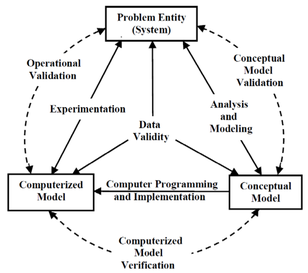
Update and Validation of LSAM

J Pyke[1]; T Weaver[1]; D Schladt[1]; A Herreid[1]; AK Israni[1,2]; BL Kasiske[1,2]; J Lake[3]; WR Kim[4]
[1]Scientific Registry of Transplant Recipients; [2]Department of Medicine, Hennepin Healthcare, Minneapolis, MN; [3]University of Minnesota, Minneapolis, MN; [4]Stanford University, Stanford, CA

Background

- The liver simulated allocation model (LSAM) is a discrete-event multiscale computer simulation combining equation, single agent, and Monte Carlo based simulation types.[1] LSAM is used to evaluate liver allocation scenarios.
- LSAM combines allocation rules, patient level predictive models, and stochastic ordering of candidate and donor arrivals to simulate transplants. These components are periodically updated.
- Performance evaluation is an important part of the LSAM update process. Simulation evaluation can be divided into two components: verification (examining the model's design assumptions and implementation) and validation (comparing simulation results with historical data from the system under study). Due to interdependence between system design and performance, this is a cyclical process with both quantitative and qualitative elements (Figure 1).

Figure 1:
Simplified version of the simulation modeling process.[2]



Methods

- LSAM uses a national average model of offer acceptance with no donation service area (DSA) or program-level predictors. However, differences in recovery rates, listing rates, and number of programs per DSA are modeled. This work focuses on verifying the acceptance model's design and validating LSAM's performance given these assumptions.
- LSAM simulates match runs for a given organ by sorting candidates according to allocation rules and then making simulated offers in order. Discards are generated using an offer cutoff; if an organ reaches the designated number of offers without acceptance, it is marked as discarded. The cutoff is used as a tuning parameter for the simulator.
- Multiple cutoff values were tested as part of the LSAM update, with the selected value of 225 giving a discard rate that most closely matched observed data. This cutoff value was compared to known values for the observed number of offers before discard (Figure 2).
- The updated LSAM using the tuned acceptance model was used to simulate liver transplants and candidate outcomes over a 3-year period (July 1, 2013-June 30, 2016), with the current liver allocation rules in place (regional sharing at model for end-stage liver disease [MELD] score 35, cap and delay for hepatocellular carcinoma exception scores, and MELD calculated with sodium). Ten simulations were run with stochastically determined sets of donors, candidates, and status updates.
- The LSAM projections were aggregated by DSA within each iteration, and the final value presented is the average by DSA over all ten runs. We compare the average simulated values to the single observed value from each DSA for several metrics of interest: overall transplant counts, local transplant counts (organs recovered and transplanted in the same DSA), local transplants as a percentage of total transplants, median travel distance, and median MELD score at transplant.
- DSAs function in the allocation system as units of both organ recovery and organ distribution, so calibration from both perspectives is important. To test this we constructed comparison plots for two DSA groupings: organs recovered in each DSA, regardless of transplant location (organ procurement organization perspective), and organs transplanted in each DSA, regardless of recovery location (program perspective).
- Simple linear regression was performed for each comparison plot to characterize the relationship between projected and observed values. Perfect calibration between LSAM and reality would give a regression slope of 1 and a y-intercept of 0.

Results

Figure 2:
Observed organ acceptance behavior. The vertical line shows the LSAM offer cutoff of 225. Median acceptance 4, mean 23.

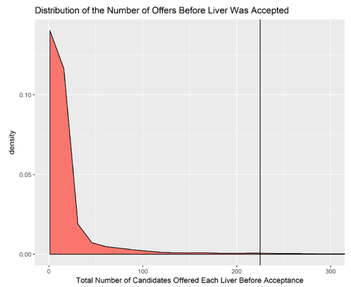


Table 1:
Regression results for multiple outcomes. Perfect calibration to observed data would give an intercept of 0 and a slope of 1.

	Transplanted within each DSA	
Metric	Intercept	Slope
Transplant Count	-11.93	1.02
Local Count	-22.50	1.01
Local Percent	0.14	0.68
Median Travel Distance	37.82	0.84
Median MELD at Transplant	7.92	0.73

	Recovered within each DSA	
Metric	Intercept	Slope
Transplant Count	-9.94	1.02
Local Count	-16.29	1.00
Local Percent	0.02	0.87
Median Travel Distance	56.91	1.00
Median MELD at Transplant	10.75	0.64

Figure 3:
Validation of transplant counts, LSAM vs. historical data.

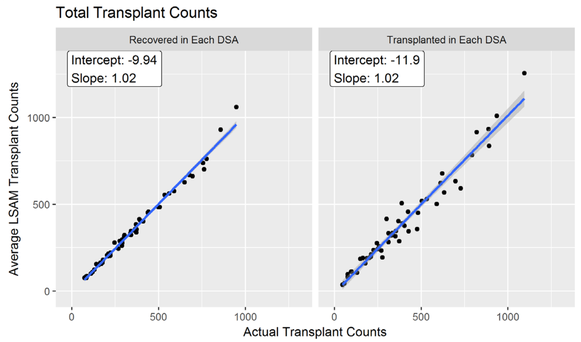
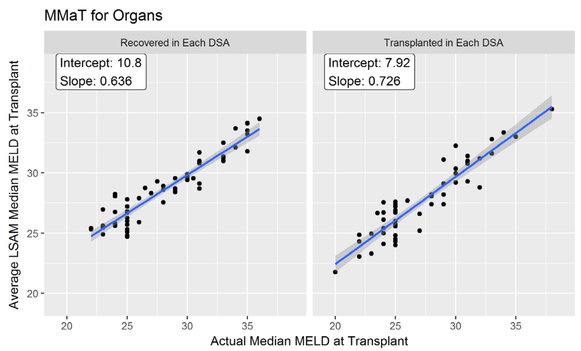


Figure 4:
Validation of median MELD at transplant (MMaT), LSAM vs historical data.



Discussion

- The LSAM offer cutoff of 225 seems reasonable. In the observed offer dataset, the vast majority of acceptances came before offer 225 (shown as the vertical line in Figure 2).
- Liver transplant metrics can vary widely across DSAs. Model verification highlighted the fact that LSAM models some sources of this variation (geographic distribution of donors and candidates) but not others (institutional differences in offer acceptance).
- LSAM predictions for both total and local transplant counts are well calibrated to observed data by DSA (Figures 3 and 4). This supports use of the more generalized acceptance model, which helps to avoid overfitting to the behavior of any particular program or DSA.
- Local percentage shows greater variation from observed values because it combines errors from two estimated values (local and total transplants).
- Predictions for median MELD score at transplant are not calibrated as well as transplant counts. This suggests future work exploring improvements to LSAM's modeling of candidate MELD progression.

References

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This work was supported wholly or in part by HRSA contract 250201000018C. The content is the responsibility of the authors alone and does not necessarily reflect the views or policies of the Department of HHS, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government.

This study used data from the Scientific Registry of Transplant Recipients (SRTR), which includes data on all donors, wait-listed candidates, and transplant recipients in the U.S., submitted by members of the OPTN. HRSA provides oversight to the activities of the OPTN and SRTR contractors.

The authors have no conflicts to report.