

ORIGINAL ARTICLE

Association of pretransplant and posttransplant program ratings with candidate mortality after listing

Andrew Wey¹ | Sally K. Gustafson¹ | Nicholas Salkowski¹ | Bertram L. Kasiske^{1,2} |
Melissa Skeans¹ | Cory R. Schaffhausen² | Ajay K. Israni^{1,2,3} | Jon J. Snyder^{1,3}

¹Scientific Registry of Transplant Recipients, Minneapolis Medical Research Foundation, Minneapolis, MN, USA

²Department of Medicine, Hennepin County Medical Center, University of Minnesota, Minneapolis, MN, USA

³Department of Epidemiology and Community Health, University of Minnesota, Minneapolis, MN, USA

Correspondence: Andrew Wey, Scientific Registry of Transplant Recipients, Minneapolis Medical Research Foundation, Minneapolis, MN.
Email: awey@cdrg.org

Funding information

Health Resources and Services Administration, Grant/Award Number: HSH250201500009C; Minneapolis Medical Research Foundation; AKI was partially supported by R01 HS 24527

The Scientific Registry of Transplant Recipients (SRTR) is responsible for understandable reporting of program metrics, including transplant rate, waitlist mortality, and posttransplant outcomes. SRTR developed five-tier systems for each metric to improve accessibility for the public. We investigated the associations of the five-tier assignments at listing with all-cause candidate mortality after listing, for candidates listed July 12, 2011–June 16, 2014. Transplant rate evaluations with one additional tier were associated with lower mortality after listing in kidney (hazard ratio [HR], 0.93 – 0.95 _{0.97}), liver (HR, 0.87 – 0.90 _{0.92}), and heart (HR, 0.92 – 0.96 _{1.00}) transplantation. For lung transplant patients, mortality after listing was highest at programs with above- and below-average transplant rates and lowest at programs with average transplant rates, suggesting that aggressive acceptance behavior may not always provide a survival benefit. Waitlist mortality evaluations with one additional tier were associated with lower mortality after listing in kidney (HR, 0.94 – 0.96 _{0.99}) transplantation, and posttransplant graft survival evaluations with one additional tier were associated with lower mortality after listing in lung (HR, 0.90 – 0.94 _{0.98}) transplantation. Transplant rate typically had the strongest association with mortality after listing, but the strength of associations differed by organ.

KEYWORDS

health services and outcomes research, organ transplantation in general, Scientific Registry for Transplant Recipients (SRTR), statistics

1 | INTRODUCTION

The Scientific Registry of Transplant Recipients (SRTR) is required to publicly report pretransplant and posttransplant outcomes.¹ Pretransplant outcomes include the transplant rate and waitlist mortality rate. The former is the relative rate of transplants performed at a program compared with the national rate; it is important because transplant typically confers a survival benefit compared

with remaining on the waiting list.^{2–4} The latter is the relative rate of mortality after listing but before transplant. Posttransplant outcomes include patient and graft survival 1 year after transplant. The Centers for Medicare & Medicaid Services (CMS) and the Organ Procurement and Transplantation Network (OPTN) monitor 1-year posttransplant outcomes for regulatory purposes, and SRTR public reporting has traditionally focused on 1-year posttransplant outcomes. Yet, posttransplant outcomes may fail to accurately inform patients regarding expected survival experiences after listing because many patients, especially candidates for kidney and liver transplant, will never undergo transplant.^{5,6} Instead,

Abbreviations: CMS, Centers for Medicare & Medicaid Services; HR, hazard ratio; OPTN, Organ Procurement and Transplantation Network; PSR, program-specific report; SRTR, Scientific Registry of Transplant Recipients.

a program's ability to quickly perform transplants in waitlisted candidates and minimize mortality on the waiting list may be more strongly associated with mortality after listing than posttransplant outcomes. Thus, additional emphasis on transplant rate and waitlist mortality may be justified in the public reporting.

We investigated the relationship of (a) adjusted transplant rate ratios, (b) adjusted waitlist mortality rate ratios, and (c) adjusted 1-year posttransplant graft survival hazard ratios [HRs] at listing with patient mortality after listing. Specifically, after categorizing each metric into five tiers that range from below average to above average,⁷ we estimated the HR for one additional tier in each metric on mortality after listing. Categorization of pretransplant and posttransplant metrics into five tiers requires calculation of a continuous score that ranges from 0 (below average) to 1 (above average). To identify potential nonlinearity in these scores, we also estimated the association of the continuous score for each outcome (referred to throughout as the five-tier score) with mortality after listing. Separate analyses were performed for kidney, liver, lung, and heart transplantation to ensure relevance to the broader transplant community.

2 | MATERIALS AND METHODS

This study used SRTR data. The SRTR data system includes data on all donors, waitlisted candidates, and transplant recipients in the United States, submitted by the members of OPTN, and has been described elsewhere.⁸ The Health Resources and Services Administration, US Department of Health and Human Services, provides oversight of the activities of the OPTN and SRTR contractors.

2.1 | Evaluated cohort

Adult candidates (age ≥ 18 years at listing) were included in the study if they were listed between July 12, 2011 (release date for the 2011 summer program-specific report [PSR] cycle), and June 16, 2014 (the day before the release of the 2014 summer PSR cycle). The primary outcome was candidate mortality after listing. Candidates were not censored because of transplant or removal from the waiting list but were administratively censored, if still alive, on December 31, 2016. The appropriate PSR release for determining the pretransplant and posttransplant tiers at listing was determined by the release dates of archived PSRs. In 2013 and 2014, the PSR release schedule was interrupted and the release dates were approximated by the prior release of the corresponding biannual PSR cycle.

2.2 | Five-tier systems for pretransplant and posttransplant metrics

Pretransplant metrics at listing were the adjusted transplant rate ratios and adjusted waitlist mortality rate ratios included in the PSR at listing. Similarly, the posttransplant metric at listing was

the 1-year posttransplant graft survival HR included in the PSR at listing. Bayesian methodology estimated program-specific posterior distributions for each metric. Specifically, because the number of observed events for each metric follows a Poisson distribution, a conjugate gamma prior with shape and rate parameters equal to 2 was used. Thus, the posterior distribution for each metric was a gamma distribution that depended only on the number of observed and expected events and can be calculated with archived PSRs.⁹

The five-tier systems for each metric used a two-step process. The first step calculates a rating between 0 and 1 by taking the expectation of a logistic-type utility function with respect to the posterior distribution. The second step assigns the rating to one of the five tiers based on a priori cutoffs. The logistic-type functions were selected to ensure that higher ratings correspond to better outcomes and that the distribution of programs was relatively bell shaped, with most programs in tier 3. For waitlist mortality and posttransplant graft survival, the logistic-type function had a relatively steep slope that assigned more weight to hazard ratios or waitlist mortality rate ratios below 1.⁷ In contrast, the function for transplant rate had a more gradual slope and assigned more weight to hazard ratios above 1. The algorithm for transplant rate was modified because high transplant rate ratios correspond to good rather than poor outcomes, and transplant rate ratios are significantly more variable than waitlist mortality and posttransplant outcomes and required a more gradual slope to ensure a relatively bell-shaped distribution across tiers. Technical details appear in the Supplementary Materials.

2.3 | Statistical analysis

Linear trends estimated the association of tier at listing for the pre- and posttransplant outcomes with mortality after listing. For the transplant rate evaluation, the interpretation is the average change in the hazard of mortality after listing for one additional tier after accounting for candidate comorbid conditions, allocation priority at listing, and the five-tier assignment for waitlist mortality and posttransplant graft survival. In a separate model, to identify potential nonlinear associations, penalized splines estimated the association of the underlying continuous five-tier score for each metric. Each five-tier score ranges from 0 to 1; a score close to 1 corresponds to above-average outcomes, and a score close to 0 corresponds to below-average outcomes. Penalized splines have wider confidence intervals than linear trends do because of the additional flexibility.

These associations were estimated with Cox proportional hazards models while adjusting for candidate risk factors at listing. A candidate factor was included if the corresponding SRTR waitlist mortality model for the January 2018 PSR release included the given factor; the Supplementary Materials list the specific candidate risk factors included in each model. Missing data were handled with multiple imputation (10 iterations). The effects of the continuous factors were estimated with penalized splines. Robust standard errors accounted for the effect of correlation among listings at the same program.

All analyses were completed in R v3.3.3,¹⁰ Cox proportional hazard models were estimated with the "survival" package,¹¹ and the multiple imputation was completed by the "mice" package.¹²

3 | RESULTS

3.1 | Kidney transplantation

During the cohort period, 104 063 candidates joined the kidney waiting list (Table 1 and Figure 1). At listing, average age was 52 years and dialysis duration was 3 years. The most common blood type was O, and the most common diagnosis was diabetes. Albumin was the most-missing risk factor, at 6.7%; most risk factors were missing less than 0.1%. See Table S1 for a summary of missing data.

Tier assignments at listing for transplant rate and waitlist mortality were associated with mortality after listing. Specifically, an additional tier in the transplant rate evaluation was associated with a 5% lower hazard of mortality after listing (HR, $_{0.93}0.95_{0.97}$), whereas an additional tier in the waitlist mortality evaluation was associated with a 4% lower hazard of mortality after listing (HR, $_{0.94}0.96_{0.99}$). Approximately two additional tiers in the transplant rate evaluation corresponded to three additional tiers in the waitlist mortality

TABLE 1 Descriptive statistics for kidney candidates listed between July 12, 2011, and June 16, 2014

Variable	Summary statistics
Number of candidates	104 063
Age, y	52.5 (13.0)
Missing	0 (0%)
Years on dialysis	3.1 (5.3)
Missing	3 (0%)
Blood type	
A	34 195 (32.9%)
AB	3898 (3.7%)
B	15 548 (14.9%)
O	50 422 (48.5%)
Missing	0 (0%)
Race	
Asian	7570 (7.3%)
Black	30 303 (29.1%)
Other	490 (0.5%)
Native American	1118 (1.1%)
Pacific Islander	519 (0.5%)
White	64 063 (61.6%)
Missing	0 (0%)
Primary diagnosis	
Congenital	1290 (1.2%)
Diabetes	33 995 (32.7%)
Glomerulonephritis	19 611 (18.8%)
Hypertension	23 586 (22.7%)
Other	23 973 (23%)
Missing	1608 (1.5%)

Continuous variables are summarized by means and standard deviations, and categorical variables are summarized by frequencies and percentages.

evaluation. In contrast, tier assignment at listing for posttransplant graft survival had no apparent association with mortality after listing for kidney candidates (HR, $_{0.97}1.00_{1.02}$). None of the evaluations had notable nonlinear associations (Figure S1). Thus, transplant rate had the strongest association with mortality after listing in kidney transplantation.

3.2 | Liver transplantation

For the 32 815 candidates who joined the liver waiting list (Table 2 and Figure 2), average age at listing was 56 years and laboratory model for end-stage liver disease (MELD) score was 18. Most candidates were white with blood type O; 9.6% had hepatocellular carcinoma exceptions at listing. The most-missing risk factors were education status (7.1%) and prior malignancy (3.6%). Most factors were missing less than 0.1%. See Table S2 for a summary of missing data.

The tier assignment for the transplant rate evaluation at listing was strongly associated with mortality after listing for liver candidates; an additional tier was associated with a 10% lower hazard (HR, $_{0.87}0.90_{0.92}$). Although the associations were not significant, an additional tier in the posttransplant graft survival evaluation was associated with a 2% lower hazard of mortality after listing (HR, $_{0.95}0.98_{1.01}$), and an additional tier in the waitlist mortality evaluation with a 2% difference in mortality (HR, $_{0.96}0.98_{1.01}$). The transplant rate evaluation had a nonlinear association, stronger for higher transplant rates (Figure S2).

3.3 | Lung transplantation

Among the 6998 candidates who joined the lung waiting list, average age at listing was 55 years and average lung allocation score was 45 (Table 3 and Figure 3). Most candidates were in diagnosis group D. The most-missing risk factor was central venous pressure, at 11.3%; missingness was between 2.5% and 5.4% for several other measures of lung function, eg, 3.1% for predicted forced expiratory volume.

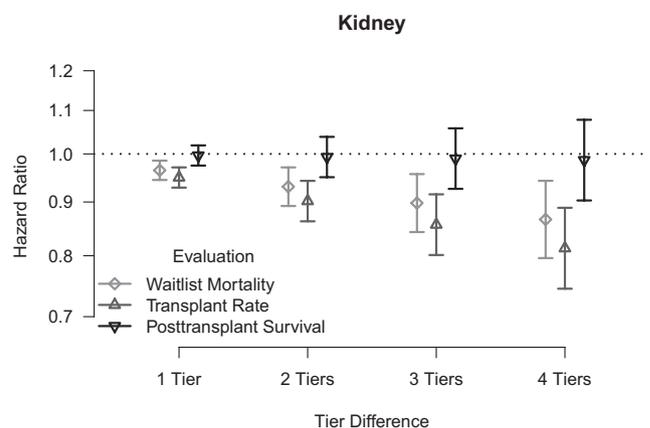


FIGURE 1 Kidney transplantation. The association of 1 to 4 additional tiers for waitlist mortality, transplant rate, and posttransplant graft survival metrics with mortality after listing for kidney candidates

TABLE 2 Descriptive statistics for liver candidates listed between July 12, 2011, and June 16, 2014

Variable	Statistics
Number of candidates	32 815
Age, y	55.5 (10.2)
Missing	0 (0%)
MELD at listing	18.0 (9.3)
Missing	5 (0.02%)
Blood type	
A	12 444 (37.9%)
AB	1233 (3.8%)
B	3939 (12%)
O	15 199 (46.3%)
Missing	0 (0%)
Race	
Asian	1462 (4.5%)
Black	3052 (9.3%)
Other	130 (0.4%)
Native American	235 (0.7%)
Pacific Islander	55 (0.2%)
White	27 881 (85%)
Missing	0 (0%)
Any HCC exception at listing	
No	29 668 (90.4%)
Yes	3147 (9.6%)
Missing	0 (0%)
Primary diagnosis	
Acute hepatic necrosis	1187 (3.6%)
Biliary atresia	78 (0.2%)
Malignant neoplasms	3826 (11.7%)
Metabolic diseases	556 (1.7%)
Other	27 160 (82.8%)
Missing	8 (0%)

Continuous variables are summarized by means and standard deviations, and categorical variables are summarized by frequencies and percentages.

HCC, hepatocellular carcinoma; MELD, model for end-stage liver disease.

For most other risk factors, missingness was less than 0.1%. See Table S3 for a summary of missing data.

Tier assignment at listing for posttransplant graft survival was associated with mortality after listing for lung candidates; an additional tier in the posttransplant graft survival evaluation was associated with a 6% lower hazard of mortality after listing (HR, _{0.90}0.94_{0.98}). An additional tier in the waitlist mortality evaluation was associated with 3% lower hazard of mortality after listing, although the difference was not significant (HR, _{0.93}0.97_{1.01}). Importantly, the transplant rate evaluation had a U-shaped association with mortality

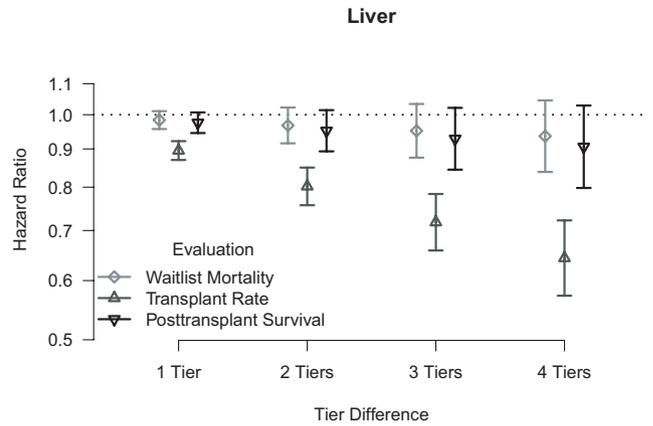


FIGURE 2 Liver transplantation. The association of 1 to 4 additional tiers for waitlist mortality, transplant rate, and posttransplant graft survival metrics with mortality after listing for liver candidates

after listing; the association decreased until a score of 0.5 and then increased (Figure S3). Thus, lung programs with average transplant rates were associated with lower mortality after listing than lung programs with below- or above-average rates.

3.4 | Heart transplantation

Among the 9637 candidates who joined the heart waiting list, average age was 53 years (Table 4 and Figure 4) and the most common blood type was O. Common primary diagnoses were cardiomyopathy (55%) and coronary artery disease (35.4%). Level of missingness was nontrivial for many cardiac measurements. For example, missingness was highest for pulmonary wedge pressure, at 11.1%, and was 4.5% for pulmonary systolic blood pressure. However, most risk factors were less than 0.1% missing. See Table S4 for a summary of missing data.

Tier assignment at listing for the transplant rate evaluation was associated with mortality after listing for heart candidates; an additional tier in the transplant rate evaluation was associated with 4% lower hazard for survival after listing (HR, _{0.92}0.96_{1.00}). The waitlist mortality and posttransplant graft survival evaluations had no apparent association. Transplant rate had a nonlinear association that was relatively constant for programs with below-average transplant rates, decreasing for programs with above-average rates (Figure S4).

4 | DISCUSSION

SRTR is required to publish PSRs that patients and their families can “accurately and efficiently” use and understand.¹ The ability of pre- and posttransplant metrics reported in the PSRs to predict mortality after listing is a fundamental component of their utility in decision making. Specifically, the relative importance of transplant rate, waitlist mortality, and posttransplant metrics at listing may better inform

TABLE 3 Descriptive statistics for lung candidates listed between July 12, 2011, and June 16, 2014

Variable	Statistics
Number of candidates	6998
Age, y	55.3 (13.5)
Missing	0 (0%)
LAS at listing	44.6 (16.5)
Missing	0 (0%)
Blood type	
A	2736 (39.1%)
AB	266 (3.8%)
B	770 (11%)
O	3226 (46.1%)
Missing	0 (0%)
Race	
Asian	118 (1.7%)
Black	620 (8.9%)
Other	13 (0.2%)
Native American	25 (0.4%)
Pacific Islander	7 (0.1%)
White	6215 (88.8%)
Missing	0 (0%)
Primary diagnosis group ^a	
A	1882 (26.9%)
B	274 (3.9%)
C	793 (11.3%)
D	4046 (57.8%)
Missing	3 (0%)

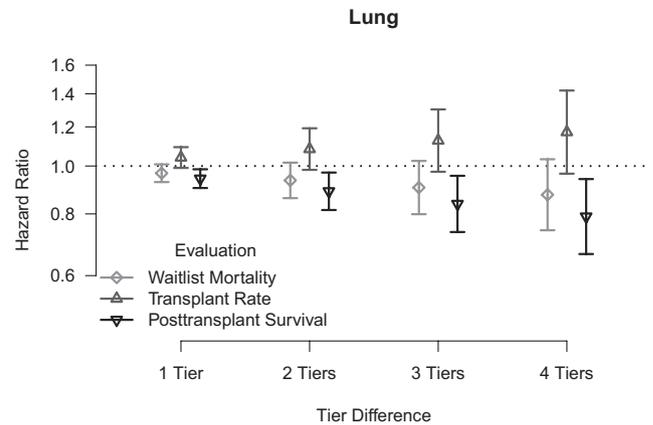
Continuous variables are summarized by means and standard deviations, and categorical variables are summarized by frequencies and percentages.

LAS, lung allocation score.

^aDisease groups: A, obstructive lung disease; B, pulmonary vascular disease; C, cystic fibrosis and immunodeficiency disorders; D, restrictive lung disease.

patients regarding the types of programs that may minimize mortality after listing. For example, in kidney transplantation, both the waitlist mortality and transplant rate metrics were associated with mortality after listing. However, transplant rate had a stronger association, and three additional tiers in waitlist mortality would be required to offset two additional tiers in transplant rate. To aid in patient decision making, these and other program differences should be conveyed to transplant candidates in the public reporting using plain language or graphical descriptions.¹³

The most effective approach for communicating to patients and their families the relative importance of different evaluations is not clear. For example, a plain language description could explicitly emphasize the relative importance of transplant rates to mortality after listing in kidney, liver, and heart transplantation, but a graphical illustration of the relative balance may provide better

**FIGURE 3** Lung transplantation. The association of 1 to 4 additional tiers for waitlist mortality, transplant rate, and posttransplant graft survival metrics with mortality after listing for lung candidates**TABLE 4** Descriptive statistics for heart candidates listed between July 12, 2011, and June 16, 2014

Variable	Statistics
Number of candidates	9637
Age, y	53.1 (12.8)
Missing	0 (0%)
Blood type	
A	3598 (37.3%)
AB	475 (4.9%)
B	1352 (14%)
O	4212 (43.7%)
Missing	0 (0%)
Race	
Asian	296 (3.1%)
Black	2160 (22.4%)
Other	55 (0.6%)
Native American	39 (0.4%)
Pacific Islander	28 (0.3%)
White	7059 (73.2%)
Missing	0 (0%)
Primary diagnosis	
Cardiomyopathy	5298 (55%)
Congenital heart disease	303 (3.1%)
Coronary artery disease	3413 (35.4%)
Other	2 (0%)
Valvular disease	155 (1.6%)
Missing	466 (4.8%)

Continuous variables are summarized by means and standard deviations, and categorical variables are summarized by frequencies and percentages.

understanding. Further research to test reports with potential users is therefore needed to determine the best approach.¹³ For example, patient interviews could provide feedback on the language used,

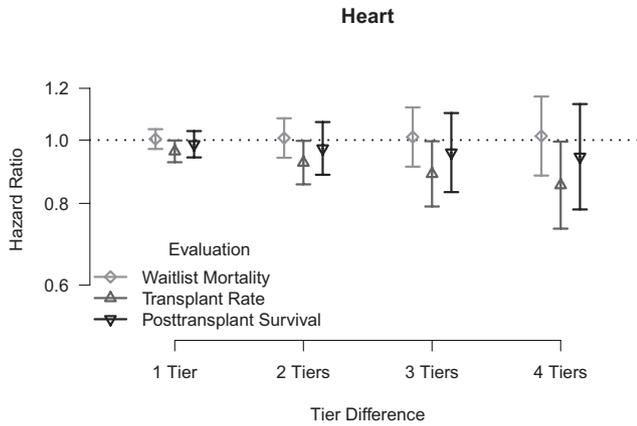


FIGURE 4 Heart transplantation. The association of 1 to 4 additional tiers for waitlist mortality, transplant rate, and posttransplant graft survival metrics with mortality after listing for heart candidates

and a randomized trial could assess the effect of different presentations on decision making in the general public. A good approach would help users interpret information by identifying outcomes associated with patient mortality after listing, eg, emphasizing transplant rate over posttransplant graft survival in liver transplantation. Meanwhile, a reasonable approach is graphical representations with simple numeric and plain language descriptions.

We found that the relative importance of pre- and posttransplant outcomes was organ specific. For example, transplant rate and waitlist mortality were associated with mortality after listing in kidney transplantation, but only posttransplant graft survival was associated with mortality after listing in lung transplantation. The different patterns of association for pre- and posttransplant outcomes suggest that a uniform approach to public reporting across each organ is not feasible. Instead, each organ should be considered separately to ensure that evaluations relevant to patient outcomes are appropriately emphasized. This is a strength, rather than a weakness, given that most patients are interested in transplants of a single organ.

Additional important considerations for public reporting pertain to the ability to predict mortality after listing. Specifically, public reporting can incentivize quality improvement efforts across all programs.¹⁴ This phenomenon has historically occurred for posttransplant metrics due to, for example, CMS's regulatory review.¹⁵ In addition, regulatory review of posttransplant outcomes could have attenuated the association of posttransplant metrics with mortality after listing because programs are actively trying to improve posttransplant outcomes, in part to avoid regulatory interventions. Transplant rate has not been subject to regulatory review or prominent public reporting. Transplant rate evaluations depend on factors both within and outside programs' control. For example, geographic variability in donor supply and demand is outside a program's control but affects the median allocation MELD (aMELD) score at transplant. In contrast, liver offer acceptance practices are arguably within a program's control and independently affect median aMELD at transplant.¹⁶ Further public reporting of transplant rates could

reduce program-level variability because some programs could improve transplant rates through modifications to offer acceptance practices. However, as a consequence, the association between transplant rate metrics and mortality after listing may attenuate over time, although, in this hypothetical example, the public reporting of transplant rate metrics would still indirectly benefit candidates through more standardized access to transplant.

These prospective associations with mortality after listing do not reflect the relative differences in evaluations within a PSR cycle. For example, an additional tier in a liver program's transplant rate was associated with a 10% lower hazard of mortality after listing despite the transplant rate ratios differing by a much larger amount, eg, approximately a 40% increase within a PSR evaluation cohort. However, none of the outcomes directly measure mortality after listing. Instead, posttransplant graft survival and waitlist mortality measure two separate causes of mortality after listing, whereas transplant rate measures the relative rate at which a program transitions candidates from the pretransplant period with a relatively high mortality risk to the posttransplant period with a relatively low mortality risk; that is, transplant rate measures a concept that is, at best, indirectly related to mortality after listing. In addition, even if the pre- and posttransplant metrics were intended to prospectively predict mortality after listing, the predictive performance of statistical methods is almost always worse than the performance on the data used to determine the metrics.¹⁷

In lung transplantation, the nonlinear association between transplant rate and mortality after listing is surprising because of the general perception that transplant conveys a survival benefit compared with remaining on the waiting list. Yet, the increased mortality after listing for candidates at lung programs with the best transplant rates suggests that aggressive acceptance behavior may not provide a survival benefit in every situation in lung transplantation, eg, acceptance of a high-risk donor for a candidate with relatively low waitlist mortality.¹⁸ A potential cause is the less severe organ shortage in lung transplantation compared with kidney and liver transplantation.^{5,6,19} A less severe organ shortage may enable lung transplant candidates to decline offers from high-risk donors because of a better probability of subsequently receiving an organ from a better donor. Alternatively, programs with high transplant rates could list candidates with unmeasured risk factors at a higher rate than programs with average transplant rates. However, such a situation could induce an association between transplant rates and posttransplant outcomes or waitlist mortality, but no such associations exist.²⁰ Regardless, further research should investigate the potential survival benefit of lung transplant with, for example, a low-quality donor organ compared with remaining on the waiting list for a better donor.

For each organ, the association of posttransplant outcomes with mortality after listing was attenuated compared with the association of posttransplant evaluations with eventual posttransplant graft survival. For example, posttransplant graft survival evaluations for liver programs were associated with eventual posttransplant graft survival but had an attenuated and nonsignificant association with

mortality after listing.²¹ This is not surprising because posttransplant outcomes are only a single component of mortality after listing. Notably, transplant rates typically had the strongest associations with mortality after listing, and the magnitude of the associations was similar to the magnitude of associations between posttransplant evaluations and eventual posttransplant graft survival.

The five-tier systems for pretransplant and posttransplant outcomes were developed in collaboration with the SRTR Visiting Committee. A general design principal of the five-tier systems was that programs should have a relatively bell-shaped distribution with most programs in the middle tier. These decisions were made without consideration of the potential association with prospective mortality after listing. Different approaches to designing the five-tier systems could lead to stronger (or attenuated) associations with mortality after listing. Although this is a potential avenue for further research, alternative systems for categorizing program performance should be evaluated with metrics directly relevant to patients; eg, programs within a tier have similar outcomes (minimizing within-tier variability)⁷ or the alternative system is associated with patient mortality after listing.

Publicly reporting pre- and posttransplant outcomes could produce unintended consequences. Kidney programs under regulatory review for posttransplant outcomes reduced volume and removed candidates from the waiting list at a higher rate than other programs.^{22,23} A similar situation could occur with more prominent public reporting of posttransplant outcomes because programs may perceive that avoiding risk improves the posttransplant metrics included in the PSR. However, the interaction of more prominent public reporting of transplant rate and posttransplant graft survival is not clear because programs would have incentives to perform well in each metric. For example, reducing transplant volume in isolation will likely cause a worse transplant rate metric. Other potential behavior changes, such as waiting to list candidates or listing candidates with relatively high allocation priority, are unlikely to improve the transplant rate metric because of adjustments for candidate allocation priority and for comorbid conditions.¹⁷ In addition, restricting overall access to the list can maintain or improve the transplant rate only if the program performs transplants at a rate similar to the national rate for candidates with the same allocation priority and comorbid conditions at listing. Regardless, a better understanding of the referral and listing practices of transplant programs would alleviate these shortcomings and help elucidate a largely unknown component of transplant program care.^{24,25}

Analyses of mortality after listing likely suffer from nonproportional hazards because candidate characteristics associated with transplant rate (eg, measures of allocation priority) characterize the potential timing of transplant: an event at which the hazard briefly increases because of perioperative mortality and then decreases to a level presumably below the hazard prior to transplant. Candidate characteristics associated with the transplant rate may not have proportional effects over time. Yet, analyses of mortality after listing cannot directly model the transplant event; for example, a time-varying covariate for transplant could likely address the nonproportional hazards but would also obscure the benefit of a

high transplant rate metric because the model-based hazard of mortality would be lower for candidates who undergo transplant. The nonproportional hazards may therefore be difficult to directly address by modeling the hazard function. Instead, alternative survival analysis techniques with different and potentially less restrictive distributional assumptions could be used. For example, censored quantile regression requires fundamentally different distributional assumptions.²⁶ A sensitivity analysis with censored quantile regression found, in general, qualitatively similar results to the Cox proportional hazards model (see Figures S5-S8). Alternative statistical methods that rely on estimators with fewer assumptions could be considered for, eg, the 3-year probability or restricted mean of mortality after listing.^{27,28}

The program-specific effect on patient mortality after listing could be a better and more direct approach to public reporting than waitlist mortality, transplant rate, or posttransplant graft survival. The program-specific effect on patient mortality is easy to understand and implicitly integrates the importance of pretransplant and posttransplant outcomes without arbitrary or imperfect selection of weights. Although mortality after listing may depend on local organ availability, the reasons for differences between programs in publicly reported metrics are less relevant to patients than to regulatory agencies, emphasizing the inappropriateness of mortality after listing for regulatory review despite its direct importance to patients. Thus, SRTR should focus on developing a program-specific metric for mortality after listing while considering potential methodological limitations, eg, nonproportional hazards.

Our analysis has significant limitations. First, the causal mechanisms responsible for the associations of pre- and posttransplant outcomes with mortality after listing are difficult to determine. For example, if programs with poor transplant and waitlist mortality rates are more likely to list candidates with unmeasured risk factors, then the programs may have worse mortality after listing *and* the unmeasured risk factors may explain the poor transplant and waitlist mortality outcomes. In this hypothetical situation, the association between transplant rate and mortality after listing may not identify differences in patient outcomes across programs but instead differences in patient populations. If the unmeasured risk factors are not contraindications to transplant, the best solution for mitigating their effect is collection of additional data. Second, the pre- and posttransplant metrics were based on old risk-adjustment models with a limited number of factors. In contrast, the risk adjustment for mortality after listing was based on new waitlist mortality models that include a broad spectrum of risk factors and flexible splines for continuous factors.^{20,29} If the new models identify a program's risk tolerance better than the old models, then the effect of pre- and/or posttransplant metrics could be attenuated.

Pre- and posttransplant evaluations at listing are associated with prospective patient mortality after listing. Although transplant rate was most important in kidney, liver, and heart transplantation, the appropriate balance among transplant rate, waitlist mortality, and posttransplant graft survival was organ-specific.

ACKNOWLEDGMENTS

This work was conducted under the auspices of the Minneapolis Medical Research Foundation, contractor for the Scientific Registry of Transplant Recipients, as a deliverable under contract number HSH250201500009C (US Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation). As a US Government-sponsored work, there are no restrictions on its use. The views expressed herein are those of the authors and not necessarily those of the US Government. AKI was partially supported by R01 HS 24527. The authors thank SRTR colleague Nan Booth, MSW, MPH, ELS, for manuscript editing.

CONFLICTS OF INTEREST

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

REFERENCES

- Department of Health and Human Services 42 CFR Part 12. Organ Procurement and Transplantation Network; Final Rule. <https://www.gao.gov/special.pubs/organ/appendd.pdf>. Accessed June 19, 2018.
- Schaubel DE, Sima CS, Goodrich NP, Feng S, Merion RM. The survival benefit of deceased donor liver transplantation as a function of candidate disease severity and donor quality. *Am J Transplant*. 2008;8(2):419-425.
- Massie AB, Luo X, Chow E, Alejo JL, Desai NM, Segev DL. Survival benefit of primary deceased donor transplantation with high-KDPI kidneys. *Am J Transplant*. 2014;14(10):2310-2316.
- Wey A, Salkowski N, Kremers WK, et al. A kidney offer acceptance decision tool to inform the decision to accept an offer or wait for a better kidney. *Am J Transplant*. 2018;18(4):897-906.
- Hart A, Smith JM, Skeans MA, et al. OPTN/SRTR 2015 annual data report: kidney. *Am J Transplant*. 2017;17(suppl 1):21-116.
- Kim WR, Lake JR, Smith JM, et al. OPTN/SRTR 2015 annual data report: liver. *Am J Transplant*. 2017;17(suppl 1):174-251.
- Wey A, Salkowski N, Kasiske BL, Israni AK, Snyder JJ. A five-tier system for improving the categorization of transplant program performance. *Health Serv Res*. 2018;53(3):1979-1991.
- Leppke S, Leighton T, Zaun D, et al. Scientific Registry of Transplant Recipients: collecting, analyzing, and reporting data on transplantation in the United States. *Transplant Rev*. 2013;27(2):50-56.
- Salkowski N, Snyder JJ, Zaun DA, et al. Bayesian methods for assessing transplant program performance. *Am J Transplant*. 2014;14(6):1271-1276.
- R Core Team. R: A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing; 2015.
- Therneau T. A package for survival analysis in S. version 2.38. 2015. <https://cran.r-project.org/web/packages/survival/index.html>. Accessed June 19, 2018.
- VanBuuren S, Groothuis-Oudshoorn K. Mice: multivariate imputation by chained equations in R. *J Stat Software*. 2011;45(3):1-67. <http://www.jstatsoft.org/v45/i03/>. Accessed June 19, 2018.
- Agency for Healthcare Research and Quality. Best practices in public reporting no. 1: How to effectively present health care performance data to consumers. <https://archive.ahrq.gov/professionals/quality-patient-safety/quality-resources/tools/pubrptguide1/pubrptguide1.pdf>. Accessed June 19, 2018.
- Hibbard JH, Stockard J, Tusler M. Does publicizing hospital performance simulate quality improvement efforts? *Health Aff*. 2003;22(2):84-94.
- Hamilton TE. Regulatory oversight in transplantation: are the patients really better off? *Curr Opin Organ Transplant*. 2013;18(2):203-209.
- Wey A, Pyke J, Schladt DP, et al. Offer acceptance practices and geographic variability in allocation model for end-stage liver disease at transplant. *Liver Transpl*. 2018;24(4):478-487.
- Hastie T, Tibshirani R, Friedman J. *The Elements of Statistical Learning: Data Mining, Inference, and Prediction*, 2nd edn. New York City: Springer; 2009.
- Vock DM, Durham MT, Tsuang WM, et al. Survival benefit of lung transplantation in the modern era of lung allocation. *Ann Am Thorac Soc*. 2017;14(2):172-181.
- Valapour M, Skeans MA, Smith JM, et al. OPTN/SRTR 2015 annual data report: lung. *Am J Transplant*. 2017;17(suppl 1):357-424.
- Wey A, Gustafson S, Salkowski N, et al. Program-specific transplant rate ratios: association with allocation priority at listing and post-transplant outcomes. *Am J Transplant*. 2018;18(6):1360-1369.
- Wey A, Salkowski N, Gustafson SK, Skeans MA, Kasiske BL, Israni AK, Snyder JJ. Comparing Scientific Registry of Transplant Recipient posttransplant program-specific outcome ratings at listing with subsequent recipient outcomes after transplant. *Am J Transplant*. In press.
- Schold JD, Buccini LD, Srinivas TR, et al. The association of center performance evaluations kidney transplant volume in the United States. *Am J Transplant*. 2013;13(1):67-75.
- Schold JD, Buccini LD, Poggio ED, Flechner SM, Goldfarb DA. Association of candidate removals from the kidney transplant waiting list and center performance oversight. *Am J Transplant*. 2016;16(4):1276-1284.
- Paul S, Plantinga LC, Pastan SO, Gander JC, Mohan S, Patzer RE. Standardized transplantation referral ratio to assess performance of transplant referral among dialysis facilities. *Clin J Am Soc Nephrol*. 2018;13(2):282-289.
- Fowler KJ. Accountability of dialysis facilities in transplant referral: CMS needs to collect national data on dialysis facility kidney transplant referrals. *Clin J Am Soc Nephrol*. 2018;13(2):193-194.
- Portnoy S. Censored regression quantiles. *J Am Stat Assoc*. 2003;98(464):1001-1012.
- Rudser KD, LeBlanc ML, Emerson SS. Distribution-free inference on contrasts of arbitrary summary measures of survival. *Stat Med*. 2012;31(16):1722-1737.
- Wey A, Vock DM, Connett J, Rudser K. Estimating restricted mean treatment effects with stacked survival models. *Stat Med*. 2016;35(19):3319-3332.
- Snyder JJ, Salkowski N, Kim SJ, et al. Developing statistical models to assess transplant outcomes using national registries: the process in the United States. *Transplantation*. 2016;100(2):288-294.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Wey A, Gustafson SK, Salkowski N, et al. Association of pretransplant and posttransplant program ratings with candidate mortality after listing. *Am J Transplant*. 2019;19:399-406. <https://doi.org/10.1111/ajt.15032>