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Via Electronic Delivery

Robert S. Higgins, MD, MSHA
President, OPTN/UNOS
Kim M. Olthoff, MD
Chair, SRTR Technical Advisory Committee

Dear Drs. Higgins and Olthoff:

The Executive Committee and Council of the American Society of Transplant Surgeons (ASTS), on behalf of our membership, which represents the majority of transplant surgeons in the United States, would like to take this opportunity to address ongoing issues with the transplant center program-specific reports (PSRs) as reported by the Scientific Registry of Transplant Recipients (SRTR). We are concerned that the PSRs are being increasingly used for purposes that are considerably different than were originally intended. In addition, we feel that many aspects of the interpretation and calculation of the PSRs can and should be improved, including redefining data elements collected, providing better incentives for centers to provide complete data reporting, developing new and more relevant risk adjustments, and developing revised statistical methods. The variables that are selected by the SRTR from the existing Organ Procurement and Transplantation Network (OPTN) data to frame these reports should be objective, clinically relevant, and not susceptible to unrecognized manipulation by individual centers to decrease their expected outcomes, thus improving the observed to expected ratio. These recommended improvements will increase the overall usefulness of these reports. We would like to address the following topics:

1) <u>The PSRs should be used as originally intended. Otherwise, their design needs to be modified to support alternative uses.</u> By design, the PSRs were developed with the goal of allowing a high ñfalse positiveò rate. This was done to capture all programs that were underperforming, knowing that many centers so identified would actually be found to be performing appropriately. The goal was to ñflagò programs for a more detailed review using a relatively broad screening standard. At the outset, it was recognized that many flagged programs would, on more detailed review, be found to be performing within national standards. In contrast to the OPTN process envisioned for the PSRs, the SRTR PSRs are now being used by the Centers for Medicare and Medicaid Services (CMS) to identify underperforming centers, and by payors for identifying ñcenters of excellence.ò

Moreover, related to data and methodological issues cited below, the adoption of the PSRs for these newer purposes may accurately identify neither deficient nor excellent centers. Contrary to the initial process envisioned by the OPTN for interpreting the PSRs, where a peer review process is used to assess centers with PSR findings outside accepted norms, CMS does not offer the same opportunity for review after identifying a program as falling below the OPTN standards. Although both the OPTN and the SRTR are aware of this expanded use of the PSRs, no action has been taken. We suggest the following steps:

a) The OPTN and the SRTR ï at every opportunity ï should clearly state that the goal when the statistical techniques for flagging centers were developed, was to maximize the likelihood of identifying programs whose performance was truly below par. This inevitably produces a high false positive rate.

b) The SRTR should either revise their analytic methods or propose a standard for deficiency to be used by CMS that has a much lower ñfalse positiveò rate. If CMS and payors are going to continue to use SRTR-generated reports, we feel it is essential that a narrower statistical cut (i.e., fewer ñfalse positivesò) is employed.

2) Current use of PSRs stifles innovation. Many of the major advances in transplantation have been as a result of clinical trials and ñpushing the envelope.ò Many of these trials involve trying to improve outcome for high risk recipients. And, by definition, clinical trials are designed to determine if new treatments are effective. If an experimental treatment proves to be inferior for a population of transplant recipients, any center participating in such a trial will demonstrate observed results that are lower than expected for patients in the experimental arm (assuming that information about the experiment itself is not available to the SRTR for adjustment). Since a programôs CMS certification depends on meeting expected outcomes, there is little benefit and significant business risk for centers pursuing clinical research protocols.

This problem is similar in concept for all transplant candidates who are at increased risk for poor transplant outcome whenever the factors conferring the increased risk are not captured in the OPTN data. For example, the clinical literature has amply documented that almost all patients with end-stage renal disease (ESRD), including those at higher risk of post-transplant graft failure or death, a kidney transplant results in better survival (and a more cost-efficient) option than dialysis. Currently, however, the OPTN and the resulting SRTR PSRs cannot account for many of these situations because the data elements are either insufficiently refined or not included in the current risk adjustment due to lack of collected data. For example, many centers have implemented ñdesensitizationò protocols for candidates with high levels of anti-HLA antibody. The literature has clearly documented that these patients survive longer with a transplant compared to remaining on dialysis, even though they have lower graft survival rates compared to average transplant patients. Inclusion of these desensitized patients in PSRs negatively affects PSR results, because the risk factor for poorer outcome (need for desensitization) is not captured. The omission of risk factors like this in the PSR risk adjustment calculations makes centers conducting such trials appear to have worse results. This can lead to review by the OPTN, and designation as underperformers by CMS and payors.

As a consequence, centers may abandon innovative approaches or markedly limit enrollment in clinical trials. CMSôs current policy for using the PSR reports imposes a negative incentive for innovation and reduces access to transplantation for higher risk candidates even though they are likely to benefit.

Our suggestion would be to exclude patients from review that participate in these innovative clinical trials. An alternative suggestion is to make a major conceptual change in the way we view outcomes under these rigorous reviews and to evaluate center outcome based on a normative population. This would allow a more ñapples to applesò comparison of observed and expected outcomes. Alternatively, changing the measurement of center performance to emphasize survival benefit over simple post-transplant patient and graft survival would provide a much better incentive for centers to pursue innovative protocols (see below).

3) Data can be manipulated by the program. We should strive to make the data utilized for these reports objective and verifiable, and to discourage interpretation and manipulation of data at the program level. Examples of this would include: functional status, ordering of multiple recipient diagnoses, and selectively reporting data as missing for variables where such designation would benefit the centerôs PSR outcomes.

It is important to consider how ñmissing dataò are handled in the PSRs. Risk adjustment methods used for missing data are designed in the current PSRs to describe the true outcome associated with data missingness, which in many cases is associated with poorer outcome. Some centers have figured this out and we are concerned about intentional and selective underreporting of some data to lower expected outcomes.

This issue should be addressed by determining thresholds for the level of missing data that would be allowed for individual variables at a given center. We would suggest that missing data in excess of the threshold should trigger a data audit of the center, with sanctions imposed as appropriate. An alternative approach would be to assign the best outcome to cases with missing data, thereby removing the incentive for a center to omit pertinent variables.

4) Observed to expected benefit. Current OPTN data and SRTR risk adjustment do not adjust for centers pursuing transplant for survival benefit of the individual patient, even though there is ample evidence in the literature for doing so. Moreover, even if risk adjustments are refined, centers choosing to use high risk grafts for high risk patients, because there is solid evidence that doing so provides a survival benefit, face being labeled as under-performers unless most of the other programs are doing the same, since current measures relate individual centersô results to national averages.

Besides stifling innovation and the impeding development of new protocols, the lack of accounting for transplant survival benefit in center performance encourages centers to instead transplant high risk grafts into low risk patients and deny transplantation altogether to high risk candidates. We feel that the ñdenominatorò for a transplant center should not be just the patients who undergo transplantation (as with the current post-transplant survival metric) but rather include outcomes of all actively listed transplant candidates.

As such, we feel that a transplant center should be evaluated by a statistic that simultaneously measures its ability to avoid deaths on the waiting list and its ability to avoid post-transplant deaths. This is the survival benefit concept.

It would be interesting to model observed to expected survival benefit for centers and compare these results to the current observed to expected patient and graft survival measures. One could examine the likelihood of a high risk patient doing less well than a normative population post-transplant compared to an even worse survival outcome if they remained on dialysis. We feel that this would much more accurately assess a centerôs performance for all patients, especially the high risk candidates, encourage appropriate utilization of higher risk grafts (see below), and help reverse the disturbing trend of restricting access of high risk patients to the transplant waiting list.

5) Donor organ risk. The current SRTR PSRs include a number of donor variables. However, we believe that the broad strokes which identify donor risk including current descriptions of expanded criteria donor (ECD) and donation after cardiac death (DCD) do not describe those risks adequately. For continuous variables such as donor age, we suggest that finer groupings and the use of linear splines be considered to better represent risk. In addition, histological parameters of the donor organ should be addressed (e.g., glomerulosclerosis in kidney donors and fatty infiltration in liver donors). We recognize that biopsies are not performed on all donors and would be pleased to participate in developing methods for including these in the future.

We would like to take this opportunity to discuss our concerns regarding some the specifics of the data used by the SRTR PSRs. These are included as follows:

1. Reevaluation of recipient risk adjustment. Age and body mass index (BMI) are adjusted using only three categories each. We believe that investigation of linear splines and finer groupings may allow more accurate accounting of risk for these variables. Listing ESRD recipient diagnosis, as currently categorized, is not only gameable, but may overlook significant interaction effects. The current model only takes into account the first diagnosis listed and in the not infrequent case of multiple diagnoses, the risk adjustment only considers the first diagnosis listed. For example, a patient with reflux nephropathy, diabetic nephropathy, and hypertensive nephrosclerosis (listed in that order) has a different risk adjustment than a patient with diabetic nephropathy, hypertensive nephrosclerosis, and reflex nephropathy. We believe that risk adjustment should be designed to take into account all of the diagnoses contributing to end-organ failure. Serious consideration should be given to revising the handling of diabetes mellitus status and hypertension. Currently, these are dichotomous entries without quantification of disease severity. Simple measures such as HgA1C or number of years on insulin or number of antihypertensive medications may considerably improve the risk adjustment for these factors.

2. Donor risk factors. There are five categories of donor age. We suggest changing the statistical approach to considering splines and smaller groupings of donor age to reflect the risk for a particular donor organ.

3. Interaction terms. Inclusion of interaction terms, or effect modification, more completely in SRTR Cox models used for the PSRs may result in models that are more predictive. Intuitively this makes sense, as physicians know from experience the combinations of certain factors (e.g., diabetes and old age) indicate that a recipient is at higher risk than the

simple sum of the risk associated with each individual factor alone. We acknowledge that systematically searching all

4. possible interaction terms is not statistically sound, and we would be happy to work with the SRTR in identifying biologically plausible interactions to be statistically explored.

5. Eliminate variables. We suggest that a number of variables be eliminated from the model as they are either gameable or donôt contribute significantly. These include functional status, insurance, and preservation type.

6. Add collected variables. As has widely been discussed, there is no variable that truly accounts for significant cardiovascular disease, which is the most common cause of death with a functioning graft in the United States. We recommend that various parameters of cardiovascular disease (Attachment A) be collected as well as the type and duration of diabetes and the duration of hypertension (as mentioned above). For the currently collected variables and variables that are added in the future, explicit definitions of the variables need to be provided. This will allow for better data collection and prevent data entry that is based upon local knowledge. Consideration should be given to collecting variables that represent a clearer picture of disease severity such as collecting data on cardiac interventions rather than angina or ñcardiovascular diseaseò.

Finally, we recommend that a consensus conference be convened to explore possible additional risk predictors that are not currently captured through the OPTN data system, with particular emphasis on the best ways to capture domains such as diabetes, cardiac, and vascular disease. We are currently in the process of organizing such an effort. We feel that it is imperative to have SRTR and OPTN participation in this process.

The American Society of Transplant Surgeons would like to thank the OPTN and the SRTR for the opportunity to present our recommendations for changes in the PSRs. We volunteer to engage in ongoing discussions with the various committees and decision makers as we move forward with refining the models in order to accurately reflect outcomes in our membersô institutions.

Sincerely yours,

John P. Roberts, MD
President

cc: Richard Durbin, HRSA

Appendix A ï Suggested Additional Variables To Be Collected

Cardiovascular Risk Factors

1) Previous interventions
    i. Coronary artery bypass grafting
    ii. Coronary artery stenting
2) Uncorrectable coronary artery disease with functional abnormality (see ejection fraction)
3) Previous myocardial infarction with functional abnormality (see ejection fraction)
4) Ejection fraction
    i. Echocardiogram
    ii. Nuclear medicine
5) Cerebrovascular and/or peripheral vascular disease with intervention
    i. Surgical bypass
    ii. Stenting
    iii. Carotid endarterectomy/stenting

Type I vs. Type II Diabetes, Duration

Duration of Hypertension