Supplementary Online Content

Parker WF, Anderson AS, Gibbons RD, et al. Association of transplant center with survival benefit among adults undergoing heart transplant in the United States. *JAMA*. doi:10.1001/jama.2019.15686

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods

Patient Record and Six-Status Coding Example:

Time Start	Time stop	Transplant	Dead	Three-Status and justification	Six-status
0	36	0	0	Status 1B (inotropes)	4
36	42	0	0	Status 1A - (Exception)	3
42	141	0	0	Status 1B (inotropes)	4
141	148	0	0	Status 1A - (High dose inotropes)	4
148	150	0	0	Status 1A - (High dose inotropes)	4
150	178	0	0	Inactive	4
178	182	0	0	Status 1A (MCS for shock)	3
182	198	0	0	Inactive	3
198	209	0	0	Status 1A - (MCS complication)	3
209	3863	1	1	Status 1A - (MCS complication)	3

1-10 of 10 rows | 1-8 of 9 columns

This patient went through the following status changes:

- status 1B with IV inotropes, six-status 4 (day 0-35)
- status 1A exception, six-status 3 (day 36-41)
- status 1B with IV inotropes, six-status 4 (day 42-140)
- status 1A with high dose IV inotropes (remained six-status 4 due to lack of cardiogenic shock) (day 141-148)
- Inactivated (day 150-177)
- re-activated at Status 1A s/p durable LVAD implantation with elective time, six-status 3 (day 178-181)
- Inactivated (day 182-197)
- re-activated at Status 1A w/ LVAD complication (not device failure), six-status 3 (day 198-208)
- transplanted and survived for over ten years (day 209- 3863)

When the candidate is inactivated from the list, we carried forward their status from the previous observed period. Because many candidates are deactivated from list before dying, this assumption allows the model to appropriately capture the risk of each active waitlist status.

Cardiogenic Shock Requirement: We identified candidates potentially overtreated by the shock requirement according to previously published methodology[1,2] which we review here. First, we identified candidates subject to the shock criteria based on the listed indication on the Status 1A justification forms. We then classified candidates based as in shock or not based on cardiac index according to the guidance in the policy for cardiac index values obtained in various circulatory support scenarios.[3] Because there are relatively few VA-ECMO and percutaneous mechanical circulatory support candidates (<50 a year) and these candidates often have missing hemodynamic data, these candidates were conservatively characterized as "in shock." We used Status 1A justification form, transplant candidate registration (TCR), and transplant recipient registration (TRR) hemodynamics. We used inotrope doses available from the Status 1A justification form to apply the minimum dose criteria to the high dose inotrope group. Body weight, height, and cardiac output were used to calculate cardiac index for each patient using the DuBois formula for body surface area.[4] For candidates with missing cardiac index data or supported with multiple support therapies simultaneously, we considered them as in shock. Because blood pressure readings were only available sporadically for candidates treated with inotropes, we conservatively did not apply this portion of the criteria. For candidates listed with IABP with hemodynamics measured while receiving IABP support, the policy does not offer specific guidance as it requires pre-IABP implantation hemodynamics for qualification. Therefore, we decided to categorize IABP candidates with post-implantation hemodynamics in shock if the cardiac index was <2.0 L/min/m^2 on IABP support. We based this threshold on the criteria for extension of Status 2, a failure to wean from IABP evidenced by a "Cardiac Index less than 2.0 L/min/m^2".[3]

Statistical Appendix: The survival benefit model in this manuscript is a **mixed-effects Cox proportional hazards model with time-dependent covariates**, represented by the following equation for patient j and center i

$$h_{ij}(t) = h_0(t) * exp(\beta_{0i} + \beta_{1i} tx_{ij}(t) + \mathbf{BX_{ij}(t)} + \mathbf{\Theta}\left(\mathbf{X_{ij}(t)} * \mathbf{tx_{ij}(t)}\right)$$

$$\beta_{0i} = \nu_{0i}$$

$$\beta_{1i} = \beta_1 + \nu_{1i}$$

This mixed effect model includes the following terms:

- a random intercept for each center β_{0i}
- a random slope β_{1i} for the time-dependent transplant variable $tx_{ij}(t)$
- a vector of covariates $X_{ij}(t)$ and their interaction terms with transplant (coefficients $\mathbf{\Theta}$)
  - Status on the wait list (time-varying until transplant)
  - High risk donor (defined as a donor risk index of >5), a validated composite measure using donor characteristics and ischemic time.[5]
  - Era of transplant (before or after 2010)
- A non-parametrically estimated baseline hazard $h_0(t)$

This model structure allows both the pre-transplant and post-transplant hazard of death to vary by center. The interaction terms with transplantation allow the benefit of transplant to vary by recipient and control for regional variation in Status utilization, donor quality, ischemic time. The year of transplant term controls for variation in center activity over time as both pre-transplant care (specifically LVAD therapy) and post-transplant care improved over time. After fitting the model, for a given center i, a case-mix adjusted empirical Bayes estimate (modal) of

relative hazard ratio of risk pre and post transplantation at a given center can be easily calculated by exponentiating the relevant estimated random component

$$HR_i(waiting\ |status, year) = \exp(v_{0i})$$

$$HR_i(transplant\ |status, donor, year) = \exp(v_{1i})$$

We fit this model by maximum likelihood using coxme package[6] for R version 3.4.3, copyright The R Foundation for Statistical Computing 2017.

Estimating the absolute 5-year survival benefit. We estimated the five-year survival benefit of transplantation for each recipient using the following procedure:

1. For each of the 19,815 recipients, calculate hazard function under transplant $h_{ij}(t|tx, X_{ij})$ for all points in time after transplant (e.g. $t > T_{transplant}$) and waiting ($h_{ij}(t|wait, X_{ij})$) using the model estimates of fixed effects (**eTable2**), a non-parametric estimate[7] of the baseline hazard function (**eFigure2),** and the empirical Bayes estimate (mode) of the intercept and transplant random effects at the center *i* they were transplanted at

$$h_{ij}\left(t\middle|wait, X_{ij}\right) = h_0(t) * exp(\beta_{0i} + \mathbf{BX_{ij}(t)})$$

$$h_{ij}\left(t\middle|tx, X_{ij}\right) = h_0(t) * exp(\beta_{0i} + \beta_{1i}tx_{ij}(t) + \mathbf{BX_{ij}(t)} + \mathbf{\Theta}\left(\mathbf{X_{ij}(t)} * \mathbf{tx_{ij}(t)}\right)$$

2. Use the estimated hazard functions to construct hypothetical "waiting forever" survival function and "observed" transplant survival functions with or without transplant (see example in **Figure 2** in main text). We reset survival to equal 100% at time $t = T_{transplant}$, making the estimates conditional upon survival to transplant

$$S_{ij}\left(t\middle|wait, X_{ij}\right) = \exp(-\int_{T\,tx}^{t} h_0(t) * exp\left(\beta_{0i} + +\mathbf{BX_{ij}(t)}\right) dt\ \mathbf{)}$$

$$S_{ij}\left(t\middle|tx, X_{ij}\right) = \exp(-\int_{T\,tx}^{t} h_0(t) * exp(\beta_{0i} + \beta_{1i}tx_{ij}(t) + \mathbf{BX_{ij}(t)} + \mathbf{\Theta}\left(\mathbf{X_{ij}(t)} * \mathbf{tx_{ij}(t)}\right)\ \mathbf{dt)}$$

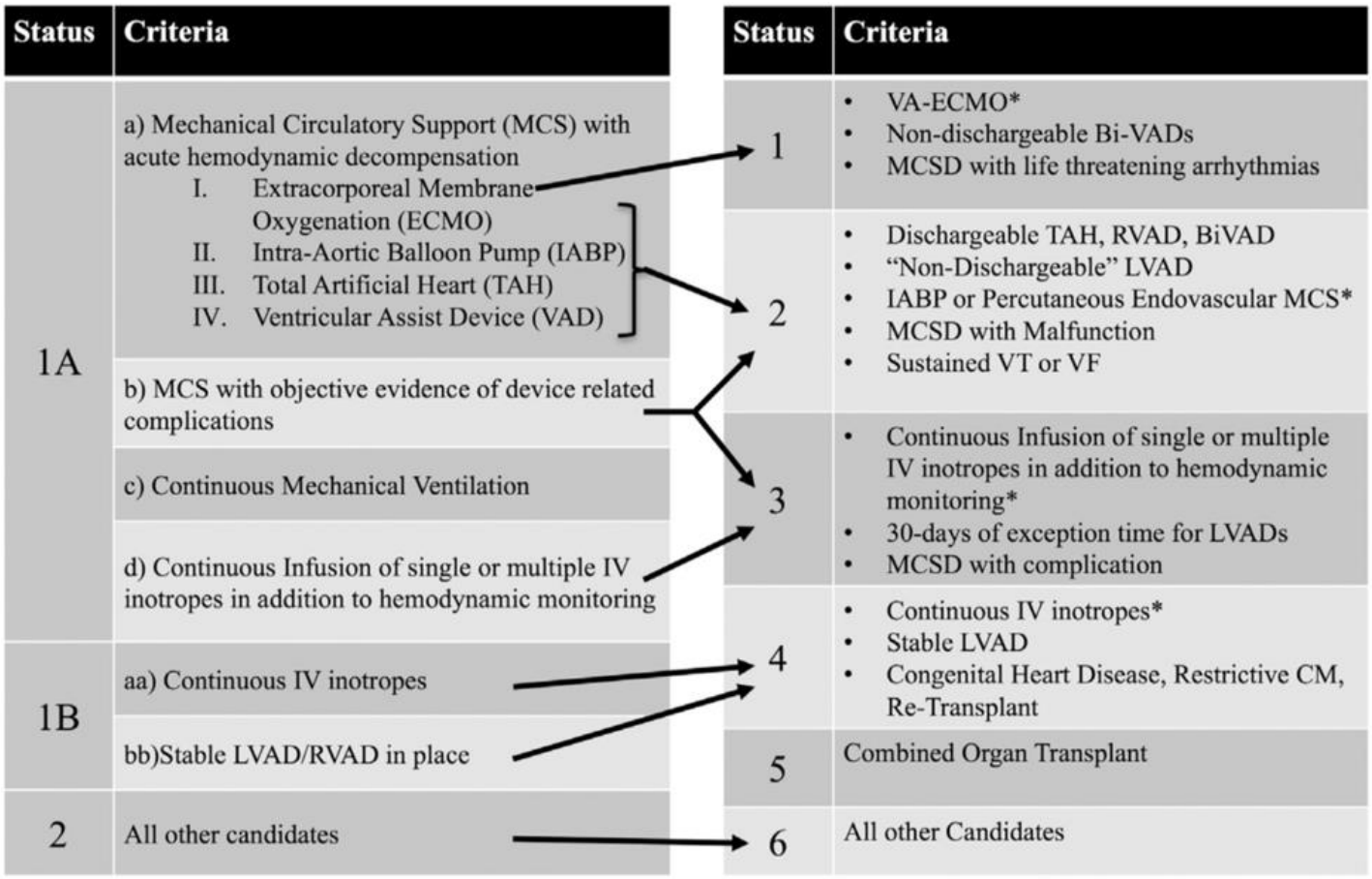
3. Finally, the 5-year survival benefit estimate for candidate *j* transplanted at center *i* is calculated by simple subtraction

$$B_{ij}(t = 5\ years) = S_{ij}\left(t = 5\ years \middle| tx, X_{ij}\right) - S_{ij}\left(t = 5\ years \middle| wait, X_{ij}\right)$$

Completing this procedure for each recipient using the random effects from the center they were actually transplanted at yields the "marginal" observed five-year survival benefit distribution. Then we used a simple linear mixed model, adjusted for Status at transplantation, to decompose the variation in the five-year survival benefit attributable to centers compared to the variance attributable to donor quality, ischemic time, year of transplant, and waiting time. Overall, the majority (76%) of the variation in survival benefit amongst recipients of the same status was attributable to center-level effects and the remaining 24% could be attributed to variation in transplant year, waiting time, donor quality and ischemic time (page 8 main text).

Case-mix adjusted center five-year survival benefit estimates. In order to estimate the mean case-mix adjusted absolute five-year survival gain from transplantation for each center, we adapted standard case-mix adjustment methodology[8,9] to account for between-center variation time to transplant and donor quality/availability. We gave each of the 113 centers the hypothetical "opportunity" to transplant each recipient, estimating 113 distributions of recipient five-year benefits by applying each center's empirical Bayes estimate of intercept and transplant random effect to each of the 19,815 recipients and following the five-year survival benefit procedure described above (e.g. **eFigure3**). To summarize each center's effect on five-year survival benefit, we calculated the mean of each center's distribution and 95% percent confidence intervals using the variance of the distribution of five-year survival estimates for the entire study population and number of transplants performed at each center during the study period (**Figure 3** in the main text).

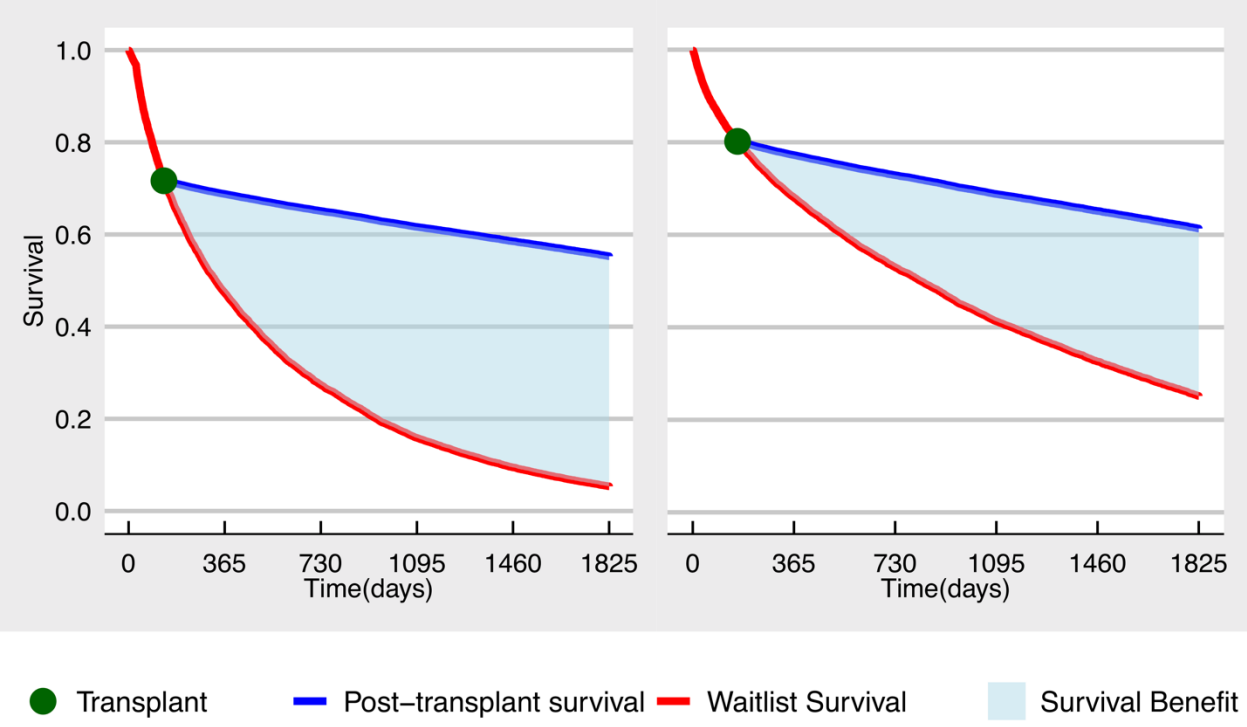
eFigure 1. Details of prior and current heart allocation system



Schematic depiction of the shift from the current adult heart allocation system to the modified system. Status 1A exception candidates were re-assigned to Status 3, Status 1B exceptions to Status 4. *Cardiogenic shock requirement applies. (Constructed with permission directly from the policy details in Organ Procurement and Transplantation Network[3]). Complete detail about each of the Status criteria are available at https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf#nameddest=Policy_06.

VT = ventricular tachycardia, VF = ventricular fibrillation, CM = cardiomyopathy, IV = intravenous.

eFigure 2. Center-specific Survival Benefit Framework

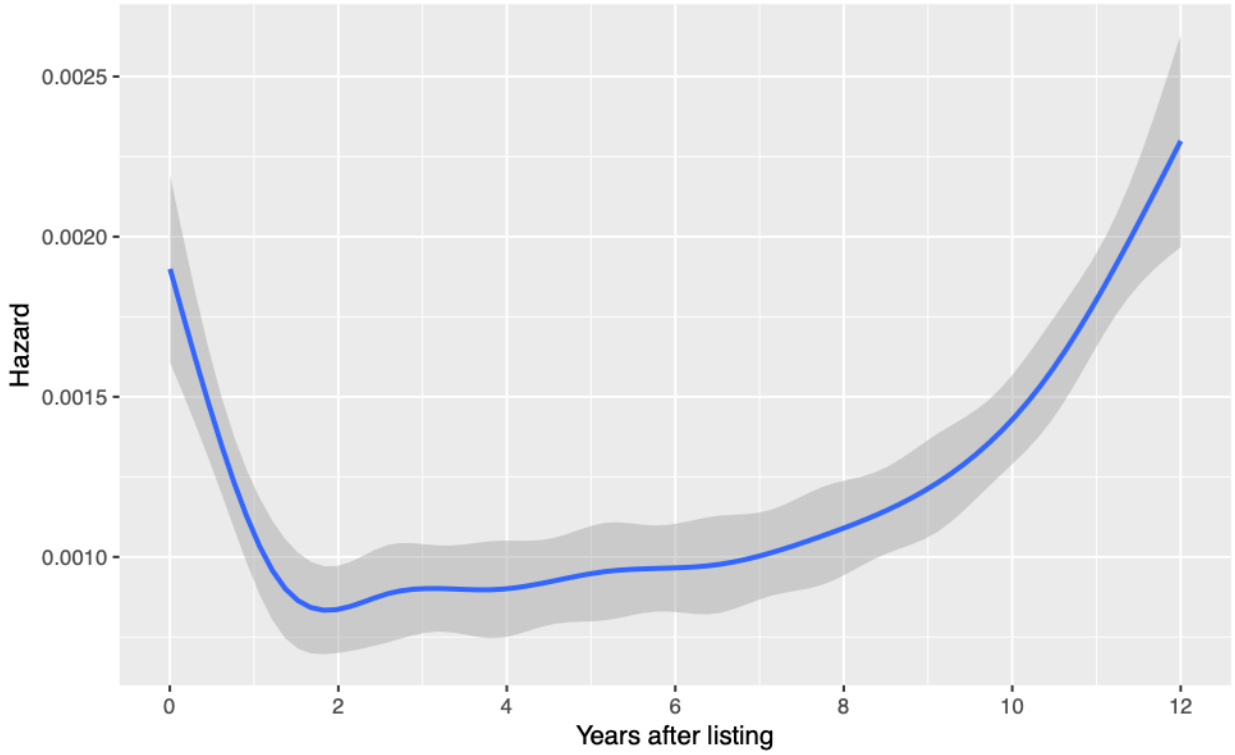


Two example survival benefit predictions incorporating the timing of transplantation, candidate status, donor quality, ischemic time, and year of transplant.

The high-benefit center (left panel) prioritizes candidates at higher risk of wait-list mortality and therefore transplantation at this center lowers risk more than the mean center. Specifically, candidates listed by this center have a risk of death 63% higher than the mean center (relative HR 1.63) and transplant lowers the risk of mortality 29% more than at the mean center (HR 0.71). The combination of these two effects leads to a large 5-year survival benefit, improving survival (conditional upon reaching transplant) from 6.1% to 75% (+69% absolute gain) for this particular Status 1A patient transplanted after waiting 135 days.

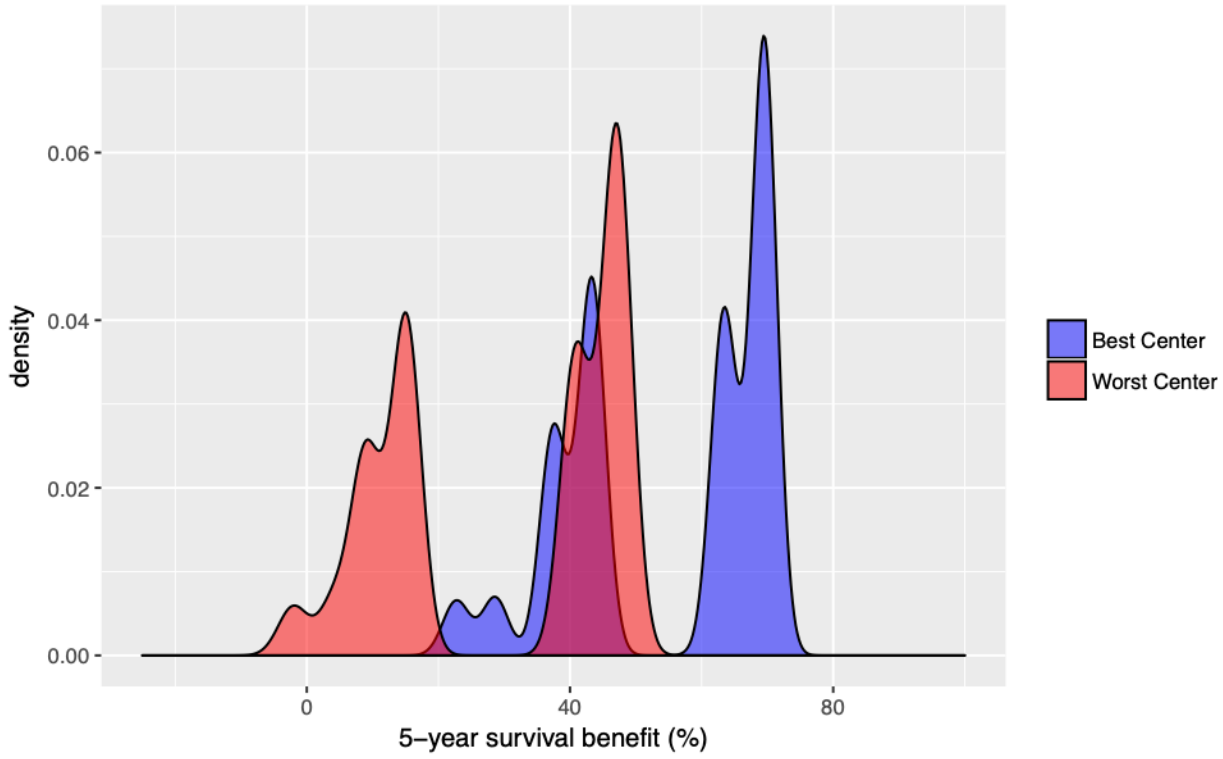
In contrast, the patients transplanted at the low-benefit center (right panel) are at lower risk of dying on the waitlist at baseline and transplantation at this center lowers risk less than the mean center. Specifically, candidates listed by this center have 26% lower risk of death than candidates at the mean center (HR 0.74) and transplant offers 60% less improvement in mortality risk than at the mean center (HR 1.60). The combination of these two effects leads to a smaller 5-year survival benefit, improving survival from 28% to 75% (+46% absolute gain) for this particular Status 1A patient transplanted after waiting 162 days

eFigure 3. Smoothed baseline hazard function from time of listing



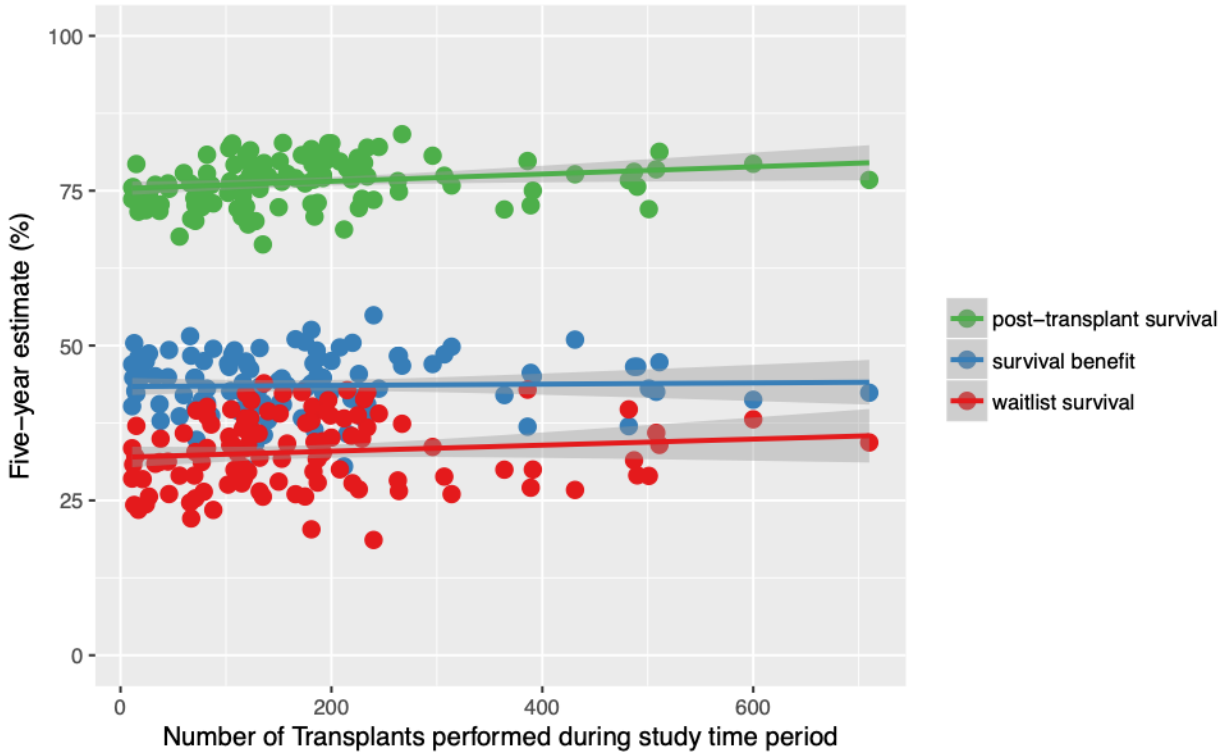
The baseline hazard function $h_0(t)$ is non-parametrically estimated, beginning at time of listing extending out to the point of maximum follow-up since listing for any candidate or recipient in the dataset. The baseline hazard function used to calculate survival benefit, representative of the hazard over time while waiting for heart transplant at the mean center. Immediately after listing for heart transplantation, candidates have increased hazard of death. More than 5 years after listing the hazard begins to rise again due to aging.

eFigure 4. Distribution of Five-year Survival Benefit at the Highest and Lowest Benefit Center, 2006-2015



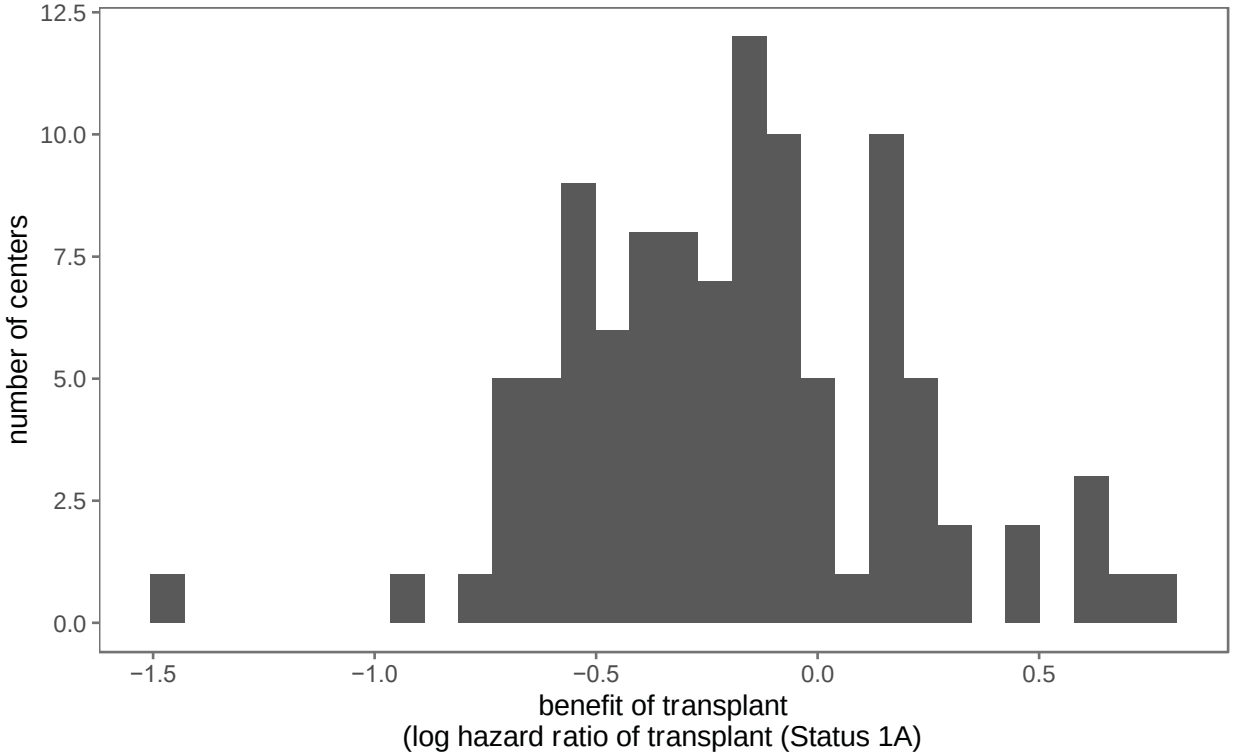
Distribution of 5-year survival benefit if the best and worst center hypothetically had transplanted all recipients during the study time period. The highest benefit center had a mean five-year survival benefit of 55% compared to only 30% at the lowest benefit center. The means and standard deviations of each center's distribution were used to create the point estimates and 95% confidence intervals in Figure 3 in the main text (standard errors calculated using the actual number of transplants performed by the center in the study time period).

eFigure 5. Association of Center Transplant Volume with Wait-List Survival, Post-Transplant Survival, and Survival Benefit from Heart Transplantation



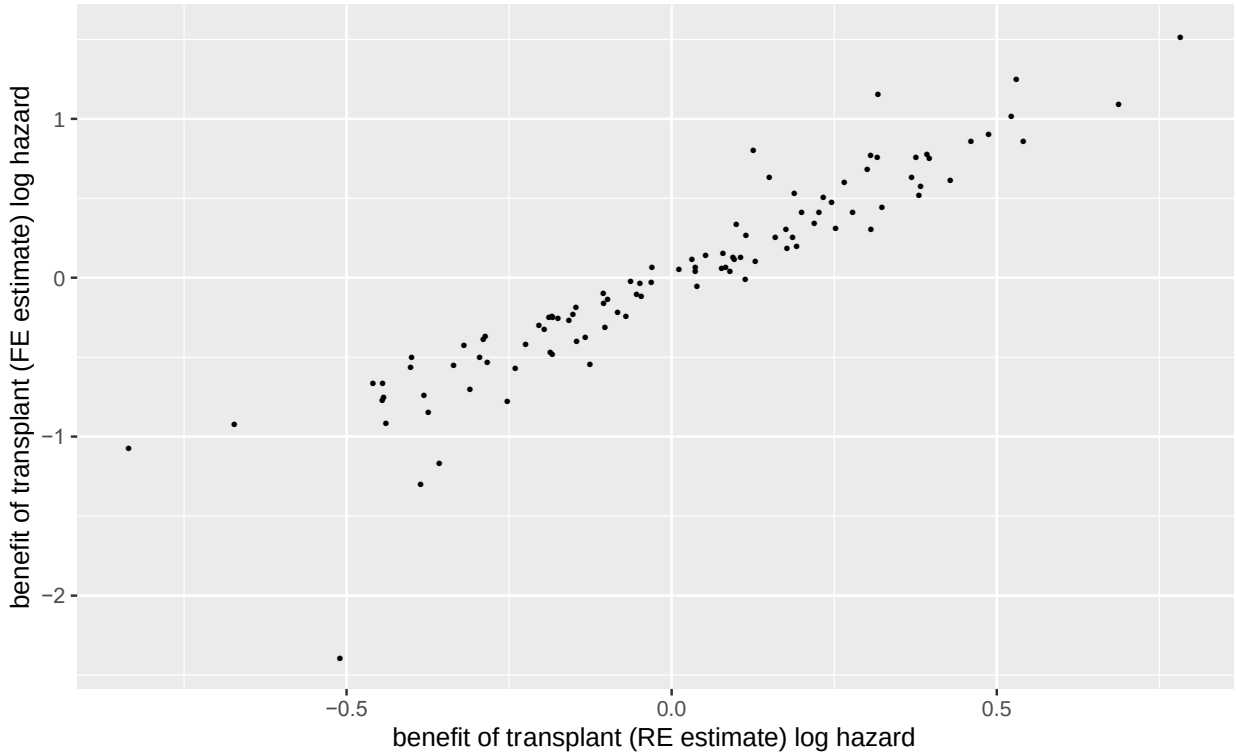
Center transplant volume was weakly associated with post-transplant survival (p = 0.03); however, it was not associated with either candidate urgency (p = 0.22) or survival benefit (p = 0.77)

eFigure 6. Histogram of center-specific survival benefits of heart transplantation as estimated by a fixed-effects model



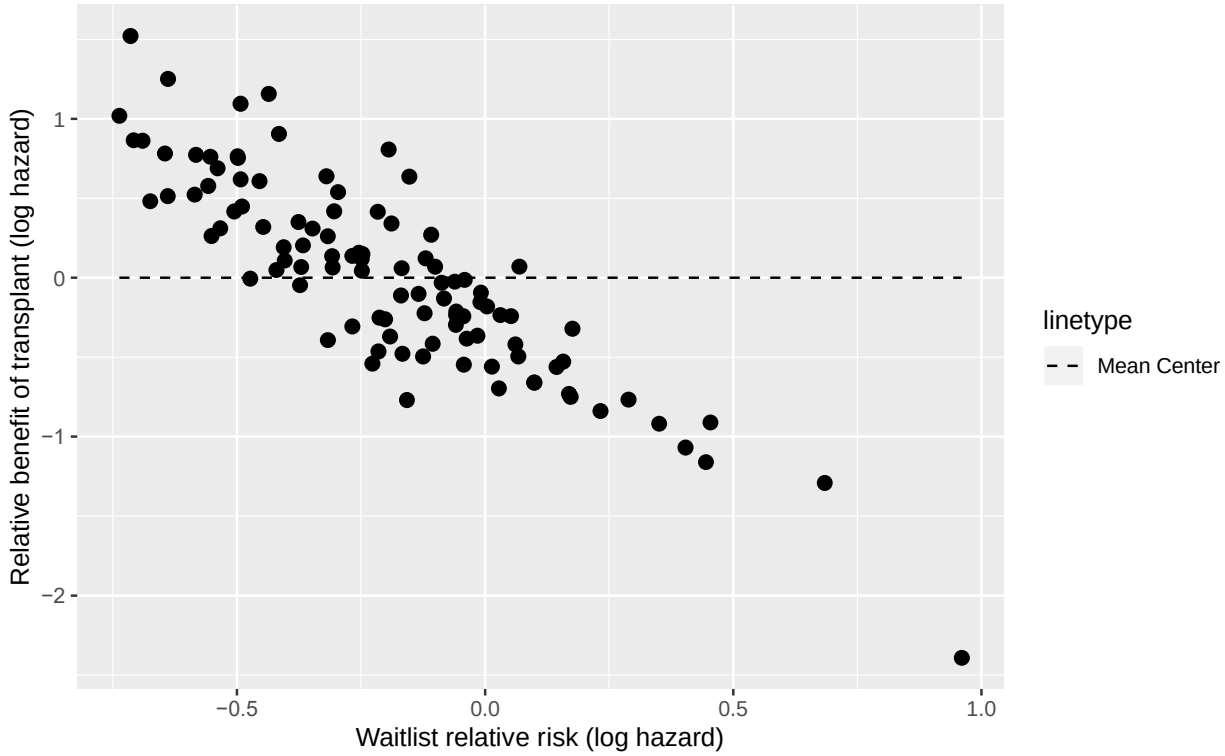
Distribution of center-specific survival benefits for a Status 1A recipient, calculated by subtracting the log hazard of waitlist from the log hazard of transplant at the center. The shapiro-wilk test for non-normality was not significant (p = 0.18).

eFigure 7. Relationship bet ween fixed-effect and random-effect center estimates of survival benefit from heart transplantation



Scatter plot of center fixed-effect (y-axis) and random-effect (x-axis) estimates of the survival benefit of heart transplantation (on log hazard scale). A spearman correlation between the two was 0.97. The log hazard ratios ore more extreme in the tails for the FE model, a well-known regression effect.

eFigure 8. Association of center waitlist risk with survival benefit from transplantation in a fixed-effects model



The association between estimated log hazard of death on waitlist at a given center (x-axis) and log hazard survival benefit (y-axis). A linear association is observed, for every one unit increase in the log hazard of waitlist risk the log hazard of transplant decreased -1.8 (95% CI 19 - 16).

eTable 1. The Detailed Cardiogenic Shock Requirements for Intra-Aortic Balloon Pumps and Multiple Inotropes or a Single High Dose Inotrope and Hemodynamic Monitoring

Candidate Groups	Status	Initial Listing Criteria
Intra-Aortic Balloon Pump	2	A candidate's transplant program may assign a candidate to adult status 2 if the candidate is admitted to the transplant hospital that registered the candidate on the waiting list, and **is supported by an IABP for cardiogenic shock** as evidenced by either of the following: • Within 7 days prior to IABP support, **all** of the following are true within one 24 hour period: a. Systolic blood pressure less than 90 mmHg b. Cardiac index less than 1.8 L/min/m2 if the candidate is not supported by inotropes or less than 2.0 L/min/m2 if the candidate is supported by at least one inotrope c. Pulmonary capillary wedge pressure greater than 15 mmHg • If hemodynamic measurements could not be obtained within 7 days prior to IABP support, at least one of the following is true within 24 hours prior to IABP support: ○ CPR was performed on the candidate ○ Systolic blood pressure less than 70 mmHg ○ Arterial lactate greater than 4 mmol/L ○ Aspartate transaminase (AST) or alanine transaminase (ALT) greater than 109 1,000 U/L
Multiple Inotropes or a Single High Dose Inotrope and Hemodynamic Monitoring	3	A candidate's transplant program may assign a candidate to adult status 3 if the candidate is admitted to the hospital that registered the candidate on the waiting list, and within 7 days prior to inotrope administration or while on inotropes meets all of the following: 1. Has one of the following: • Invasive pulmonary artery catheter • Daily hemodynamic monitoring to measure cardiac output and left ventricular filling pressures 2. Is in cardiogenic shock, as evidenced by all of the following within one 24 hour period: a. Systolic blood pressure less than 90 mmHg b. Pulmonary Capillary Wedge Pressure greater than 15 mmHg c. Cardiac index of either: • Less than 1.8 L/min/m2 for candidates without inotropic or mechanical support within 7 days prior to inotrope administration • Less than 2.2 L/min/m2 for candidates with inotropic or mechanical support 3. Is supported by one of the following: • A continuous infusion of at least one high-dose intravenous inotrope: ○ Dobutamine greater than or equal to 7.5 mcg/kg/min ○ Milrinone greater than or equal to 0.50 mcg/kg/min ○ Epinephrine greater than or equal to 0.02 mcg/kg/min • A continuous infusion of at least two intravenous inotropes: ○ Dobutamine greater than or equal to 3 mcg/kg/min ○ Milrinone greater than or equal to 0.25 mcg/kg/min ○ Epinephrine greater than or equal to 0.01 mcg/kg/min ○ Dopamine greater than or equal to 3 mcg/kg/min mcg/kg/min

Table constructed (with permission) directly from the policy details available at https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf#nameddest=Policy_06.

eTable 2. Three-status (old system) Model

Observations: 163,240

Total Events (death or re-transplant): 11,058

	NULL	Integrated	Fitted
Log-likelihood	-107,600	-105,890.7	-105,702

Fixed Effects Covariate	**log hazard ratio**	**95% CI**
Status 1B	-0.942	(-1.00, -0.88)
Status 2	-1.36	(-1.43, -1.28)
Transplant	-1.95	(-2.04, -1.87)
Transplant: Status 1B	0.90	(0.82, 0.99)
Transplant: Status 2	1.32	(1.20, 1.45)
Transplant before 2010	-0.05	(-0.11, 0.01)
Donor Risk Score > 5	0.26	(0.21, 0.32)

Base case is a candidate waiting at Status 1A. The mean hazard ratio of transplantation and 95% CI dependent on status and donor is displayed in graphical form on the next page

Status 1A candidates had a hazard ratio of transplant 0.14 (95% CI 0.13-0.15), Status 1B candidates had a HR of 0.35 (95% CI 0.32-0.38) and Status 2 candidates had a HR of 0.53 (95% CI 0.47-0.61).

Model random effects

Variable	Standard Deviation	Variance	Correlation
Intercept	0.224	0.050	-0.509
Transplant	0.238	0.057	

The random intercept and slope in this model were strongly negative correlated (-0.51), indicating that center-specific hazard ratio of transplantation decreased with increased center-specific waitlist risk. The variance in the survival benefit of transplant (waitlist subtracted from transplant) was 0.161 on log hazard ratio scale.

eTable 3. Status at Heart Transplantation by Center Level of Benefit

	Low-Benefit (N =5,430)	High-Benefit (N =6,878)	p-value
Status (Old)			<0.001
Status 1A	3430 (63.2)	3447 (50.1)	
Status 1B	1800 (33.1)	2908 (42.3)	
Status 2 (Old)	200 (3.7)	523 (7.6)	
Status (Current)			<0.001
Status 1	66 (1.2)	110 (1.6)	
Status 2	407 (7.5)	349 (5.1)	
Status 3	2079 (38.3)	1820 (26.5)	
Status 4	2725 (50.2)	4214 (61.3)	
Status 6	153 (2.8)	385 (5.6)	
Non-shock at transplant	N = 2,878	N = 4,599	
Status 1A qualifying IABPs or high-dose inotropes despite no cardiogenic shock	878 (30.5)	1,168 (25.4)	<0.001

Status calculated at time of transplantation. P-values calculated with Fisher exact tests (two-tailed)

eTable 4. Status 1A Candidate Characteristics at Time of Transplant by Center Benefit

	Low-Benefit (N =3,430)	High-Benefit (N =3,447)	p-value
	Mean ±SD	Mean ±SD	
Age	52.3 ±12.8	52.1 ±12.8	0.50
Body Mass Index (m/kg^2)	27.5 ±5.0	26.9 ±6.2	<0.001
	N (%)	N (%)	
Women	727 (21.2)	779 (22.6)	0.16
Race			<0.001
White	2246 (65.5)	2186 (63.4)	
Black	775 (22.6)	709 (20.6)	
Hispanic	288 (8.4)	359 (10.4)	
Other	121 (3.5)	193 (5.6)	
Diagnosis at listing			0.07
Dilated cardiomyopathy, non-ischemic	1563 (45.6)	1577 (45.7)	
Ischemic cardiomyopathy	1232 (35.9)	1191 (34.6)	
Restrictive cardiomyopathy	368 (10.7)	352 (10.2)	
Other	267 (7.8)	327 (9.5)	
Candidate Blood Type			0.64
A	1328 (38.7)	1295 (37.6)	
AB	139 (4.1)	132 (3.8)	
B	450 (13.1)	478 (13.9)	
O	1513 (44.1)	1542 (44.7)	
Diabetic	997 (29.1)	945 (27.4)	0.13
Renal Function			<0.001
GFR ≥ 60 mL/min	1995 (58.2)	1860 (54.0)	
GFR ≥30 mL/min & < 60 mL/min	1238 (36.1)	1329 (38.6)	
GFR ≤30 mL/min	87 (2.5)	131 (3.8)	
On Dialysis	110 (3.2)	107 (3.1)	
Functional Status			<0.001
Limited Impairment, 10-30%	907 (26.4)	593 (17.2)	
Moderate Impairment, 40-60%	920 (26.8)	817 (23.7)	
Severe Impairment, 70-100%	1455 (42.4)	1907 (55.3)	
Unknown/Missing	148 (4.3)	130 (3.8)	
History of Non-transplant Cardiac Surgery	1366 (39.8)	1346 (39.0)	0.51
ICD at listing	2653 (77.3)	2572 (74.6)	0.008

	Low-Benefit (N =3,430)	High-Benefit (N =3,447)	p-value
Insurance			<0.001
Medicaid	426 (12.4)	442 (12.8)	
Medicare	1251 (36.5)	1039 (30.1)	
Other	188 (5.5)	96 (2.8)	
Private	1565 (45.6)	1870 (54.3)	
Cardiac index (L/min/m^2)			
Missing	179 (5.2)	240 (6.96)	0.003
Mean ± s.d.	2.29 ±0.7	2.24 ±0.7	0.02
Pulmonary Capillary Wedge Pressure (mmHg)			
Missing	269 (7.8)	427 (12.4)	<0.001
Mean ± s.d	18.9 ±9.0	20.1 ±9.0	<0.001
< 15	1106 (32.2)	868 (25.2)	<0.001
Continuous flow LVAD in place at the time of transplant	2643 (48)	2415 (35)	<0.001
Status 1A Justification			<0.001
Mechanical Support for acute hemodynamic decompensation	1045 (30.5)	1297 (37.6)	
Mechanical circulatory support with objective medical evidence of significant device-related complications	1266 (36.9)	690 (20.0)	
Mechanical Ventilation	12 (0.3)	12 (0.3)	
Continuous infusion of a single high-dose intravenous inotrope or multiple intravenous inotropes and continuous hemodynamic monitoring	858 (25.0)	1149 (33.3)	
Exception	246 (7.2)	299 (8.7)	
No justification listed	3 (0.1)	0 (0.0)	

320

For continuous variables, mean and standard deviation were calculated and group comparison testing p-values calculated using Student's t-test. For categorical variables, number (%) are presented and group comparison testing p-values calculated with Fisher's exact test. Functional status is on the Karnofsky scale.[10] Applying the Bonferroni correction for multiple testing, only p-values < 0.003 were considered statistically significant.

eTable 5. Classification of Heart Transplant Recipients from 2006-2015 Based on the New Status 1-6 System

	Status 1A (N =11,227)	Status 1B (N =7,250)	Status 2 (Old) (N =1,338)
	N (%)	N (%)	N (%)
Status 1	255 (2)	0 (0)	0 (0)
Status 2	1254 (11)	0 (0)	0 (0)
Status 3	6255 (56)	0 (0)	0 (0)
Status 4	3462 (31)	7250 (100)	288 (22)
Status 6	1 (0)	0 (0)	1050 (78)

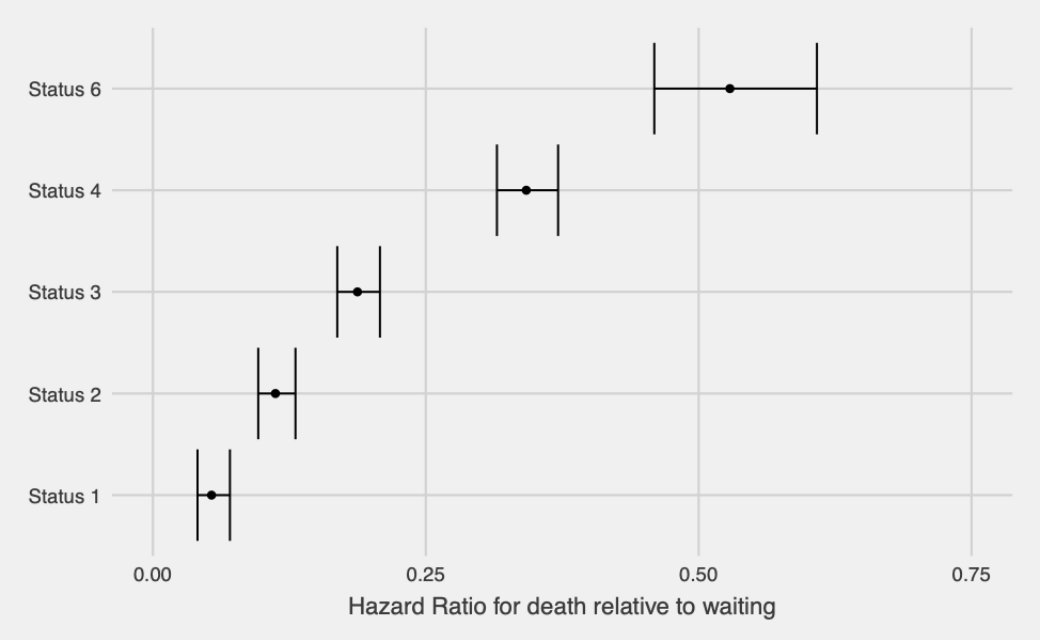
The majority (56%) of Status 1A recipients were coded as Status 3. A substantial portion (31%) of Status 1A candidates would have been downgraded to Status 4 because of violation of the cardiogenic shock requirement. A small number of recipients 288 were assigned a higher status because of restrictive cardiomyopathy, congenital heart disease, or hypertrophic cardiomyopathy. Intractable angina was not available as a specific data field in dataset so this was omitted as a status 4 qualifying diagnosis. Dischargeable vs. non-dischargeable ventricular support devices were distinguished via a list provided by the SRTR.

eTable 6. Six-status Model Results
Total observations: 163,240
Total Events (death or re-transplant): 11,058

	NULL	Integrated	Fitted
Log-likelihood	-107,600	-105,838	-105,665

Fixed Effects Covariate	**log hazard ratio**	**95% CI**
Status 2	-0.87	(-1.04, -0.69)
Status 3	-1.53	(-1.69, -1.36)
Status 4	-2.17	(-2.32, -2.02)
Status 6	-2.61	(-2.78, -2.45)
Transplantation	-2.92	(-3.2, -2.65)
Transplant: Status 2	0.74	(0.44, 1.04)
Transplant: Status 3	1.25	(0.97, 1.53)
Transplant: Status 4	1.85	(1.58, 2.12)
Transplant: Status 6	2.29	(1.99, 2.58)
Donor Risk Score > 5	0.26	(0.21, 0.32)
Transplant before 2010	-0.05	(-0.11, 0.01)

Base case is a candidate waiting at Status 1 requiring ECMO, non-dischargeable bi-VAD support, or life-threatening arrhythmias. The HR of transplantation dependent on six-status is displayed below



Hazard ratios of transplantation by 6-Status Justification at transplantation as estimated by mixed-effects model, adjusted for donor risk, ischemic time, and year of transplant. Status 1 candidates had hazard ratio of transplant of 0.054 (95% CI 0.041-0.071), Status 2 had a hazard ratio of 0.11 (95% CI 0.096-0.13), Status 3 had a HR of 0.19 (95% CI 0.17-0.21), Status 4 had a HR of 0.34 (95% CI 0.32-0.37), and Status 6 had a HR of 0.53 (95% CI 0.46-0.61). Status 5 is reserved for multi-organ candidates who were excluded from this study.

Model random effects (log hazard scale)

Variable	Standard Deviation	Variance	Correlation
Intercept	0.195	0.038	-0.386
Transplant	0.212	0.045	

Compared to model 1 (three-status), the calculated variance in the survival benefit of transplant decreased by a factor of 0.28 from 0.161 to 0.115 on log hazard ratio scale compared to the three-status system.

eTable 7. Fixed-effects Model Results

$$h(t) = h_o(t) * \exp(center + status + tx * (center + status + donorRisk + year))$$

n= 162054
number of events = 10962
Likelihood ratio test=3849 on 213 df, p<0.001

covariate	*log hazard ratio*	*Lower border 95% CI*	*Upper border 95% CI*
Status 1B	-0.95	-1.01	-0.89
Status 2	-1.38	-1.46	-1.31
Transplantation	-1.78	-2.21	-1.36
Transplantation: Status 1B	0.92	0.83	1.01
Transplantation: Status 2	1.35	1.22	1.48
Donor Risk Score > 5	0.26	0.21	0.32
Transplant before 2010	-0.05	-0.11	0.01
center7	-0.06	-0.42	0.30
center8	-0.50	-0.94	-0.06
center18	-0.42	-0.83	-0.01
center25	-0.11	-0.53	0.32
center33	-0.25	-0.59	0.10
center47	0.14	-0.37	0.66
center55	0.45	-0.04	0.95
center63	-0.25	-0.78	0.29
center64	0.17	-0.27	0.61
center65	-0.50	-1.01	0.02
center67	-0.17	-0.58	0.25
center72	0.10	-0.28	0.47
center78	-0.04	-0.39	0.30
center79	-0.11	-0.52	0.31
center91	-0.17	-0.59	0.25
center94	-0.65	-1.14	-0.15
center96	-0.25	-0.68	0.17
center108	-0.22	-0.58	0.15
center119	-0.04	-0.41	0.33
center128	-0.56	-0.97	-0.15
center131	-0.49	-0.87	-0.11
center136	-0.30	-0.67	0.06
center141	-0.02	-0.36	0.33
center147	-0.19	-0.69	0.30
center149	-0.30	-0.83	0.24

center165	-0.47	-0.94	0.00
center171	-0.71	-1.15	-0.28
center178	-0.59	-0.98	-0.19
center183	-0.38	-0.78	0.03
center185	0.23	-0.25	0.71
center190	0.05	-0.34	0.44
center195	-0.13	-0.59	0.32
center199	-0.19	-0.72	0.34
center201	0.00	-0.38	0.39
center210	-0.04	-0.40	0.32
center213	-0.54	-1.06	-0.02
center221	0.01	-0.33	0.35
center234	0.45	-0.15	1.04
center298	0.10	-0.26	0.45
center301	-0.53	-0.88	-0.19
center303	-0.45	-0.82	-0.07
center307	-0.31	-0.70	0.08
center313	0.35	-0.01	0.71
center324	-0.35	-0.77	0.08
center337	-0.20	-0.55	0.14
center338	-0.23	-0.70	0.25
center348	-0.12	-0.47	0.22
center350	-0.41	-0.76	-0.05
center351	0.07	-0.26	0.40
center359	-0.71	-1.19	-0.23
center372	0.29	-0.14	0.72
center377	-0.64	-1.25	-0.03
center380	-0.21	-0.65	0.22
center382	-0.06	-0.40	0.28
center388	-0.09	-0.50	0.33
center402	-0.74	-1.22	-0.25
center404	-0.12	-0.50	0.26
center408	-0.45	-0.96	0.05
center434	-0.37	-0.68	-0.05
center442	-0.27	-0.62	0.08
center445	-0.37	-0.80	0.05
center446	-0.49	-0.88	-0.11
center459	-0.17	-0.61	0.27
center465	-0.21	-0.54	0.12
center479	-0.25	-0.69	0.19

center484	0.68	0.05	1.32
center486	-0.44	-0.97	0.10
center487	-0.01	-0.39	0.37
center507	-0.55	-1.02	-0.08
center512	-0.27	-0.66	0.12
center520	-0.42	-0.83	0.00
center523	-0.01	-0.50	0.48
center527	-0.08	-0.45	0.28
center532	-0.12	-0.53	0.29
center534	0.16	-0.31	0.63
center536	-0.31	-0.68	0.06
center588	0.96	0.30	1.62
center595	0.03	-0.43	0.48
center615	0.18	-0.30	0.65
center620	-0.04	-0.37	0.30
center633	0.07	-0.34	0.48
center640	-0.40	-0.77	-0.04
center642	-0.55	-1.02	-0.09
center643	-0.10	-0.42	0.22
center645	0.17	-0.23	0.58
center648	-0.15	-0.73	0.43
center656	0.40	0.06	0.74
center667	-0.32	-0.72	0.09
center670	-0.06	-0.72	0.60
center675	0.03	-0.34	0.40
center688	-0.67	-1.23	-0.12
center690	-0.51	-1.00	-0.01
center696	-0.49	-0.87	-0.11
center700	-0.32	-0.71	0.07
center701	-0.64	-1.13	-0.15
center703	-0.69	-1.10	-0.28
center708	-0.19	-0.62	0.24
center733	-0.16	-0.59	0.27
center736	-0.32	-0.69	0.06
center742	-0.06	-0.64	0.52
center746	0.06	-0.29	0.41
center749	-0.37	-0.80	0.06
center838	-0.58	-1.14	-0.03
tx:center7	-0.35	-0.91	0.20
tx:center8	0.26	-0.37	0.88

tx:center18	-0.37	-0.97	0.23
tx:center25	0.16	-0.42	0.75
tx:center33	-0.13	-0.61	0.35
tx:center47	-0.42	-1.11	0.27
tx:center55	-0.46	-1.15	0.24
tx:center63	-0.10	-0.88	0.69
tx:center64	-0.56	-1.19	0.06
tx:center65	0.27	-0.46	0.99
tx:center67	-0.64	-1.30	0.01
tx:center72	-0.56	-1.08	-0.04
tx:center78	-0.29	-0.77	0.20
tx:center79	-0.52	-1.11	0.07
tx:center91	-0.28	-0.88	0.32
tx:center94	0.14	-0.54	0.81
tx:center96	-0.10	-0.74	0.54
tx:center108	0.20	-0.38	0.78
tx:center119	-0.59	-1.14	-0.04
tx:center128	0.02	-0.55	0.59
tx:center131	0.13	-0.39	0.64
tx:center136	0.11	-0.41	0.64
tx:center141	-0.38	-0.90	0.14
tx:center147	0.61	-0.22	1.44
tx:center149	0.24	-0.46	0.95
tx:center165	-0.48	-1.20	0.25
tx:center171	0.81	0.18	1.44
tx:center178	-0.06	-0.65	0.53
tx:center183	-0.03	-0.59	0.54
tx:center185	-0.61	-1.36	0.15
tx:center190	-0.19	-0.73	0.35
tx:center195	-0.24	-0.87	0.40
tx:center199	0.15	-0.56	0.86
tx:center201	-0.18	-0.73	0.38
tx:center210	-0.05	-0.61	0.50
tx:center213	0.15	-0.56	0.86
tx:center221	-0.55	-1.08	-0.01
tx:center234	-0.72	-1.63	0.20
tx:center298	-0.56	-1.11	-0.01
tx:center301	-0.22	-0.78	0.33
tx:center303	-0.13	-0.69	0.44
tx:center307	-0.24	-0.85	0.36

tx:center313	-0.57	-1.11	-0.03
tx:center324	-0.04	-0.66	0.58
tx:center337	-0.46	-0.98	0.06
tx:center338	-0.77	-1.53	-0.01
tx:center348	-0.62	-1.17	-0.07
tx:center350	-0.21	-0.75	0.32
tx:center351	-0.43	-0.93	0.07
tx:center359	0.16	-0.44	0.76
tx:center372	-0.48	-1.11	0.16
tx:center377	-0.13	-0.97	0.72
tx:center380	-0.68	-1.30	-0.06
tx:center382	-0.09	-0.57	0.40
tx:center388	-0.12	-0.73	0.49
tx:center402	0.28	-0.36	0.92
tx:center404	-0.35	-0.87	0.18
tx:center408	0.15	-0.52	0.83
tx:center434	-0.16	-0.63	0.30
tx:center442	-0.57	-1.18	0.04
tx:center445	-0.42	-1.04	0.21
tx:center446	0.60	0.06	1.14
tx:center459	-0.11	-0.73	0.52
tx:center465	-0.46	-0.95	0.02
tx:center479	-0.20	-0.82	0.41
tx:center484	-0.61	-1.55	0.33
tx:center486	0.72	-0.10	1.54
tx:center487	-0.10	-0.67	0.47
tx:center507	-0.29	-0.93	0.36
tx:center512	-0.13	-0.69	0.43
tx:center520	0.49	-0.09	1.07
tx:center523	-0.16	-0.85	0.53
tx:center527	-0.21	-0.72	0.29
tx:center532	0.00	-0.59	0.60
tx:center534	-0.37	-1.06	0.32
tx:center536	-0.17	-0.68	0.34
tx:center588	-1.43	-2.28	-0.58
tx:center595	-0.67	-1.32	-0.02
tx:center615	-0.14	-0.80	0.51
tx:center620	-0.42	-0.94	0.10
tx:center633	0.14	-0.43	0.71
tx:center640	-0.30	-0.85	0.26

tx:center642	0.21	-0.49	0.90
tx:center643	-0.03	-0.51	0.44
tx:center645	-0.58	-1.17	0.01
tx:center648	0.48	-0.27	1.24
tx:center656	-0.66	-1.18	-0.15
tx:center667	-0.06	-0.63	0.52
tx:center670	-0.29	-1.25	0.66
tx:center675	-0.20	-0.72	0.31
tx:center688	-0.19	-0.92	0.53
tx:center690	-0.09	-0.76	0.59
tx:center696	-0.04	-0.62	0.54
tx:center700	0.32	-0.24	0.87
tx:center701	0.61	-0.10	1.32
tx:center703	0.17	-0.44	0.79
tx:center708	-0.56	-1.21	0.09
tx:center733	-0.93	-1.64	-0.21
tx:center736	-0.71	-1.29	-0.13
tx:center742	-0.27	-1.26	0.72
tx:center746	-0.36	-0.87	0.16
tx:center749	-0.30	-0.91	0.31
tx:center838	0.19	-0.62	1.00

eTable 8. Three-status + expanded donor factors and listing year model results

Observations: 163,109

Total Events (death or re-transplant): 11,052

	NULL	Integrated	Fitted
Log-likelihood	-107535	-105726	-105540

Fixed Effects Covariate	**log hazard ratio**	**95% CI**
Status 1B	-0.946	(-1.01, -0.884)
Status 2	-1.43	(-1.5, -1.36)
Listing year 2007	-0.0392	(-0.168, 0.0894)
Listing year 2008	-0.103	(-0.227, 0.0215)
Listing year 2009	-0.153	(-0.275, -0.0316)
Listing year 2010	-0.231	(-0.354, -0.108)
Listing year 2011	-0.312	(-0.439, -0.184)
Listing year 2012	-0.305	(-0.43, -0.179)
Listing year 2013	-0.403	(-0.528, -0.278)
Listing year 2014	-0.335	(-0.457, -0.213)
Listing year 2015	-0.483	(-0.612, -0.353)
Transplant	-2.4	(-2.56, -2.25)
Transplant: Status 1B	0.919	(0.833, 1.01)
Transplant: Status 2	1.4	(1.28, 1.53)
Transplant: Listing year 2007	-0.0313	(-0.195, 0.132)
Transplant: Listing year 2008	0.0583	(-0.104, 0.221)
Transplant: Listing year 2009	0.119	(-0.0434, 0.282)

Transplant: Listing year 2010	0.113	(-0.0538, 0.28)
Transplant: Listing year 2011	0.257	(0.0827, 0.43)
Transplant: Listing year 2012	0.235	(0.0598, 0.411)
Transplant: Listing year 2013	0.454	(0.277, 0.632)
Transplant: Listing year 2014	0.444	(0.264, 0.625)
Transplant: Listing year 2015	0.705	(0.513, 0.897)
Donor BUN/Cr Ratio	-0.0336	(-0.0882, 0.0209)
Donor Age ≤30	-0.384	(-0.474, -0.295)
Donor Age 30-50	-0.182	(-0.283, -0.0816)
Donor-Recipient race mismatch	0.17	(0.111, 0.229)
Ischemic time (hours)	0.146	(0.0996, 0.192)

Base case is a candidate waiting at Status 1A, donor >50, no race mismatch, ischemic time <1 hour.

Model random effects

Variable	Standard Deviation	Variance	Correlation
Intercept	0.213	0.045	-0.481
Transplant	0.238	0.057	

The random intercept and slope in this model were strongly negative correlated (-0.48), indicating that center-specific hazard ratio of transplantation decreased with increased center-specific waitlist risk. The variance of the survival benefit of transplant was 0.151 on log hazard ratio scale, 6.3% lower than the three-status model.

eTable 9. Three-status + expanded donor factors and listing year + candidate variables model results

Observations: 163,109

Total Events (death or re-transplant): 11,052

	NULL	Integrated	Fitted
Log-likelihood	-1075345	-105459.5	-105275

Fixed Effects Covariate	**log hazard ratio**	**95% CI**
Status 1B	-0.939	(-1, -0.877)
Status 2	-1.46	(-1.53, -1.39)
Listing year 2007	-0.0346	(-0.164, 0.0944)
Listing year 2008	-0.0893	(-0.214, 0.0353)
Listing year 2009	-0.135	(-0.257, -0.0124)
Listing year 2010	-0.226	(-0.349, -0.103)
Listing year 2011	-0.3	(-0.428, -0.172)
Listing year 2012	-0.287	(-0.413, -0.161)
Listing year 2013	-0.375	(-0.501, -0.248)
Listing year 2014	-0.289	(-0.413, -0.165)
Listing year 2015	-0.45	(-0.581, -0.32)
Age	0.0149	(0.0124, 0.0173)
Female	0.0161	(-0.0482, 0.0803)
BMI < 25th percentile	0.0636	(-0.00685, 0.134)
BMI > 75th percentile	0.0562	(-0.00631, 0.119)
Ischemic Cardiomyopathy	0.133	(0.0692, 0.198)
Restrictive cardiomyopathy	0.191	(0.0891, 0.292)
Other Diagnosis	0.53	(0.447, 0.614)
Cross Match requested	0.396	(0.328, 0.465)
Blood type: AB	0.138	(-0.0252, 0.302)

Blood type: B	-0.000891	(-0.0913, 0.0895)
Blood type: O	0.00624	(-0.0526, 0.0651)
Transplant	-1.49	(-1.74, -1.24)
Transplant: Status 1B	0.912	(0.825, 0.998)
Transplant: Status 2	1.44	(1.31, 1.57)
Transplant: Listing year 2007	-0.0342	(-0.198, 0.13)
Transplant: Listing year 2008	0.0499	(-0.113, 0.213)
Transplant: Listing year 2009	0.11	(-0.0534, 0.273)
Transplant: Listing year 2010	0.118	(-0.0495, 0.286)
Transplant: Listing year 2011	0.251	(0.0768, 0.426)
Transplant: Listing year 2012	0.23	(0.0537, 0.407)
Transplant: Listing year 2013	0.436	(0.257, 0.615)
Transplant: Listing year 2014	0.411	(0.229, 0.594)
Transplant: Listing year 2015	0.693	(0.5, 0.886)
Donor BUN/Cr Ratio	-0.0195	(-0.0745, 0.0355)
Donor Age ≤30	-0.38	(-0.47, -0.29)
Donor Age 30-50	-0.186	(-0.287, -0.0851)
Donor-Recipient race mismatch	0.187	(0.127, 0.247)
Ischemic time (hours)	0.139	(0.0932, 0.186)
Transplant: age	-0.0163	(-0.0197, -0.0128)
Transplant: female	0.00115	(-0.0904, 0.0927)
Transplant: BMI < 25th percentile	-0.125	(-0.223, -0.0274)
Transplant: BMI > 75th percentile	0.123	(0.0303, 0.216)
Transplant: Ischemic cardiomyopathy	0.117	(0.0263, 0.208)
Transplant: Other Diagnosis	-0.376	(-0.505, -0.246)
Transplant: Restrictive cardiomyopathy	-0.105	(-0.253, 0.0423)
Transplant: cross match requested	-0.294	(-0.409, -0.18)
Transplant: blood type AB	-0.133	(-0.338, 0.0712)

Transplant: blood type B	0.0612	(-0.0604, 0.183)
Transplant: blood type O	0.0848	(6.94e-05, 0.17)

412 Base case is a male candidate waiting at Status 1A, dilated cardiomyopathy, blood type A, no
413 cross-match requested, BMI 25th-75th percentile.

414 **Model random effects**

Variable	Standard Deviation	Variance	Correlation
Intercept	0.220	0.048	-0.462
Transplant	0.222	0.049	

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416 The random intercept and slope in this model were strongly negative correlated (-0.462,
417 indicating that center-specific hazard ratio of transplantation decreased with increased center-
418 specific waitlist risk. The variance of the survival benefit of transplant was 0.143 on log hazard
419 ratio scale, 11% lower than the three-status model.

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eTable 10. Three-status + LVAD + UNOS Region

Observations: 163,109

Total Events (death or re-transplant): 11,052

	NULL	Integrated	Fitted
Log-likelihood	-1075345	-105678.7	-105520.1

Fixed Effects Covariate	**log hazard ratio**	**95% CI**
Status 1B	-0.914	(-0.977, -0.852)
Status 2	-1.57	(-1.65, -1.49)
UNOS Region 2	0.163	(-0.0878, 0.414)
UNOS Region 3	0.102	(-0.15, 0.355)
UNOS Region 4	0.242	(-0.0155, 0.499)
UNOS Region 5	0.137	(-0.116, 0.391)
UNOS Region 6	0.11	(-0.242, 0.462)
UNOS Region 7	0.104	(-0.155, 0.363)
UNOS Region 8	0.0085	(-0.294, 0.311)
UNOS Region 9	0.0338	(-0.262, 0.33)
UNOS Region 10	0.151	(-0.119, 0.42)
UNOS Region 11	0.133	(-0.118, 0.384)
LVAD	-0.485	(-0.549, -0.421)
Transplant	-2.36	(-2.62, -2.09)
Transplant: Status 1B	0.913	(0.827, 1)
Transplant: Status 2	1.63	(1.5, 1.76)
Transplant: UNOS Region 2	0.0861	(-0.211, 0.383)
Transplant: UNOS Region 3	0.127	(-0.174, 0.428)
Transplant: UNOS Region 4	0.117	(-0.187, 0.422)

Transplant: UNOS Region 5	-0.0121	(-0.311, 0.287)
Transplant: UNOS Region 6	-0.516	(-0.945, -0.0868)
Transplant: UNOS Region 7	-0.0164	(-0.325, 0.293)
Transplant: UNOS Region 8	0.0695	(-0.284, 0.423)
Transplant: UNOS Region 9	0.0719	(-0.277, 0.42)
Transplant: UNOS Region 10	0.0132	(-0.307, 0.333)
Transplant: UNOS Region 11	0.0736	(-0.225, 0.372)
Transplant: LVAD	0.678	(0.59, 0.766)
Donor Risk Score > 5	0.265	(0.21, 0.32)
Transplant before 2010	-0.0254	(-0.0855, 0.0347)

Base case is a candidate waiting at Status 1A, UNOS Region 1, without an LVAD.

Model random effects

Variable	Standard Deviation	Variance	Correlation
Intercept	0.198	0.0391	-0.55829070
Transplant	0.198	0.0390	

The random intercept and slope in this model were strongly negative correlated (-0.56), indicating that center-specific hazard ratio of transplantation decreased with increased center-specific waitlist risk. The variance of the survival benefit of transplant in the model including UNOS region and LVAD was 0.122 on log hazard ratio scale, 24% lower than the three-status model.

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