SRC Analytical Methods Subcommittee Meeting Minutes

Analytical Methods Subcommittee Teleconference

October 19, 2021, 1:30 PM – 4:00 PM CDT

Voting Members:	**HRSA:**	**SRTR Staff:**
Brent Logan, PhD (Chair)	Shannon Dunne, JD	Ryutaro Hirose, MD
Andrew Schaefer, PhD	Adriana Martinez	Ajay Israni, MD, MS
David Vock, PhD		Jon Miller, PhD
Shu-Xia Li, PhD		Josh Pyke, PhD
Katherine Panageas, PhD		Jon Snyder, PhD, MS
		David Zaun, MS
Not in Attendance:		
Andrew Schaefer, PhD		

Welcome and opening remarks

Dr. Jon Snyder called the Analytical Methods Subcommittee (AMS) meeting to order. He informed the subcommittee that Dr. Andrew Wey had moved on from the Scientific Registry of Transplant Recipients (SRTR) and that Dr. Snyder would replace him as the staff co-chair. He reviewed the agenda and conflict of interest management.

Risk-adjustment model-building: Selection of appropriate risk factors

In the previous meeting, Dr. Wey had reviewed changes SRTR intends to make to the process for developing risk-adjustment models using the period-prevalent framework, which will extend to other model-building frameworks in general.

SRTR is exploring the period-prevalent approach, in which a 24-month calendar window would replace the 30-month window. Any patient alive with a functioning graft during the calendar window would be included. Previous recommendations supported looking for a wider range of covariates with less penalization given that penalization is not the best approach for program evaluation versus prediction. The committee also had previously recommended deeper engagement with the transplant community on the factors included in the models.

SRTR used these previous recommendations to continue development of the alternative process for building period-prevalent transplant models. This process was pared from four steps to three. Step one is to estimate an initial model with all potential risk factors (all data SRTR has in the 24-month window), with penalization and variable selection performed using the Least Absolute Shrinkage and Selection Operator (LASSO) framework. Continuous risk factors would consider left and right linear splines. For categoric factors, each level of risk factor is put into the LASSO, and with binary factors,

the level with the highest prevalence is fed to the LASSO. Step two is to estimate a new model with only the risk factors from step one that have a non-zero effect. In this step, only effects that add flexibility are penalized (ie, the LASSO penalty is removed except for any linear splines terms beyond the overall linear component and/or any time-varying effects).

Dr. Snyder said that during the model build process, missing data are imputed. Two different model-building approaches were explored. The first is to nest the entire two-step process within each multiple imputation (MI) iteration. The second option is to run initial variable selection within only 1 MI dataset and then build the final model within each of the 10 MI datasets using the predictors selected from step 1. Step 3 is to average across the 10 MI results to derive the final model.

Dr. Snyder favored the first option, in which the entire model-build process is run within each of the 10 MI datasets. Dr. Brent Logan said the concern with the first approach is getting a different variable selection within each MI iteration and the uncertainty that averaging parameters would work because zeroes are averaged. Dr. Shu-Xia Li said that option one is better, and Dr. David Vock suggested doing a sensitivity analysis. Dr. Snyder added that the proposal was to shift the process to a build every 6 months. Dr. Katherine Panageas asked if a 6-month period was too short to see changes in risk factors, and Dr. Snyder said that it may be a reason to still have a build once every 3 years. Dr. Ryutaro Hirose recommended not remaining fixed in a model for too long, because the transplantation field moves quickly, and the effects of this movement manifest in different outcomes.

Overall, the subcommittee recommended evaluating the choices in terms of stability and practicality. Dr. Logan suggested reviewing a few articles[1,2] for a possible third option. Members said they generally preferred the first option to run the full process within each multiply-imputed dataset.

COVID-19 update

Dr. Snyder noted that the main SRTR Review Committee (SRC) recommended carving out the cohort period from March 13 to June 12, 2020, from risk-adjusted performance metrics presented in program-specific reports (PSRs) and organ procurement organization (OPO)-specific reports (OSRs). Clinical practice was seriously disrupted early in that period but had generally stabilized by June. Since then, the AMS has received 2 letters recommending that SRTR reestablish monthly updates to the COVID-19 monitoring application (which was updated monthly for 1 year) and reconsider how COVID-19 is handled in performance reports. SRTR also received 9 emails from transplant programs concerned that the 3-month carve out is too short.

Dr. Snyder reviewed the COVID-19 application for the subcommittee, in which viewers can see the effects of COVID-19 during the first year of the pandemic. Dr. Snyder also shared the United Network for Organ Sharing (UNOS) application, available at www.UNOS.org, which contains data on the impact of the pandemic on the transplant system.

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[1] Wood AM, White IR, Royston P. How should variable selection be performed with multiply imputed data? Stat Med. 2008 Jul 30;27(17):3227-46. doi: 10.1002/sim.3177. PMID: 18203127.

[2] Zhao Y, Long Q. Variable selection in the presence of missing data: imputation-based methods. Wiley Interdiscip Rev Comput Stat. 2017;9(5):e1402. doi:10.1002/wics.1402.

Dr. Snyder said he felt comfortable with the previous recommendation of the SRC and the AMS to carve out the first quarter of the pandemic and the recommendation that SRTR not pursue further modifications given limitations in available data sources. Dr. Logan agreed.

Dr. Hirose said the subcommittee should consider the clinical experience, which recognizes geographic variation and time-dependent variation in the effects of COVID-19 beyond the first 3 months of the pandemic. While the national transplantation field has recovered, the pandemic impacts different programs at different times. However, the subcommittee previously recommended not pursuing special or temporal adjustments due to lack of data that would accurately capture these effects.

Dr. Snyder also suggested that the SRTR could take direction from the AMS to evaluate available resources to resume updating the COVID-19 application. Dr. Logan recommended that the AMS create a written response to the 2 letters received and to include that it has asked SRTR to evaluate the possibility of resuming the COVID-19 application and that the AMS does not recommend alteration to the 3-month carve-out at this time. Dr. Logan offered to draft the response letter and circulate the draft to AMS members by email. The committee agreed with this approach.

Sociodemographic adjustment

Dr. Snyder reviewed the concept of sociodemographic adjustment in risk-adjustment models. In recent literature, there was controversy as to whether sociodemographic factors should or should not be considered in both medical equations (eg, glomerular filtration rate estimating equations or the Kidney Donor Risk Index) and in models used to assess transplant program and OPO performance.

The National Kidney Foundation (NKF) recently released a statement opposed to using race in estimated glomerular filtration rate (eGFR) equations. Two additional articles supported measuring the risks of not including race in deceased donor kidneys. The Centers for Medicare & Medicaid Services (CMS) advanced new OPO metrics in the Final Rule that will not adjust for race, while SRTR published a paper in the *American Journal of Transplantation* that supported adjusting for race.

Dr. Snyder also pointed out a 2014 paper from the National Quality Forum, "Risk Adjustment for Socioeconomic Status or Other Sociodemographic Factors," which recommended incorporating sociodemographic data into risk adjustment and stratification when certain criteria are satisfied: 1) A plausible relationship between race and the outcome of interest; 2) Empirical evidence of a relationship; and 3) A standardized model-building process.

SRTR said that there are biological arguments within transplantation. For example, certain races may have difficulty finding a matching donor due to blood type differences across races and/or HLA profiles. Race may also be associated with social risk factors not measured or available to SRTR. SRTR also acknowledged that negative outcomes in racial subgroups may be a result of inherent bias within the healthcare system or society in general.

Dr. Snyder presented the results of a study SRTR performed in which models used to assess posttransplant outcomes were rebuilt without race, analyzing the effects at the patient-level risk-prediction and program-level evaluations. In general, the ability of the models to discriminate high-

risk from low-risk patients decreased slightly because other variables absorbed some of the risk previously captured through the inclusion of race. Patient-level predictions changed in predictable ways when race was removed from consideration, and program-level evaluations generally were not affected greatly. Dr. Snyder said that, the absence of more refined factors may better explain any racial effect adjustment for race and was preferable to excluding race as a possible risk predictor. SRTR plans to advance editorial publications on this issue to a journal and welcomes collaborations with the subcommittee.

Dr. Hirose said that SRTR should push back on arguments to exclude race from consideration when building risk-adjustment models. Race is a complex construct in which many underlying causes may explain observed associations with outcome, but they are not available to SRTR. For example, organ donation is an act of trust in the medical system. Bias against certain communities may justify mistrust, which may also result in low organ donation rates among certain ethnic groups. If race is not included as a risk adjustor, the performance of OPOs with a generally homogenous population may hide disparities rather than bring them to light. Dr. Hirose noted that only through adjustment can we truly elucidate which OPOs or transplant programs have better or worse outcomes in all the populations they serve.

Dr. Snyder agreed. Dr. Li said that her organization does not adjust for race but stratifies results to elucidate any disparities. Drs. Vock and Panageas agreed with SRTR's approach to continue to adjust for race and expressed interest in manuscript preparation. A majority of the subcommittee members supported SRTR's proposed stance and further investigation of stratification of performance metrics in public reports.

Closing business

Hearing no other business, the meeting concluded. The next meeting will take place in about 3 months via teleconference.