OPTN

Concept Paper

Continuous Distribution of Livers and Intestines Concept Paper

OPTN Liver and Intestinal Organ Transplantation Committee

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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 point-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 allocation system will create a more equitable and transparent allocation system.

The purpose of this paper is educate the community on the concept of continuous distribution, provide an update on the progress the Committee has made on the project thus far, and solicit feedback from the community on the Committee's work to date.

Background

In 2018, the OPTN Board of Directors chose to replace the current classification-based allocation system with a points-based continuous distribution framework.[1] 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 Liver and Intestinal Organ Transplantation Committee (the Committee) began developing a framework for the continuous distribution of livers and intestines. Also in December 2021, the OPTN Board of Directors approved a proposal to establish the continuous distribution of lungs.[2] In addition, the OPTN Kidney Transplantation Committee and OPTN Pancreas Transplantation Committee are collaborating on a project to convert the kidney and pancreas allocation systems to continuous distribution. The goal is for all organs to eventually transition to a continuous distribution allocation system.

Purpose

The purpose of this concept paper is two-fold. First, it is intended to educate and inform the liver and intestine transplant community on what continuous distribution is and the progress the Committee has made in developing a continuous distribution framework for the allocation of livers and intestines.

Second, the Committee is seeking the community's feedback on their progress to date, the plan for the project moving forward, and any other relevant aspects of the larger effort to develop a points-based allocation system. This is not a final 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 the time this concept paper was drafted, the Committee has been working on continuous distribution for six months. The effort to convert the current allocation to continuous distribution will require many steps, more data analysis and discussion, and ongoing communication between the Committee and the community.

The Committee requests community feedback on any of the ideas presented below. However, they are most interested in feedback on which attributes should be included in the first iteration of the continuous distribution framework. More detail on these attributes is provided in subsequent sections of the document.

[1] OPTN Board of Directors. 2018, December 3-4. Executive Summary. Available at https://optn.transplant.hrsa.gov.
[2] 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.

What is Continuous Distribution? [3]

A continuous distribution system prioritizes candidates based on a combination of points awarded for factors related to medical urgency, expected post-transplant outcomes, candidate biology, patient access, and the efficient management of organ placement. Continuous distribution will eliminate 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.[4,5] In a point-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.

There are many complex decisions that must be made to fully realize the potential of continuous distribution and the Committee intends to continuously seek the community's feedback throughout the develop of this project.

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 concept paper describes a points-based framework for organ allocation, otherwise known as continuous distribution.

Luckily, livers and intestines are not the first organ systems to make the transition from a classification-based system to continuous distribution. In December 2021, the OPTN Board of Directors approved a proposal to establish the continuous distribution of lungs.[6] The OPTN Kidney Transplantation Committee and the OPTN Pancreas Transplantation Committee are also working on continuous distribution and have released their own concept paper that is currently available for public comment.[7]

While the concept of a points-based 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.

The goal of continuous distribution is to convert all aspects of liver and intestine allocation that rely on distinct classifications, such as model for end-stage liver disease (MELD) score or pediatric end-stage

[3] 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 https://optn.transplant.hrsa.gov/policies-bylaws/a-closer-look/continuous-distribution/

[4] 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

[5] Jon Snyder, "Systems without Geographic Boundaries". Presented to the OPTN Ad Hoc Geography Committee meeting, March 26, 2018.

[6] 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.

[7] See public comment documents available at https://optn.transplant.hrsa.gov/

liver disease (PELD) score and distance from donor hospital to transplant program, to a more flexible and transparent continuous distribution system.

Composite Allocation Score

A continuous distribution framework will rank candidates by a composite allocation score, or CAS, that aligns with the different requirements found in NOTA and the OPTN Final Rule. **Figure 1** shows the five sub-scores, or goals, that constitute the overall CAS. These five goals are explained in more detail below.

Figure 1: Components of Composite Allocation Score

Medical urgency score The Final Rule requires that allocation policies "seek to achieve the best use of donated organs"[8] and requires priority of organ allocation to be based upon "objective and measurable medical criteria."[9] OPTN policies use several different approaches to prioritize candidates based upon their medical urgency such as MELD score, PELD score, heart statuses, etc. Within the current liver allocation system, medical urgency already plays a prominent role. The most medically urgent candidates are provided Status 1A and Status 1B priority. After these priority statuses, candidates are then sorted based on their MELD or PELD scores. These scores, which rank candidates based on their risk of 90-day waitlist mortality, are examples of sorting candidates based on medical urgency (i.e. sickest first). Similarly, OPTN policy for the allocation of intestines classifies candidates' medical condition based on statuses, with the sickest candidates receiving the highest priority status.[10]

Post-transplant survival score: The Final Rule requires the consideration of allocation policies that would avoid futile transplants.[11] In other words, the Final Rule requires consideration of post-transplant outcomes. OPTN policies use several approaches to incorporate post-transplant outcomes, such as human leukocyte antigen (HLA) mismatching or ischemic time, which can impact post-transplant outcomes.[12,13] However, none of these factors currently play a direct role in liver and intestine allocation. The Committee will consider if there are specific attributes related to post-transplant survival that could be incorporated into a continuous distribution system.

Candidate biology score: The Final Rule calls for allocation policies to "promote patient access to transplantation."[14] Some candidates have difficulty finding a suitable donor due to biological incompatibilities. The OPTN has long used different mechanisms, for example the calculated panel reactive antibodies (CPRA) sliding scale found in kidney and pancreas allocation policy, to reduce

[8] 42 C.F.R. §121.8(a)(2)
[9] *Id.*at §121.8(b)(2)
[10] OPTN Policy 7.1: Status Assignments
[11] 42 C.F.R. §121.8(a)(5)
[12] A. Nikaein et al., "HLA Compatibility and Liver Transplant Outcome: Improved Patient Survival by HLA and Crossmatching," *Human Immunology* 40 (1994): p. 6, https://doi.org/10.1016/0198-8859(94)91670-5.
[13] Vladimir J. Lozanovski et al., "The Impact of Major Extended Donor Criteria on Graft Failure and Patient Mortality after Liver Transplantation," *Langenbeck's Archives of Surgery* 403, no. 6 (2018): pp. 719-731, https://doi.org/10.1007/s00423-018-1704-z.
[14] 42 C.F.R. §121.8(a)(5).

these biological differences in transplant access.[15] Another example, more pertinent to liver and intestine allocation, is blood type compatibility between donors and candidates on the match.[16]

Patient access score: The Final Rule requires allocation polices be designed to "promote patient access to transplantation."[17] Additionally, NOTA requires that allocation policies "recognize the differences in health and in organ transplantation issues between children and adults throughout the system and adopt criteria, policies, and procedures that address the unique health care needs of children."[18] The prioritization of pediatric candidates and the prioritization of prior living donors in kidney allocation are examples of current OPTN policies that are designed to promote patient access to transplantation.

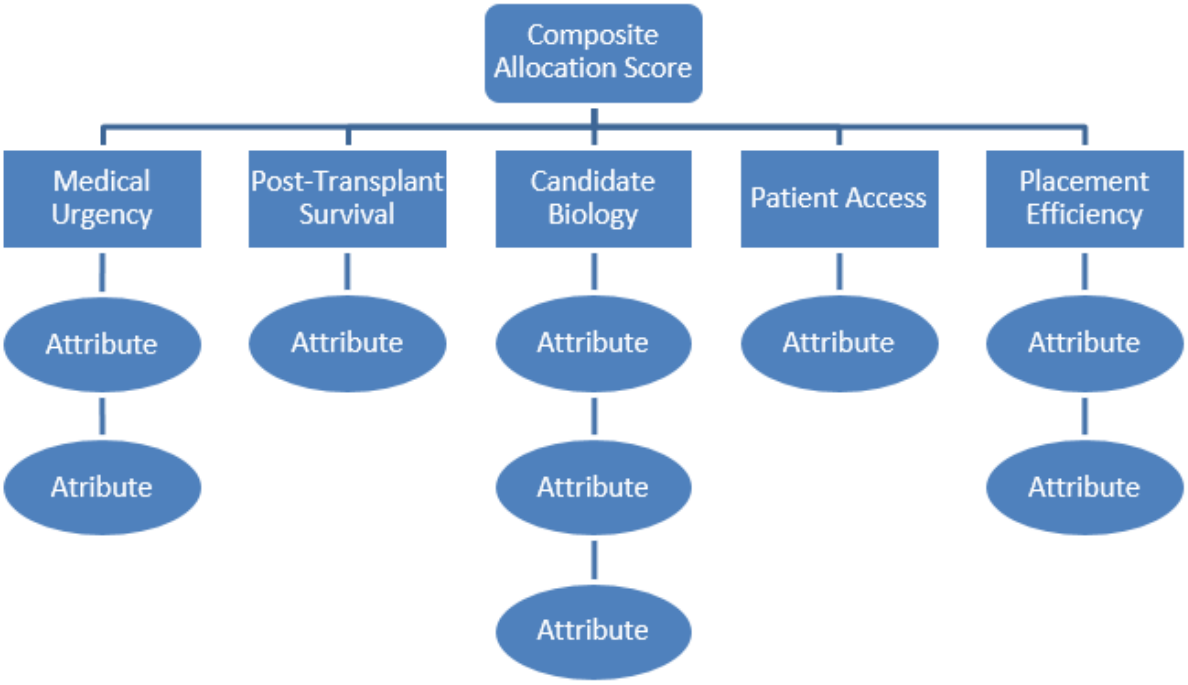
Placement efficiency score: The Final Rule requires that organ allocation policies be designed to promote the "efficient management of organ placement."[19] This can be impacted by many things, such as the time it takes from organ offer to final acceptance, travel time between the transplant program and the donor hospital, and the costs associated with organ procurement and travel.

These five goals form the basis of the continuous distribution framework. Within each goal, the Committee has listed different attributes. 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, which are then weighted against each other to create the overall CAS.

One can liken CAS to a hierarchy. At the bottom are the different attributes aligned under the five goals. The goals are then combined to form the CAS. This hierarchy is depicted below in **Figure 2**.

[15] OPTN Policy 8.3: Table 8-2 Points for CPRA
[16] OPTN Policy 9.8.C: Allocation of Livers by Blood Type
[17] 42 C.F.R. §121.8(a)(5)
[18] 42 U.S.C. §274(b)(2)(M).
[19] 42 C.F.R. §121.8(a)(5)

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 post-transplant outcomes 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.[20]

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 is just a rough example, but it depicts how candidates could receive points for different attributes, which are then combined to calculate the overall CAS. The amount of points given to each candidate would depend upon the candidate's specific situation, the rating scale for that attribute, and the amount of weight given to that goal within the overall CAS.

In the below example (see **Figure 4**), the amount of points given to a candidate varies depending upon the candidate's specific circumstances and donor characteristics. The current classification-based system precludes all candidates in a lower classification from being prioritized ahead of any candidates in a higher classification, irrespective of other factors (See **Figure 3**). For example, in the current allocation system, classifications are built around MELD or PELD score, distance between the donor hospital and transplant program, and blood type compatibility. In this system, a candidate with an identical blood type to the donor will always be ranked ahead of a candidate with a compatible blood type when the two candidates are in the same allocation classification and have the same MELD or PELD score, irrespective of other factors. Under continuous distribution, such classifications will be removed and the

[20] 42 CFR §121.8

allocation system will take a more nuanced approach to such cases by incorporating attributes using a points-based framework that considers multiple candidate characteristics simultaneously.

Figure 3: Sample Allocation Policy (Current)

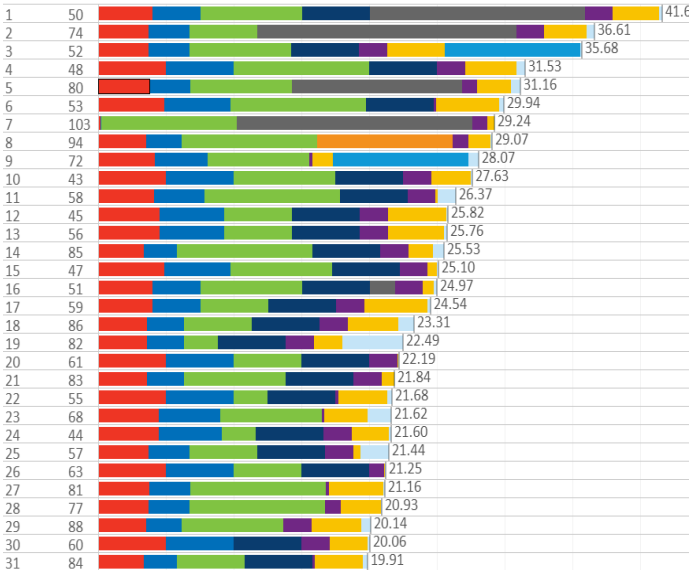
Note that candidates are placed into specific classifications and cannot move between them.

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)

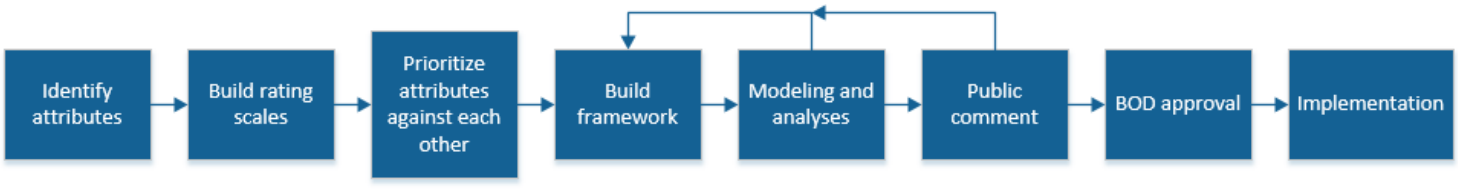
Each color represents a different attribute and the length of the bar shows the points credited to that attribute. Note that candidates receive points for multiple considerations and can move up or down depending on each attribute.



Project Plan

The Committee is tasked with developing a comprehensive proposal for the continuous distribution of livers and intestines, an effort that represents the most significant change to liver and intestine allocation perhaps in the history of liver and intestine transplantation. The project will progress through several phases, as seen in **Figure 5**. Each step is explained in more detail below.

Figure 3: Project Overview



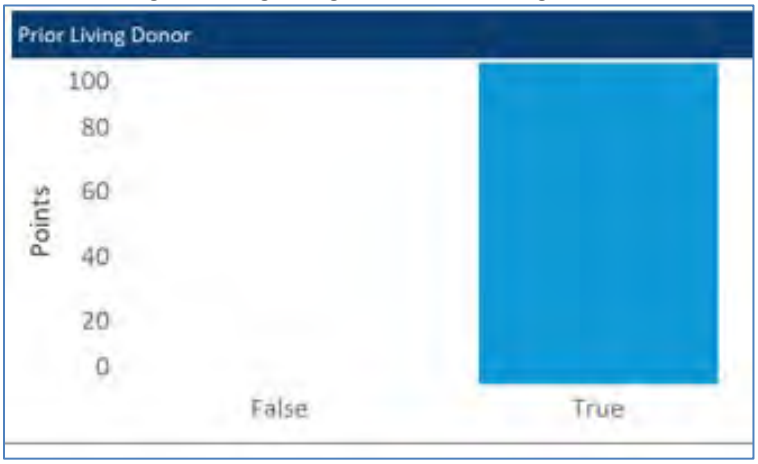
Identify attributes: The first step in the development of continuous distribution for livers and intestines is identifying all attributes that should be included in the new allocation system.[21] To do so, the Committee started by identifying all attributes that currently exist in liver and intestine allocation policy. These attributes are listed below in **Table 2**. In addition to the attributes that already exist in the current allocation system, the Committee is also considering incorporating other attributes that do not exist in current allocation. While the primary focus of the project is to convert the current system to continuous distribution, the Committee recognizes that they can also use the opportunity to improve the allocation system by incorporating additional attributes. It is not possible to include every potential attribute in the first version of continuous distribution and the Committee is interested in the community's feedback on which attributes should be added to the allocation system as part of the first iteration.

In addition to identifying the different attributes, the Committee has also categorized each of them into one of the five goals, based on their purpose in allocation.

Build Rating Scales: Once the Committee has finalized the list of attributes for inclusion in the first iteration of continuous distribution, they will begin the task of constructing rating scales for each attribute.[22] **Figures 5, 6, and 7** below depict rating scales for different attributes in the continuous distribution of lungs. Generally speaking, rating scales are the mathematical curves or the way in which points will be assigned to individual candidates for each attribute.

Figure 5 shows the lung rating scale for prior living donors. This rating scale is dichotomous. Either a candidate is a prior living donor or they are not. If they are, they get the maximum number of points available for prior living donors.[23]

Figure 5: Lung Rating Scale for Prior Living Donors



[21] Attributes are criteria used to classify then sort and prioritize candidates. Refer to *Appendix: Glossary of Terms* for more information.
[22] Rating scales describe how much preference are provided to candidates within each attribute. Refer to *Appendix: Glossary of Terms* for more information.
[23] The Committee will determine the maximum number of points available to those candidates who were prior living donors. These points are relative to the attribute of prior living donor, not relative to the maximum number of total composite allocation score points.

Figure 6 shows the rating scale the OPTN Lung Transplantation Committee constructed for the height attribute. This rating scale incorporates three U-shaped curves for different diagnoses. Generally, the curves provide more points to candidates who are short and candidates who are tall, with fewer points being assigned as height approaches approximately 170 centimeters (cm). The intent of this rating scale is to provide additional points within the overall CAS for candidates who are either short or tall, thereby prioritizing candidate populations that have difficulty finding size appropriate donors.

Figure 6: Lung Rating Scale for Height

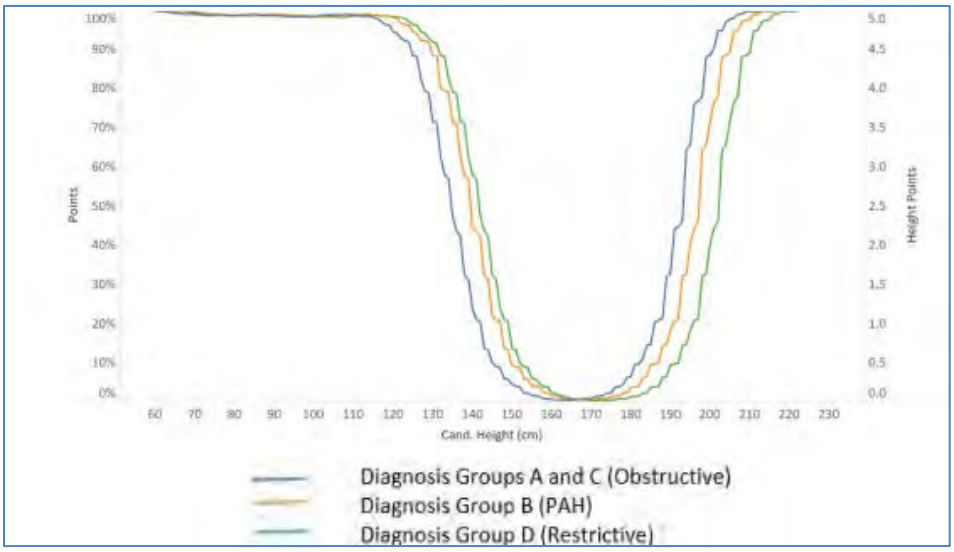
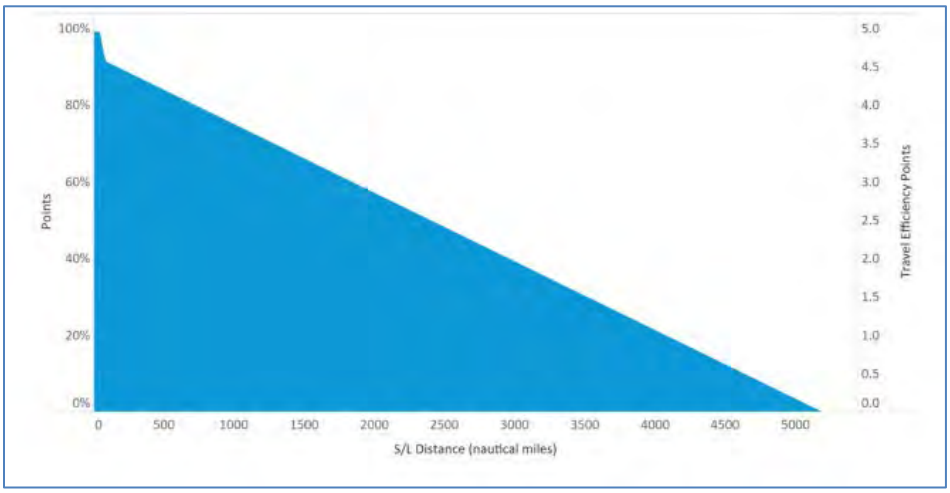


Figure 7 depicts the rating scale for travel efficiency. This rating scale was constructed to reflect the changes in cost associated with traveling differing distances to procure and transplant lungs. The proposed scale for travel efficiency (cost) gradually decreases from 0-45 NM, reflecting small differences in costs associated with driving greater distances. The rating scale then declines more drastically from 45 to 90 NM, due to the fact that air travel may be needed in this range of distances and the costs increase more rapidly. After 90 NM, the rating scale follows a more shallow, steady slope, which reflects the fact that all lungs will be flown beyond 90 NM and the associated cost is incremental.[24] The Committee will have the ability to develop a travel efficiency rating scale that reflects the specific needs of liver and intestine distribution.

[24] 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.

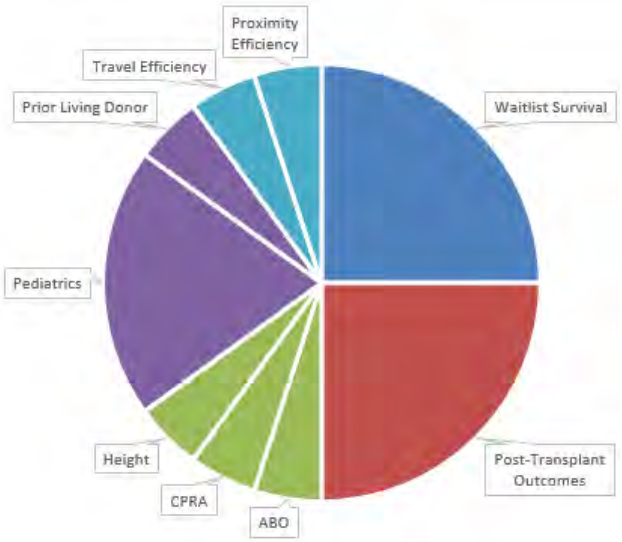
Figure 7: Lung Rating Scale for Travel Efficiency (Cost)



The Committee will construct rating scales for each of the attributes included in the continuous distribution of livers and intestines. These rating scales will be built from objective clinical or operational data as much as possible.

Prioritize attributes against each other: After building the rating scale for each attribute, the Committee will then decide how much weight or relative importance each goal and attribute should have within the CAS. The Committee, with input from the transplant community, must weigh the relative importance of each attribute against each other and determine how much importance each attribute should have in the overall CAS. For example, **Figure 8** below shows the weights assigned to each attribute and goal within the lung continuous distribution system.

Figure 8: Percent of Lung Composite Allocation Score (by Attribute)



Attribute	Weight
Waiting list Survival	25%
Post-Transplant Survival	25%
Candidate Biology	15%
Blood Type	5%
CPRA	5%
Height	5%
Patient Access	25%
Pediatric	20%
Prior Living Donor	5%
Placement Efficiency	10%
Travel Efficiency	5%
Proximity Efficiency	5%

The Committee will utilize a number of tools to inform the discussion about attribute weights. The larger transplant community will be asked for their input via a structured exercise, called the

analytical hierarchy process of AHP.[25] This exercise will ask participants for their opinion on how the different attributes should be weighed against each other in a quantitative and systematic fashion. The Committee will also consider the results of a Revealed Preference Analysis (RPA) to approximate the weights of the attributes in the current policy and will work with experts in mathematical optimization to understand the tradeoffs between different attributes to help them select the optimal combination of rating scales and weights .[26,27,28] The Committee will utilize additional tools and consult with other subject matter experts as needed throughout this process.

Build framework: Once the Committee has constructed rating scales and determined the weights for the different attributes, they will put everything together in one comprehensive framework. In addition to attributes, rating scales, and weights, the Committee will also need to consider how to incorporate donor factors (ex. donor age, DCD status, etc.), MELD and PELD exceptions, and the National Liver Review Board (NLRB).

Modeling and Analysis: The Committee will then submit their proposed framework to the Scientific Registry of Transplant Recipients (SRTR) for Liver Simulated Allocation Modeling (LSAM) analysis in order to understand the impact of the proposal on candidates and recipients. The Committee will review these results and make final determinations to develop a proposal. If the Committee is not satisfied with the predicted outcomes, they could consider tweaking the framework and re-submitting for additional modeling.

Public comment: Once SRTR modeling is complete and the Committee is supportive of the proposed framework, the proposal will then be sent out for public comment and community feedback. If public comment suggests that additional work is needed on the framework, the Committee could again revise the proposal and send it back out for public comment.

BOD approval and implementation: Once public comments are considered and the proposal is finalized by the Committee, it will move to the BOD for final consideration and approval. Once approved by the BOD, the proposal will be implemented in the OPTN computer system. Any new data collection could require OMB approval and delay the implementation of the proposal.

At multiple steps throughout the project, the OPTN will provide education to and solicit feedback from the transplant community. These outreach efforts include the release of this concept paper and will continue through the lifecycle of this project.

Community Input

As noted above, the Committee is still in the early stages of this project and no decisions or recommendations have been finalized. The Committee has primarily focused on deciding which attributes to include in the first version of continuous distribution. Therefore, the Committee is most interested in community feedback on the proposed attributes.

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[25] OPTN, *Continuous Distribution,* Help build the framework. Available at https://optn.transplant.hrsa.gov/policies-bylaws/a-closer-look/continuous-distribution/#CD_BuildTheFramework.

[26] Darren E. Stewart et al., "A Revealed Preference Analysis to Develop Composite Scores Approximating Lung Allocation Policy in the U.S," *BMC Medical Informatics and Decision Making* 21, no. 1 (June 2021), https://doi.org/10.1186/s12911-020-01377-7.

[27] 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 (January 2022), https://doi.org/10.1093/jlb/lsac012.

[28] Mankowski M, Wood N, Segev D, Gentry S. Designing Continuous Distribution for Liver Allocation [abstract]. *Am J Transplant.* 2022; 22 (suppl 3). https://atcmeetingabstracts.com/abstract/designing-continuous-distribution-for-liver-allocation/. Accessed July 5, 2022.

At later points in the development of the project, the Committee will seek more specific feedback on rating scales, weights, and other operational aspects of the effort.

Progress So Far

The Committee began discussing a continuous distribution framework for livers and intestines in December 2021 and is currently in the first phase of identifying attributes related to liver and intestine allocation. More details on the Committee's discussions can be found in the subsections below.

Identifying Attributes

As part of the first phase of the project, the Committee reviewed the five goals used across organs to organize the continuous distribution discussion. These goals and their definitions are outlined in **Table 1** below.

Table 1: Goals for Liver and Intestine Continuous Distribution Allocation

Goals	Medical Urgency	Post-Transplant Survival	Candidate Biology	Patient Access	Placement Efficiency
	Prioritize those with highest risk of mortality on the waitlist	Increasing graft and recipient post-transplant survival /longevity matching	Increase transplant opportunities for candidates who are medically harder to match	Appropriate transplant access for all candidates	Consider resource requirements required to match, transport, and transplant an organ

The Committee reviewed how other organ systems categorized their attributes then identified and categorized attributes that were specific to liver and intestine allocation. The Committee started by identifying attributes that exist in the current liver and intestine allocation policy, before discussing attributes that are not currently in policy but should be considered for inclusion in the continuous distribution framework. **Table 2** shows a list of the attributes and their associated goal as developed by the Committee. The attributes are further grouped by those attributes in current policy versus those attributes not in current policy, which will be considered for inclusion in the continuous distribution framework.

Not every attribute listed below will be included in the first iteration of continuous distribution. Currently, the Committee is reviewing available data and literature on each attribute to determine which attributes can and should be incorporated into the first version of continuous distribution.

Table 2: OPTN Liver & Intestinal Transplantation Committee Identified Attributes

	Medical Urgency	Post-Transplant Survival	Candidate Biology	Patient Access	Placement Efficiency
In Current Policy	• Status 1A/1B, MELD, PELD • Candidate Diagnosis points (Status 1B) • Liver-intestine registration		• Candidate blood type	• Candidate Age • Waiting time • Liver-intestine registration	• Travel Efficiency • Proximity Efficiency
Not in Current Policy	• Hepatocellular carcinoma (HCC) stratification • OPOM	• Post-transplant survival	• Donor-recipient size matching • Frailty • Surgical Complexity/re-transplant • HLA Sensitization	• Candidate social Determinants of Health (SDoH) • Prior living donor • Willingness to accept a split liver transplant • Supply/demand	

Medical Urgency

The OPTN Final Rule calls for allocation policies to "seek to achieve the best use of donated organs."[29] One way to achieve the best use of a donated organ is to transplant the organ into a candidate who has the greatest medical urgency. Also, the Final Rule calls for the OPTN to "[set] priority rankings … for patients or categories of patients who are medically suitable candidates for transplantation to receive transplants. These rankings shall be ordered from most to least medically urgent…"[30]

Within current policy, the Committee identified the following attributes related to medical urgency:

- **Status 1A, Status 1B, MELD, and PELD**: While these four factors are different from each other, together they form the basis of the current liver and intestine allocation system, which is largely centered around transplanting the sickest candidates first. Candidates listed as Status 1A receive the highest priority in liver allocation. These candidates have a life expectancy of less than seven days without a liver transplant. Status 1B is reserved for pediatric candidates with a higher need for transplant than other candidates with MELD or PELD scores. Candidates listed as Status 1B are typically offered organs after Status 1A candidates. After these priority statuses, candidates are then ranked by decreasing MELD and PELD scores, which are calculations based on a number of clinical lab values that predict a candidate's likelihood of waitlist mortality within 90 days. The Committee will need to discuss how to convert these already-existing measures of medical urgency into a point-based framework. As part of this conversation, the Committee will consider how to put each of these factors on a common rating scale within the CAS.

[29] 42 CFR Sec. 121.8(a)(2).
[30] 42 CFR Sec. 121.8(b)(2).

- **Candidate Diagnosis Points (Status 1B)**: During their meeting in June 2022, the OPTN BOD approved a proposal to sort candidates within Status 1B based on diagnosis points.[31] These points will prioritize Status 1B candidates with chronic liver disease, who are at the highest risk of mortality, ahead of other Status 1B candidates.

- **Liver-Intestine Registration:** Adult candidates registered for an intestine as well as a liver automatically receive a 10% increase in the risk of 3-month mortality in their MELD score. Pediatric candidates listed for an intestine as well as a liver are provided 23 additional MELD or PELD points. This additional priority reflects the fact that these candidates are more medically urgent than otherwise similar candidates who are only listed for a liver.[32,33]

In addition to the attributes already existing in current policy, the Committee identified two attributes that they plan to discuss more for potential inclusion in the first or future iterations of continuous distribution – HCC stratification and OPOM.

- **HCC stratification**: Currently, HCC candidates meeting specific criteria in OPTN policy are provided a MELD or PELD exception score. After a six month delay, adult HCC candidates are assigned an exception score equal to medium MELD at transplant (MMaT) minus three. Pediatric and adolescent HCC candidates are assigned a score equal to MELD or PELD 40. However, the same scores are assigned regardless of differing tumor burden between candidates. The Committee intends to explore the feasibility of incorporating an attribute that would further stratify HCC candidates based on additional clinical factors to ensure the most urgent candidates are provided sufficient priority over less sick candidates.[34,35]

  The Committee is interested in public feedback on HCC stratification and if it should be considered for inclusion in the first or future iterations of continuous distribution.

- **OPOM**: OPOM, or optimized prediction of mortality, was developed in 2019 and uses machine-learning to predict a candidate's 3-month waitlist mortality or waitlist removal. Proponents suggest OPOM is superior to MELD and PELD in ranking liver transplant candidates based on mortality risk. The Committee intends to review the OPOM model and associated data for potential incorporation into the continuous distribution framework.[36]

  The Committee seeks the community's thoughts on the inclusion of OPOM in the first or future iterations of continuous distribution allocation system.

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[31] OPTN Liver and Intestinal Organ Transplantation Committee, *Briefing Paper,* Improving Liver Allocation: MELD, PELD, Status 1A, Status 1B. Public Comment Period January 27, 2022-March 27, 2022. https://optn.transplant.hrsa.gov/media/kxhdo0h4/improving-liver-allocation_meld-peld-status-1a-and-status-1b_winter-2022-pc.pdf

[32] J Fryer, "Mortality in Candidates Waiting for Combined Liver-Intestine Transplants Exceeds That for Other Candidates Waiting for Liver Transplants," *Liver Transplantation* 9, no. 7 (2003): pp. 748-753, https://doi.org/10.1053/jlts.2003.50151.

[33] J. Kaplan et al., "The Impact of Meld/Peld Revisions on the Mortality of Liver-Intestine Transplantation Candidates," *American Journal of Transplantation* 11, no. 9 (September 2011): pp. 1896-1904, https://doi.org/10.1111/j.1600-6143.2011.03628.x.

[34] Tsuyoshi Shimamura et al., "Liver Transplantation for Hepatocellular Carcinoma: How Should We Improve the Thresholds?," *Cancers* 14, no. 2 (2022): p. 419, https://doi.org/10.3390/cancers14020419.

[35] Neil Mehta et al., "Liver Transplantation for Hepatocellular Carcinoma. Working Group Report from the ILTS Transplant Oncology Consensus Conference," *Transplantation* 104, no. 6 (2020): pp. 1136-1142, https://doi.org/10.1097/tp.0000000000003174.

[36] 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.

Post-Transplant Survival

The OPTN Final Rule calls for allocation policies "to avoid futile transplants."[37] Currently, the liver and intestine allocation system does not include a factor for post-transplant survival. However, other organs, namely kidney allocation, do account for post-transplant survival. Current kidney allocation includes a factor called Expected Post Transplant Survival (EPTS), which is used to predict a candidate's projected longevity with a functioning graft. The EPTS score works together with the Kidney Donor Profile Index (KDPI) of the donor kidney to match the organ to the appropriate candidate to maximize graft and patient survival.[38,39] Similarly, the policy for the continuous distribution of lungs includes an attribute that quantifies the expected number of days a candidate will live during the first five years post-transplant.[40]

While there is no factor for post-transplant survival in current liver allocation, the Committee will discuss if some form of post-transplant survival should be considered for inclusion in the first or future iterations of continuous distribution of livers and intestines. The Committee is seeking the community's feedback on if post-transplant survival should be a factor in liver allocation. If yes, the Committee asks for additional feedback on potential ways to incorporate such an attribute.

Candidate Biology

NOTA requires the OPTN to consider candidates "whose immune system makes it difficult for them to receive organs,"[41] and the OPTN Final Rule calls for allocation policies to "promote patient access to transplantation."[42] Some candidates have difficulty finding a suitable donor due to biological incompatibilities and the OPTN has long used different mechanisms such as CPRA in kidney allocation and prioritizing candidates with specific blood types for certain donors to equalize access to transplant for biologically disadvantaged candidates.

The Committee identified one attribute for candidate biology in the current allocation system – candidate blood type.

- **Candidate blood type**: In the current allocation system, candidates with blood type O and blood type B are provided additional priority for blood type O donors. This prioritization is intended to improve access to transplant for a population of candidates who, due to their specific biology, are expected to have a more difficult time accessing transplant.[43] The current allocation policy also sorts candidates within a classification based on their blood type compatibility with the donor. Within a given classification, if multiple MELD/PELD scores are equal, candidates with an identical blood type are ranked ahead of candidates with a compatible blood type who are then ranked ahead of candidates with an incompatible blood type.[44]

[37] 42 CFR §121.8(a)(5).
[38] OPTN Policy 8.5.A: Candidate Classifications
[39] 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
[40] 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.
[41] 42 U.S.C. §274(b)(2)(A)(ii)
[42] 42 CFR §121.8(a)(5).
[43] OPTN Liver and Intestinal Organ Transplantation Committee, *Briefing Paper*, Liver and Intestine Allocation Using Distance from Donor Hospital. Public Comment Period October 8, 2018-November 1, 2018. Available at https://optn.hrsa.gov.
[44] OPTN Policy 9.8.D: Sorting Within Each Classification

In addition to blood type compatibility in current policy, the Committee identified four additional attributes not in current policy that they will discuss for potential inclusion in the continuous distribution framework:

- **Donor-recipient size matching:** Published research has consistently documented that liver transplant candidates who are shorter have reduced access to transplant, as many livers from larger donors are not size-appropriate.[45,46,47] In fact, while developing MELD 3.0, the Committee strongly considered including a factor for candidate height, but data suggested that height is more correlated to reduced access to transplant, as opposed to the risk of waitlist mortality.[48] Therefore, the Committee will discuss potential ways to address this well-documented issue through continuous distribution.[49] To note, the OPTN Lung Transplantation Committee addressed donor-recipient size matching by developing a height rating scale that awards more points to the shortest and tallest candidates, as those are the lung candidates who have the most trouble finding an appropriate match.[50]

  For liver, this could entail developing a rating scale that provides additional points to candidates of a certain height range irrespective of any donor characteristics. Conversely, the Committee could consider a solution that would more strategically prioritize certain candidates based on the height of the donor. Whichever way the Committee pursues, the intent is to improve access to transplant for a population with reduced access due to their biological situation.

  The Committee is seeking public feedback on donor-recipient size or size-matching as a potential attribute in continuous distribution.

- **Frailty:** Sarcopenia and frailty are common complications in patients suffering from end-stage liver disease.[51] These complications are associated with increased risk of mortality and can impact a candidate's ability to access transplant. On the other hand, these complications are also associated with adverse post-transplant outcomes and can be difficult to measure objectively.[52,53] The Committee will consider if an attribute for frailty should be included in the continuous distribution system, and asks for community input on the topic.

- **Surgical complexity and re-transplant:** The Committee noted that candidates who have already received a liver transplant and are subsequently re-listed for transplant are more difficult to transplant surgically and therefore have a more difficult time finding a suitable donor organ due

[45] J. C. Lai et al., "Height Contributes to the Gender Difference in Wait-List Mortality under the Meld-Based Liver Allocation System," *American Journal of Transplantation* 10, no. 12 (2010): pp. 2658-2664, https://doi.org/10.1111/j.1600-6143.2010.03326.x.
[46] Alina M. Allen et al., "Reduced Access to Liver Transplantation in Women," Transplantation 102, no. 10 (October 2018): 1710–16, https://doi.org/10.1097/tp.0000000000002196.
[47] Jin Ge and Jennifer C. Lai, "Identifying a Clinically Relevant Cutoff for Height That Is Associated with a Higher Risk of Waitlist Mortality in Liver Transplant Candidates," *American Journal of Transplantation* 20, no. 3 (April 2019): pp. 852-854, https://doi.org/10.1111/ajt.15644.
[48] OPTN Liver and Intestinal Organ Transplantation Committee, *Meeting Summary,* August 27, 2021
[49] Ibid.
[50] 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.
[51] Yedidya Saiman and Marina Serper, "Frailty and Sarcopenia in Patients Pre– and Post–Liver Transplant," *Clinics in Liver Disease* 25, no. 1 (2021): pp. 35-51, https://doi.org/10.1016/j.cld.2020.08.004.
[52] Elizabeth J. Carey et al., "A Multicenter Study to Define Sarcopenia in Patients with End-Stage Liver Disease," Liver Transplantation 23, no. 5 (2017): pp. 625-633, https://doi.org/10.1002/lt.24750.
[53] Ching-Sheng Hsu and Jia-Horng Kao, "Sarcopenia and Chronic Liver Diseases," Expert Review of Gastroenterology & Hepatology 12, no. 12 (2018): pp. 1229-1244, https://doi.org/10.1080/17474124.2018.1534586

to technical considerations.[54] As such, the Committee intends to discuss if data exists to support prioritizing candidates who are surgically complex or listed for re-transplant in the continuous distribution framework.

The Committee is interested in the public's feedback on prioritization of candidates who are surgically complex or listed for re-transplant.

- **HLA sensitization:** Calculated panel reactive antibody (CPRA) values directly estimate the proportion of donors with which an HLA-sensitized candidate is HLA incompatible. CPRA is already in use in kidney allocation and will be incorporated into lung allocation as part of continuous distribution. These policies are intended to grant greater access for candidates who might otherwise struggle to receive organ offers due to being biologically unable to accept organs from many donors. As such, the Committee will determine if HLA-sensitized candidates should receive some form of priority in the future liver allocation system and is seeking community input on this potential attribute. To note, the OPTN Lung Transplantation Committee addressed HLA sensitization by aligning all three candidate biology rating scales (blood type, CPRA, and height) to a single curve, most clearly represented by the CPRA curve, because all three are measures of how hard it is for the candidate to match with a compatible donor or incompatibility.[55]

Patient Access

The OPTN Final Rule requires allocation policies to "promote patient access to transplantation,"[56] and NOTA requires the OPTN to "recognize the differences in health and in organ transplantation issues between children and adults throughout the system and adopt criteria, polices, and procedures that address the unique health care needs of children."[57] Accordingly, the patient access goal is intended to ensure appropriate access to transplant for all liver transplant candidates.

Within patient access, the Committee identified three attributes that already exist in liver and intestine allocation policy:

- **Candidate age**: There are a number of instances where the current liver and intestine allocation system addresses the unique needs of the pediatric population. This includes areas such as the pediatric-specific criteria for Status 1A, the creation of Status 1B priority (which is reserved for pediatric candidates), assignment of higher exception scores for pediatric candidates, the prioritization of pediatric candidates for pediatric donors, and sorting pediatric candidates ahead of adults when MELD or PELD and blood type compatibility are equal.[58] These pediatric-specific policies reflect the unique clinical needs of the pediatric population and are in alignment with the Ethical Principles of Pediatric Organ Allocation.[59]

  In initial discussions about continuous distribution, the Committee agreed that it is vital to continue to include similar, if not additional, forms of pediatric priority in the points-based framework.

[54] P.S. Yoo et al., "Retransplantation of the Liver: Review of Current Literature for Decision Making and Technical Considerations," *Transplantation Proceedings* 45, no. 3 (2013): pp. 854-859, https://doi.org/10.1016/j.transproceed.2013.02.063.
[55] 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.
[56] 42 CFR §121.8(a)(5).
[57] 42 U.S.C. §274(b)(2)(M)
[58] This is not an exhaustive list of all areas where pediatric candidates are treated differently than adult candidates within OPTN Policy.
[59] OPTN, *Ethical Considerations,* Ethical principles of pediatric organ allocation. Updated November 2014. Available at https://optn.transplant.hrsa.gov/

Throughout the development of continuous distribution, the Committee will collaborate with pediatric stakeholders to ensure pediatric candidates are appropriately considered and provided sufficient priority and access to transplant.

- **Waiting time**: In current liver allocation, waiting time is used in certain circumstances to sort candidates when other factors are equal. For instance, when candidates with a calculated MELD or PELD score are in the same classification, have the same MELD or PELD score, have the same blood type compatibility with the donor, and are in the same age category (pediatric vs. adult), they are then ranked based on time at their current MELD or PELD score or higher. Exception candidates are sorted similarly, except they are further ranked by time since submission of earliest approved exception. In effect, waiting time is used to prioritize the candidates who have been on the waiting list longer, when all else is equal. The Committee will discuss how and if waiting time should continue to play a role in the allocation of livers and intestines.

- **Liver-intestine registration**: Liver-intestine registration was also included as an attribute in the medical urgency goal. The Committee decided to also include it in the patient access goal because liver-intestine candidates need access to higher quality donors where the liver, intestine, and pancreas are available for transplant in addition to having higher waitlist mortality than liver-alone candidates.[60] Recent research has also shown that liver-intestine candidates have lower transplant probability after the implementation of the AC policy.[61] Therefore, the Committee has discussed providing points for candidates registered for a liver-intestine combination in both the medical urgency and patient access goals.

In addition to the attributes that already exist in policy, the Committee also identified four attributes related to patient access that are not currently included in liver and intestine allocation policy.

- **Candidate Social determinants of health:**[62] The United States Department of Health and Human Services defines the social determinants of health as, "the conditions in the environments where people are born, live, learn, work, play, worship, and age that affect a wide range of health, functioning, and quality-of-life outcomes and risks."[63] Within the context of liver and intestine allocation, the social determinants of health have been demonstrated to play a role across the transplant process. Factors such as age, sex, race/ethnicity, insurance/socioeconomic status, and geography have all been shown to impact candidate access to transplant, waitlist outcomes, and post-transplant survival.[64]

  The Committee will need to weigh the potential benefits of incorporating an attribute that could account for a candidate's social determinants of health against the reality that such factors are also correlated with worse post-transplant outcomes. In addition, the Committee will need to consider if including such an attribute is feasible within NOTA and the Final Rule. The Committee is interested in community feedback on incorporating aspects of the social determinants of health in the continuous distribution system.

[60] Tommy Ivanics et al., "Impact of the Acuity Circle Model for Liver Allocation on Multivisceral Transplant Candidates," *American Journal of Transplantation* 22, no. 2 (2021): pp. 464-473, https://doi.org/10.1111/ajt.16803.
[61] Ibid.
[62] 42 C.F.R. §121.4(a)(3) permits the OPTN to develop "Policies that reduce inequities resulting from socioeconomic status, including…(iv) Reform of allocation policies based on assessment of their cumulative effect on socioeconomic inequities;"
[63] See https://health.gov/healthypeople/objectives-and-data/ social-determinants-health.
[64] Nabeel A. Wahid, Russell Rosenblatt, and Robert S. Brown, "A Review of the Current State of Liver Transplantation Disparities," *Liver Transplantation* 27, no. 3 (2021): pp. 434-443, https://doi.org/10.1002/lt.25964.

- **Prior living donor:** In the current liver allocation system, prior living donors are not provided any form of additional priority. However, in the current kidney allocation system all prior living donors, regardless of which organ they donated, receive priority. Similarly, continuous distribution of lungs includes additional points for prior living donors, again, regardless of which organ the candidate previously donated. The inclusion of this prioritization for prior living donors is supported by the OPTN Ethics Committee and the OPTN Living Donor Committee.[65,66] Further, there are both ethical and legal justifications for providing a form of priority for prior living donors.[67]

  The Committee will need to decide if they believe liver and intestine allocation should mirror kidney and lung allocation and offer priority for candidates who have previously donated an organ and is interested in feedback on the topic.

- **Willingness to accept a split liver segment**: A split liver transplant is when a transplant program accepts a donor liver and decides to split the liver into two segments, thereby transplanting two candidates from one donor organ. In current OPTN policy, there are two variances aimed at increasing the number of split liver transplants. Both of these variances are focused on making the logistical and surgical aspects of the procurement and transplantation process simpler, by allowing a program to transplant the second segment of a split liver into a candidate at the same transplant program. The variances further incentivize the procedure by allowing them to transplant two of their candidates with a single liver.[68,69]

  However, the number of split liver transplants has decreased post-acuity circles (AC) and initial monitoring of the Region 8 split liver variance does not suggest it has been effective at increasing split liver transplants.[70,71] Committee members have attributed these results both to the implementation of the AC policy and the associated logistical changes, as well as the onset of the COVID 19 pandemic.[72]

  More recently, the Committee has discussed taking a different approach to increasing split liver transplant in the context of continuous distribution. They have suggested that the most effective way to increase split liver transplantation may be to provide an incentive to individual candidates to accept a split liver segment.[73] The general idea the Committee has suggested is to provide some form of priority, such as additional CAS points, for candidates who are willing to accept a split within the continuous distribution framework.

  If candidates who are willing to accept a split are prioritized on the match run, there is a higher likelihood they will receive the offer, increasing the chance of a split liver transplant. Increasing the

[65] OPTN Ethics Committee, *Meeting Summary,* March 11, 2021.
[66] OPTN Living Donor Committee, *Meeting Summary,* May 12, 2021.
[67] 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.
[68] OPTN Policy 9.12.A: Open Variance for Segmental Liver Transplantation as of June 2022
[69] OPTN Policy 9.12.C: Closed Variance for Any Segment Liver Transplantation as of June 2022
[70] Descriptive Data Request: 18 Month Monitoring Report of Liver and Intestine Acuity Circle Allocation Removal of DSA and Region as Units of Allocation, Prepared for the OPTN Liver and Intestinal Organ Transplantation Committee, December 3, 2021
[71] Descriptive Data Request: OPTN Region 8 Split Liver Variance Two Year Report, Prepared for the PELD/Status 1B Work Group, April 4, 2022
[72] OPTN Liver and Intestinal Organ Transplantation Committee, Meeting Summary, April 4, 2022. https://optn.transplant.hrsa.gov/media/rgcloilq/20220404_liver_summary.pdf
[73] Ibid.

number of split liver transplants will be especially beneficial for pediatric candidates and adult candidates who are of smaller stature, as they are more likely to accept the second segment of a split liver, which are smaller grafts.

There are a number of outstanding questions on this topic the Committee will continue to consider but they are interested in community feedback on the feasibility of including some form of priority for candidates who are willing to accept a split liver transplant.

- **Supply/demand**: Donor availability, or the number of liver donors available in a certain geographic area, differs across the nation.[74] In addition, there is variability in rates of mortality due to liver disease in different geographic areas.[75] The use of MMaT as a means to assign exception scores reflects the fact that different MELD scores are needed to access transplant in different areas of the country, despite the fact that the variation in median MELD score at transplant (MMaT) has decreased by OPTN Region, DSA and state since the implementation of the AC policy.[76]

  The Committee will need to discuss if and how a continuous distribution system can account for these differences across the nation and seeks public feedback on the topic.

Placement Efficiency

The OPTN Final Rule does not define the "efficient management of organ placement." [77] However, a Federal Register notice related to the development of the OPTN Final Rule can provide some guidance for interpreting this clause. It states:

> Broad geographic sharing should not come at the expense of wasting organs through excessive transportation times. Efficient management of organ allocation will sometimes dictate less transportation when the highest ranking patient can wait a day or two for the next available organ. Sound medical judgment must be exercised before a final decision on whether to transplant a particular organ into a particular patient.[78]

The placement efficiency goal encompasses the amount of resources required to identify a suitable candidate willing to accept the organ and deliver the organ for transplant.

Placement efficiency is factored into the current liver and intestine allocation system by using concentric circles and prioritizing candidates closer to the donor hospital when other factors are similar. However, the Committee has an opportunity to consider the impact of placement efficiency in a more nuanced way within continuous distribution.

That being said, it is important to reiterate that the goal of continuous distribution is smarter distribution, not broader distribution of livers and intestines. The intent of continuous distribution is to remove the hard boundaries between classifications that exist in the current allocation system, such as

[74] Raymond J. Lynch et al., "Moving Past 'Think Local, Act Global': A Perspective on Geographic Disparity," *American Journal of Transplantation* 19, no. 7 (2018): pp. 1907-1911, https://doi.org/10.1111/ajt.15079.
[75] David Goldberg, Katherine Ross-Driscoll, and Raymond Lynch, "County Differences in Liver Mortality in the United States: Impact of Sociodemographics, Disease Risk Factors, and Access to Care," *Gastroenterology* 160, no. 4 (2021), https://doi.org/10.1053/j.gastro.2020.11.016.
[76] Descriptive Data Request: 24 Month Monitoring Report of Liver and Intestine Acuity Circle Allocation Removal of DSA and Region as Units of Allocation, Prepared for the OPTN Liver and Intestinal Organ Transplantation Committee, July 8, 2022
[77] 42 CFR §121.8(a)(2).
[78] 63 FR 16315 (1998).

the use of concentric circles. Removing these concentric circles does not necessarily mean that continuous distribution will result in livers and intestines being allocated over larger areas for all donors and candidates; instead, continuous distribution should permit broader access for the most urgent candidates and more localized allocation for organs that cannot travel as far. The transition to a points-based framework allows the Committee and the community to consider the impact of placement efficiency with more precision and nuance.

The Committee has identified two attributes – travel efficiency and proximity efficiency – in the placement efficiency goal. These attributes align with the continuous distribution of lungs policy that was recently approved by the Board.

- **Travel efficiency:** Current liver and intestine allocation uses a series of concentric circles (150, 250, and 500 NM) to categorize candidates of decreasing MELD and PELD score into distinct classifications of decreasing allocation priority. The Committee chose to utilize a 150 NM circle as it is approximately the distance at which the transplant surgeon was more likely to fly to recover the organ rather than drive.[79] Flying represents a significant increase in costs of transportation for a transplant, and increased costs make the process less efficient. The Committee then chose a distance of 500 NM as they sought to balance the need to distribute organs as broadly as feasible against the inefficiencies of national organ distribution.[80] They then agreed to include a 250 NM circle to account for variations in geography and logistics across the county.[81] Using different sized circles allows for some geographical variation while attempting to minimize the additional costs and potential risks of flying that impact the efficiency of organ placement.[82]

  In general, travel distance impacts travel time; the farther an organ is transported, the more likely it is to travel by air than ground; and air travel is more expensive than ground travel for the same distance. [83,84]And finally, financial costs are only one aspect of overall placement system efficiency.

  Even though the current circle sizes used in allocation were selected based on the available data and clinical input of the Committee, there remains opportunity to improve the way that travel is considered within the allocation of livers and intestines. Continuous distribution will allow the Committee, similar to the lung example above, to construct a rating scale for travel efficiency that better reflects the costs associated with organ procurement and transplantation.

  The Committee is interested in community feedback on the best way to incorporate travel efficiency into continuous distribution.

- **Proximity efficiency**: Travel efficiency, or cost, is only one relevant aspect of placement efficiency, however. Importantly, geographic proximity (e.g., distance between donor and transplant candidate's hospital) may be considered to the extent necessary to satisfy requirements in the Final

[79] OPTN Liver and Intestinal Organ Transplantation Committee, *Briefing Paper*, Liver and Intestine Allocation Using Distance from Donor Hospital. Public Comment Period October 8, 2018-November 1, 2018. Available at https://optn.hrsa.gov.
[80] Ibid.
[81] Ibid.
[82] Ibid.
[83] S. Gentry, E. Chow, N. Dzebisashvili, et al. The Impact of Redistricting Proposals on Health Care Expenditures for Liver Transplant Candidates and Recipients. Am J Transplant. 2016; 16(2):583-93
[84] Dubay DA, Maclennan PA, Reed RD, et al. The impact of proposed changes in liver allocation policy on cold ischemia times and organ transportation costs. Am J Transplant. 2015; 15(2):541-6

Rule: e.g., efficient management of organ placement and the avoidance of futile transplants due to increased ischemic time.[85] The proximity efficiency attribute measures the efficiency of transporting livers shorter distances other than decreased transportation costs. These include differences such as the time in transit for transplant teams, additional effort required to coordinate longer travel, and differences in the chance of something going wrong in transit the farther the personnel and liver/intestine must travel.

The Committee will consider how to incorporate this attribute in the continuous distribution based system and is seeking community feedback on the topic.

Next Steps

As described previously, the Committee is still in the early phases of this project and much work remains to be done.

Most immediately, the Committee will finalize the list of attributes to include in the first version of continuous distribution. Again, the primary goal of this project is to convert the current classification-based system into a points-based framework. While doing so, the Committee has the opportunity to include new attributes, such as donor-recipient size-matching, HCC stratification or post-transplant survival, in the new allocation system. But they will not be able to incorporate every possible attribute. Any attempt to do so would be far beyond the scope of this project and delay the immediate benefits of transitioning to a continuous distribution framework.

With that in mind, the next step is to finalize which attributes the Committee wants to consider for further incorporation in continuous distribution. To guide this discussion, the Committee is considering the following questions for each potential new attribute:

- What solutions, if any, have already been developed?
    - *Utilizing a solution that has already been developed and vetted will be simpler and faster than the Committee developing a new solution.*
- Are there competing solutions to this problem?
    - *Topics that have clear consensus around a single solution will be easier to incorporate than topics where there are competing solutions.*
- What research exists to show this is an effective solution(s)?
    - *The Committee is only interested in solutions that have been demonstrated to effectively address the problem they intend to solve.*
- Is there community consensus on a solution?
    - *Solutions that already have community consensus on their effectiveness and feasibility will be easier to incorporate than solutions for which there is no consensus.*
- What would the committee need to do to develop a solution?
    - *If a solution does not already exist but the Committee is still interested in incorporating the attribute into continuous distribution, they will need to weigh the time and resources needed to develop the solution against the value of the potential solution.*
- How complex are potential solutions?
    - *Transitioning from a classification-based framework to appoints-based framework will be a complex effort in and of itself. Incorporating additional attributes that do not already exist in allocation policy will increase the complexity of the project. As such, the*

[85] 42 C.F.R. §121.8(a)(8)

Committee is interested in new attributes that will minimize the complexity of the overall project to the extent possible.

- Are there options that can be more easily incorporated than others?
    - *The Committee will weigh the ease with which each new attribute and associated solution could be incorporated against the time and resources needed to incorporate the solution and its anticipated effectiveness. For example, within the context of donor-recipient size matching, the Committee could consider including a solution that will provide additional points for candidates who are below a specific height threshold that is correlated with decreased access to transplant. Alternatively, they could consider a more nuanced solution that would prioritize certain candidates who are close to the donor's size. The former option is simpler to implement but might not have the same impact as the latter solution. The Committee will need to weigh the anticipated impact of potential solutions compared to the complexity with which they could be developed and incorporated.*
- How does the solution align with Final Rule, NOTA, committee/community sentiment?
    - *All aspects of the new framework will need to align with the requirements outlined in the Final Rule and NOTA. In addition, the Committee will want to ensure the attributes they recommend to include in continuous distribution align with the values of the larger transplant community.*
- Does the OPTN currently collect necessary data? If not, what needs to be collected?
    - *If the OPTN does not already collect the data needed to incorporate a certain attribute or associated solution, it will be difficult to incorporate that attribute/solution into continuous distribution. Similarly, the Committee may identify certain data elements that should be collected in order to implement future improvements to the allocation system.*
- Does this impact other organs?
    - *One benefit of utilizing a points-based framework is the ability for consistency across organs. The Committee will consider any impact their proposed attributes/solutions may have on other organs. Where appropriate, the liver allocation system should align with the other allocation systems.*
- Would the attribute benefit from additional time and research before incorporating into liver allocation?
    - *The Committee will consider if additional time and research are needed before incorporating a certain attribute or solution into the new allocation system. If additional work is needed, the attribute or solution will likely need to be incorporated into future iterations of continuous distribution.*

Once the Committee has a finalized the list of attributes, they will construct rating scales for each attribute. Many of these attributes already have existing rating scales or there exists precedent in other organ allocation systems.

Once they have constructed rating scales, the focus will shift to weighting the different attributes against each other in a points-based system. Similar to lung, the Committee has sought a Revealed Preference Analysis (RPA) to approximate the weights of the attributes in the current policy.[86]Also,

[86] Darren E. Stewart et al., "A Revealed Preference Analysis to Develop Composite Scores Approximating Lung Allocation Policy in the U.S," *BMC Medical Informatics and Decision Making* 21, no. 1 (June 2021), https://doi.org/10.1186/s12911-020-01377-7.

similar to the other organs transitioning to continuous distribution, the Committee expects to work with experts in mathematical optimization to understand the tradeoffs between the attributes and select the optimal combination of rating scales and weights.[87,88] Throughout these steps, the Committee will use all available data, subject matter expertise, and will continue to seek community feedback as they progress through the project.

Once the Committee constructs rating scales and attribute weights, they will then build the overall framework for the continuous distribution system. More detail on the items the Committee will need to consider when constructing the comprehensive framework is included below.

Additional Considerations

- **Exceptions and the NLRB:** Transplant programs can submit exception requests when they believe a candidate's MELD or PELD score does not accurately reflect their need for transplant. The review board framework – or chiefly the ability of transplant programs to request changes to their candidates' prioritization and for that request to be evaluated by a group of peers – is an important part of current liver allocation. As the OPTN transitions to points based scores for all organs, this component will be a necessary and consistent part of continuous distribution for all organs. The Committee expects to continue to utilize some form of review board to evaluate instances where a candidate's clinical situation is not appropriately represented by their CAS.

  It is likely that what constitutes a MELD or PELD exception and the process through which exceptions are considered will need to change within the context of continuous distribution. While the Committee has not yet discussed how to handle exceptions in depth, they have reviewed general options.

  First, it is important to clarify that the current way in which exceptions are considered is a bit of a misnomer. There are nine diagnoses in OPTN policy with specific criteria, and if a candidate meets the criteria for one of these diagnoses, they are automatically approved for an "exception." However, if an exception is something that does not follow a rule, then these standard "exceptions" are not actually exceptions in the true sense of the word. If the criteria in policy are the rules, then candidates meeting those rules are provided additional MELD or PELD points. This situation is not an exception to the rule; it follows a rule.

  That may seem like a trivial distinction at first but it begins to highlight how such "exceptions" could be handled under continuous distribution. When constructing the comprehensive framework, the Committee could consider incorporating these "exceptions" directly into the allocation system and reserve the review board process for peer review of clinical cases.

  Table 3 and **Figure 9** below depict a high-level, hypothetical example of what this might look like in the new system. This sample scenario is simplified but imagine the case of the following four candidates:
  - **Candidate A**: Medical urgency sub-score is driven by calculated MELD

[87] 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 (January 2022), https://doi.org/10.1093/jlb/lsac012.
[88] Mankowski M, Wood N, Segev D, Gentry S. Designing Continuous Distribution for Liver Allocation [abstract]. *Am J Transplant.* 2022; 22 (suppl 3). https://atcmeetingabstracts.com/abstract/designing-continuous-distribution-for-liver-allocation/. Accessed July 5, 2022.

- **Candidate B:** Calculated MELD is low, but the candidate receives more medical urgency points for cholangiocarcinoma (CCA)
- **Candidate C:** HCC candidate, is not medically urgent but receives more points in the patient access sub-score
- **Candidate D:** Calculated MELD is low, but the candidate receives more medical urgency points for hepatic artery thrombosis (HAT)

Candidate A does not have an exception and has a calculated MELD score equal to 25. In the hypothetical system, having a MELD score of 25 is converted to a medical urgency sub-score equal to 50 CAS points.

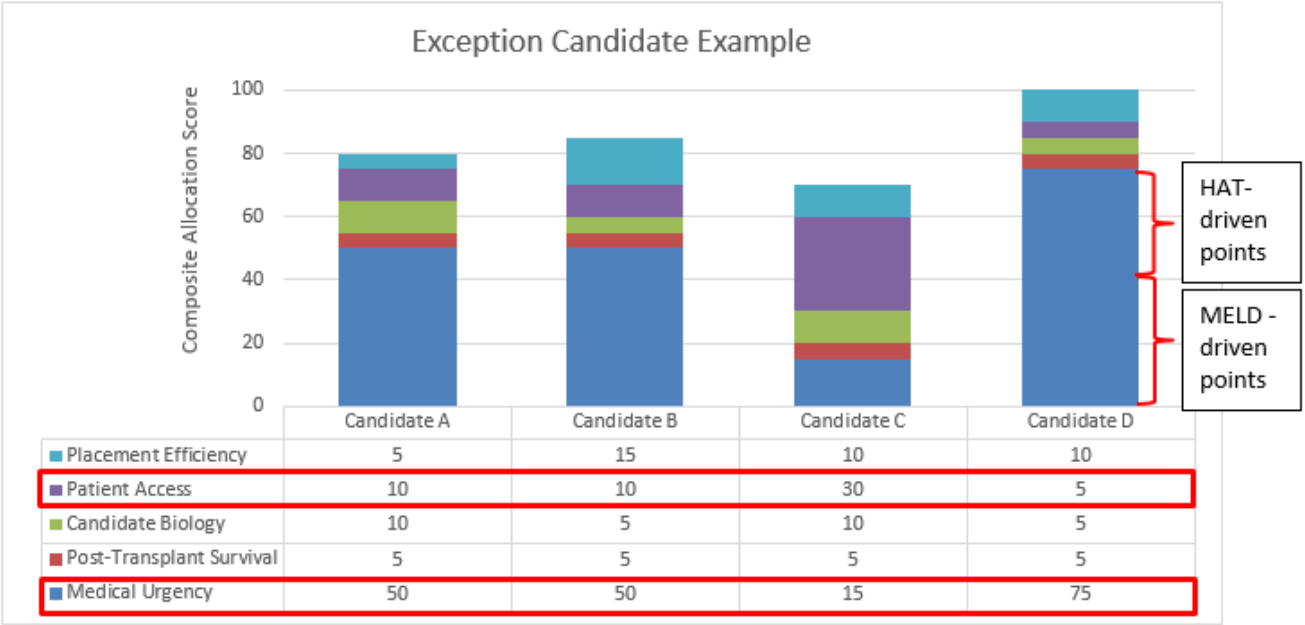
The next three candidates all have what is now considered an "exception." For each of these "exceptions," the candidates are assigned a certain number of points either in the medical urgency sub-score or patient access sub-score. For instance, candidate B has a CCA diagnosis with a calculated MELD score of 17. However, this candidate is provided additional medical urgency points because he or she meets the criteria for a CCA "exception." Similarly, Candidate C is provided additional patient access points because he or she has an HCC "exception" and Candidate D is assigned more medical urgency points because he or she has an HAT "exception."

This framework provides additional points for certain attributes when candidates meet the standard criteria for an "exception." **Figure 9** below shows how Candidate D is assigned 75 total points within the medical urgency sub-score. However, some of these points are assigned due to the candidate's underlying calculated MELD score while the rest are assigned because the candidate meets the criteria for what is now called a HAT "exception." This system recognizes that the MELD and PELD scores underestimate mortality risk for certain candidates meeting specific criteria and includes additional points for these candidates within the framework.

Table 3: Exception Candidate Example

Candidate	Calculated MELD Score	Exception Diagnosis	Medical Urgency	Post-Transplant Survival	Candidate Biology	Patient Access	Placement Efficiency	Total CAS
Candidate A	25	None	50	5	10	10	5	80
Candidate B	17	CCA	50	5	5	10	15	85
Candidate C	6	HCC (after delay)	15	5	10	30	10	70
Candidate D	20	HAT	75	5	5	5	10	100

Figure 9: Exception Candidate Example



	Candidate A	Candidate B	Candidate C	Candidate D
Placement Efficiency	5	15	10	10
Patient Access	10	10	30	5
Candidate Biology	10	5	10	5
Post-Transplant Survival	5	5	5	5
Medical Urgency	50	50	15	75

Again, this is just one potential way the Committee could consider incorporating standard exceptions into the new framework and they will still need to discuss how non-standard exceptions, or those exceptions that do not meet the criteria in policy and are reviewed by the NLRB, will be adjudicated. One potential option is to create a system to allow for goal-based exceptions, rather than tying the exception to the candidate's MELD or PELD score. Under this framework, transplant programs would be able to submit an exception to get more medical urgency points, more patient access points or more placement efficiency points. These cases would then be reviewed by a body in a similar way to the NLRB.

The Committee will focus on these operational aspects of the new system at a later date but is open to community feedback on how MELD and PELD exception and the NLRB could be incorporated into the new allocation system.

- **Donor factors:** In current liver allocation, there are different match runs based on specific donor-related factors. Generally, pediatric candidates are prioritized for pediatric donors and candidates at transplant programs located closer to the donor hospital are prioritized when the donor is either over the age of 70 or is a donation after circulatory death (DCD) donor. The Committee has not yet discussed how to incorporate such donor factors in the continuous distribution system but will have the ability to adjust attribute rating scales or weights based on different donor factors. The OPTN Kidney Transplantation Committee and the OPTN Pancreas Transplantation Committee have already begun considering how to incorporate donor factors in their concept paper currently out for public comment.[89]

- **Intestine Allocation:** Thus far, the Committee has focused on liver and liver-intestine allocation. However, they will also need to also convert the intestine allocation system to a points-based

[89] See Update on Continuous Distribution of Kidneys and Pancreata. Available for public comment at https://optn.transplant.hrsa.gov/

framework. This will include converting the current classifications of statuses, distance, and blood type compatibility into a points-based allocation system.

Compliance Analysis

NOTA and OPTN Final Rule

The Committees submit this concept paper 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."[90] 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," 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 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."[91] While this paper does not propose policy changes at this time, the concepts presented in this paper:

Are based on sound medical judgment:[92] The construction of the individual ratings 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 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:[93] 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:[94] In this case, the allocation systems will be tailored to livers and intestines.

Are designed to avoid wasting organs:[95] The Committee identified multiple attributes specifically designed to avoid wasting organs. Additionally, before the policy proposal is released for public comment, it will be modeled by the SRTR to assess the impact on discarded organs, as well as the impact on total number of transplants. If necessary, the Committee will be able to adjust the weighting of the attributes to balance the number of transplants against other attributes.

[90] 42 CFR §121.4(a).
[91] 42 C.F.R. §121.8(a)
[92] 42 CFR §121.8(a)(1).
[93] 42 CFR §121.8(a)(2).
[94] 42 CFR §121.8(a)(4).
[95] 42 CFR §121.8(a)(5).

Are designed to…promote patient access to transplantation:[96] 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:[97] 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]:[98] The Committee is considering the candidate's place of listing to the extent that is required for the purpose of achieving efficient placement of the organs, specifically for travel efficiency, placement efficiency, and supply/demand.

Consider whether to adopt transition procedures:[99] 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. This would allow members and patients time to prepare for these changes.

Conclusion

This concept paper represents the first step in a multi-phase 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 specific attributes and developing attribute 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.

This project serves as an opportunity to rethink how the OPTN and the transplant community develops organ allocation policies. This concept paper explains the work that the Committee has completed to date and seeks community feedback on which attributes should be included in the first iteration of continuous distribution. The Committee is also interested the Community's input on the overall project plan and any other aspects of the allocation system that are relevant to continuous distribution.

Consideration for the Community

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

- Which attributes should the Committee continue to consider for inclusion in the first iteration of continuous distribution?

[96] 42 CFR §121.8(a)(2).
[97] 42 CFR §121.8(a)(5).
[98] 42 CFR §121.8(a)(8).
[99] 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.

- Are there other attributes the Committee should consider that are not included in the list provided above?
- Are there any attributes that exist in current policy that should not be included in continuous distribution?
- Any other feedback on the plan to develop continuous distribution of livers and intestines.

Appendix: Glossary of Terms

The following terms are used throughout the concept paper.

Analytical Hierarchy Process (AHP): An AHP is an example of a stated preference analysis. This analysis asks participants to state their preferences in a pairwise comparison.

Attribute: Attributes are criteria used to classify, sort and prioritize candidates.

Classification-based framework: A classification-based framework groups similar candidates into classifications or groupings. The candidates are then sorted within those classifications. This is the framework currently used to allocate organs.

Composite Allocation Score: A composite allocation score combines points from multiple attributes together. This concept paper proposes the use of composite allocation scores in a points-based framework.

Concentric Circles: This distribution framework utilizes the distance between the donor hospital and the candidate's transplant hospital to prioritize organ offers to candidates. These distances are grouped into zones at specific nautical mile distances.

Calculated Panel Reactive Antibody (CPRA): The percentage of deceased donors expected to have one or more of the unacceptable antigens indicated on the waiting list for the candidate. The CPRA is derived from HLA antigen/allele group and haplotype frequencies for the different ethnic groups in proportion to their representation in the national deceased donor population.

Exception (standardized): When the calculated MELD or PELD score does not reflect the candidate's medical urgency, a liver transplant program may request an exception score. A candidate that meets the criteria for one of nine diagnoses in OPTN policy is approved for a standardized exception.

Exception (non-standard): When the calculated MELD or PELD score does not reflect the candidate's medical urgency, a liver transplant program may request an exception score. If the candidate does not meet the criteria for standardized exception as outlined in OPTN policy, the request is considered by the National Liver Review Board (NLRB).

Framework: A collection of policies and procedures used to distribute organs. Examples include concentric circles and continuous distribution.

Goals: Five goals constitute the overall composite allocation score. These goals align with the requirements in NOTA and the OPTN Final Rule: Medical urgency, post-transplant survival, candidate biology, patient access, placement efficiency**.**

Human leukocyte antigen (HLA): A type of molecule found on the surface of most cells in the body. Human leukocyte antigens play an important part in the body's immune response to foreign substances.

Ischemic Time: Ischemic time is broken into three subparts: procurement, transit, and transplant time.

Procurement time begins at cross-clamp and ends at transit departure time. OPO and procurement practices, among other things, influence procurement related ischemic time. Transit time is the time in between departure from the procurement location and delivery at the transplant hospital. Transplant time is then the time between delivery at the transplant hospital and the start of anastomosis.

MELD: Model for End Stage Liver Disease; the scoring system used to measure illness severity in the allocation of livers to adults and adolescents.

MMaT: Medium MELD at transplant; The MMaT is calculated by using the median of the MELD scores for transplants performed within 150 nautical miles (NM) of each donor hospital. Exception candidates on a match run are assigned an exception score relative to the MMaT for the donor hospital where match is run and ranked against each other based on time since submission of earliest approved exception

NLRB: National Liver Review Board; A review board of members drawn from a nationwide pool of liver transplant physicians and surgeons, who review non-standard exception requests from transplant programs for candidates whose calculated MELD score or PELD score does not accurately reflect the candidate's medical urgency for transplant.

PELD: Pediatric End Stage Liver Disease; The scoring system used to measure illness severity in the allocation of livers to candidates under the age of 12.

Points-based framework: A points-based framework gives each candidate a score or points. Organs are then offered in descending order based upon the candidate's score. This concept paper proposes a points-based framework for organ allocation.

Rating Scale: A rating scale describes how much preference is provided to candidates within each attribute. Applying the rating scale to each candidate's information and combining it with the weight of the attribute results in an overall composite score for prioritizing candidates.

Revealed Preference: A revealed preference analysis looks at actual decisions to determine the implicit preferences of the decision maker. This is compared with a stated preference analysis (for example, AHP) that asks the decision maker to state their preferences in an experiment.

Weight: Weights are the relative importance or priority of each attribute toward our overall goal of organ allocation. Combined with the ratings scale and each candidate's information, this results in an overall composite score for prioritizing candidates.