

**OPTN Lung Transplantation Committee
Updating Mortality Models Subcommittee
Meeting Summary
February 25, 2021
Conference Call**

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

Introduction

The Lung Transplantation Committee's Updating Mortality Models Subcommittee met via Citrix GoTo teleconference on 02/25/2021 to discuss the following agenda items:

1. Introduction to the Subcommittee
2. SRTR 5-Year Modeling Results Overview

The following is a summary of the Subcommittee's discussions.

1. Introduction to the Subcommittee

The Chair welcomed members to the Updating Mortality Models (UMM) Subcommittee and explained the focus of the Subcommittee is to review and update waitlist mortality and post-transplant mortality models to better predict outcomes, identify new variables that are not currently collected or used in the lung allocation score (LAS), identify ways to improve and refine current fields, determine length of outcomes to use, and determine the cadence for future updates. SRTR staff noted that there are data being collected that are not currently being used in the LAS calculation and the workgroup can consider any possibilities or opportunities to incorporate that information.

2. SRTR 5-Year Modeling Results Overview

SRTR staff presented an overview of the findings of their modeling on 5-year post-transplant outcomes.

Summary of discussion:

The Lung Committee previously requested this analysis because they were concerned that the 1-year post-transplant mortality model may fail to capture the possibility of worse long-term survival of older recipients. There are two primary avenues that a different post-transplant mortality model approach can affect ranking on the match run. Moving from a 1-year to 5-year model could change the ranking of candidates and/or change the relative importance of post-transplant mortality compared to waitlist mortality.

The SRTR analysis sought to identify two effects: the transition from a 1-year to 5-year post-transplant mortality model and the difference between models that allow covariate effects to evolve over the post-transplant follow-up time period. SRTR staff considered different models because the Lung Committee previously expressed concern that the age effect gets larger over the course of post-transplant follow-up, and traditional survival models would not be able to capture that because they assume that these variables remain constant after transplant. The SRTR used six models to identify the specific effects (e.g. the effect of age vs. the effect of shifting from one-year to five-year post-transplant survival) instead of confounding any effects. Each model included the covariates in the recently approved LAS post-

transplant model and these covariates allowed a more direct comparison with the post-transplant mortality score under consideration for continuous allocation.¹

The 5-year post-transplant mortality model did show that outcomes for older recipients get worse at longer time intervals, but this might not actually change the rankings. This supported the Committee's initial prediction of older recipient outcomes. Allowing a 5-year model to have time-varying effects did not improve the predictive performance of the model but the 5-year model had slightly better predictive performance than the 1-year model. The time-varying effects also did not meaningfully change the rankings of the patients and it is significantly more complicated than the proportional hazards model.

SRTR staff stated that it seems unlikely that different modeling frameworks and/or extending post-transplant follow-up will meaningfully change candidate rankings within the post-transplant mortality scale. However, placing different relative weights on waitlist mortality and the 5-year post-transplant mortality may change the impact of the 5-year post-transplant mortality model. The difference between 35-50 year old candidates to 65+ year old candidates from the 1-year to 5-year model could change ranking on the match run depending on the variability in the waitlist mortality scale. For the urgent candidates regarding waitlist mortality, their values are small with large differences between them so it is less likely that the change from a 1-year to a 5-year post-transplant mortality model will affect the extremely urgent candidates. Also, smaller shifts in how the differences in the post-transplant mortality scale line up with waitlist mortality could affect allocation priority for many recipients between the 50th and 90th quantile. SRTR did a Thoracic Simulation Allocation Modeling (TSAM) study to clarify this point, which was different than the TSAM used for the continuous distribution data request. This TSAM study compared the 1-year and 5-year post-transplant mortality models across three allocation systems (the current allocation system; a 1:1 LAS continuous distribution system; and a 2:1 LAS continuous distribution system). The continuous allocation systems had noticeable differences in outcomes between the 1-year and 5-year post-transplant models as they generally increased transplant rate for candidates ages 18 to 50 and decreased transplant rates for candidates over age 65 relative to the current allocation system. Across allocation systems, there was an increase in transplant rate for candidates in diagnosis groups B and C and decrease in transplants for candidates in diagnosis group D between the 1-year and 5-year post-transplant mortality models. SRTR staff also looked at the percentage of transplants, which showed similar patterns to the transplant rates, although the differences were smaller for candidates ages 18-50 and candidates with diagnoses C and D. For candidates 65+ years old, the percentage of transplants for the 1:1 LAS model had a 4% difference between the 1-year to 5-year models which is a large difference considering the only thing that is being changed for the allocation systems is how the post-transplant mortality scale is defined.

A member said it is agreeable to see the 5-year model had the impact that was expected by the Committee, at least for the continuous distribution models, in that many of the older patients are lost between the 2 and 5-year mark, and it has been difficult to change allocation by age alone. The member supported using 5-year post-transplant outcomes in allocation. A member said this approach looks great overall. The Committee was having trouble understanding how changing the weight of post-transplant mortality did not result in much change in the modeling, so it is encouraging to see that there were differences in age group once SRTR used 5-year post-transplant outcomes. The member said it was exciting to see how this approach could work in continuous distribution. The Chair agreed with this sentiment. A member said this means that this extra element needs to be included in allocation.

¹ Updated Cohort for Calculation of the Lung Allocation Score (LAS), OPTN, December 7, 2020. Accessed March 24, 2021: <https://optn.transplant.hrsa.gov/media/4244/updated-cohort-for-calculation-of-the-las.pdf>

A member asked if the Lung Committee has the authority to approve a change from a 1-year to 5-year post-transplant mortality model for continuous distribution. The Chair said this is within the Lung Committee's purview, but SRTR staff had some other suggestions for first steps. SRTR staff explained that they would like to have peer-review of the model. UNOS staff noted that next steps would be to refine the model more and walk through the assumptions that SRTR staff made in the analysis to confirm they are the correct assumptions and then make the shift to the 5-year model with continuous distribution. As the Subcommittee starts thinking about variables that can be added to the model, they can think about it in terms of 5-year outcomes.

HRSA staff asked if there were interactions between the patients over the age of 65 and the group D diagnosis patients. SRTR staff said they did not observe interactions, but they could investigate that if there was clinical interest. HRSA staff said it seems intuitive that transplants would decrease for the 65+ age group looking at 5-year post-transplant outcomes and asked if he was missing anything since it seemed that would be obvious. SRTR staff explained that the spread of the entire post-transplant mortality scale is much larger at 5 years than 1 year so that is the primary driver of the changes. HRSA staff said there may be future public comments regarding the fairness or ethical approach of decreasing transplants for older candidates. HRSA staff recommended that the Committee think about how to respond to these concerns. The Chair said this comes down to the utility issue of managing a limited resource, but agreed the Committee will have to be clear about their reasoning. SRTR staff explained that based on the fair innings principle, an older candidate has had access to opportunities over their life whereas younger candidates have not had as much access or as many "innings." In this sense it would be unfair to give lungs to a candidate with worse projected outcomes when they have had the benefit of more life-years. HRSA staff said the Committee may benefit from reviewing the Kidney Committee's response when this question came up around the Kidney Allocation System (KAS). UNOS staff explained the legal context because that is where KAS ran into issues. It is not a problem if there are disparate impacts for different age groups. It is a problem if decisions are being made solely on the basis of age. It is acceptable if age is an indicator of post-transplant success, even if it causes a disparate impact based on age, because this is based on clinical data instead of using age as an arbitrary factor.

A member asked for clarification on if it is based on intent, or if we intend to transplant older patients less, that is not allowable, but it is allowable to look at longer-term post-transplant outcomes, even if it decreases transplants for older patients. UNOS staff said that is correct as long as that decision is supported by the clinical data such as the work that the SRTR has done on this project.

Next steps:

SRTR staff will work with the Subcommittee to refine the 5-year model and the Subcommittee will start work on refining existing data fields.

Upcoming Meetings

- March 18, 2021 (Committee)
- March 25, 2021 (Committee)

Attendance

- **Subcommittee Members**
 - Erika Lease, Chair
 - Marie Budev, Vice Chair
 - Whitney Brown
 - Dennis Lyu
 - John Reynolds
- **HRSA Representatives**
 - Jim Bowman
 - Marilyn Levi
- **SRTR Staff**
 - Katie Audette
 - Ajay Israni
 - Melissa Skeans
 - Maryam Valapour
 - Andrew Wey
- **UNOS Staff**
 - James Alcorn
 - Julia Chipko
 - Rebecca Goff
 - Elizabeth Miller
 - Janis Rosenberg
 - Leah Slife
 - Kaitlin Swanner
 - Susan Tlusty
 - Sara Rose Wells
 - Karen Williams