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Impact of incorporating long-term survival for calculating transplant benefit in the US lung transplant allocation system

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KEYWORDS:
continuous distribution;
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BACKGROUND: The lung allocation score prioritizes candidates for a lung transplant in the United States. As the country adopts the continuous distribution framework for organ allocation, we must reevaluate lung allocation score assumptions to maximize transplant benefit.

METHODS: We used Scientific Registry of Transplant Recipients data to study the impact of these changes: (1) updating cohorts; (2) transitioning from 1- to 5-year posttransplant survival; (3) using time-varying effects for non-proportional hazards; and (4) weighting waitlist and posttransplant area under the curve differently. Models were compared using Spearman correlations and C-statistics. The thoracic simulation allocation model characterized transplant rates and proportions of recipient subgroups under the current and new systems.

RESULTS: Posttransplant areas under the curve models were estimated with recipients aged ≥12 from January 1, 2014, to December 31, 2018. All models had similar C-statistics and Spearman correlations, indicating similar predictive performance and posttransplant area under the curve rankings. Five-year posttransplant area under the curve across age and diagnosis groups varied more than 1-year groups. Using the thoracic simulation allocation model, 1- and 5-year posttransplant model under the curve models showed similar transplant rates and recipient characteristics under the current system, but under continuous distribution, 5-year posttransplant area under the curve resulted in increased transplant rates with more recipients younger and in diagnosis groups B and C.

CONCLUSION: Incorporating equally weighted waitlist and posttransplant models using 5-year posttransplant survival detected the largest variability in survival under the continuous distribution system, which could improve long-term survival in the United States.

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The lung allocation score (LAS) prioritizes candidates for a lung transplant in the United States based on the estimated net survival benefit of a transplant. The LAS is derived using two Cox proportional hazards (PH) models to calculate the waitlist area under the curve (WLAUC) and posttransplant area under the curve (PTAUC) to represent expected survival without and with transplant over the next year, respectively.[1] The WLAUC currently receives twice the weight of the PTAUC, a structural element borne out of the preference of the lung transplant community to give risk of waitlist mortality greater relative weight in allocation priority after the LAS was first implemented in 2005.[1] Implementation of the LAS resulted in broad changes to the

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practice of lung transplant in the United States, including an exponential increase in the listing and transplant of candidates at high risk for waitlist mortality—a practice not feasible in the preceding time-based allocation system.

Despite major shifts in practice and characteristics of transplant candidates and recipients over the past 16 years, the LAS system has undergone few structural changes.[2] At the same time, long-term survival for lung transplant recipients has plateaued at approximately 60% at 5 years.[2] This trend has been partially attributed to the structure of the LAS, which includes 2:1 weighting of WLAUC to PTAUC in its calculation of transplant benefit and exclusion of long-term survival in modeling, elements that may perpetuate transplant without long-term survival benefit.[2-5]

The US lung allocation system is poised to undergo major changes, moving from the LAS to the continuous distribution (CD) system. CD makes explicit how equity is balanced with utility by providing relative value to all considerations in organ allocation, including: waitlist urgency, posttransplant survival, candidate biology, pediatric status, and placement efficiency.[6-8] A major goal of CD is to reduce consideration of proximity of the donor to the candidate in organ allocation, allowing the sickest candidates wider geographic access to donors. This, in effect, would expand the geographic reach of the LAS survival models, potentially amplifying the access and survival trends brought about by the LAS.[3]

We hypothesized that alterations in LAS modeling structure, follow-up time, and weighting would have a greater impact on transplant trends in a CD allocation system than under the current allocation system. We examined the population effects of specific survival models for waitlists and posttransplant in the CD system recently approved by the Organ Procurement and Transplantation Network (OPTN) Lung Transplantation Committee.

Table 1 Descriptive Statistics for the Risk Factors Included in the PTAUC Model

Variable	Mean/N (SD/Percent)
Age	57 (14)
Creatinine	0.84 (0.31)
Cardiac Index	2.9 (0.8)
Missing	502 (4.5%)
Ventilation Status	859 (8%)
Diagnosis Group	
A	2921 (26%)
B	434 (4%)
C	1245 (11%)
D	6610 (59%)
Diagnosis: Bronchiectasis (A)	2 (0%)
Diagnosis: Lymphangioleiomyomatosis (A)	193 (1.7%)
Diagnosis: Sarcoidosis with PA < 30 mmHg (A)	167 (5.5%)
Diagnosis: Sarcoidosis with PA > 30 mmHg (D)	991 (8.8%)
Diagnosis: Pulmonary Fibrosis not Idiopathic (D)	116 (1.0%)
Diagnosis: Obliterative Bronchiolitis (D)	42 (0.4%)
Functional Status	
No assistance	609 (5%)
Some assistance	9545 (85%)
Full assistance	1058 (9%)
6-minute walk distance (feet)	725 (448)

Group A, obstructive lung disease; Group B, pulmonary vascular disease; Group C, cystic fibrosis and immunodeficiency disorders; Group D, restrictive lung disease; PTAUC, posttransplant area under the curve.

Mean and standard deviations summarized continuous variables, and frequencies and percents summarized categorical variables. The descriptive statistics for the continuous variables were calculated before trimming outlier values to the 1st and 99th percentiles.

Methods

The Scientific Registry of Transplant Recipients (SRTR) database, which includes data on all US donors, transplant candidates, and recipients, was used for this analysis. Oversight of the acquisition of this data is provided by the Health Resources and Services Administration, US Department of Health and Human Services.[9] This work follows the International Society for Heart and Lung Transplantation ethics statement.

Population

The cohort for the PTAUC analyses included lung transplant recipients from January 1, 2014, to December 31, 2018. Recipient follow-up was administratively censored at the earliest of 1 or 5 years or July 31, 2020. The cohort for the thoracic simulation allocation model (TSAM) included the most updated candidate and recipient cohort from January 1, 2018, to December 31, 2019.

Modeling framework

The LAS measures expected survival through two components: WLAUC over 1 year and PTAUC over 1 year. To compare effects of model covariates on 1- and 5-year posttransplant outcomes, the same cohort was used to build all models, which included all covariates in the updated LAS posttransplant model, including age, serum creatinine, cardiac index, ventilation status, diagnosis group, functional status, and 6-minute walk distance (Table 1).[10] Continuous variables were trimmed to the first and 99th percentiles to reduce the influence of outliers. Ten iterations of multiple imputations handled missing data, and Rubin's rules combined estimates across multiple imputations iterations.[11]

Multiple models were fit to the data to understand the impact of model structure on lung transplant candidates. First, traditional Cox proportional hazard models with updated LAS parameterizations (changes to parameters and coefficients recently approved by the OPTN board) for continuous risk factors (e.g., reconsidering the relationship of candidate age with posttransplant outcomes) were fit to both 1- and 5-year posttransplant follow-up data. Next, piecewise exponential models (PEMs) with and without time-varying effects, which relax the proportional hazards assumption of the Cox proportional hazards model,[12] were fit to both 1- and 5-year posttransplant follow-up data. The least absolute shrinkage and selection operator (LASSO) was used to select predictive covariates and estimate effects for the PEMs and Cox proportional hazards models with updated LAS parameterizations. The tuning parameter which minimized the deviance, as estimated through 10-fold cross-validation, was chosen. The LASSO also selected

intervals with important time-varying effects in the PEM with time-varying effects. Time-dependent C-statistics compared the predictive performance across models 1 and 5 years after transplant.[13] The C-statistics used 10-fold cross-validation to minimize the risk of overly optimistic estimates.

A series of 6 models were estimated to understand the effect of the different modeling decisions: (1) a new parameterization for the posttransplant LAS model; (2) using PEMs instead of Cox proportional hazards models; and (3) the integration of time-varying effects. The specific models were:

1. A Cox proportional hazards model for 1-year survival with the current LAS parameterization
2. A Cox proportional hazards model for 1-year survival with an updated LAS parameterization
3. A PEM for 1-year survival without time-varying effects
4. A Cox proportional hazards model for 5-year survival with an updated LAS parameterization
5. A PEM for 5-year survival without time-varying effects
6. A PEM for 5-year survival with time-varying effects

Transplant priority

PTAUC was calculated, and Spearman correlations compared the similarity in recipient PTAUC rankings resulting from each of the 6 models. A Spearman correlation of 1 indicated identical ranks, and 0 indicated unrelated ranks, between the normalized values of PTAUC. PTAUC values, which are generally interpreted as the number of expected days of survival after transplant over 1 or 5 years, were normalized on a scale from 0 to 1 as used in the CD system. This allows for a direct comparison of PTAUC over different time scales. Means and standard deviations of the PTAUC were examined by recipient age subgroups (12-<18, 18-<35, 35-<50, 50-<65, and ≥65) and diagnosis group (group A—obstructive lung disease, group B—pulmonary vascular disease, group C—cystic fibrosis and immunodeficiency disorders, and group D—restrictive lung disease). These prespecified subgroups were chosen for illustrative purposes, and the full list of variables adjusted for in the PTAUC is included in Table 1.

Simulation

We used the SRTR TSAM, a validated Monte Carlo simulation, to simulate impact of each of the 6 models.[14,15] A TSAM two-factor factorial study was performed to determine the effect of transitioning from a 1- to a 5-year PTAUC model. The first factor was the PTAUC model (1- or 5-year), and the second was the base allocation system (current allocation system), 1:1 WLAUC:PTAUC CD system, and 2:1 WLAUC:PTAUC CD system. The TSAM lung offer acceptance models are described in the Appendix. Simulations were run 10 times, the standard number of TSAM software runs.

Results

The cohort for estimating PTAUC consisted of 11,212 lung transplant recipients with a mean age of 57 years; 59% of recipients were in diagnosis group D. Most variables did not have missing data, although 4.5% of recipients had missing values for cardiac index (Table 1).

Time-varying effects

The continuous risk factors did not have dramatic time-varying effects on survival. The relationship between survival and age was a U-shaped curve, with the youngest and oldest recipients experiencing worse relative survival (Supplemental Figure 1). The pattern was similar over time, although the slope increased for older recipients as time from transplant increased. The cardiac index had a relatively weak association with posttransplant survival, and the effect had relatively small differences over time. Creatinine had a moderate association, although the effects were notably stronger for a recipient follow-up period of 0 to 90 days after transplant. Lastly, 6-minute walk distance also had a notable and mostly linear relationship, although recipients with longer 6-minute walk distances had notably better relative survival rates between 3 and 5 years after transplant than before 3 years. Thus, the time-varying effects had some differences over the period of follow-up, although the differences were relatively small.

Model discrimination

Performance was comparable among the 6 models, as evidenced by similar C-statistics in the 1-year (60.2%, 60.6%, and 60.5%) and 5-year models (58.9%, 58.9%, and 59.2%). The PEM with time-varying effects had only marginally better C-statistics than the Cox proportional hazards model at 1 and 5 years and the PEM without time-varying effects. The inclusion of flexible time-varying effects did not meaningfully improve the predictive performance of the posttransplant component of the LAS (Supplemental Table 1).

Transplant priority

Spearman correlations were used to compare recipient rankings between models. The Cox proportional hazards models with updated LAS parameterizations and the PEMs without time-varying effects had nearly perfect correlations for the 1- and 5-year models (0.96 and 0.97, respectively), suggesting that the transition from a Cox proportional hazards model to a PEM without time-varying effects did not meaningfully change the ranking of recipients (Supplemental Table 2). The Spearman correlation between the 5-year PEMs with and without time-varying effects was 0.96, suggesting that the integration of time-varying effects did not meaningfully alter recipient rankings. The transition from a 1- to a 5-year model for a Cox proportional hazards model or a PEM without time-varying effects had a Spearman correlation of 0.90 and 0.89, respectively. Thus, the transition from a 1- to 5-year outcome changed rankings more than the other modeling decisions.

PTAUC and WLAUC across candidate subgroups

The updated Cox proportional hazards models were selected over alternative PEMs because the C-statistics were not meaningfully different and moving to PEMs led to

a large increase in model complexity without significant improvements in discrimination (Supplemental Table 2). Transitioning from a 1- to a 5-year model magnified differences in the PTAUC for some recipient subgroups. When comparing the updated Cox proportional hazards models, the average difference between recipients 35 to 50 years and those 65 and older was 0.02 for the updated 1-year model and increased to 0.08 for the updated 5-year model, a 4-fold difference. The differences across disease groups were less pronounced. The larger differences in the 5-year PTAUC across age groups may alter the relative ranking of candidates under the CD system because older candidates would then require correspondingly larger differences in the WLAUC to achieve the same relative ranking (Table 2).

Updating LAS parameterizations did not meaningfully affect PTAUC, except for recipients 12 to 17 years. Their PTAUC declined from 0.96 to 0.89, on average, due to the U-shaped relationship between recipient age and posttransplant survival, a relationship not seen in the current LAS model, in which age had a linear effect only for recipients 45 years and older (Supplemental Figure 1).

The difference in 5-year PTAUC between recipients aged 35 to 50 and 65 and older was similar in magnitude to an expected difference between occupying the 50th (higher illness severity) and 70th (lower illness severity) quantiles of the WLAUC (Table 3). For example, an average individual aged 35 to 50 in the 70th WLAUC quantile would have a 1:1 normalized LAS value of 1.02 with the 1-year PTAUC and 0.90 with the 5-year PTAUC. In contrast, an average individual aged 65 or older in the 50th quantile of WLAUC would have a 1:1 LAS value of 1.07 with the 1-year PTAUC and 0.89 with the 5-year PTAUC (Table 4). In a 1-year PTAUC model, the older candidate with higher illness severity would receive priority for transplant. In a 5-year PTAUC model, the same older candidate with higher illness severity would receive similar priority as the younger candidate with lower illness severity due to the impact of PTAUC. Greater variability in the 5-year PTAUC model leads to larger changes in the PTAUC's contribution to the LAS.

Table 3 The 10th, 30th, 50th, 70th, and 90th Quantiles for the WLAUC and PTAUC

	Quantile				
Model Component	10th	30th	50th	70th	90th
WLAUC	0.29	0.74	0.85	0.92	0.98
1-year PTAUC: Cox PH (updated)	0.89	0.92	0.93	0.94	0.95
5-year PTAUC: Cox PH (updated)	0.70	0.75	0.78	0.80	0.83

PH, proportional hazards; PTAUC, posttransplant area under the curve; WLAUC, waiting list area under the curve.

The PTAUC was reported for the 1-year Cox model with a new parameterization [1-year: Cox proportional hazards (new)] and the 5-year Cox model with an updated parameterization [5-year: Cox proportional hazards (updated)]. The smaller differences between higher quantiles of WLAUC indicate that changes in the relative differences across PTAUC affect candidates with relatively low risk of waitlist mortality than high risk.

Simulation results

Transplant rates and recipient characteristics were similar in the current allocation system when moving from a 1- to a 5-year PTAUC model (Figure 1, Supplemental Table 3). Both CD allocation systems (1:1 WLAUC:PTAUC and 2:1 WLAUC:PTAUC) had major differences in transplant rates and recipient characteristics when moving from a 1- to a 5-year PTAUC model. Candidates aged 18 to 65 experienced higher transplant rates and encompassed a greater proportion of transplant recipients, while candidates 65 and older experienced lower transplant rates and comprised a lower proportion of transplant recipients in the 5-year PTAUC model. This correlated with higher transplant rates in Groups B and C and lower transplant rates in Group D. Posttransplant survival was similar in simulations using 1-year and 5-year PTAUC models.

Table 2 The Mean and Standard Deviation for the PTAUC Across Recipient Age and Diagnosis Subgroups

Variable	1-year Cox PH (current)	1-year Cox PH (updated)	5-year Cox PH (updated)
Overall	0.93 (0.03)	0.93 (0.03)	0.77 (0.06)
Recipient Age			
12-<18	0.96 (0.01)	0.89 (0.02)	0.67 (0.07)
18-<35	0.94 (0.03)	0.93 (0.03)	0.78 (0.07)
35-<50	0.94 (0.03)	0.94 (0.03)	0.82 (0.05)
50-<65	0.93 (0.02)	0.93 (0.03)	0.78 (0.04)
65+	0.92 (0.02)	0.92 (0.03)	0.74 (0.05)
Diagnosis Group			
A	0.94 (0.02)	0.94 (0.02)	0.79 (0.05)
B	0.89 (0.03)	0.89 (0.04)	0.75 (0.06)
C	0.94 (0.02)	0.94 (0.03)	0.81 (0.06)
D	0.92 (0.02)	0.92 (0.03)	0.76 (0.05)

PH, proportional hazards; PTAUC, posttransplant area under the curve.

The PTAUC was reported for the 1-year Cox model with the current parameterization [1-year: Cox proportional hazards (current)], the 1-year Cox model with a new parameterization [1-year: Cox proportional hazards (new)], and the 5-year Cox model with an updated parameterization [5-year: Cox proportional hazards (updated)]. Each area under the curve is reported as a standardized value of 0 to 1, regardless of the original length of follow-up.

Table 4 PTAUC Comparison by Age and WLAUC Quantile

Candidate age	WLAUC quantile	WLAUC	PTAUC	1:1 LAS (normalized)[a]
1-year PTAUC				
35-<50	70th	0.92	0.94	1.02
65+	50th	0.85	0.92	1.07
5-year PTAUC				
35-<50	70th	0.92	0.82	0.90
65+	50th	0.85	0.74	0.89

PTAUC, posttransplant area under the curve; WLAUC, waiting list area under the curve.

Demonstration of the change in WLAUC and PTAUC by candidate aged 35-<50 and 65+ and moving from the 70th WLAUC quantile (lower illness severity) to the 50th WLAUC quantile (higher illness severity).

[a]1:1 LAS (normalized) = (1 - WLAUC) + PTAUC.

Discussion

Principal findings

Five-year posttransplant survival models can achieve equally precise survival estimates as 1-year models in the newly proposed CD lung allocation system in the United States. Simulations predict that incorporating long-term survival models in the CD allocation system will result in candidates younger than 65 years experiencing relatively greater access to lung transplants than older candidates.

Rationale for reconsidering long-term survival in lung allocation

The primary purpose of this analysis was to evaluate the impact of alternative modeling strategies for the posttransplant component of the current LAS risk calculation. The implementation of the LAS system in 2005 led to significant improvements in the US lung transplant system, allowing access to transplant for those most in need, and likely drove many of the recent innovations for the management of critically ill transplant candidates; however, like most policies, it led to some unintended consequences, namely its impact on long-term survival. The LAS calculation assigns waitlist urgency (WLAUC) twice the value of posttransplant survival (PTAUC), perpetuating a trend of providing transplants to older and sicker candidates at the highest risk for death without transplant but who may not achieve substantial gains in posttransplant survival. In consort with this effect on survival has come an exponential rise in transplant-related costs and accrual of significant posttransplant morbidity.[16,17]

The US lung allocation is poised to adopt the CD system, in which the distribution of organs will be less bound by strict geographic constraints and more driven by estimates of waitlist and posttransplant survival. The potential consequences of the LAS were somewhat curbed in a system in which geographic proximity played a large role in organ allocation, allowing lower-urgency candidates who were also more likely to experience longer posttransplant survival to access transplant. The diminishing importance of geographic proximity in the CD system could make the effects of survival models more far-reaching, potentially exacerbating poor posttransplant survival trends and unrealized life-years gained from lung transplants.

Analytic approach to evaluating long-term survival in lung allocation

Before and soon after the implementation of the LAS, efforts to identify long-term survival models that could reliably predict survival were believed to have diminishing accuracy as time from transplant increased.[1] Posttransplant models were found to have poor predictive performance, and efforts to model longer-term survival were subsequently abandoned.[5] We explored modeling strategies that could impact waitlist and posttransplant survival estimates and tested them using validated simulation programs[14] to predict how these changes would impact allocation of donor organs among US lung transplant candidates. Specifically, we focused on 4 key strategies: (1) using short-term (1-year) compared to long-term (5-year) posttransplant models; (2) comparison of the current LAS allocation framework and CD with altered weights of the waitlist and posttransplant models; (3) updating model cohorts to reflect the current transplant population; and (4) assessing assumptions intrinsic to currently used Cox models, including the proportional hazard assumption and consideration of time-varying effects.

We built 1- and 5-year posttransplant models and studied changes in the current population accessing transplants. One criticism of the current LAS-based lung allocation system is that the LAS considers only 1-year posttransplant survival, which may not maximize the utility of transplanted organs.[5] Predicting longer-term survival based on candidate factors known at the time of transplant has proven difficult because contributions from donor characteristics, intraoperative and perioperative factors and postoperative complications may have a differential impact on long-term survival.[5] Measures of model discrimination—the ability of the LAS model to reliably discriminate between candidates who are likely to survive versus not—is often measured with the C-statistic and has led to conclusions that posttransplant models perform poorly compared with the waitlist models. However, C-statistics for WLAUC are expected to be higher than for PTAUC because there is greater variability in risk of death for candidates while on

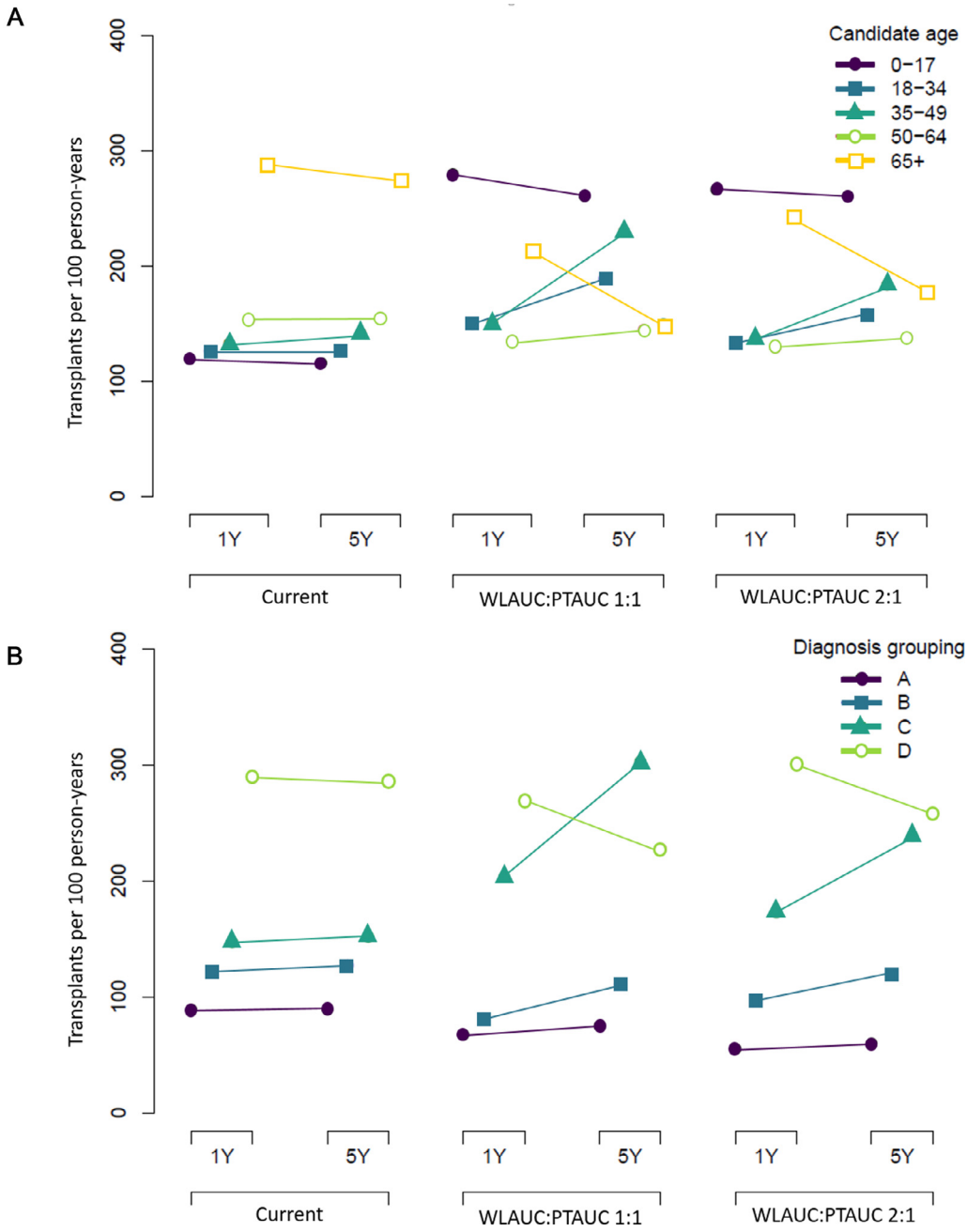

Figure 1 Deceased donor transplant rates by A) candidate age and B) diagnosis groups across different allocation systems (current allocation system, with and without a 5-year PTAUC [5-year Cox proportional hazards (new)]. The different allocation systems were (1) the current allocation system, (2) the 1:1 WLAUC:PTAUC weighting, and (3) the 2:1 WLAUC:PTUAC weighting. Data presented in a tabular format in Supplemental Table 3.

PTAUC, posttransplant area under the curve; WLAUC, waiting list area under the curve.

the waiting list compared with posttransplant (e.g., transplants likely to achieve very low survival are not performed), which led us to explore the differences between posttransplant models.

Next, the OPTN adopted the CD framework to comply with the Final Rule requirement to minimize the role of geography to the extent possible in candidates' ability to access transplant.[18-20] The CD framework of organ allocation avoids strict geographic cut-points, which can seem arbitrary; rather, it allows a continuum of geographic distance (or placement efficiency), which can expand or contract in relation to other key allocation considerations, including candidate biology, pediatric status, history of living donation, WLAUC, and PTAUC.[6,21] Models were compared between the current LAS system (2:1 WLAUC:PTAUC and 250 nautical miles as the first unit of allocation) and the proposed CD system (2:1 WLAUC:PTAUC, 1:1 WLAUC:PTAUC and a 10% placement efficiency metric in which geographic proximity accounts for 10% of the final allocation decision). The impact of changing the weights of the WLAUC and PTAUC models was explored to address concerns that the current weighting of the waitlist

and posttransplant survival priorities would exacerbate the unrealized potential life-years gained from transplants if it were to carry forward into the CD system.

The importance of cohort selection for model parameterization cannot be overstated, as the use of outdated models can lead to poor performance in out-of-sample populations. This has significant consequences in lung transplant allocation because the LAS has selected an increasingly older waitlist candidate population, with more candidates with idiopathic pulmonary fibrosis and on mechanical support.[2,3] From inception, the LAS relied on outdated models due to the time and analysis required for large-scale policy decisions and institutional oversight, and its cohort has been updated only minimally, with even fewer updates to the structure of the underlying models. We have shown the impact of updating cohorts in prior analyses, including changing beta values and goodness-of-fit measures, which can lead to changes in how candidates are prioritized for transplant.[2,14] We used updated LAS and TSAM cohorts in this work to overcome this barrier.

Finally, the current waitlist and posttransplant models are Cox proportional hazards models, which require compliance with the proportional hazards assumption, in which each covariate has a constant multiplicative effect on a common hazard function for the entirety of posttransplant follow-up. However, hazard ratios are unlikely to remain constant because some risk factors may lead to worse short-term outcomes but better long-term outcomes (e.g., bilateral vs single lung transplant).[2,22-24] For this reason, we built PEMs to determine if consideration of time-varying effects improved model performance, but these complex PEMs had C-statistics that were similar or very marginally better than the simpler traditional Cox proportional hazards models.

The key finding of this work was that moving from a 1- to a 5-year posttransplant model did not affect the current LAS allocation system but led to meaningful changes in the predicted patient population undergoing transplants in the CD system. Consideration of long-term survival allowed increased variability in the PTAUC, magnifying differences among transplant recipients over time. This effect and the relative increase in the importance of PTAUC in the CD model resulted in a notable impact on transplant priority when long-term survival was considered. While candidates aged 65 and older and those in diagnosis group D had lower transplant rates, this resulted in only a slightly lower proportion of simulated transplants when a 5-year posttransplant model was used. This effect was more pronounced when using models with 1:1 WLAUC:PTAUC as opposed to models in which waitlist priority is prioritized (e.g., 2:1 WLAUC:PTAUC).

Ethical considerations in using long-term survival in allocation

The scarcity of donor organs worldwide, including in the United States, has required the establishment of systems of rationing that rely on ethical principles that protect patients' interest while acknowledging that utility must be considered in the allocation of severely limited life-saving resources. The core ethical principles that guide the US organ allocation systems first drafted in 1992 and reaffirmed repeatedly in the last two decades define the core ethical principles of organ allocation as "justice," "respect for persons," and "utility."[8] These principles were also upheld by the recently published International Society for Heart and Lung Transplantation guidelines on the selection of lung transplant candidates and the systems that allocate donor lungs.[25] This statement considered the principle of utility on the societal level and made recommendations explicitly to maximize net survival for society in aggregate, arguing that "unsuccessful lung transplant affects not only the individual who was transplanted but also a potential alternative recipient who did not have the opportunity to be transplanted due to the prevailing organ shortage."[25] The US LAS system has considered utility more narrowly at the individual patient level, primarily due to the inability to reliably estimate long-term survival. The analysis presented here provides a framework for estimating survival up to 5 years after transplant that may provide a policy path towards considering a system of allocation that gives more serious consideration to aggregate survival while remaining steadfast in the equally important principles that protect patients' autonomy and individual value in society.

Limitations

The TSAM is limited by use of retrospective populations, although the cohort used candidates, offers, recipients, and donors from January 1, 2018, to December 31, 2019. This analysis was limited by variables used in the current allocation survival models and did not include new variables that may improve prediction or discrimination. This was done because incorporating new variables into the system requires policy initiatives that have not yet been implemented. The CD allocation system is not yet implemented into policy and may undergo changes as a result of the public comment cycle; however, the overall theoretical framework is anticipated to remain the same. Posttransplant survival models used for risk stratification and prioritization for transplant are inherently limited to only factors known before transplant and cannot account for surgical events associated with short- and long-term survival. However, we have shown a nearly identical C-statistic for 1- and 5-year models in a large cohort highlighting the stability of the relationship of candidate characteristics with survival—be it short- or long-term. Not all recipients reached the full follow-up time, which was the result of an analytic decision made to ensure the most up-to-date cohort was used due to changing cohort effects seen in lung allocation.

Conclusion

Incorporating long-term posttransplant survival into the CD lung allocation system could curtail an unintended and far-reaching consequence of the LAS-based system of limiting long-term survival. This strategy may lead to future gains

in posttransplant survival, especially in conjunction with the implementation of the CD allocation system.

Author contributions

All authors were involved in the conception and design of the work. Data analysis was performed by AW and MS, and data interpretation was performed by all authors. All authors contributed to drafting, revision, and final approval of the work.

Disclosure statement

This work was conducted under the auspices of the Hennepin Healthcare Research Institute (HHRI), contractor for the SRTR, as a deliverable under contract no. HHSH75R60220C00011 (US Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation). The US Government (and others acting on its behalf) retains a paid-up, nonexclusive, irrevocable, worldwide license for all works produced under the SRTR contract, and to reproduce them, prepare derivative works, distribute copies to the public, and perform publicly and display publicly, by or on behalf of the government. The data reported here have been supplied by HHRI as the contractor for SRTR. The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy of or interpretation by SRTR or the US Government. The authors thank SRTR colleagues Mary Van Beusekom, MS, ELS, and Anna Gillette for manuscript editing. No authors report a financial conflict of interest.

Supplementary materials

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