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On behalf of the Cystic Fibrosis Foundation (CFF) and the below signed individuals of the CF Lung Transplant Consortium, we write in response to the OPTN/ UNOS Public Comment Proposal, *Establish Continuous Distribution of Lungs*.

Background on Cystic Fibrosis and the Foundation

Cystic fibrosis (CF) is a rare genetic disease that affects over 35,000 people in the United States. In people with CF, a defective gene causes a thick buildup of mucus in the lungs, pancreas and other organs. In the lungs, the mucus obstructs the airways and traps bacteria leading to infections, extensive lung damage and eventually, respiratory failure. Over 280 people with CF received transplants in 2018, the majority of which were lung transplants. However, some people with CF also may require liver or kidney transplants due to the disease.

In order to address the needs of people with CF living with advanced lung disease, as well as those considering transplant, the CF Foundation launched the Lung Transplant Initiative in 2016. Through this initiative, the Foundation is working to improve and standardize the care received by people with CF for whom transplant is an option and to find solutions to barriers that may adversely impact the chance of a person with CF receiving a donor organ.

Continuous Distribution Model

We applaud OPTN/UNOS for this proposal focused on what matters most: the people on the waiting list. They deserve an allocation system that aspires to reduce waitlist mortality to zero, transplants the most medically urgent, minimizes the risk of post-transplant complications and provides the opportunity for long term survival for as many as possible, and does so in a resource efficient manner. The current classification system has hard boundaries that can create barriers for a candidate with higher medical urgency to receive an organ if they are farther from the donor than someone closer, with less medical urgency.

Developing an allocation system that prioritizes the most appropriate recipient when an organ becomes available without substantially jeopardizing the viability of the organ or creating unacceptable barriers to getting the organ to the appropriate person is a challenging task. The new Composite Allocation Score (CAS) moves beyond the classification system of the Lung Allocation Score (LAS) and prioritizes accommodating individuals who are medically harder to match or have other special considerations.

We believe the categories of attributes identified by OPTN/UNOS included in this proposal are appropriate. In particular, we are pleased to see that OPTN/UNOS has addressed issues for harder to match recipients, such as, blood type, and candidate stature. We appreciate the additional consideration of the impact of sensitization on lung allocation in the update system as well. This will hopefully impact the gender inequality present under the current allocation system with lower transplant rates among women, who tend to be more highly sensitized. Future guidance from the OPTN Histocompatibility Committee on how to account for differences in center specific classification of sensitization (MFI thresholds, laboratory techniques, epitope level differences) may be helpful in standardizing practices across centers. We appreciate that OPTN/UNOS will still allow for exception requests where additional points can be requested if a transplant center believes the score does not properly or fully reflect the candidate's profile. This will ensure a candidate's transplant team will be allowed to provide a more nuanced perspective on prioritization.

As this new allocation model is implemented, we ask OPTN/UNOS to closely monitor data on the immediate effects for any strong signal of unintended consequences, particularly for prioritization of pediatric candidates, and adjust as appropriate.

Two aspects of the proposal related to pediatric patients will warrant monitoring if the proposal is adopted without change:

1) As allocation will no longer be stratified by donor age, pediatric candidates will not have explicit priority for pediatric donor lungs in the new system. This is mitigated in large measure by the addition of pediatric access points and also by the points provided for smaller candidates. Nonetheless, TSAM modeling suggested a significant shift in the age of donors transplanted into adolescent recipients (from 73% in the current system to over 80% from adults in continuous distribution). Although the modeling suggested 41-46% of these adult donors would be from 18-34-year olds, because the post-transplant survival model includes donor age as a factor, the SRTR report suggested that donor age may contribute to the predicted increase in adolescent 2 year post-transplant mortality. Although the committee anticipates that transplant center behavior will mitigate this concern, if post-transplant mortality in the adolescent age group increases as predicted it will warrant revisiting this aspect of policy.
2) Pediatric candidates less than 12 years old will no longer have explicit priority for pediatric donors ahead of adolescent candidates within 1500 miles of the donor hospital. Although the points for pediatric access and recipient height will combine to rank these candidates ahead of the majority of adult candidates in most scenarios, the prioritization within the two pediatric age groups is less clearly defined. The Tableau tool provided by the Committee is somewhat reassuring, but as Priority 1 candidates in the 0-11 age group will have no ability to increase their composite score as their disease progresses, waiting list mortality for this age group will warrant close monitoring

Geographical Prioritization Changes

We are pleased to see that the new CAS allows for more dynamic flexibility in addressing the distance from a donor hospital, taking into consideration a continuous scale, rather than a categorical scale. This will result in less emphasis on the distance than the current LAS that prioritizes hard geographic boundaries and ultimately limits patient access.

Post-Transplant Survival

We are encouraged to see that OPTN/UNOS took our previous comments and the analytic hierarchy process (AHP) exercise into consideration when establishing that five-year survival be included in the continuous distribution model. The one-year survival measure currently accounted for through the LAS does not accurately reflect how beneficial a transplant is for any given patient. In fact, it is unlikely that people decide to undergo lung transplantation with the aim of only surviving for one year. The longer-term outcome of 5-year post-transplant survival will optimize the quality-adjusted life year (QALYs) and transplant benefit.

Multi-Organ Allocation

We are pleased to see the establishment of OPTN Multi Organ Transplant Committee in order to address future improvements to the allocation of multiple organs to one recipient. As other organs transition to a continuous distribution allocation model, we ask OPTN/UNOS to closely monitor the impact of the new integrated systems and provide a potential mitigation plan if the data demonstrates inappropriate allocation and prioritization. We look forward to partnering with OPTN/UNOS and provide feedback on the effects this system may have on lung allocation.

Conclusion

We believe the continuous distribution framework has the potential to best address the need to appropriately weigh meaningful factors in organ allocation as proposed, and we are pleased to see OPTN/UNOS moving forward with this model. As the CAS is implemented, we expect to see decreased regional variation in transplant rates and increased patient access across the country. We hope to see OPTN/UNOS continue to respond to data and make necessary changes in the future in order to get the most benefit out of the shift to continuous distribution.

We are happy to serve as a resource and look forward to working alongside OPTN/UNOS in the future on this issue.

Sincerely,

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