OPTN

Committee Update

Update on Continuous Distribution of Livers and Intestines

OPTN Liver and Intestinal Organ Transplantation Committee

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Contents

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Update on Continuous Distribution of Livers and Intestines

Sponsoring Committee: *Liver and Intestinal Organ Transplantation*
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Executive Summary

In December 2021, the OPTN Liver and Intestinal Organ Transplantation Committee (the Committee) began their work to convert the current classification-based allocation system for livers and intestines to a points-based framework, otherwise known as continuous distribution. Continuous distribution will replace the current classification-based approach, which draws hard boundaries between types of candidates (for example, blood type compatible vs. identical; inside vs. outside a circle), with a composite score that simultaneously takes into account donor and candidate attributes. This points-based framework will create a more equitable and transparent allocation system.

This committee update is the third public comment document from the Committee on the development of continuous distribution of livers and intestines.[1,2] The purpose of this committee update is to continue to inform the community about the development of continuous distribution, share the results of the values prioritization exercise (VPE) which was released as part of the previous public comment request for feedback, and solicit community input on specific topics including post-transplant survival, medical urgency scoring, and geographic equity. This committee update also outlines the expected next steps in the development of continuous distribution.

[1] OPTN Liver and Intestinal Organ Transplantation Committee, Concept Paper, Continuous Distribution of Livers and Intestines Concept Paper. Public Comment Period August 3, 2022 – September 28, 2022. https://optn.transplant.hrsa.gov/media/fzmjii35/continuous-distribution-of-livers-and-intestines-concept-paper_liver_pc-summer-2022.pdf.
[2] OPTN Liver and Intestinal Organ Transplantation Committee, Request for Feedback, Update on Continuous Distribution of Livers and Intestines. Public Comment Period January 19, 2023-March 15, 2023. https://optn.transplant.hrsa.gov/media/zc3lti1y/continuous-distribution-of-livers-and-intestines_liver_pc_winter-2023.pdf

Background

In 2018, the OPTN Board of Directors sought a consistent allocation system to use across all organs and chose to replace the current classification-based allocation system with a points-based continuous distribution framework.[3] Continuous distribution aims to eliminate the hard boundaries between classifications that exist in the current liver and intestine allocation system, ultimately resulting in more equity for candidates on the waitlist and increased transparency in the allocation of livers and intestines. In addition to the benefits of removing hard boundaries between classifications, continuous distribution also has more potential for flexibility, producing efficiencies not only in allocation but also in policy development and implementation.

In December 2021, the OPTN Liver and Intestinal Organ Transplantation Committee (the Committee) began developing a framework for the continuous distribution of livers and intestines. The continuous distribution of lungs was implemented in March 2023 and the OPTN Kidney and Pancreas Transplantation Committees are collaborating on a project to convert the kidney and pancreas allocation systems to continuous distribution. The OPTN Heart Transplantation Committee has begun their work on the continuous distribution of hearts as well. The goal is for all organs to eventually transition to a continuous distribution allocation system.

Purpose

This update provides information on the anticipated next steps and the progress the Committee has made on the development of a continuous distribution framework for the allocation of livers and intestines.

Additionally, the Committee's update includes the results of the values prioritization exercise (VPE), which was released during the previous public comment cycle and asked community members to compare the relative importance of different factors that will be included in the new allocation system. New information on the Committee's deliberations on post-transplant survival and geographic equity as potential attributes in the points-based framework, as well as Committee discussions on the use of model for end-stage liver disease (MELD)/pediatric end-stage liver disease (PELD) or optimized prediction of mortality (OPOM) as the medical urgency score in continuous distribution, are also included here. Finally, this update details information on how the Committee plans to continue to develop the continuous distribution and allocation system for livers and intestines.

This is not a policy proposal and the Committee has not finalized any specific decisions or recommendations. With such a significant change to the allocation system, community input is particularly important, and the Committee is eager for feedback from the transplant community at every step of the project.

[3] OPTN Board of Directors. 2018, December 3-4. Executive Summary. Available at https://optn.transplant.hrsa.gov.

What is Continuous Distribution? [4]

As a reminder, a continuous distribution system prioritizes candidates based on a combination of points awarded for factors such as those related to medical urgency, candidate biology, patient access, and the efficient management of organ placement. Continuous distribution will remove hard boundaries between classifications, which currently preclude a candidate from being prioritized ahead of candidates on the other side of the boundary, despite other factors that could impact each candidate's prioritization for transplant.[5,6] In a points-based system, candidates will be ranked on a match run based on a combination of donor and candidate clinical characteristics, as well as placement efficiency.

Classification-based framework: A classification-based framework places similar candidates into ordered classifications or groupings. Candidates are then sorted within those classifications. This is the framework currently used to allocate livers and intestines.

Points-based framework: A points-based framework assigns a composite allocation score (CAS) to each candidate for each match run. Organs are then offered in descending order based upon the candidate's score for that match run. This committee update document describes a points-based framework for organ allocation, otherwise known as continuous distribution.

While the concept of a points-based allocation system may seem foreign in the context of liver and intestine, it is already used in some areas of allocation. For example, *OPTN Policy 9.7.A Liver Allocation Points* explains how points are used in the current allocation system to sort candidates within Status 1A and Status 1B. Specifically, Status 1B candidates on a match run are sorted using three different types of points: diagnosis points, waiting time points, and blood type compatibility points. On a particular match run, Status 1B candidates are sorted based on the total number of points they receive across these three categories.

This existing policy is an example of a points-based allocation framework. Rather than saying, for example, that *all* blood type identical candidates will be sorted ahead of *all* blood type compatible candidates regardless of other factors, the points-based system allows for increased flexibility based on specific candidate characteristics. In this way, the framework is agnostic as to its goals and is flexible enough to achieve the desired outcomes of the community.

The goal of continuous distribution is to convert all aspects of liver and intestine allocation that rely on distinct classifications, such as MELD score or PELD score and distance from donor hospital to transplant program, to a more flexible and transparent continuous distribution system.

Composite Allocation Score

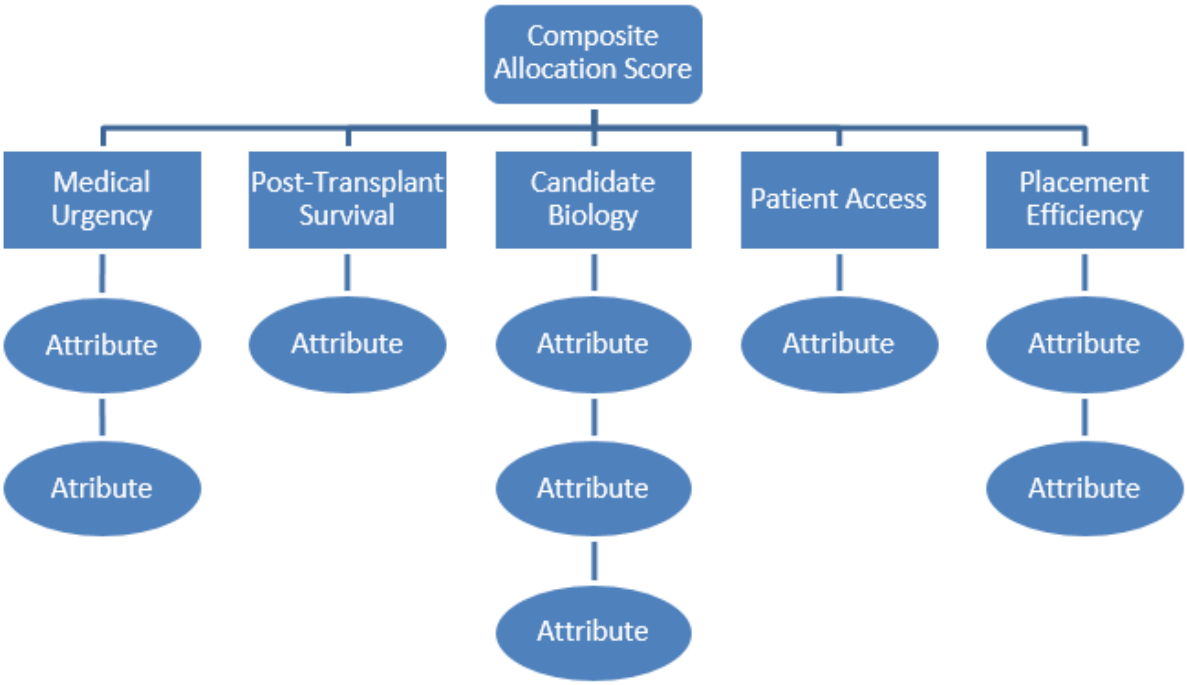
The continuous distribution framework will rank candidates using a composite allocation score, or CAS, that aligns with the different requirements found in the NOTA and the OPTN Final Rule.[7,8] **Figure 1** shows the five sub-scores, or goals, that could constitute the overall CAS.

[4] Continuous distribution aims to create a more fair and patient-focused system for organ allocation. For additional information on the continuous distribution framework and the work of the OPTN, visit http://optn.transplant.hrsa.gov/policies-bylaws/a-closer-look/continuous-distribution/.
[5] J. J. Snyder et al., "Organ distribution without geographic boundaries: A possible framework for organ allocation," Am J Transplant 18, no. 11 (Nov 2018), https://doi.org/10.1111/ajt.15115.
[6] Jon Snyder, "Systems without Geographic Boundaries". Presented to the OPTN Ad Hoc Geography Committee meeting, March 26, 2018.
[7] 42 CFR §121.8.
[8] 42 U.S.C. §274

Figure 1: Components of Composite Allocation Score

These five goals form the basis of the continuous distribution framework.[9] Within each goal, there may be different potential attributes, or factors that can be used to assign points to candidates based on different characteristics. Candidates will be assigned a certain number of points for each attribute, which will then be combined to create sub-scores that align with the different goals. One can liken CAS to a hierarchy depicted below in **Figure 2.** At the bottom are the different attributes aligned under the five goals. The goals are then combined to form the CAS.

Figure 2: CAS Hierarchy Depiction



Combining multiple scores allows the OPTN to simultaneously utilize all the factors that must be considered to satisfy the regulatory requirements for organ allocation policies. It will also allow the OPTN to understand the role of each score across organs. For example, some organ systems may place more weight on medical urgency than other organs. Finally, by constructing the CAS around the performance goals in the OPTN Final Rule, the rationale for compliance will more explicitly align with the requirements in the OPTN Final Rule.[10]

[9] OPTN Liver and Intestinal Organ Transplantation Committee, Concept Paper, Continuous Distribution of Livers and Intestines Concept Paper. Public Comment Period August 3, 2022 – September 28, 2022. https://optn.transplant.hrsa.gov/media/fzmjii35/continuous-distribution-of-livers-and-intestines-concept-paper_liver_pc-summer-2022.pdf

[10] 42 CFR §121.8.

Figures 3 and 4 show how the current liver allocation system functions and how a potential liver and intestine allocation system utilizing a CAS could work. This rough example depicts how candidates could receive points for different attributes, which are combined to calculate the overall CAS. The number of points given to each candidate will depend upon the candidate's specific situation, the rating scale for that attribute, and the amount of weight given to that goal or attribute within the overall CAS.

Figure 3: Sample Allocation Policy (Current)

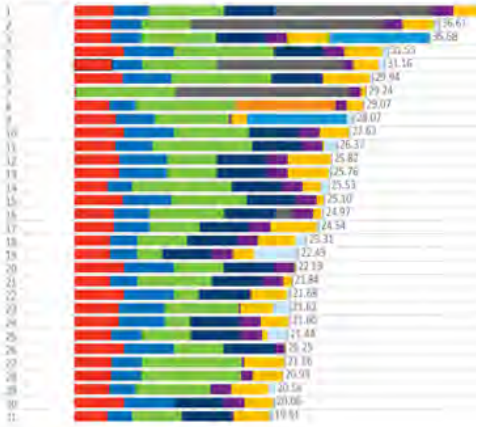
Note that candidates are placed into specific classifications and cannot move between them unless their status changes.

Table 9-11: Allocation of Livers from Non-DCD Deceased Donors at Least 18 Years Old and Less than 70 Years Old

Classification	Candidates with a MELD or PELD score of at least	And registered at a transplant hospital that is at or within this distance from a donor hospital	Donor blood type	Candidate blood type
1	Status 1A	500NM	Any	Any
2	Status 1B	500NM	Any	Any
3	Status 1A	2,400NM and candidate is registered in Hawaii or 1,100NM and candidate is registered in Puerto Rico	Any	Any
4	Status 1B	2,400NM and candidate is registered in Hawaii or 1,100NM and candidate is registered in Puerto Rico	Any	Any
5	37	150NM	O	O or B
6	37	150NM	Non-O	Any

Figure 4: Example Match Run (Proposed)

Each color represents a different attribute and the bar's length shows the points credited to that attribute. Candidates receive points for multiple considerations and can move up or down depending on each attribute.



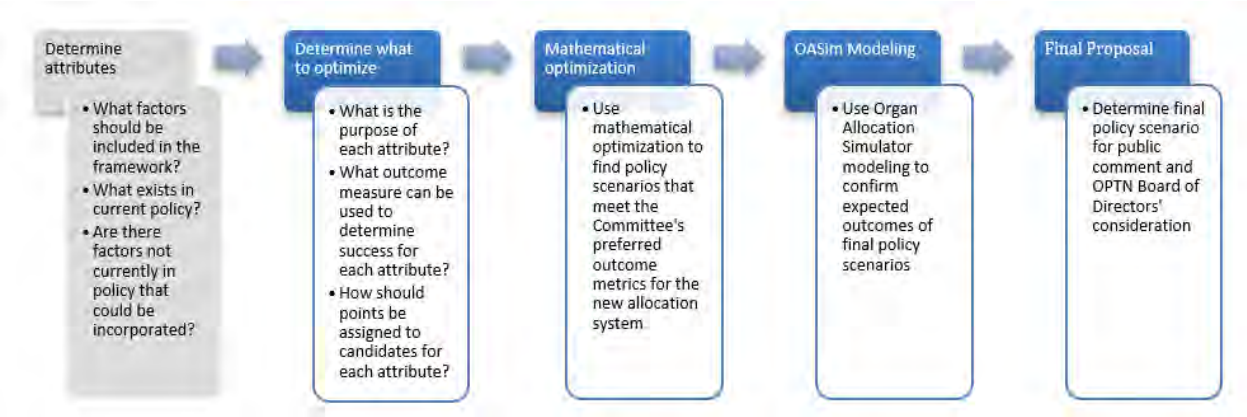
Project Plan

The Committee is tasked with developing a comprehensive proposal for the continuous distribution of livers and intestines, an effort that represents perhaps the most significant change to liver and intestine allocation in recent history.

With the continuous distribution of lungs already implemented and the development of continuous distribution for kidneys and pancreata farther along in the policy development process, the Committee has gained valuable insight from the other organ systems and has refined their project plan based on this feedback.

The project plan for developing the continuous distribution of livers and intestines is depicted in **Figure 5** below. The project plan represents a new approach to the OPTN policy development process, whereby the Committee will be able to iterate and understand the potential impact of many different policy scenarios before finalizing a proposal for public comment.

Figure 5: Overview of Project Development Process

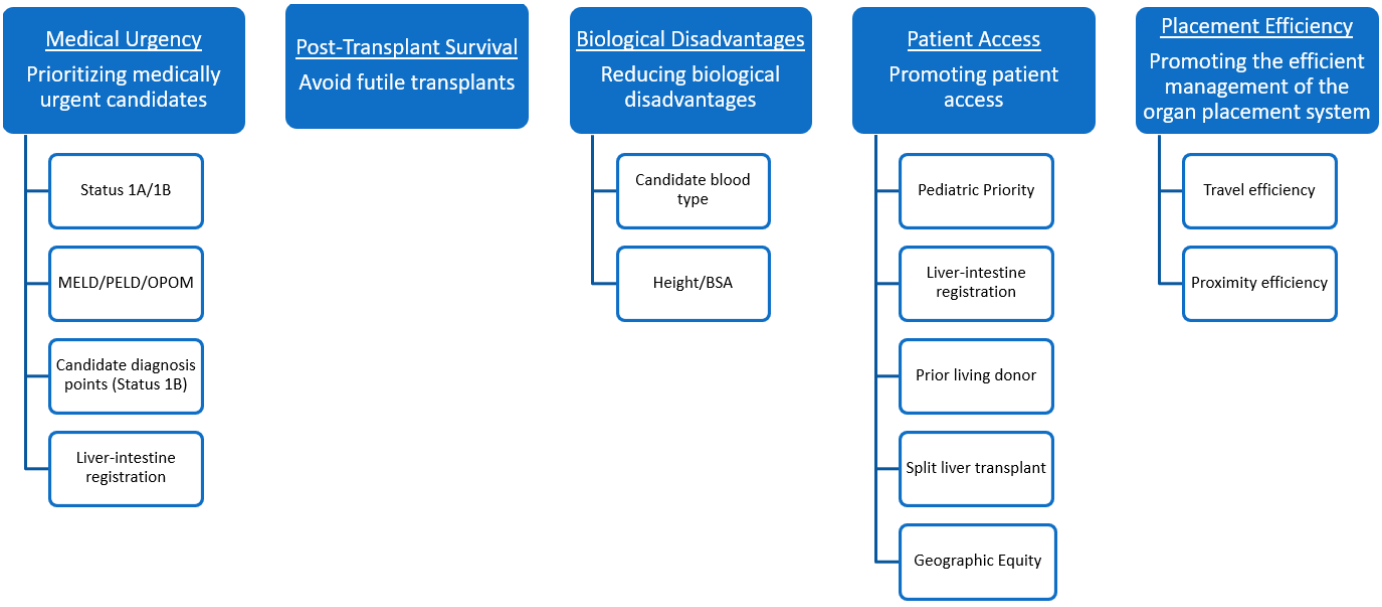


Progress to Date

The previous request for feedback described the Committee's deliberations on which attributes to include in the points-based framework.[11] Since then, the Committee has continued to consider several attributes, including post-transplant survival, medical urgency scoring, and geographic equity (formerly referred to as population density). More details on these continued discussions are included in the sections below.

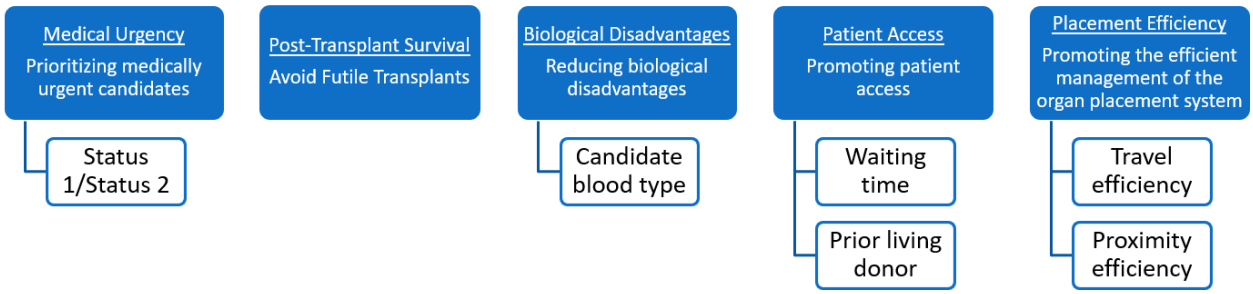
Currently, the Committee is focused on the second step in **Figure 5**, which is preparing for the mathematical optimization analysis. For reference, **Figure 6** shows the updated list of attributes that the Committee intends to include in the continuous distribution allocation system for livers and **Figure 7** shows the attributes for intestines.

Figure 6: Liver Attributes



[11] OPTN Liver and Intestinal Organ Transplantation Committee, *Update on Continuous Distribution of Livers and Intestines.* Public comment period: January 19, 2023 – March 15, 2023. Available at https://optn.transplant.hrsa.gov/media/zc3lti1y/continuous-distribution-of-livers-and-intestines_liver_pc_winter-2023.pdf

Figure 7: Intestine Attributes



Mathematical Optimization Analysis

Overview

The next major step in developing the continuous distribution of livers and intestines is mathematical optimization, which uses machine learning and artificial intelligence to augment Liver Simulated Allocation Modeling (LSAM) data to quickly and accurately predict outcomes from thousands of potential policy scenarios.[12] The use of mathematical optimization, machine learning, and artificial intelligence in the development of continuous distribution represents a significant improvement in how the OPTN develops organ allocation policy by allowing for a more iterative and flexible approach to policy development.

In the previous approach to modeling the potential impact of policy changes, OPTN committees would first develop a handful of policy scenarios to address specific problems and then work with the Scientific Registry of Transplant Recipients (SRTR) to model the potential impact of each policy scenario using LSAM, now known as the Organ Allocation Simulator (OASim). This process could take several months per round of modeling, may require multiple rounds of modeling, and would require OPTN Committees to develop potential policy solutions to their identified problem before knowing to what extent each potential solution would (or would not) solve the identified problem. OASim modeling would then quantify how the policy scenarios developed by the Committee may perform in accomplishing their stated goals.

However, with mathematical optimization, the Committee will be able to iterate through thousands of potential policy scenarios in near real time, making the entire policy development process more flexible and responsive to the deliberations of the Committee. Rather than deciding on the policy scenarios they expect will achieve the desired outcomes first, and then seeing if those policy scenarios accomplish the intended outcomes, mathematical optimization reverses the order of this process by allowing the Committee first to determine the specific outcomes they intend to achieve and then find the policy scenario(s) that will achieve those outcomes.

A simple example of the benefits of mathematical optimization within the context of continuous distribution would be assigning relative weights to each attribute. Rather than assigning initial weights

[12] Theodore P Papalexopoulos et al., "Ethics-by-Design: Efficient, Fair and Inclusive Resource Allocation Using Machine Learning," *Journal of Law and the Biosciences* 9, no. 1 (2022), https://doi.org/10.1093/jlb/lsac012.

to each attribute and then seeing what outcomes those weights would achieve through OASim modeling, mathematical optimization starts with determining the outcomes the Committee wants to achieve and then finds the policy scenarios with the relative weights that will accomplish those desired outcomes. With mathematical optimization, the Committee first needs to determine what outcomes they want the allocation system to optimize, and the mathematical optimization analysis finds policy scenarios that meet those specifications.

In addition, mathematical optimization will allow the Committee to better quantify, understand, and deliberate over tradeoffs between attributes that may conflict with one another. As an example, if the Committee wants to focus on prioritizing the most medically urgent candidates with less regard for other attributes, that would likely cause an increase in the median distance between the donor hospital and transplant program, as the allocation system would be primarily focused on getting organ offers to the most medically urgent candidates, with less regard for distance. However, with mathematical optimization, the Committee can have a more nuanced discussion about the tradeoff between prioritizing the most medically urgent candidates and proximity. The mathematical optimization tool will be able to provide insight into *how much* an increase in priority for the most medically urgent candidates may influence median travel distance. For example, mathematical optimization may show that increasing the weight of the medical urgency attribute in the CAS by 10% may decrease waitlist mortality/removal for too sick for transplant by 15%, but it would increase median travel distance by 25%. Alternatively, mathematical optimization could show that increasing the weight of the proximity attribute by 10% will decrease median travel distance by 20% but may cause an increase in the waitlist mortality rate. With mathematical optimization, the Committee will be able to understand the tradeoffs between different attributes and make more informed decisions about the relative weights and rating scales for each attribute in the final policy proposal.

Preparing for Mathematical Optimization

As mathematical optimization is the next major step in developing continuous distribution, the Committee has begun to focus its work on the inputs that will go into the mathematical optimization tool. At a high level, for each attribute, the Committee will need to determine a specific outcome measure to quantify the impact of the attribute in the optimization tool and decide on a general method by which points will be assigned for each attribute. The Committee is currently working through this process for each attribute. **Table 1** below shows how the Committee will organize their work preparing for mathematical optimization.

First, the Committee created a plain language purpose for each attribute, which is included in the second column of **Table 1**. Next, the Committee will focus on determining specific outcome metrics for each attribute to include in mathematical optimization. These outcome metrics will be used to show if, and to what extent, any particular policy scenario accomplishes the stated purpose for the given attribute. And finally, the Committee will create potential frameworks for assigning points to candidates for each attribute in mathematical optimization. Importantly, with mathematical optimization, the Committee will have increased flexibility to include multiple frameworks for each attribute and iterate between different variations of these frameworks to compare the impact of each different policy scenario.

Table 1: Preparing for Mathematical Optimization

Attribute	What is the purpose?	How to measure for success?	How will points be assigned?
Medical Urgency	Prioritize candidates who are most likely to die/be removed from the waitlist for too sick for transplant		
Blood type	Provide equal access to transplant for candidates regardless of their blood type		
Height/BSA	Provide equal access to transplant for candidates regardless of their stature		
Pediatric Priority	Minimize time on the waitlist for pediatric candidates		
Liver/Intestine	• Provide increased access to appropriate donors for liver-intestine (MVT) candidates • Prioritize liver-intestine (MVT) candidates who are most likely to die/be removed from the waitlist without a transplant		
Living Donors	Prioritize living donors		
Split liver transplant	Prioritize those candidates (ex. pediatric candidates and small statured adults) willing and likely to initiate a split liver transplant for appropriate donors		
Geographic equity	Provide equal access to transplant regardless of geographic location of transplant program		
Travel efficiency	Reduce distance between donor hospital and transplant program		
Proximity efficiency	Increase efficiency in organ placement system		

As an example, the Committee intends to include an attribute for either height or body surface area (BSA) to account for the fact that candidates of smaller stature have reduced access to transplant.[13] Within mathematical optimization, the Committee must determine which metric can be used to understand if a given policy scenario appropriately corrects this disparity.

In addition, the Committee will create potential frameworks, or rating scales, for how points will be assigned to candidates for each attribute. Continuing with the height/BSA example, potential frameworks could involve providing additional points to candidates under a certain height/BSA threshold, developing a height/BSA-based curve, similar to the height curve used in the lung continuous distribution framework, or creating a donor-recipient size-matching system whereby candidates below a certain stature are prioritized for similarly sized donor organs.[14]

While the Committee has begun some of this work, they have not yet determined the specific outcome metric for each attribute or finalized potential rating scales. The Committee is interested in any public

[13] Ex. Catherine E. Kling et al., "Association of Body Surface Area with Access to Deceased Donor Liver Transplant and Novel Allocation Policies," *JAMA Surgery* 158, no. 6 (2023): 610, https://doi.org/10.1001/jamasurg.2023.0191.
[14] OPTN Lung Transplantation Committee, *Briefing Paper,* Establish Continuous Distribution of Lungs. Public Comment Period August 3, 2021 – September 30, 2021. https://optn.transplant.hrsa.gov/media/esjb4ztn/20211206-bp-lung-establish-cont-dist-lungs.pdf.

comment feedback on the outcome metrics and rating scales and plans to provide more information on these topics as part of the next continuous distribution update.

Once the Committee has used mathematical optimization to identify a handful of specific policy scenarios that accomplished their desired outcomes, the Committee will submit a request to the SRTR to model the policy scenarios using OASim, which will provide more detailed and robust analysis of the potential impact of these policy scenarios before submitting a final proposal to public comment and OPTN Board of Directors consideration.[15]

Values Prioritization Exercise Results

During the previous public comment cycle, the public was asked to participate in a Values Prioritization Exercise, or VPE, for liver allocation. The purpose of the VPE was to provide a structured way for the community to provide input on the relative importance of each attribute the Committee intends to include in continuous distribution of livers.

The VPE utilized an Analytical Hierarchy Process (AHP), a multi-criteria decision-making methodology that asks participants a series of questions to compare the relative importance of a set of criteria through multiple pairwise comparisons.[16] Participants were asked to weigh their preferences between pairs of attributes, described as patient profiles, in terms of how important each attribute should be when prioritizing candidates for liver transplantation.

The exercise prompted participants to respond to 15 pairwise comparisons and select which of the two attributes being compared they would prioritize in each situation if all other aspects of the patient profiles were the same (**Figure 1**). Additionally, participants were asked to indicate on a scale ranging from 1 (equally important) to 9 (extremely important) how important they believe it is for their selected attribute to be prioritized in organ allocation over the other. The following attributes were included in the VPE: 1) A Highly Medically Urgent Candidate, 2) A Biologically Difficult to Match Candidate, 3) A Pediatric Candidate, 4) A Candidate who has been Waiting a Long Time, 5) A Prior Living Donor, and 6) A Very Nearby Candidate.[17] These attributes were determined after Committee deliberations on which factors to incorporate into a potential CAS, as outlined in the previous Committee update.[18] The pairwise comparisons were then aggregated into overall preferences, or relative importance "weights," for the different attributes.

In addition to pairwise comparison selections and rankings, participants were given the option to enter free-text comments after each pairwise comparison to elaborate on their response or provide additional feedback. The VPE was available on the OPTN website and presented at eleven regional meetings and

[15] Mathematical optimization will only provide analyses for liver allocation due to the tool using Liver Simulated Allocation Modeling (LSAM) data, which does not include information on intestine or liver-intestine allocation.
[16] *See generally*, Lin, Carol and Harris, Shannon 2013. A Unified Framework for the Prioritization of Organ Transplant Patients: Analytic Hierarchy Process, Sensitivity, and Multifactor Robustness Study. Journal of Multi-Criteria Decision Analysis.
[17] The Final Rule requires that when developing policies for the equitable allocation of cadaveric organs, such policies must be developed "in accordance with §121.8,"[17] which requires that allocation …(8) Shall not be based on the candidate's place of residence or place of listing, except to the extent required by paragraphs (a)(1)-(5) of this section." The Committee will continue to balance the allocation of organs based on a candidate's place of residence or place of listing against the other factors outlined in the Final Rule throughout the development of continuous distribution.
[18] OPTN Liver and Intestinal Organ Transplantation Committee, *Update on Continuous Distribution of Livers and Intestines Request for Feedback.* Public comment period, January 19, 2023 – March 15, 2023. Available at https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/update-on-continuous-distribution-of-livers-and-intestines/.

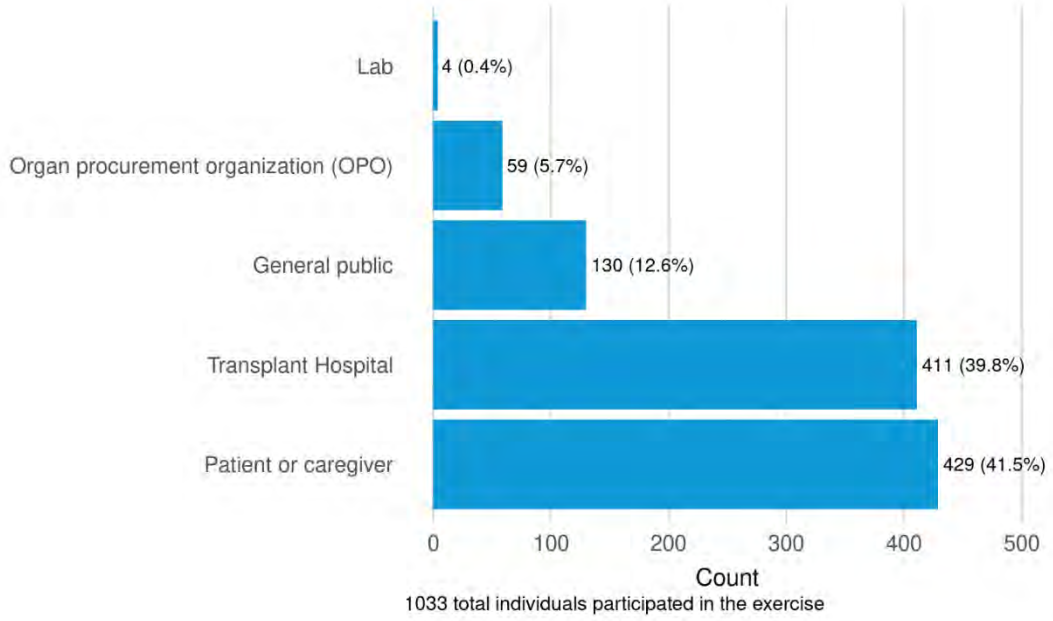
eight OPTN committee meetings. The results of the VPE were presented to the Committee during their meeting on May 19, 2023.[19]

In the context of developing continuous distribution, the Committee will use the results of the VPE to inform their deliberations about which attributes or goals to prioritize and optimize in the mathematical optimization analysis. The following section provides an overview of the VPE results, while a full report is also available on the OPTN website.[20]

Participation

1,033 individuals submitted responses to the VPE, far exceeding participation in previous exercises for other organ systems.[21] During the exercise, participants were asked to select their affiliation to transplant from five pre-determined choices. **Figure 8** below represents the breakdown of VPE participants by their affiliation to transplant. The most frequent participant group was patient or caregiver (41.5%), followed by transplant hospital professional (39.8%), general public (12.6%), organ procurement organization (OPO) professional (5.7%), and laboratory professional (0.4%). It is especially important to note that 429 patients or caregivers participated in the VPE, the largest group of respondents by transplant affiliation, and represents a significant increase in participation by patients and caregivers in OPTN policy development.

Figure 8: Participation by Transplant Affiliation



[19] OPTN Liver and Intestinal Organ Transplantation Committee, *Meeting Summary,* May 19, 2023. Available at https://optn.transplant.hrsa.gov/about/committees/liver-intestinal-organ-transplantation-committee/.
[20] Continuous Distribution of Livers: Winter 2023 Values Prioritization exercise – Community Results; Available at https://optn.transplant.hrsa.gov/media/0g5l3qpa/05122023_vpe_researchreport_final.pdf
[21] The OPTN Lung, Kidney, and Pancreas Transplantation Committees had 196, 431, and 390 participants respectively for each values prioritization exercise.

Overall Ratings

Figure 9 below represents the overall, unweighted ratings from the VPE. Since patients, caregivers, and transplant hospital professionals participated in greater volume than other transplant affiliation groups, these ratings skew toward their preferences.

Figure 9: Overall Ratings

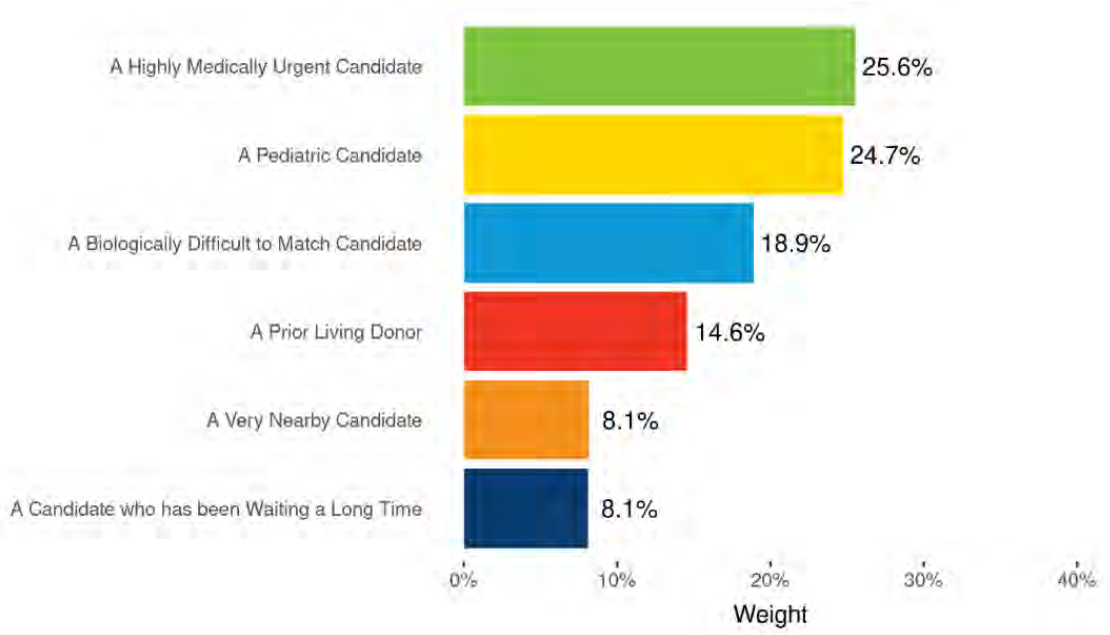
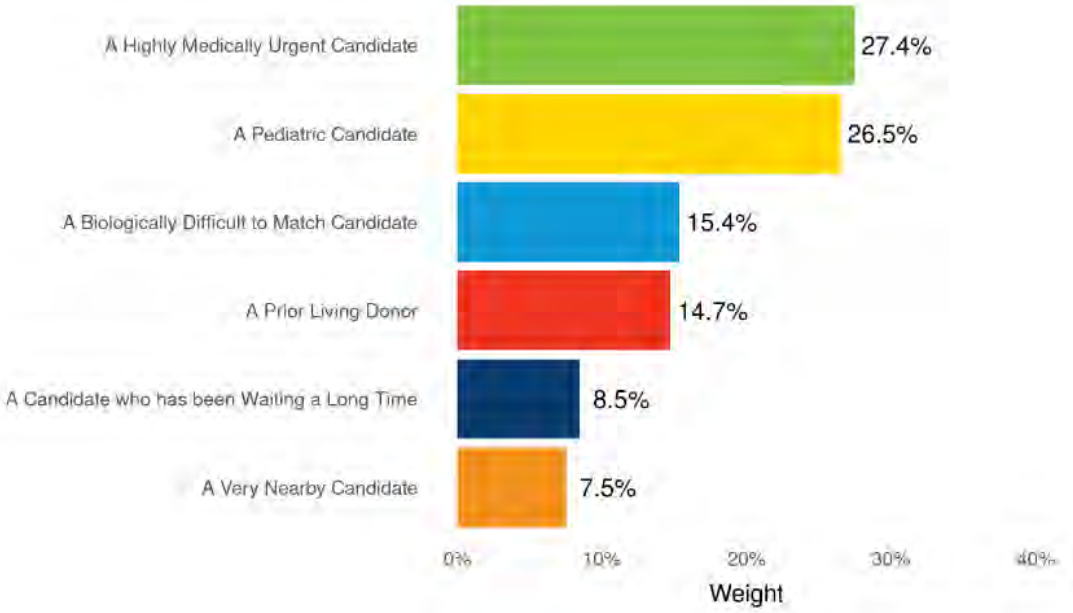


Figure 10 shows the overall ratings with the five transplant affiliation groups equally weighted, or population adjusted. Population-adjusting the overall ratings gives the ability to see the ranking of attributes without the influence of the transplant affiliations groups that participated the most. However, the population-adjusted overall ratings do not differ greatly from the overall ratings that were not population-adjusted (**Figure 9**).

Figure 10: Overall Ratings, Population-Adjusted



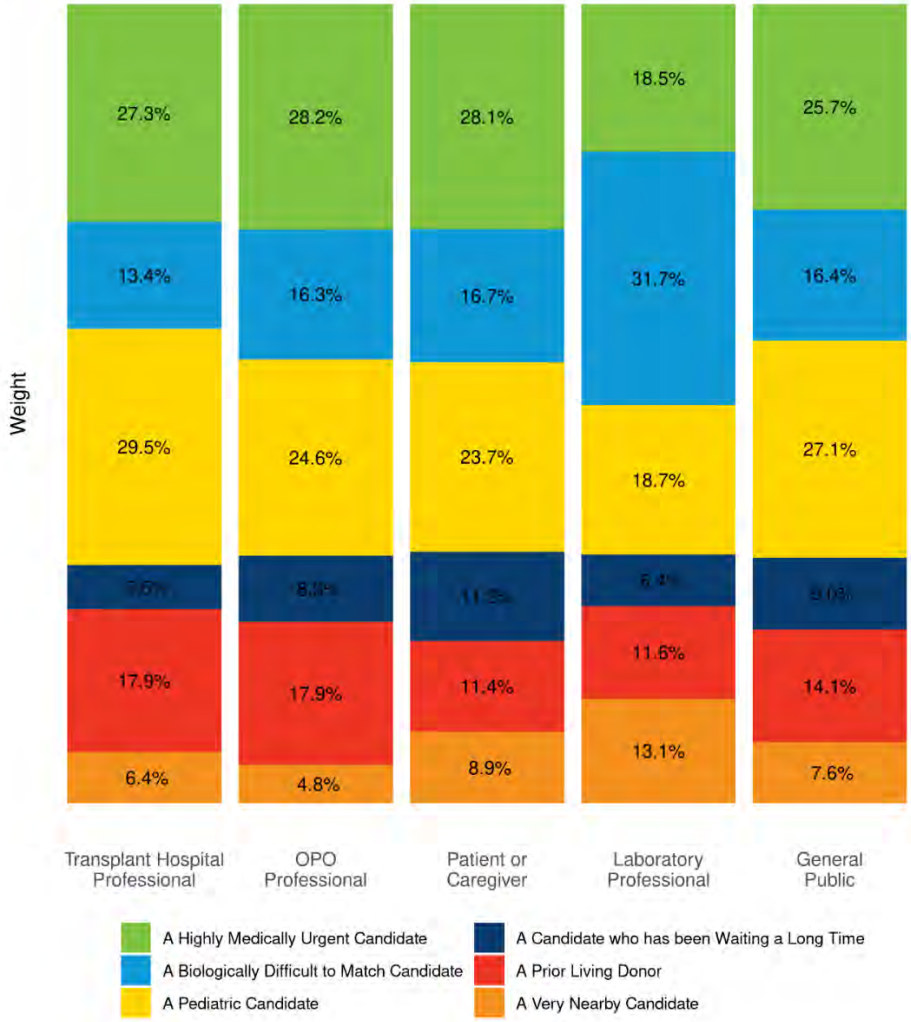
These results show that, overall, the community values prioritizing medically urgent candidates and pediatric candidates the most in the new allocation system. The results also show that the community places an emphasis on biologically difficult to match candidates, which would include candidates with blood type O or blood type B or those who have a more difficult time finding a size appropriate donor due to height or BSA limitations. The community also sees value in providing some priority to prior living donors, although not as much as highly medical urgent candidates, pediatric candidates, or candidates who are biologically difficult to match.

Generally, the community deprioritized waiting time and proximity as attributes in the allocation system. These are all important considerations for the Committee to understand as they continue to discuss which attributes and outcomes to optimize in continuous distribution.

Priorities by Participation Groups

The figure below shows the overall preferences of participants by transplant affiliation groups and shows the variability in priorities between the different participant groups (**Figure 11**).

Figure 11: Ratings by Transplant Affiliation



Results stratified by transplant affiliation show many similarities across the different respondent categories, although there was some slight variation across the groups. For instance, transplant hospital professionals and members of the general public placed slightly higher priority on pediatric candidates than medical urgency, whereas organ procurement organizations (OPO) professionals and patients/caregivers placed medical urgency above pediatric candidates.

Transplant hospital professionals and OPO professionals placed more priority on prior living donors than biologically difficult to match candidates, while patients/caregivers and the general public ranked biologically difficult to match candidates ahead of prior living donors. Across all respondent groups (except for laboratory professionals, which only had 4 respondents), waiting time and proximity were the lowest ranked attributes.

The Committee is interested in additional feedback on the importance of proximity and travel efficiency in the new allocation system, especially from OPO professionals. Early discussions after implementation of the lung continuous distribution policy have noted a desire for increased efficiency in the allocation

system. Discussions about the allocation system include the rank order on the match run as well as the operational rules such as expedited placement, offer filters, etc. The Committee is eager to hear feedback from OPO professionals or other transplant professionals on their experience with proximity and overall efficiency within lung continuous distribution.

VPE Next Steps

As noted above, the Committee will use the results from the VPE to inform their discussions about which attributes or goals to prioritize in the mathematical optimization analysis. Similarly, these results will help guide the Committee as they discuss tradeoffs between different attributes. As the results of the VPE show, the community prioritized both medical urgency and pediatric priority as the most important attributes in a new liver allocation system. Based on this information, the Committee has discussed optimizing the system for these two attributes by finding policy scenarios that ensure the most medically urgent candidates are prioritized for transplant, and pediatric candidates are given increased priority.

Ongoing Committee Discussions about Attributes

The request for feedback that was released as part of the previous public comment period outlined the Committee's deliberations and decisions about which attributes to include in the first iteration of continuous distribution.[22] Since that time, the Committee has continued to discuss three specific attributes in light of the feedback submitted on the previous request for feedback. The following sections include updated information on the Committee's discussions related to the following attributes: post-transplant survival, medical urgency score (MELD/PELD vs. OPOM), and geographic equity.

Post-Transplant Survival

The OPTN Final Rule calls for allocation policies "to avoid futile transplants," which can be interpreted as maximizing the utility of organ transplantation by incorporating expected post-transplant survival into organ allocation.[23] Other organ allocation policies, namely kidney and lung allocation, include specific attributes for post-transplant survival. Current kidney allocation includes Expected Post Transplant Survival (EPTS), which is used to predict a kidney candidate's projected post-transplant survival with a functioning graft. The EPTS score works together with the Kidney Donor Profile Index (KDPI) to match donor organs to candidates based on organ quality and expected survival of the candidate in order to maximize graft and recipient survival.[24,25] Similarly, the continuous distribution of lungs includes an attribute that quantifies the expected number of days a lung recipient is expected to survive during the first five years post-transplant.[26] In this model, the longer a candidate is expected to survive after

[22] OPTN Liver and Intestinal Organ Transplantation Committee, Request for Feedback, Update on Continuous Distribution of Livers and Intestines. Public Comment Period January 19, 2023-March 15, 2023. https://optn.transplant.hrsa.gov/media/zc3lti1y/continuous-distribution-of-livers-and-intestines_liver_pc_winter-2023.pdf

[23] 42 CFR §121.8(a)(5).

[24] OPTN Policy 8.5.A: Candidate Classifications

[25] OPTN Kidney Transplantation Committee. 2020, September 25. Kidney Continuous Distribution Workgroup Meeting Summary. https://optn.transplant.hrsa.gov/media/4128/20200925_kidney_continuousdistribution_wg_summary.pdf.

[26] OPTN Lung Transplantation Committee, *Briefing Paper,* Establish Continuous Distribution of Lungs. Public Comment Period August 3, 2021 – September 30, 2021. https://optn.transplant.hrsa.gov/media/esjb4ztn/20211206-bp-lung-establish-cont-dist-lungs.pdf.

transplant, the more points they receive in the composite allocation score for the post-transplant survival attribute.

As outlined in the previous request for feedback document, the Committee does not intend to include an attribute for post-transplant survival in continuous distribution.[27] The request for feedback document outlined how there were no post-transplant survival models readily available that could be incorporated into the new allocation system.[28]

However, during the previous public comment period, the Committee received feedback that supported the inclusion of a post-transplant survival attribute in the continuous distribution framework. In particular, patient/donor family respondents voiced strong support for including an attribute for post-transplant survival, citing not only the importance of including post-transplant survival in the new allocation system but also the need for consistency across organ allocation systems.

In addition, after the request for feedback was released, a new model for incorporating post-transplant survival in liver allocation was published. This paper, titled, "A model for calculating the long-term estimated post-transplant survival of deceased donor liver transplant patients," aimed to quantify the estimated long-term survival benefit in deceased donor liver transplant candidates, akin to the EPTS score in kidney allocation.[29] The proposed liver model is called the Liver Estimated Post-Transplant Survival (L-EPTS) score.

Given these two new pieces of information (public comment feedback in support of a post-transplant survival attribute and the new L-EPTS model), the Committee reconsidered their initial decision to not include a factor for post-transplant survival in the new allocation system during their in-person meeting on April 3, 2023.[30] During the meeting, the Committee reviewed all feedback provided during the previous public comment period and the primary author of the L-EPTS paper joined the meeting to provide an in-depth overview of the new model for the Committee to consider. However, the Committee ultimately reaffirmed their initial decision to not include an attribute related to post-transplant survival in the new allocation system.[31]

While the L-EPTS model seems to have an improved ability to predict long term (5 and 10 year) post-transplant survival compared to other available models, the Committee agreed that longer term post-transplant survival should not be incorporated into the continuous distribution framework, due to methodological concerns around model development, limitations of the model in terms of predictive performance, and because the separation in likelihood of recipient survival can be better accounted for in a shorter post-transplant timeframe rather than five or ten years after transplant.

In addition, the allocation system already accounts for short-term post-transplant survival in other ways. Specifically, the MELD score is capped at MELD 40, which helps avoid futile transplants by not giving increased priority to candidates with increasing MELD scores who are unlikely to do well after

[27] OPTN Liver and Intestinal Organ Transplantation Committee, Request for Feedback, Update on Continuous Distribution of Livers and Intestines. Public Comment Period January 19, 2023-March 15, 2023. https://optn.transplant.hrsa.gov/media/zc3lti1y/continuous-distribution-of-livers-and-intestines_liver_pc_winter-2023.pdf
[28] Ibid.
[29] John S. Malamon et al., "A Model for Calculating the Long-Term Estimated Post-Transplant Survival of Deceased Donor Liver Transplant Patients," *eBioMedicine* 90 (2023): 104505, https://doi.org/10.1016/j.ebiom.2023.104505.
[30] OPTN Liver and Intestinal Organ Transplantation Committee, *Meeting Summary*, April 3, 2023. Available at https://optn.transplant.hrsa.gov/about/committees/liver-intestinal-organ-transplantation-committee/.
[31] Ibid.

transplant. In addition, there are very specific criteria for MELD and PELD exceptions for diagnoses, such as hepatocellular carcinoma (HCC) and cholangiocarcinoma (CCA), so that only candidates expected to benefit from transplant are provided a higher MELD or PELD score. Similar to other organs, liver transplant programs are also monitored by the SRTR on one year survival after liver transplant. Because of this monitoring, transplant programs generally only choose to list and transplant candidates who are expected to survive more than one year after transplant. Although these approaches may not be as transparent or explicit as a specific post-transplant survival attribute, the Committee agreed that they are effective in accounting for post-transplant survival in liver allocation. Each of these aspects of the current liver allocation system will be carried over to continuous distribution, and the Committee felt that these aspects are likely to achieve the desired post-transplant outcomes in continuous distribution, without a specific post-transplant survival attribute.

The Committee also noted that there is no strong data to suggest increased utility in matching higher quality liver offers to candidates expected to survive longer after transplant, likely due to the fact that hepatocytes regenerate.[32]

Ultimately, the Committee reaffirmed their decision to not include a post-transplant survival attribute as the available models for longer-term post-transplant survival are not ready to be incorporated into continuous distribution and short-term post-transplant survival is already accounted for by other measures in the allocation system. While the Committee does not intend to include an attribute for post-transplant survival in the first iteration of continuous distribution, they are encouraged by the opportunity to incorporate it as an attribute in future iterations should a more appropriate model become available.

The Committee is interested in additional feedback, especially from the patient population, about the decision to not include an attribute for post-transplant survival in continuous distribution.

Medical Urgency Scoring in Continuous Distribution

In the previous request for feedback document, the Committee asked for community input on the medical urgency score that should be used to rank candidates based on mortality risk within the continuous distribution framework. The current system uses MELD and PELD, which were recently updated in July 2023 to better predict mortality for liver transplant candidates.

The Committee is considering converting the medical urgency score from MELD and PELD to Optimized Prediction of Mortality or OPOM, which uses machine learning techniques to rank adult liver transplant candidates based on their medical urgency for transplant.[33] The previous request for feedback explained the Committee's interest in considering OPOM to replace MELD and PELD as the medical urgency score used in continuous distribution due to its potential to better rank candidates based on risk of waitlist mortality and interdigitate candidates with HCC, thereby reducing waitlist mortality. However, other Committee members were concerned about the increased complexity that converting to OPOM at the same time as continuous distribution would entail. Further, given that MELD and PELD were recently updated, some Committee members felt it was important to allow for some time for the new MELD and PELD scores to be in the system to be able to understand their impact before converting to OPOM.

[32] Ibid.
[33] Dimitris Bertsimas et al., "Development and Validation of an Optimized Prediction of Mortality for Candidates Awaiting Liver Transplantation," American Journal of Transplantation 19, no. 4 (June 2018): pp. 1109-1118, https://doi.org/10.1111/ajt.15172.

During the previous public comment cycle, members of the community provided feedback on which medical urgency score to use in the new allocation framework. Those in support of converting to OPOM felt that it represented an important step forward in liver allocation by reducing waitlist mortality through better ranking candidates based on medical urgency and that implementing OPOM and continuous distribution simultaneously would be beneficial to the allocation system. Those opposed to converting to OPOM at the same time as continuous distribution noted that it would be an unprecedented amount of concurrent change and highlighted that there is no validated OPOM score for adolescent or pediatric candidates. Commenters also stated that OPOM itself needs to be independently validated before being incorporated into the allocation system.

The Committee reviewed all public comment on MELD/PELD and OPOM and received an update from the developers of OPOM regarding improvements to the medical urgency score based on previous feedback from the Committee.[34] Specifically, the presenters removed age and added MELD 3.0 as a variable in the OPOM calculation without materially changing the results. In addition, the authors presented a pediatric version of OPOM, also known as POPOM, which showed similar results to the current PELD calculation.[35]

After reviewing this feedback, the Committee remains interested in the potential for OPOM to better predict mortality risk and interdigitate HCC candidates as part of continuous distribution. Therefore, the Committee intends to include policy scenarios with both MELD/PELD and OPOM in the mathematical optimization analysis. Once the Committee is better able to understand the impact of OPOM on the allocation system within the context of continuous distribution, they will then be more informed to make a final decision on whether to use MELD/PELD or OPOM as the medical urgency score in continuous distribution. As such, the Committee is currently tabling discussions on MELD/PELD and OPOM until they are able to see the results of each medical urgency score in the mathematical optimization analysis.

Geographic Equity as an attribute in Continuous Distribution

In the previous request for feedback, the Committee included population density as a potential attribute in the points-based allocation framework.[36] Initially, the Committee intended to include a population density attribute to account for differences in travel practices between densely populated areas and sparsely populated areas. The Committee also posited that incorporating population density could improve geographic equity. Public comment feedback indicated support for including an attribute that would help account for differences in population density around the country.

Since the time of the previous request for feedback, the Committee has had more detailed discussions regarding this attribute, which has subsequently been broadened and re-named as “geographic equity,” to reflect the fact that the fundamental purpose of the attribute is to reduce inherent differences in the ratio of donor supply and demand across the country.[37] While differences in population density likely

[34] OPTN Liver and Intestinal Organ Transplantation Committee, *Meeting Summary*, April 3, 2023. Available at https://optn.transplant.hrsa.gov/about/committees/liver-intestinal-organ-transplantation-committee/.
[35] Ibid.
[36] OPTN Liver and Intestinal Organ Transplantation Committee, *Update on Continuous Distribution of Livers and Intestines Request for Feedback.* Public comment period, January 19, 2023 – March 15, 2023. Available at https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/update-on-continuous-distribution-of-livers-and-intestines/.
[37] OPTN Liver and Intestinal Organ Transplantation Committee, *Meeting Summary*, April 3, 2023. Available at https://optn.transplant.hrsa.gov/about/committees/liver-intestinal-organ-transplantation-committee/.

play a factor in differences in the ratio of donor supply and demand, population density is just one aspect of a larger conversation about geographic equity in liver allocation and therefore the Committee is broadening the scope of this attribute from population density to geographic equity. In a related change, the Committee has moved the geographic equity attribute from the Placement Efficiency goal to the Patient Access goal to reflect the attribute's purpose of addressing equity in access to transplant rather than improving system efficiency.

While the Final Rule requires policies to not be based on the location of a candidate, there are other requirements that allow for policies to incorporate constraints related to geographic distribution. The OPTN Ad Hoc Committee on Geography determined five *Principles of Distribution* in which geographic distribution may be constrained that are in alignment with Final Rule requirements.[38] The purpose of the geographic equity attribute, as defined by the Committee, is in agreement with the Final Rule requirement to design policies that promote patient access to transplantation.[39]

The Committee also discussed how geographic equity could be measured in mathematical optimization. The Committee focused on objective measures that would be independent, to the extent possible, of transplant program and OPO behavior and performance, such as offer rates and match run sequence order. The Committee expressed interest in analyzing offer rates because candidates at similar MELD scores should receive similar access to liver offers regardless of the location of their transplant program.

The Committee expressed additional interest in analyzing sequence order for candidates, which would examine the percentage of match runs where a candidate from a set geographic (e.g. donation service area, OPTN region, state, etc.) unit is in a defined range at the top of the match run. Alternatively, another option may be analyzing the difference between geographic units with the highest percent of match runs where candidates are in a defined top range of each match run compared to the geographic unit with the lowest percent of match runs where liver candidates are in a defined top range of each match run. By finding a policy scenario that reduces this difference, the policy scenario could reduce the difference in the ratio of donor supply and demand across the country.

The Committee is interested in public comment feedback on the geographic equity attribute, including ways to address differences in the supply/demand ratio across the county and outcome metrics that could be used to measure if policy scenarios successfully reduce this disparity.

NOTA and Final Rule Analysis

The Committees submit this Committee update under the authority of the OPTN Final Rule, which states the OPTN Board of Directors shall be responsible for developing "policies for the equitable allocation for cadaveric organs."[40] The Final Rule requires that when developing policies for the equitable allocation of cadaveric organs, such policies must be developed "in accordance with §121.8,"[41] which requires that allocation policies "(1) Shall be based on sound medical judgment; (2) Shall seek to achieve the best use of donated organs; (3) Shall preserve the ability of a transplant program to decline an offer of an organ or not to use the organ for the potential recipient in accordance with §121.7(b)(4)(d) and (e); (4) Shall be

[38] OPTN Ad Hoc Committee on Geography, *Mini-Brief,* Geographic Organ Distribution Principles and Models Recommendations Report. June 2018. Available at https://optn.transplant.hrsa.gov/media/2506/geography_recommendations_report_201806.pdf.
[39] 42 CFR §121.4(a).
[40] Ibid.
[41] 42 C.F.R. § 121.4(a)(1).

specific for each organ type or combination of organ types to be transplanted into a transplant candidate; (5) Shall be designed to avoid wasting organs, to avoid futile transplants, to promote patient access to transplantation, and to promote the efficient management of organ placement;…(8) Shall not be based on the candidate's place of residence or place of listing, *except to the extent required by paragraphs (a)(1)-(5) of this section*" (emphasis added).[42] While this paper does not propose policy changes at this time, the concepts presented in this paper:

Are based on sound medical judgment:[43] The construction of the individual rating scales and weights will be based on objective data, including simulation modeling and published research. The Committee will rely upon peer-reviewed literature and data analyses as well as their own clinical experience and judgment in making determinations regarding assigning weights and ratings to each attribute.

Seek to achieve the best use of donated organs:[44] The Committee will need to balance how to prioritize the most medically urgent candidates against the need to optimize post-transplant outcomes, ultimately resulting in the best use of donated organs. Before the policy proposal is released for public comment, it will be modeled by the SRTR to assess its impact on waitlist mortality and post-transplant outcomes. If necessary, the Committee will adjust the weighting of the attributes to balance these outcomes.

Are specific for each organ:[45] In this case, the allocation systems will be tailored to livers and intestines.

Are designed to avoid wasting organs:[46] The Committee identified multiple attributes specifically designed to avoid wasting organs, including proximity efficiency and travel efficiency. If necessary, the Committee will be able to adjust the weighting of the attributes to balance the number of transplants against other attributes.

Are designed to… promote patient access to transplantation:[47] The Committee identified several attributes that specifically ensure similarly situated candidates have equitable opportunities to receive an organ offer. The inclusion of these attributes is likely to increase access to transplantation for these candidates.

Are designed to… promote the efficient management of organ placement:[48] The Committee will consider indicators of efficiency associated with procuring and transplanting livers and intestines, including travel costs and the proximity between the donor and transplant hospitals.

Not be based on the candidate's place of residence or place of listing, except to the extent required [by the aforementioned criteria]:[49] The Committee is considering the candidate's place of listing to the extent that is required for the purpose of achieving equity in access to transplantation and efficient placement of organs, specifically for travel efficiency and placement efficiency.

[42] 42 C.F.R. §121.8(a)
[43] 42 CFR §121.8(a)(1).
[44] 42 CFR §121.8(a)(2).
[45] 42 CFR §121.8(a)(4).
[46] 42 CFR §121.8(a)(5).
[47] 42 CFR §121.8(a)(5).
[48] 42 CFR §121.8(a)(5).
[49] 42 CFR §121.8(a)(8).

Consider whether to adopt transition procedures:[50] A points-based framework will facilitate the use of transition procedures for existing candidates. For example, the OPTN may be able to compare the policy proposal with the results of a revealed preference analysis and modeling to determine who is impacted and if there is a need for transition procedures. Similarly, exception candidates might need a process to transition to the new system. This would allow members and patients time to prepare for these changes.

Conclusion

This Committee update represents one step in a long-term project to convert the current classification-based allocation system to a continuous distribution framework. Continuous distribution utilizes a points-based system for organ allocation and will be more equitable, transparent, and flexible than the current allocation system. By separating the attributes and developing specific rating scales and weights, there will be more nuanced solutions for how certain candidate populations are prioritized, thereby improving equity in access to organ transplantation.

In the development of continuous distribution, the Committee has used and will continue to utilize novel approaches to policy development including the VPE and mathematical optimization. This Committee update shares the results of the VPE, explains the next steps in the development of continuous distribution and how the Committee will utilize mathematical optimization. It also includes information about ongoing Committee deliberations regarding post-transplant survival, medical urgency scoring, and geographic equity. The Committee is interested in community feedback on any of the information included in this document or any other aspects of the continuous distribution project.

Considerations for the Community

The Committee is seeking public comment feedback on the following items related to the continuous distribution of livers and intestines:

- Do you agree with the Committee's decision to not include an attribute for post-transplant survival in the first iteration of continuous distribution?
- Do you have any feedback for how geographic equity should be incorporated as an attribute in liver candidate's composite allocation score?
- Do you have any feedback for ways to increase efficiency in the organ allocation and placement process, especially given the low priority assigned to proximity in the VPE?
- Do you agree with the purpose for each attribute outlined in Table 1?
- Do you have any feedback on outcome metrics or ways to assign points to candidates for each attribute in the optimization analysis?

[50] 42 C.F.R. § 121.8(d). The Final Rule requires the OPTN to "consider whether to adopt transition procedures that would treat people on the waiting list and awaiting transplantation prior to the adoption or effective date of the revised policies no less favorably than they would have been treated under the previous policies" whenever organ allocation policies are revised.