Received: 8 July 2024 | Accepted: 8 July 2024

DOI: 10.1097/LVT.0000000000000440

EDITORIAL

Principles for simulating the organ allocation system

A *simulator* is a program designed to mimic a complex system like the organ allocation system. Such a simulator allocates organs as they become available while dynamically updating the waiting list of candidates. Data about candidates and donors, rules governing allocation, and submodels specifying features of the organ allocation system are simulator inputs. A *simulation* is the concrete execution of the simulator using these inputs to generate data. With different inputs, a researcher can execute many simulations using a single simulator.

A *simulation study* begins with a set of research questions to be analyzed using simulated data. Simulation studies are useful for answering research questions *where no empirical data exist*. For this reason, when evaluating a simulation study, we should ask not only "What are the results?" but also "Why should we believe them?" A credible simulation study must be anchored to historical data and provide positive information that the reader should trust the simulated results. Each component in a credible simulation study should be designed and assessed, both individually and jointly, in relation to a historical era in transplantation to answer the specific research questions. This process is called validation, and the results should be reported with each simulation study.

Submodels must accurately replicate historical data without overfitting to it. Validation results provide insight into how to interpret the simulated data. Simulation study submodels may not be suitable to answer the research questions,[1,2] or they may be suitable to answer them, provided the results are interpreted within the boundaries described during validation.[3]

The Scientific Registry of Transplant Recipients (SRTR) performs simulation studies to guide allocation policymakers. SRTR simulates the organ allocation system during a historical era and compares simulated results of the current allocation policy with those from proposed allocation policies. These studies are *counterfactual* (ie, they answer the question, "What *would have happened* had the allocation policy been different?"). For example, "How would the proposed policies have affected access to transplant for pediatric candidates had they been in place during the historical period?"[1,2] In these simulation studies, only the allocation policy varied between simulation scenarios. All other aspects of the organ allocation system were assumed unchanged. There are 2 reasons for this. First, we cannot reliably predict the future landscape of transplantation—new technologies, changing donor/candidate populations, changes in offer acceptance practices, etc. Second, concurrently changing several factors deviates the simulation further from reality and creates ambiguity about the interactions of the many counterfactual assumptions, making the simulated results more difficult to interpret credibly.

For some research questions, it is reasonable to change factors other than the allocation policy in a simulation study. In this issue of *Liver Transplantation*, Blandon et al[4] used the Liver Simulated Allocation Model (LSAM) for one such study. LSAM is one member of a family of SRTR simulators that are publicly available for research and policymaking purposes. SRTR provides 1 set of input files and submodels that were developed to simulate the liver allocation system between 2013 and 2016. Recognizing changes since that time, Blandon and colleagues show one way to alter these input files and submodels to better reflect the modern landscape of liver transplantation. In particular, they increased the number of donors, but they did not update the donor composition to reflect the increasing percentage of recovered livers from donation after circulatory death (DCD) and older donors, nor did they model the changing size/composition of the liver waiting list (Figure 1). This counterfactual scenario massively diverges from recently observed cohorts, and so is not actionable/informative; our recommended approach would be to build new input files for both donors and candidates to resemble data from the recent past.

Separately, Blandon and colleagues suggest changes to the input files to reflect their hypotheses about behavior changes (to organ acceptance) to be used as a sensitivity analysis. They increased the number of offers after which a liver is not used for transplant, and they changed the offer acceptance models to increase acceptance of DCD and nearby donors and decrease

Abbreviations: DCD, donation after circulatory death; LSAM, Liver Simulated Allocation Model; SRTR, Scientific Registry of Transplant Recipients.

SEE ARTICLE ON PAGE 1123

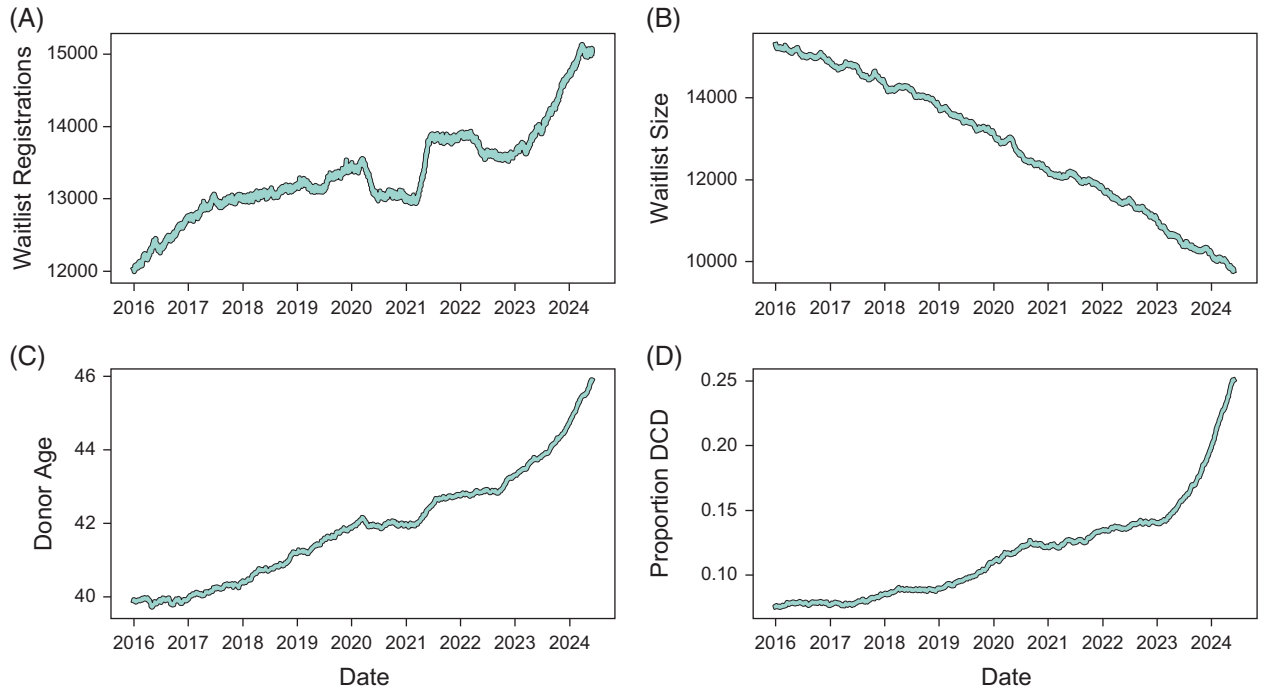

FIGURE 1 Liver transplantation time trends. On each day, we calculated the number of (A) liver waitlist registrations, (B) the average size of the liver waiting list, (C) the average donor age in years, and (D) the proportion of recovered livers from DCD donors in the previous 365 days. Abbreviation: DCD, donation after circulatory death.

acceptance of offers that appear early on the match run. They made crude adjustments to the beta parameters of a regression model without justifying the magnitude of the adjustments or indicating why they believed all other elements of the acceptance model would be unchanged. In contrast, our recommended approach would be to build a new accept/decline model using recent data on increased acceptance of DCD donors and to show validation graphs comparing the magnitude of their hypothesized decrease in acceptance for highest match-run positions to changes in acceptance after recently observed allocation changes.

SRTR encourages more simulation studies. However, using the above principles, we recommend the following steps:

(1) Define the specific research questions to be answered using simulation.

- One research question might be, "How do changes in offer acceptance practice affect the transplant rate for high MELD candidates?" This step includes specifying figures or other methods to present the simulated data to answer the questions.

(2) Design simulation submodels to answer the specific research questions.

- Given that "high MELD candidates" are of interest to the research question, this factor should be considered as a predictor of acceptance.

(3) Report validation results, both individually and jointly, in relation to a recent historical era. Some example questions to address with the validation process include the following:

- Do the donors and candidates simulated resemble those in the recent cohort?
- Does the updated acceptance model have better predictive power on the recent cohort than the prior models?
- Do the updated inputs and submodels produce simulated results that more closely reflect the recent cohort than the prior LSAM models as measured by the figures and methods identified in step 1?

(4) Based on the validation results, place limitations and interpretive bounds on the simulation study.

- Only after validation can other aspects of the organ allocation system be changed to answer the research question. These simulation studies should not be interpreted as predictions of the future but rather as counterfactual predictions of what would have happened.

(5) Limit deviation. The further simulations deviate from the observed organ allocation system, the less confidence one can have in the simulated results.

- Validation anchors a simulation study to historical data. Results generated by hypothesizing future

changes require an exceptionally compelling rationale and should be viewed as speculative.

ACKNOWLEDGMENTS

This work was conducted under the auspices of the Hennepin Healthcare Research Institute (HHRI), contractor for the Scientific Registry of Transplant Recipients (SRTR), under contract no. 75R60220C00011 (US Department of Health and Human Services, Health Resources and Services Administration, Health 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 acknowledge SRTR colleague Joshua Pyke, PhD, for his contribution to our simulation methodology.

CONFLICTS OF INTEREST

The authors have no conflicts to report.

Nicholas L. Wood[1,2]
Tim Weaver[1]
Allison J. Kwong[3]
Sommer E. Gentry[4]

[1]*Scientific Registry of Transplant Recipients, Hennepin Healthcare Research Institute, Minneapolis, Minnesota, USA*
[2]*Department of Medicine, Hennepin Healthcare, University of Minnesota, Minneapolis, Minnesota, USA*
[3]*Division of Gastroenterology and Hepatology, Department of Medicine, Stanford University School of Medicine, Stanford, California, USA*
[4]*Department of Surgery, New York University Grossman School of Medicine, New York, New York, USA*

Correspondence
Allison J. Kwong, Division of Gastroenterology and Hepatology, Department of Medicine, 430 Broadway Street, 3rd Floor, Redwood City, CA 94063, USA.
Email: ajk@stanford.edu

ORCID

Nicholas L. Wood https://orcid.org/0000–0003–0768–3759
Allison J. Kwong https://orcid.org/0000–0002–3874–6612
Sommer E. Gentry https://orcid.org/0000–0003–4530–8917

REFERENCES

1. Mogul DB, Perito ER, Wood N, Mazariegos GV, VanDerwerken D, Ibrahim SH, et al. Impact of acuity circles on outcomes for pediatric liver transplant candidates. *Transplantation*. 2020;104:1627–32.
2. Wood NL, Mogul DB, Perito ER, VanDerwerken D, Mazariegos GV, Hsu EK, et al. Liver simulated allocation model does not effectively predict organ offer decisions for pediatric liver transplant candidates. Am J Transplant. 2021;21:3157–62.
3. Wood NL, VanDerwerken D, Segev DL, Gentry SE. Correcting the sex disparity in MELD-Na. Am J Transplant. 2021;21:3296–304.
4. Blandon C, Karp SJ, Shah M, Lynch RJ, Goldberg DS. Assessing LSAM's ability to account for changes in organ donation and transplant center behavior. Liver Transpl. 2024;30:1123–31.