OPTN Lung Transplantation Committee
Continuous Distribution Data Workgroup
Meeting Summary
August 13, 2020
Conference Call

Erika Lease, MD, Chair
Marie Budev, DO, Vice Chair

Introduction
The Lung Transplantation Committee’s Continuous Distribution Data Workgroup met via Citrix GoTo teleconference on 08/13/2020 to discuss the following agenda items:

1. Biological Disadvantages and Equity Rating Scales

The following is a summary of the Workgroup’s discussions.

1. Biological Disadvantages and Equity Rating Scales

The Chair and UNOS staff led the Workgroup in a discussion on rating scales for attributes associated with biological disadvantages in transplant access: sensitization, blood type, and candidate size.

Summary of discussion:
UNOS staff reviewed the integrated analytical hierarchy process (AHP) approach to reducing biological disadvantages. This approach recognizes that a candidate’s access to transplant can vary depending on biological factors that affect the ability to find a compatible donor. Relatively more points should be awarded to candidates that are less likely to be transplanted due to challenges in finding a biologically compatible match, like candidates that have a high Calculated Panel Reactive Antibodies (CPRA) score (indicating that they are highly sensitized).

UNOS staff noted that CPRA 50% candidates are human leukocyte antigen (HLA) antibody-incompatible with about 50% of donors. Blood type O candidates are ABO-incompatible with about 50% of donors. Candidates with restrictive lung disease that are 5’0” tall are height-incompatible with about 50% of donors. Accordingly, the proportion of lung donors with which a candidate is biologically incompatible provides a common scale for aligning sensitization/CPRA, blood type, and height.

Sensitization
UNOS staff presented an approach for creating a rating scale for CPRA. By definition, CPRA reflects the proportion of donors who are HLA-incompatible based on candidate antibody sensitivities. The rating scale would map the probability to AHP rating, e.g., a CPRA of 50% would equate to a score of 0.5 on the rating scale. UNOS staff noted that the Committee could also consider using nonlinear approaches.

Blood Type
The Chair explained that points will be awarded by candidate blood type (e.g., A, B, O) in the continuous distribution framework, not by ABO identical versus compatible. In 2019, the Continuous Distribution of Lungs Workgroup concluded that the purpose of prioritizing ABO identical matches was solely for equity,
not post-transplant outcomes. Accordingly, the Workgroup decided that awarding points based on “absolute” blood type allows for a more refined, graded approach for addressing blood type-induced access disparities. For example, for a blood type O donor, a policy based on ABO identical versus compatible would give blood type O candidates the most points, and candidates with blood type A, B, and AB would all receive zero points. A policy based on “absolute” ABO can award points along a continuum, such as $O > B > A > AB$.

UNOS staff presented an approach for creating a rating scale for blood type. UNOS staff computed the probability of compatible donors for a cohort of 2,751 deceased lung donors from 2019. Because candidates with blood type AB can receive organs from any blood type, they would receive a score of 0. Because blood type O candidates are incompatible with 50% of donors, they would receive a score of 0.5. In this cohort, blood type A candidates had a 14% probability of being incompatible with donors, so they would receive a score of 0.14. Blood type B candidates had a 38% probability of being incompatible with donors, so they would receive a score of 0.38. This approach assumes a linear scale. UNOS staff said they considered looking at offer and transplant rate data, but did not think that data would provide any guidance, since current policy prioritizes ABO identical matches over other matches and that would bias the data. A member said this approach would not make sense if the Committee intends for the policy to continue to prioritize identical blood type over compatible. UNOS staff agreed, noting that the Continuous Distribution of Lungs Workgroup previously decided that the continuous distribution framework would not need to prioritize identical candidates over compatible candidates.

**Candidate Height**

The Chair noted that the continuous distribution framework will account for candidate size rather than donor-candidate height matching. While height matching might improve system efficiency by reducing offer refusal rates, the Continuous Distribution of Lungs Workgroup agreed previously that transplant programs should have both the prerogative and the responsibility to set appropriate minimum and maximum donor height acceptance criteria for their candidates. Furthermore, the primary purpose of incorporating candidate height is to reduce inequities in access, not to increase efficiency.

UNOS staff presented an approach for creating a rating scale for candidate height. For each possible candidate height, it is possible to estimate the proportion of lung donors that are height-incompatible. UNOS staff shared graphs depicting the distribution of recipient-donor height differences, both in aggregate and by diagnosis group. A member said that the curves for diagnosis groups A, C, and B are not surprising, but that they would expect the curve for diagnosis group D to be farther to the right, rather than centered around zero. The Chair agreed. The Vice Chair suggested that since group D includes patients with chronic obstructive pulmonary disease (COPD) and idiopathic pulmonary fibrosis (IPF), those patients may have shifted the distribution to the left. HRSA staff noted that there appears to be a broad range of height differences on either side of zero across diagnosis groups, suggesting that the height differences might not be as important as expected. A member explained that there are a lot of variables that factor into this. For example, a younger recipient would have less space in the chest cavity than an older recipient, since the chest tends to get deeper with age and have more space. Gender can also result in a difference in height, particularly if there is a female to male lung transplant. If the donor is large, the surgeon has the option to remove some of the lung tissue to fit it to the chest of a smaller recipient. UNOS staff asked the Workgroup to consider if there should be a different curve for each

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diagnosis group in the continuous distribution framework, or if they should be combined in one curve. Members did not immediately offer a recommendation.

Next, UNOS staff shared a graph depicting the proportion of height-compatible donors by height and diagnosis group, and then shared an inverted graph of the proportion of height-incompatible donors by height and diagnosis group. UNOS staff shared a linear rating scale that assigns more points to candidates who are less likely to find height-compatible donors. UNOS staff noted that since policy currently does not prioritize height, risk-adjusted transplant rate data could provide some guidance as to whether it is appropriate for this rating scale to be linear.

UNOS staff asked if the Workgroup believes that the 95% height-compatibility windows are clinically plausible and appropriately used in this approach. A member said it would be helpful to see a slide illustrating the 95% height-compatibility windows, and how very short and very tall candidates end up with a smaller donor pool based on that. UNOS staff said that sensitivity analysis will allow members to enter sample candidate data and attribute weights to observe the impact on the composite score.

**Combined Equity Rating Scale**

UNOS staff shared a graph of the proposed sensitization, blood type, and height rating scales aligned on a common scale. A member asked if it makes sense to add points or to multiply points across the three rating scales. UNOS staff said the proposed approach is additive, but the member’s question raises a broader question about whether these factors are independent. The proposed approach assumes that these traits are independent across donor profiles based on feedback from experts, but UNOS staff could potentially look into this further. The member said he did not know the answer but noted that the goal is to provide equal access to donors across these three traits, so the Workgroup should consider whether summing the score achieves that goal. UNOS staff said that sensitivity analysis and SRTR modeling will help the Workgroup to answer that question. The Vice Chair noted that a lot of women are of shorter height and sensitized but was not sure if there is a dependency between those traits. UNOS staff said this approach is looking more at donor traits than candidate traits. UNOS staff shared examples of how the rating scales would work, assuming a weight of 15% on this attribute:

- Biological disadvantage score = weight * (CPRA score + blood type score + height score)/3
  - Candidate 1 (least biologically disadvantaged)
    - CPRA = 0%, blood type AB, 5’5”, diagnosis group D
    - Score = 0.15 * (0 + 0 + 0.06)/3 = 0.003
  - Candidate 2 (more biologically disadvantaged)
    - CPRA = 50%, blood type A, 5’1, pulmonary arterial hypertension
    - Score = 0.15 * (0.50 + 0.14 + 0.35)/3 = 0.05
  - Candidate 3 (highly biologically disadvantaged)
    - CPRA = 95%, blood type O, 6’6”, diagnosis group D
    - Score = 0.15 * (0.95 + 0.5 + 0.81)/3 = 0.113
  - Candidate 4 (small pediatric candidate)
    - CPRA = 95%, blood type O, 3’7”
    - Score = 0.15 * (0.95 + 0.50 + 0.99)/3 = 0.122

Since all the rating scales are relative, these scores could be multiplied by 100 to achieve the desired impact on candidate rankings. The Committee will have the opportunity to revise this at a later date if needed.
**Nonlinear Approach**

UNOS staff shared an example of what a nonlinear combined rating scale could look like, noting that an exponential function might better ensure that extremely hard-to-match patients receive a sufficient boost in points. UNOS staff asked if the Workgroup has a strong opinion on whether the rating scale should be linear or nonlinear, or if both should be examined in sensitivity analysis. A member noted that the weight placed on this rating scale will impact how much the shape of the curve influences the candidate’s overall score. The member suggested waiting until the model was more developed to revisit the shape of the curve. UNOS staff agreed that the weight on the attribute and the shape of the curve go hand-in-hand. A member said that the linear approach makes sense, and agreed that the Committee should wait to select the shape of the curve until the model is more developed.

HRSA staff said it seems like the framework for considering a nonlinear scale might depend on the relative compatibility, analogous to kidney, where CPRA for kidney is not linear. For kidney, the CPRA curve is fairly linear up until about 70-80% and then slopes up very steeply, especially from 98% CPRA upwards. It seems worth exploring whether it would be equitable to incorporate nonlinear approaches. UNOS staff agreed that the kidney allocation score (KAS) can provide insights. The analytical hierarchy process approach inherently goes from zero to one, and there are some reasons to stick to this approach, but it doesn’t absolutely have to be that way – it can be adapted. For example, maybe someone with a 99.999% CPRA needs a score above one. First, the Committee can explore linear vs. nonlinear, and then another option on the table is to consider assigning scores greater than one.

**Summary**

- The probability of biological incompatibility concept provides a unified framework for developing rating scales to address biological disadvantages
- The choice of rating scale shape (linear vs. nonlinear) may require assessment during sensitivity analysis and/or SRTR modeling
  - Linear mapping is the easiest to interpret and understand, but may not sufficiently boost priority for very hard-to-match patients
- This approach is data-driven, though not necessarily “optimal”
  - Whether the combination of the assigned weight and chosen rating scales will lead to an acceptable degree of disparities in access, in light of other policy goals, is unknown; SRTR modeling may help determine whether refinements are needed
  - The weight is assumed equal for sensitization, blood type, and height, but factor-specific weights could be “tuned” if unacceptably high disparities persist for one or more factors

UNOS staff asked the Workgroup if members believe that this is a reasonable approach for incorporating biological disadvantages into the composite allocation score. Members thought that this approach was both reasonable and understandable, and did not have any concerns about these three traits being aligned on the same scale. UNOS staff noted that this is a big change since these traits used to be handled as separate classifications in allocation, but now the traits will be on the same scale. This is an approach that the Committee can follow with other biological disadvantages in the future, if need be, and this approach can be used for other organs.

**Next steps:**
The rating scales will be shared with the full Lung Committee during an upcoming meeting. The Committee will revisit the shape of these rating scales following sensitivity analysis and SRTR modeling.
Upcoming Meetings

• August 20, 2020 – Lung Committee
• September 10, 2020 – Continuous Distribution Data Workgroup
Attendance

- **Committee Members**
  - Erika Lease, Committee Chair
  - Marie Budev, Committee Vice Chair
  - Whitney Brown
  - Rocky Daly
  - Ryan Davies
  - Jasleen Kukreja
  - Marc Schecter

- **HRSA Representatives**
  - Jim Bowman
  - Marilyn Levi
  - Adriana Martinez

- **SRTR Staff**
  - Yoon Son Ahn
  - Katie Audette
  - Melissa Skeans
  - Maryam Valapour
  - Andrew Wey

- **UNOS Staff**
  - James Alcorn
  - Julia Chipko
  - Rebecca Goff
  - Elizabeth Miller
  - Janis Rosenberg
  - Leah Slife
  - Darren Stewart
  - Kaitlin Swanner
  - Sara Rose Wells
  - Karen Williams

- **Other Attendees**
  - Belinda Udeh