Accounting for Selection Bias in Transplant Benefit and Waitlist Urgency Models

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Background & Motivation

- Lung transplant candidates In the U.S. are prioritized based on estimated pre- and post-transplant survival via Lung Allocation Scores (LAS).
- **These models do not account for selection bias:**
  - Individuals being removed from the waitlist due to receipt of transplant (dependent censoring)
  - Transplanted individuals necessarily having survived long enough to receive transplant (survivor bias)
- Such selection bias leads to inaccurate predictions
- **We developed a modified LAS using inverse probability weighting to improve the accuracy of the LAS by accounting for selection bias in the pre- and post-transplant survival models**

Methods

- **Data Source**: Pre- and post-lung transplant data from the United Network for Organ Sharing (UNOS)
  - Development cohort: Patients ≥18 years old listed for single or bi-lateral lung transplantation in the U.S. between January 1, 2010 and December 31, 2013
  - Testing cohort: Patients meeting above criteria listed between January 1, 2016 and December 31, 2017
- **Weights**: Constructed time-varying inverse probability of treatment weights (IPTW) and inverse probability of censoring weights (IPCW) to mitigate selection bias
- **Outcome Models:** Fit weighted Cox proportional hazards models to the pre- and post-transplant data using the same variables as the existing pre- and post-transplant LAS, but weighted by each patient's final, cumulative weight or their post-transplant weight, respectively.
- **Assessing Model Performance**
  - **Discrimination**: time-dependent receiver operating characteristic (ROC) curves evaluated at 1-year post-waitlist registration or 1-year post-transplant
  - **Calibration**: observed (Kaplan-Meier) vs. predicted survival curves based on tertiles of the linear predictor of the pre and post-transplant outcome models

Comparing Modified & Existing LAS

- Applied weighted outcome models to the testing cohort to estimate a modified LAS score for each patient considering all possible offer dates between 2016-2017
- Ranked patients at each offer date based on their modified and existing LAS scores
- Assessed the difference between the modified and existing LAS models via:
  - Bland-Altman plots of the modified vs. existing scores and ranks
  - Scatterplots of differences in predicted pre- and post-transplant survival

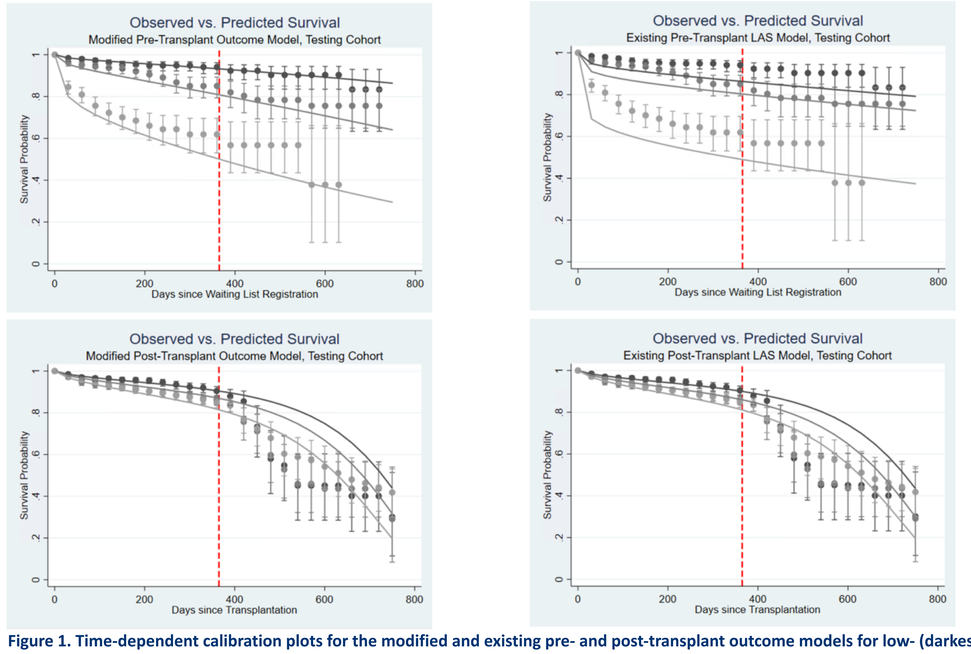

Figure 1. Time-dependent calibration plots for the modified and existing pre- and post-transplant outcome models for low- (darkest lines), medium- (medium-shaded lines), and high-risk (lightest lines) patients.

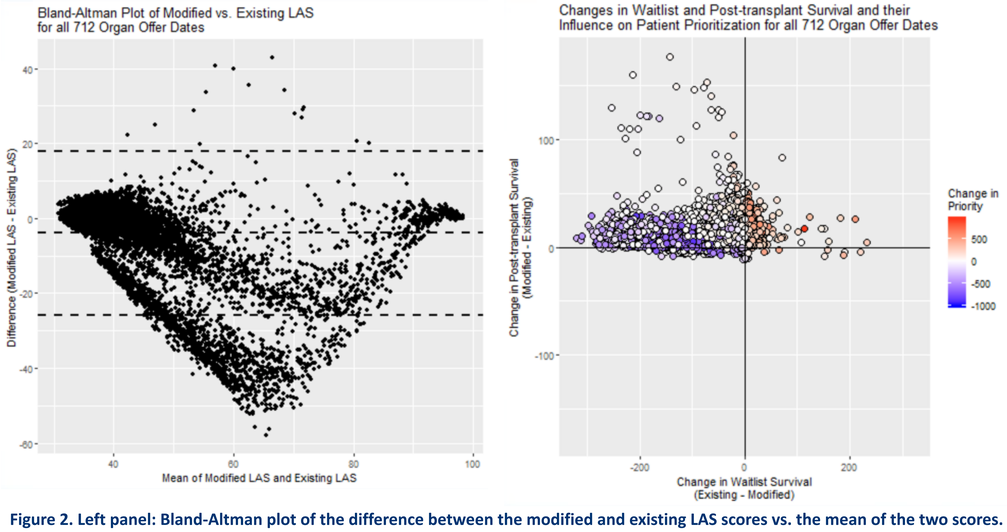

Figure 2. Left panel: Bland-Altman plot of the difference between the modified and existing LAS scores vs. the mean of the two scores. Right panel: scatter plot of the difference in predicted post-transplant survival vs. the difference in predicted pre-transplant survival obtained under the modified and existing LAS models, with points shaded based on the magnitude of change in priority.

Results

Table 1. Time-dependent AUC (with bootstrap standard error) at 1-year post-waitlist registration and 1-year post-transplant for the modified and existing LAS

Cohort	Data	Existing LAS	Modified LAS
Development	Pre-tx	0.68 (0.01)	0.74 (0.01)
	Post-tx	0.56 (0.01)	0.60 (0.01)
Testing	Pre-tx	0.67 (0.03)	0.75 (0.02)
	Post-tx	0.54 (0.02)	0.57 (0.02)

Abbreviations: tx=transplant

- Modified model has better discrimination than the existing LAS in both the development and testing cohorts
- Calibration improved under the modified pre-transplant model, and was comparable under the modified post-transplant model
- Patients at the extremes tend to receive similar LAS scores under the two models; intermediate patients experience more changes under the modified model, with a distinct group receiving lower scores
- Changes in priority were explained more by differences in predicted pre-transplant survival than differences in predicted post-transplant survival
- Predicted post-transplant survival under the modified LAS tends to be the same or greater than that under the existing LAS

Conclusions & Next Steps

- **Inverse probability weighting can mitigate selection bias in lung transplant allocation scores**
- **Our approach can be applied to any organ allocation system that relies on estimates of pre- and post-transplant survival to prioritize patients**
- Further research will explore:
  - The demographic and clinical characteristics of patients who tend to receive higher or lower priority under the modified LAS relative to the existing LAS
  - How the modified LAS would impact observed pre- and post-transplant survival if it were implemented in clinical practice

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