AST recommends adding language that moving DCD donors to an OPO recovery center can only happen when the donor care unit is within a licensed hospital.
- In response to the questions included in the proposal:

- What information should be disclosed to potential donors and next of kin regarding NRP, and how should one approach disclosure?
  - The committee may wish to reference or incorporate key recommendations from the AST guidelines on this topic: Guidelines Regarding Communication to Donor Families in Cases Where Normothermic Regional Perfusion (NRP) is Planned - https://www.myast.org/sites/default/files/DTO%20COP_NRP%20Guidance_final%20%281%29.pdf
  - This question would also benefit from input outside of the transplant community. Qualitative research of the public as well as donor families may help develop a robust understanding of what information is relevant in decision-making about organ donation and about the acceptability of different procedural aspects.
  - When authorization for donation occurs, the OPO may not know if NRP is going to be used so we recommend that authorization for all DCD donation include information about the possibility of using NRP as well as that of using ex-situ machine perfusion (which may also pose ethical concerns particularly with heart donation) so that the family is not approached multiple times for additional authorizations.
- Are there any additional ethical considerations or evidence that should be taken into account in the analysis?
  - The committee may want to consider the ethical obligation that we have to the deceased donor and their family with regards to maximizing the number of organs utilized from the DCD process. While the implementation of new technology or organ recovery strategies should always remain within ethical boundaries, it is also an ethical obligation of the transplant community to explore all options that can lead to increased numbers of patients transplanted with better outcomes than the current standard of care.