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Great Variability in Donor Heart Acceptance Practices across the United States

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Abstract

Disparities in organ acceptance practices exacerbate donor heart non-use and lead to increased waiting times and mortality for heart transplant candidates. We studied disparities in donor heart acceptance among US transplant centers and their relations to post-transplant outcomes. Candidate, potential transplant recipient match run, and deceased donor data were obtained from the United Network for Organ Sharing. We analyzed donor, candidate, and transplant center characteristics with respect to organ acceptance, offer acceptance, number of offers before acceptance (organ sequence number), and association with post-transplant mortality. A total of 693,420 donor heart offers made between April 2007 and December 2015 were included. We identified great variability in donor heart acceptance practices among US heart transplant centers. We identified donor and recipient characteristics that were strongly associated with heart organ and offer acceptance, and organ sequence number, and identified inconsistencies among centers with respect to how these characteristics influenced acceptance decisions. Finally, we identified characteristics that were highly predictive of donor heart non-use and were not associated with increased recipient mortality, which may guide future efforts aimed at increasing use of available hearts for transplantation.

INTRODUCTION

The great shortage of donor hearts deemed acceptable for transplantation continues to restrict heart transplantation to a minority of patients with end-stage heart disease who could benefit from this life-saving procedure. Despite this shortage, an analysis of the United Network for Organ Sharing (UNOS) heart transplant registry from 1995-2010 revealed disparities in donor heart acceptance rates across the United States (US), even after adjusting for key donor characteristics that may influence heart acceptance decisions.(1) This

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DISCLOSURE

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

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

SUPPORTING INFORMATION

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

variability in donor heart acceptance practices among geographical regions, transplant centers, and even individual physicians likely exacerbates the current problem of donor heart non-use for transplantation, which ultimately increases transplant waiting times and mortality for critically ill patients.(2)

Recent efforts have been made to develop consensus guidelines for donor heart acceptance, with the hope of standardizing practices across the US and ultimately improving use of available donor hearts.(3) These efforts, however, are greatly hampered by a lack of systematic studies on this topic and analyses that could provide evidence-based recommendations for donor heart selection.

Prior work by our group and others have identified predictors of donor heart non-acceptance for transplantation in various cohorts.(4–7) Of great interest, however, was the observation that many of these donor characteristics did not necessarily portend increased recipient mortality after transplantation, suggesting that these donor risk factors are not absolute contraindications to transplantation.

The first step in systematically studying donor heart under-utilization is to identify where the greatest disparities exist—specifically: (1) Which donor and candidate characteristics are most predictive of offer acceptance, organ acceptance, and organ sequence number in the US?, (2) Which of these highly predictive donor and candidate characteristics are inconsistently applied across transplant centers to guide offer acceptance and organ acceptance decisions?, (3) Which of these inconsistently applied donor and candidate characteristics are actually predictive of post-transplant mortality or re-transplantation?, and (4) Can we identify donor and candidate characteristics that can be targeted to increase consistency in offer and organ acceptance decisions across heart transplant centers? The identification of disparities in donor heart use across the country will inform and guide future research and policy efforts focused on this issue.

METHODS

Study design

This is a retrospective study of heart transplant candidates, potential donors, and transplant centers in the US. The study was approved by the Stanford University Institutional Review Board. All transplant services in the country are joined under the nationwide Organ Procurement and Transplantation Network (OPTN), which is managed by UNOS. We requested and received the following data: thoracic candidate data (09/1985-12/2015), potential transplant recipient (PTR) match run data for thoracic transplant candidates (record of each time a donor heart offer is made to a transplant candidate, 04/2007-12/2015), and thoracic deceased donor data (09/1987-12/2015). These analyses were based on OPTN data as of February 10, 2017.

Waitlist identifiers were used to link candidates awaiting heart transplantation to transplant centers and potential donors. Exclusion criteria for candidates, donors, and offers are presented in Figure 1. Supplemental Table 1 summarizes the list of donor heart refusal codes

included in the study, the percent of donors with each refusal code, and the list of refusal codes that were excluded from this analysis.

Outcomes

The primary objective of this study was to identify and examine the donor, candidate, and transplant center characteristics that were inconsistently used to guide offer acceptance, organ acceptance, and organ sequence number decisions across transplant centers in the US. There are two ways to analyze the decision process to accept or reject a donor heart offer. An organ may be deemed acceptable or unacceptable for all candidates listed at a transplant center based on the characteristics of the organ, or it may be evaluated on an offer-by-offer basis for each eligible candidate at a program (by position on the match run), based on the characteristics of each donor and candidate pair. These two approaches require separate analyses. We therefore analyzed donor, candidate, and transplant center characteristics with regard to (1) organ acceptance, (2) offer acceptance, (3) the number of offers before acceptance (organ sequence number), and (4) the association with post-transplant mortality or re-transplantation. Finally, we identified characteristics that are inconsistently applied across transplant centers and determined whether these characteristics predict mortality or re-transplantation within 30 days and 1 year (see Statistical Analyses section).

Candidate and donor characteristics

Based on previous literature, we identified key candidate and donor characteristics to consider,(4–11) as summarized in Tables 1 and 2. Categorical characteristics that had missing values or were coded as “unknown” were grouped together and treated as “unknown”.

Transplant center volume and access to transplantation

Center volume was included as a covariate in all models and was calculated according to the convention described by Shuhaiber et al.(12) Centers were characterized as very low-, low-, medium-, or high-volume centers (0-12, 13-21, 22-33, and >33, respectively) based on the average number of transplants per year from 2007-2015. The access rate for each transplant center was calculated as the number of candidates at the center divided by the sum of the proportion of the time that each candidate spent waiting. Access rate is similar in calculation to the “person-years” waiting metric reported by the Scientific Registry of Transplant Recipients (SRTR), but is calculated per center and over the entire time period for which data was available (see Detailed Methods in the Supplemental Material).

Statistical analyses

Figure 2 illustrates the statistical analyses performed for this study. For donor heart *offer* acceptance and *organ sequence number*, we identified candidate, donor, and transplant center characteristics predictive of the outcome using elastic net regularized regression.(13) Donor and transplant center characteristics, but not candidate characteristics, were included in models of *organ* acceptance. Similar to the LASSO (Least Absolute Shrinkage and Selection Operator) method,(14) elastic net uses the penalized likelihood to select characteristics that are most predictive of the outcome; however, unlike LASSO, elastic net

allows highly correlated characteristics to be included in the model. We chose this method because we aimed to identify characteristics that were most predictive of the outcomes of interest, while also allowing for correlation among these characteristics.

Logistic regression models were used for the dichotomous outcomes (offer acceptance, organ acceptance, and mortality/re-transplantation) while a Poisson regression model was used to model organ sequence number for organs that were ultimately accepted. Since not all candidates have equal access to transplantation and since access is known to influence mortality/re-transplantation, we included access rate as a covariate in the mortality/re-transplantation models. All analyses were completed in the R statistical computing environment,(15) utilizing the *glmnet* package.(16)

To gain a better understanding of the interactions among candidate and donor characteristics on the outcomes of interest, we used conditional inference trees (17) with the 15 most predictive characteristics as input. The conditional inference trees were implemented with the *partykit* (18) package in R.(15)

Identification of characteristics that are inconsistently applied across transplant centers

For each outcome of interest, we identified the 15 most predictive donor, candidate, and transplant center characteristics, based on the rank of the characteristic in the elastic net model results. Next, using these top 15 characteristics, we independently fit ridge regression models to data from each center, such that a separate model was fit for each center. Ridge regression includes all characteristics in the model, but also accounts for correlation among characteristics.(19)

For each outcome and characteristic, we calculated the median absolute deviation (MAD) of the centers' ridge regression coefficients. Characteristics with MAD in the lowest quartile were considered to vary the least. Characteristics with MAD in the highest quartile were considered to vary the most and represented characteristics that were inconsistently applied across centers.

Finally, we separately identified donor and recipient characteristics that were highly predictive of mortality or re-transplantation within 30 days or 1 year, adjusting for transplant center access rates. We compared these characteristics to those that were inconsistently applied across transplant centers, as determined previously. We thereby identified characteristics that could be targeted for more consistent donor heart utilization across centers.

For additional details, please see Detailed Methods in the Supplemental Material.

RESULTS

A total of 28,088 potential donors, 26,320 heart transplant candidates, and 693,420 donor heart offers made in the US between April 2007 and December 2015 were included in this study (Figure 1). As shown in Supplemental Table 1, most donor hearts (67%) were turned down by transplant centers due to concerns about donor heart "quality" (code 830). The majority of candidates included in this study (63.1%) received a heart transplant, although

some received a heart from a donor that was excluded from this analysis, most commonly due to donor age less than 18 years. Only data on candidates and donors who met study inclusion criteria were used for subsequent analyses. Of the donor hearts included in this study, 55.8% were ultimately transplanted (this is higher than the average national donor heart utilization rate of 30-35%,⁽¹⁾ as only donor hearts that were offered for transplantation were included). Candidate and donor characteristics are summarized in Tables 1 and 2.

Most transplant centers were very low- or low-volume centers: 55.9% were very low (0-12 transplants/year), 26.2% were low (13-21 transplants/year), 9.0% were medium (22-33 transplants/year), and 9.0% were high volume centers (>33 transplants/year). Centers had a median access rate of 8.62 (IQR 5.17-11.74). Not surprisingly, median access rate generally increased as transplant center volume increased (Figure 3) but there was considerable variability among very low-volume centers, with a median access rate of 7.52 (IQR 3.96-11.16). For this reason, access rate was added as a covariate to the mortality models.

Offer acceptance

The characteristics that were most predictive of donor heart *offer* acceptance, by ranked order, were: candidate total days waiting, candidate days as status 1B, donor age, candidate days as status 2, candidate days as status 1A, candidate BMI, donor/candidate weight ratio, donor LVEF>50%, candidate blood type O, and donor weight. Standardized coefficients (which indicate the direction and magnitude of the effect) and rankings for the 15 most predictive characteristics are shown in Table 3A and for all characteristics can be seen in Supplemental Table 2A. Note that negative coefficients indicate that the offer was less likely to be accepted, while positive coefficients indicate that the offer was more likely to be accepted. For example, heart offers were *less* likely to be accepted for candidates who were waiting longer or if the donors were older, had LVEF < 50%, or if there was a donor/candidate weight mismatch. Conversely, heart offers were *more* likely to be accepted if the candidate had blood type O or if the donor was larger (higher weight and height).

The conditional inference tree analysis indicated that donor age and LVEF were the primary determinants of offer acceptance, followed by the length of time that the candidate was waiting, candidate blood type, and donor height (Supplemental Figure 1).

Organ acceptance

The donor characteristics that were most predictive of donor heart *organ* acceptance were, by ranked order: age, LVEF, height, cause of death, PHS high risk designation, hypertension, blood type, cigarette use, race, BUN, history of myocardial infarction, diabetes, sex, and BMI. Standardized coefficients and rankings for the 15 most predictive donor characteristics are shown in Table 3B and for all donor characteristics can be seen in Supplemental Table 2B. These results show that donor hearts were *more* likely to be accepted if the donor's LVEF was >50%, if the cause of death was head trauma, or if the donor was blood type O, and were *less* likely to be accepted if the donor was older, had blood type AB, or was Public Health Service (PHS) high risk, for example.

The conditional inference tree analysis (Supplemental Figure 2) indicated that donor age was again the primary determinant of organ acceptance, followed by donor LVEF and donor

height. Donor cause of death and history of hypertension were important, but lesser factors, in organ acceptance decisions.

Organ sequence number

The median organ sequence number of hearts accepted for transplantation was 3 (IQR 1-10). Figure 4 illustrates the variability in median sequence numbers across the US, by transplant centers' donation service areas. The characteristics that were most predictive of the *number of offers* before acceptance of a donor heart were, in order of importance: recipient days waiting, recipient days as status 2, transplant center volume, donor blood type, ischemic time, recipient age, donor age, recipient blood type, donor height, donor BMI, donor cause of death, and donor race. Standardized coefficients and rankings for the 15 most predictive characteristics are shown in Table 3C, and for all characteristics can be seen in Supplemental Table 2C. Negative coefficients indicate that fewer offers were made prior to heart acceptance (lower sequence number), while positive coefficients indicate that more offers were made prior to acceptance (higher sequence number). These results indicate that high volume transplant centers had higher sequence numbers. This is most likely due to the fact that high volume centers were more likely to accept hearts that were turned down by other centers; however, there may be other reasons for this finding, including the possibility that high volume centers were turning down offers for the first candidate on their waitlist in favor of candidates who were lower down on their list. Blood type O donors also had higher sequence numbers (hearts were likely to be accepted after more offers), while sequence numbers were lower (hearts were likely to be accepted after fewer offers) if the candidate had been waiting longer, if the candidate had blood type AB, or if the donor was taller.

The conditional inference tree analysis (Supplemental Figure 3) indicated that transplant center volume was the primary determinant of the organ sequence number. Ischemic time, donor age, and donor cause of death were also important contributing factors.

Variation across transplant centers

The donor and candidate characteristics that varied most among transplant centers with respect to offer acceptance, organ acceptance, and organ sequence number are summarized in Supplemental Figures 4–6.

Among the characteristics that were most predictive of offer acceptance, organ acceptance, and organ sequence number, transplant centers varied the most in how they weighed donor age and height in the decision process (Figure 5). Those characteristics that were most predictive of organ acceptance and organ sequence number but were inconsistently treated across centers were donor race and donor cause of death. Candidate characteristics highly predictive of offer acceptance and organ sequence number but inconsistently treated across centers were days waiting as status 2, while for offer acceptance the greatest inconsistency across centers was related to candidate days on the waiting list.

Mortality

A total of 15,042 recipients were included in the 30 day mortality analysis and 12,979 recipients were included in the 1 year mortality analysis. In total, these transplants occurred

across 145 centers. Two hundred two recipients died and 31 were re-transplanted (1.5%) within 30 days, while 1,862 died and 37 were re-transplanted (14.6%) within one year.

Tables 3D and 3E list the 15 donor and candidate characteristics most predictive of mortality or re-transplantation within 30 days and one year, respectively, after adjusting for access to transplantation. The standardized coefficients and rankings for all characteristics are provided in Supplemental Tables 3A and 3B. Note that positive coefficients indicate an increased risk of mortality.

Transplant center donor heart acceptance practices and recipient mortality

Factors predictive of both 30 day and 1 year mortality, after adjusting for access to transplantation, are shown in Figures 6A and 6B. The characteristics that were most predictive of both 30-day and 1-year mortality or retransplantation were ischemic time, recipient cigarette use, donor cocaine use, recipient race, recipient diabetes, donor hypertension, transplant center volume, and recipient hypertension.

The characteristics that were most predictive of recipient death or retransplant within 30 days but did not predict one year mortality were recipient height, recipient prior cardiac surgery, donor PHS high risk designation, donor last serum sodium value, donor blood type, and recipient weight. The strength and direction of association are shown in Figure 6A. Thirty six percent of patients who died or were retransplanted within 30 days were from low volume centers, compared to 26% who were from high volume centers.

Characteristics most predictive of death or retransplant within 1 year, but were not predictive of mortality or retransplantation within 30 days, were recipient days at Status 1B, donor race, donor diabetes, recipient sex, donor cause of death, donor creatinine, and recipient hypertension. The strength and direction of association are shown in Figure 6B. Notably, the difference in mortality by center volume was not explained by transplant access rates.

Transplant centers demonstrated great variability with regards to the following candidate and donor characteristics that *were highly predictive of recipient post-transplant mortality*: candidate days at status 1B, ischemic time, donor blood type, donor cause of death, and donor race.

Transplant center practices were also highly variable with respect to other characteristics that *were not predictive of recipient post-transplant mortality*: candidate total days spent waiting, candidate days at status 1A or status 2; and donor age, height, BUN, and LVEF. These final results identify key opportunities to safely expand acceptance of available donor hearts (Figure 5).

DISCUSSION

Much of the recent discussion surrounding the processes by which hearts are distributed for transplantation in the US has focused on allocation policies that determine the order in which offers are made to candidates on the waiting list. Indeed, the US heart allocation system was extensively reviewed and a revised allocation system was implemented in October 2018.(20, 21) Comparatively little attention, however, has been paid to assessing

whether donor heart offers are accepted in an efficient manner that best serves the needs of the growing number of patients on the waiting list. Low organ and offer acceptance leads to inefficiency, longer waiting times (and subsequent higher candidate mortality), and underutilization of available organs. As shown previously by Wey et. al, donor heart offer acceptance practices contribute significantly to program-level variability in the probability of waitlist mortality.(22)

Various reasons for low heart acceptance rates have been proposed, including expectations of poor post-transplant survival based upon perceived donor risk factors, anticipated interactions between donor and recipient characteristics, and a reluctance to accept a “high risk” donor heart for a clinically stable recipient or a recipient with uncomplicated, durable mechanical circulatory support. A single-center effort to liberalize donor heart acceptance criteria at the University of Washington, however, led to an increase in use of available donor hearts within the region from 46% to 75%, with an accompanying decrease in waitlist mortality from 17% to 12%, while maintaining 90% recipient 1-year survival.(23)

Although the effects of individual donor and candidate characteristics on recipient post-transplant survival have been well studied, we sought to advance the field by analyzing the complex relationship between donor and candidate characteristics in combination, to better understand which characteristics are viewed inconsistently across centers during donor heart acceptance decisions. In other words, we hypothesized that variation in acceptance practices, beyond that which can be explained by isolated donor and recipient characteristics, exists among transplant centers. We hope that our efforts will help standardize (and thereby improve) donor heart acceptance.

The likelihood of donor heart acceptance varied greatly among transplant centers and across the US. This variation in sequence numbers (as shown in Figure 4) reflects differential organ availability across regions of the country, differential willingness to accept organs that are perceived to be “high risk”, and differential transplant center waiting list sizes, clinical practices, and candidate characteristics.

We found great variation between transplant centers when examining their likelihood of accepting a donor heart, according to donor and candidate characteristics. As shown in Table 3A, the length of time that a candidate spent as status 1B varied the most across centers for *offer* acceptance. This observation may be related to the extended waiting times for stable patients bridged with left ventricular assist device support—a practice that is often center-specific.(24, 25) Donor age, on the other hand, was highly variable between centers when examining *organ* acceptance, reflecting great variability in centers’ willingness to accept older donor hearts. Finally, candidate waiting time, transplant center volume, and ischemic time varied the most across centers in terms of *organ sequence number*. This finding suggests that there is great variability in centers’ willingness to accept less desirable (e.g. higher sequence number) donor hearts for critically ill candidates, especially those with prolonged waiting times.

It is important to recognize that acceptance decisions are made by evaluating donor and candidate characteristics in combination. This decision-making process is illustrated by the results of the decision tree analyses presented in Supplemental Figures 1–3.

The great heterogeneity identified in transplant centers' acceptance practices should help to focus future research efforts. Studies focused on the optimal timing for transplantation, and the trade-offs between donor risk and candidate waiting time should inform these decisions. Similarly, rigorous studies focused on defining acceptable donor and recipient age and size combinations are required, as donor age, height, and BMI were variable across centers with respect to offer acceptance, organ acceptance, and organ sequence number. Finally, transplant centers continue to demonstrate variability in their willingness to accept donor hearts with LV dysfunction (EF 50%), despite several recent studies showing that recipients of carefully-selected donors with LV dysfunction have excellent post-transplant outcomes. (26, 27)

A key finding of this study is that acceptance of hearts for transplant based on donor age, BMI, BUN, and LVEF varied greatly between centers, and yet was not predictive of recipient post-transplant mortality. This finding thereby identifies opportunities for centers to safely liberalize their donor heart acceptance practices in order to increase access to transplantation for candidates on their waiting lists.

In summary, this study demonstrated that transplant centers across the US vary greatly with respect to donor heart acceptance practices. Currently, regulatory efforts in transplantation focus on monitoring post-transplant survival, such that centers with lower-than-expected survival may be placed on probation or otherwise penalized. Another approach could be to flag centers with low donor heart acceptance rates. Such data are now available via the SRTR online program-specific reports. Indeed, we observed great variability between centers in access rates for heart transplantation.

This study has several limitations. Our analyses were limited by the availability and quality of data submitted by OPOs and transplant centers to UNOS. While some variables (such as mortality) are mandatory, other variables had missing values and/or quality may have been affected by accuracy of entry by OPO and transplant center personnel. As is seen in the results, "unknown" characteristics were often strongly associated with the outcomes of interest. We cannot determine whether these features were truly unknown, were simply not entered, or if the characteristic was not present. We chose to keep these "unknown" characteristics in order to present our results in the most accurate way possible. As with any study that relies on "turndown" codes for donor heart declines, we relied on the single code entered into DonorNet. In reality, however, the decision to decline a heart is often based on a combination of donor and candidate factors. Moreover, there are unmeasured variables that an experienced clinician incorporates into the evaluation of a potential donor that may not be captured. Certainly, organ acceptance may be influenced by variability in organ donation and recovery, population density, and the number of OPOs and transplant centers within a given region. Organ acceptance may also be influenced by the particular transplant center personnel evaluating the offer, and whether centers use standardized criteria and decision-making tools to guide offer acceptance. In addition, organ offers are based upon the donor

inclusion/exclusion criteria listed by individual transplant centers. While some centers may list very few exclusions, other centers may be more selective and may therefore receive fewer offers. Organ selection may also be influenced by the practices of the local OPO. Transplant centers served by under-performing OPOs may be more likely to accept “marginal” donor organs due to fewer offers. Conversely, transplant centers served by high-performing OPOs may decline donor hearts with elevated perceived risk, due to their expectation of receiving a “better” offer. In addition, there may have been small changes in donor heart acceptance practices after December 2015 that are not captured in this data set.

Finally, a new donor heart allocation system was introduced in the United States in October 2018, which changed the 3-status candidate prioritization system to a more granular 6-status system. The impact of the new allocation system cannot be wholly known from this current analysis; however, we can still conclude that, all other factors remaining the same, the results regarding Status 1A roughly translate to the new Statuses 1-3, the results regarding Status 1B roughly translate to the new Status 4, and the findings related to Status 2 roughly translate to the new Statuses 5-6. While it remains to be seen the extent to which our findings related to Status 1A, 1B, and 2 map to the new allocation system, our central findings about donor heart selection practices and strategies to safely expand donor heart utilization remain unchanged. Despite these limitations, we present the results of rigorous analyses involving a very large sample size in the contemporary transplant era.

CONCLUSIONS

Low donor heart acceptance rates continue to result in allocation inefficiency, inequity in access to transplantation, and the discard of potentially suitable organs in the US. We demonstrated great variability in donor heart acceptance decisions among transplant centers. We identified donor and recipient characteristics associated with offer and organ acceptance, and identified inconsistencies among centers with respect to how these characteristics influenced acceptance decisions. Finally, we demonstrated that several key risk factors that were highly predictive of donor heart non-use (and variability in acceptance across centers) were not associated with increased recipient mortality. These findings may help focus efforts on increasing use of available donor hearts for transplantation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

BMI body mass index

BUN	blood urea nitrogen
LV	left ventricular
LVEF	left ventricular ejection fraction
MAD	median absolute deviation
OPO	organ procurement organization
OPTN	organ procurement and transplantation network
PHS	public health service
PTR	potential transplant recipient
UNOS	United Network for Organ Sharing
US	United States

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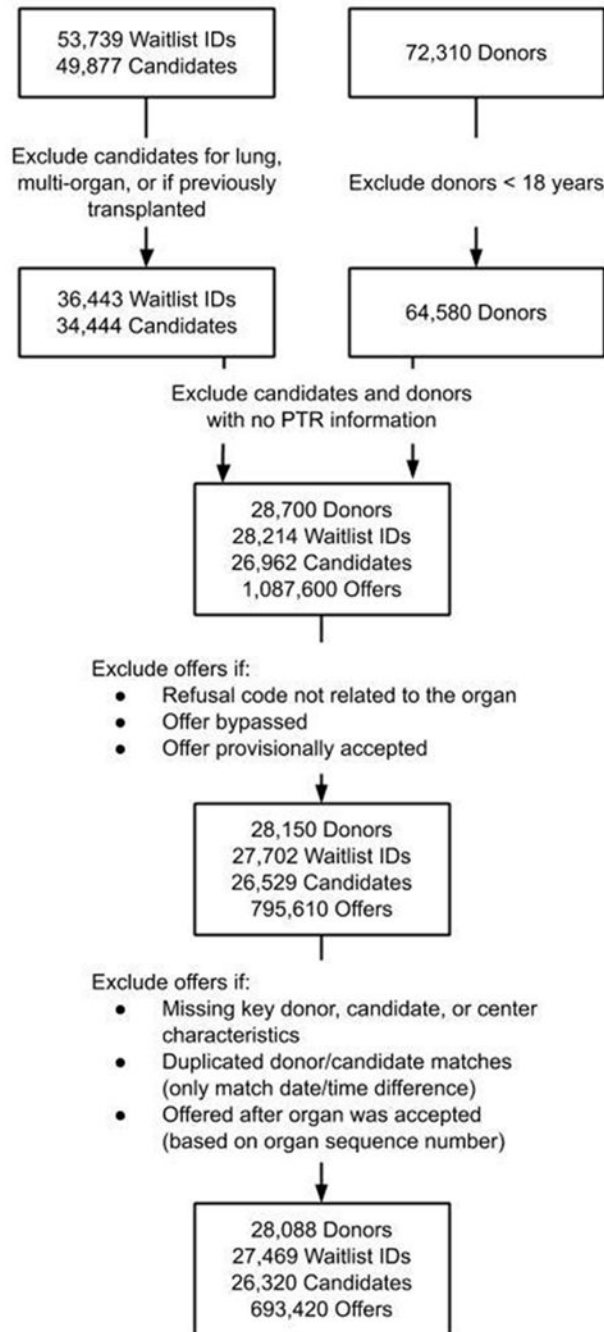


Figure 1: Exclusion criteria for transplant candidates, donors, and donor heart offers from April 2007 to December 2015

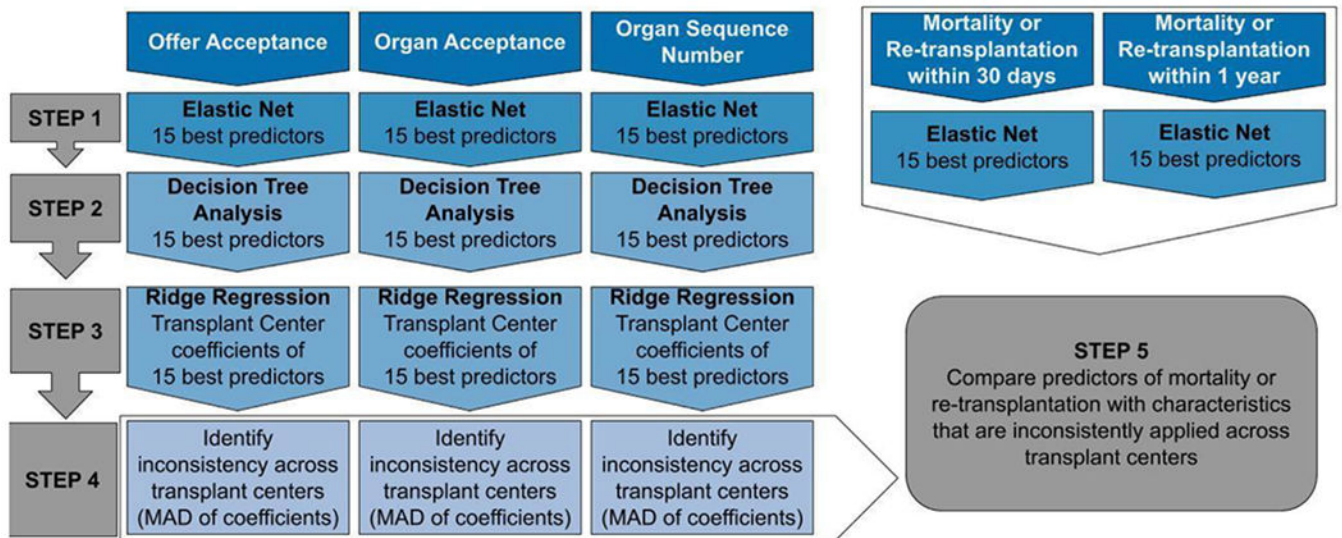


Figure 2:
Overview of statistical analyses performed (MAD: median absolute deviation)

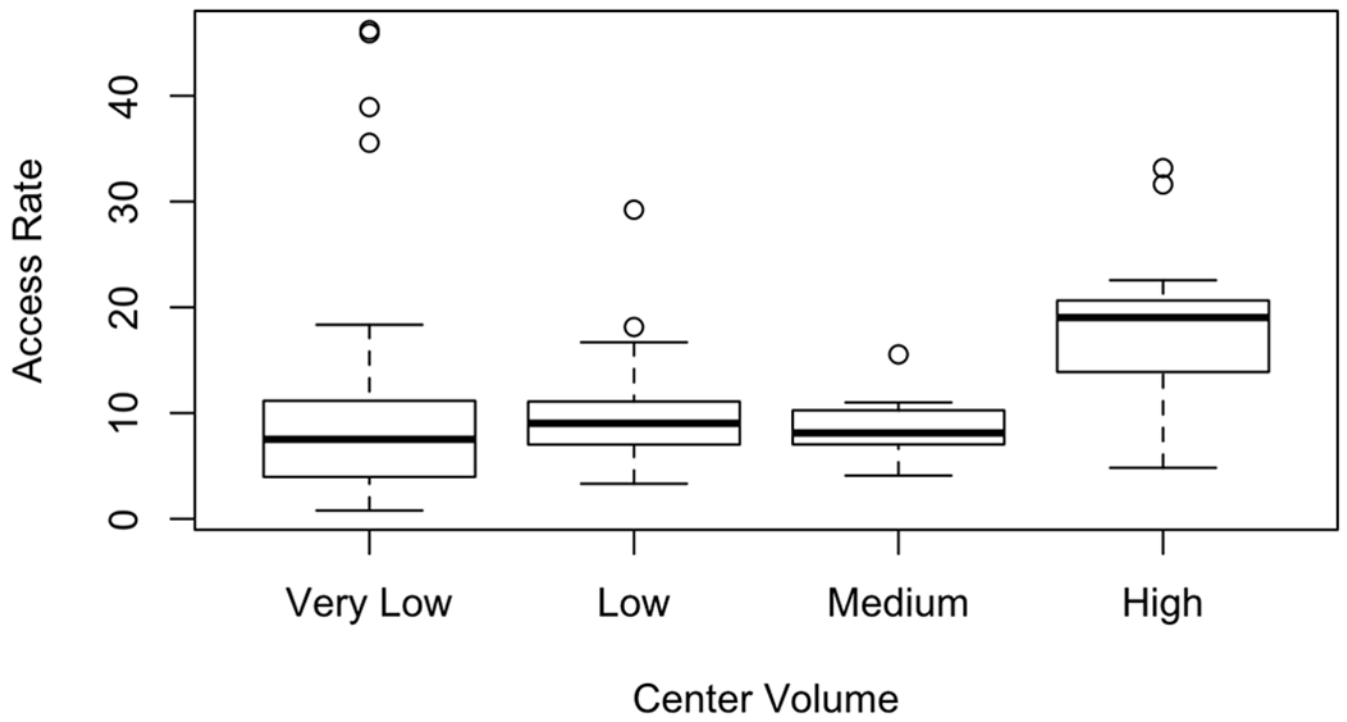


Figure 3: Access rate, by transplant center volume (very low=0-12/year, low=13-21/year, medium=22-33/year, high>33/year)

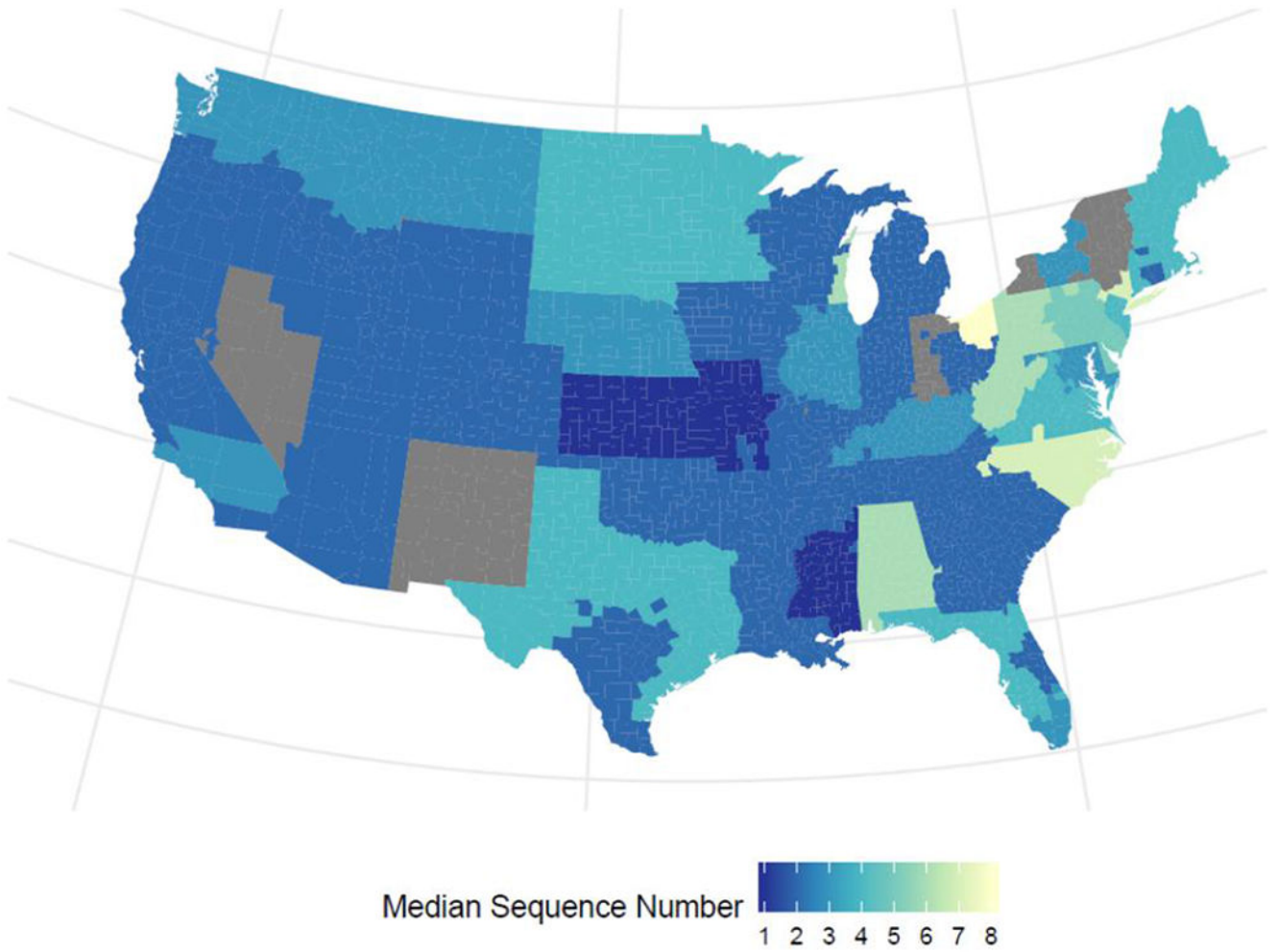


Figure 4: Median organ sequence number, by transplant centers' donation service area. Grey areas indicate areas excluded due to lack of data (see Detailed Methods in the Supplemental Material)

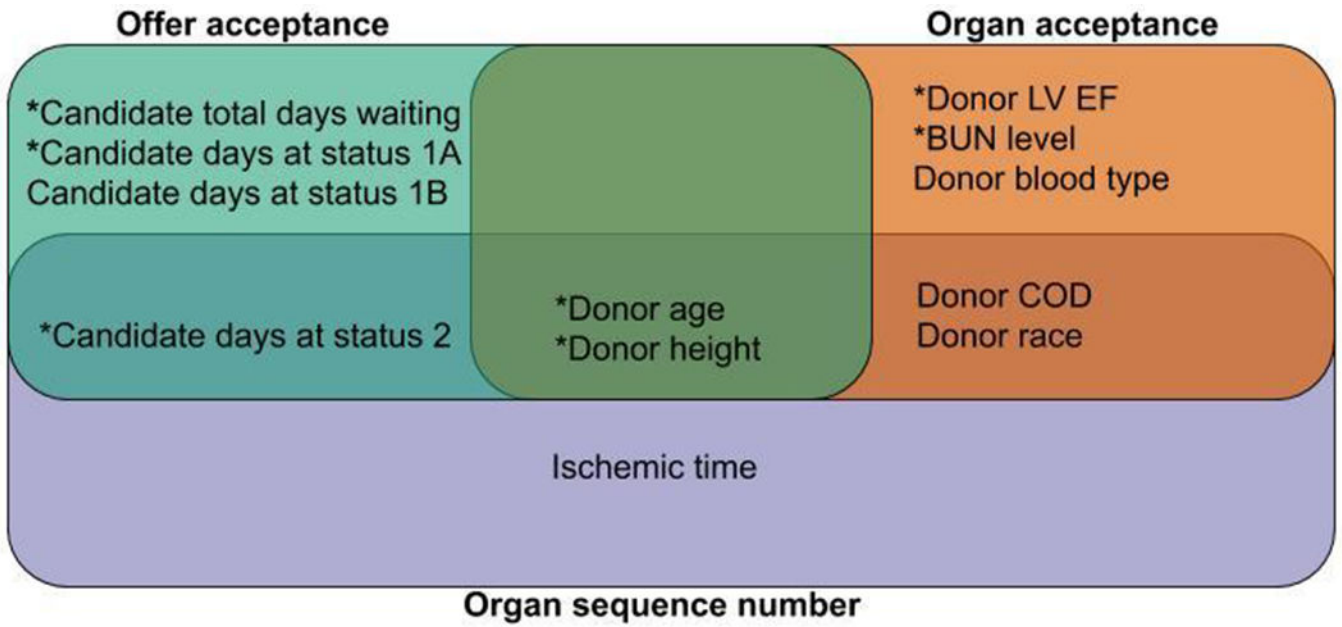


Figure 5: Donor and candidate characteristics that demonstrated the greatest inconsistency between transplant centers, by offer acceptance, organ acceptance, and organ sequence number. Transplant centers were most inconsistent in how they weighed donor age and height in the decision process. Characteristics that were not predictive of recipient post-transplant mortality are highlighted with an asterisk (*) and represent key characteristics that can be targeted to safely increase donor heart utilization. BUN: blood urea nitrogen, LV: left ventricular, EF: ejection fraction, COD; cause of death

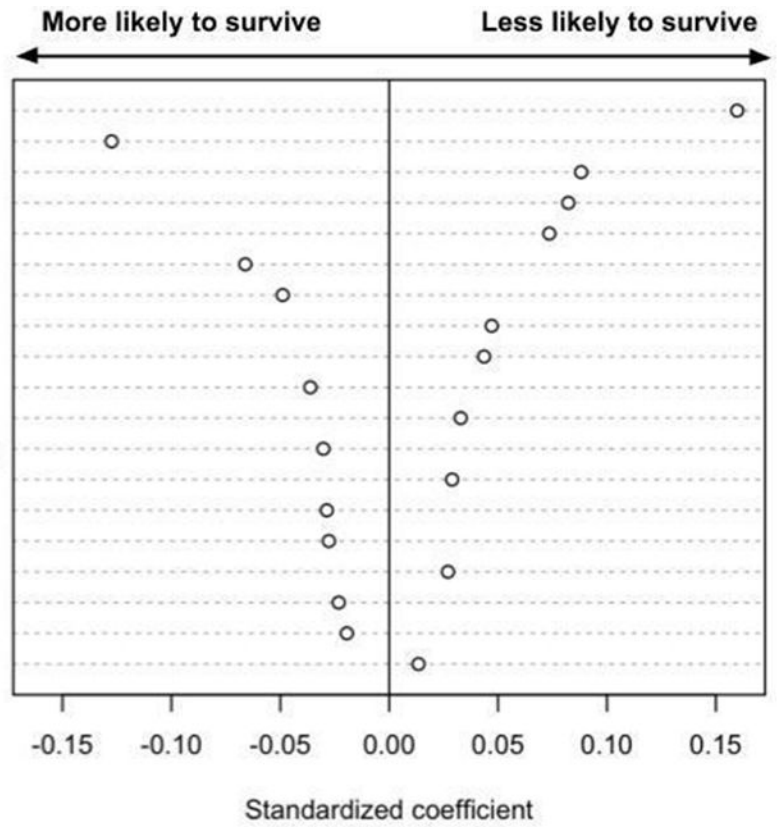
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- Donor ischemic time unknown
- Recipient height
- Recipient unknown cigarette use
- Recipient prior cardiac surgery at listing
- Donor history of cocaine use
- Donor ischemic time < 4 hours
- Donor did not have PHS risk factors
- Recipient race Asian
- Recipient race Multiracial
- Donor unknown history of cocaine use
- Recipient unknown history of diabetes
- Recipient no prior cardiac surgery at listing
- Donor had PHS risk factors
- Donor last serum sodium value
- Donor no history of hypertension
- Donor blood type AB
- Recipient weight
- Center volume high
- Donor unknown history of hypertension



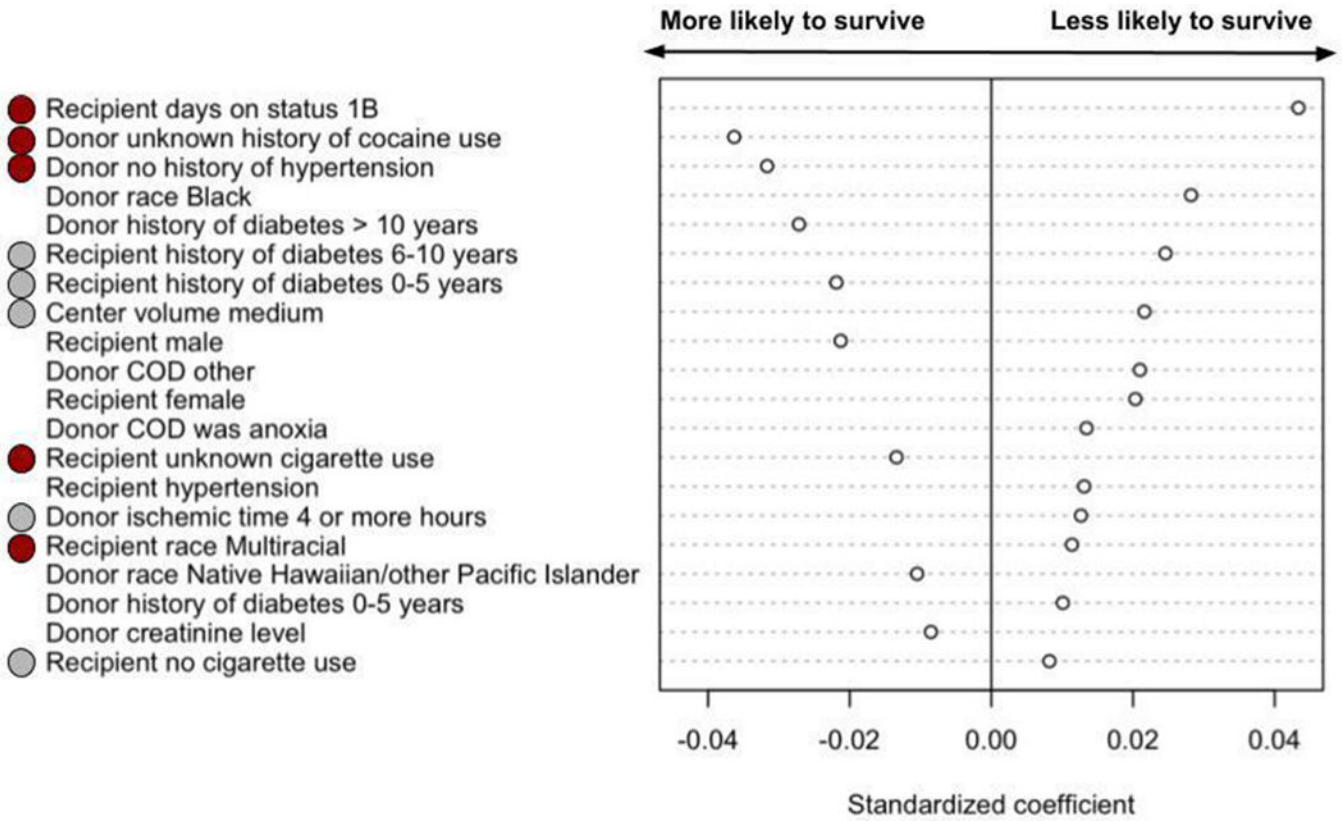


Figure 6:

A: Donor and recipient characteristics most predictive of mortality or re-transplantation within 30 days. Red circles indicate that the characteristic (e.g. race) and the category (e.g. multiracial) were predictive of *both* 30-day and 1-year mortality or re-transplantation. Grey circles indicate that the characteristic is predictive of both 30-day and 1-year mortality or re-transplantation, but not the category (for example, transplant center volume is associated with both 30-day and 1-year mortality or re-transplantation, but high volume is associated with 30-day mortality and medium volume is associated with 1-year mortality).

B: Donor and recipient characteristics most predictive of mortality or re-transplantation within 1 year. Red circles indicate that the characteristic (e.g. race) and the category (e.g. multiracial) were predictive of *both* 30-day and 1-year mortality or re-transplantation. Grey circles indicate that the characteristic is predictive of both 30-day and 1-year mortality or re-transplantation, but not the category (for example, transplant center volume is associated with both 30-day and 1-year mortality or re-transplantation, but high volume is associated with 30-day mortality and medium volume is associated with 1-year mortality).

Table 1.

Candidate characteristics

Candidate characteristics	Overall	Not transplanted	Transplanted
N	26320	9706 (36.9)	16614 (63.1)
Waitlist organ = Heart only vs Heart-Lung (%)	26180 (99.5)	9566 (98.6)	16614 (100.0)
Male (%)	19425 (73.8)	7230 (74.5)	12195 (73.4)
Blood type (%)			
A	9903 (37.6)	3176 (32.7)	6727 (40.5)
AB	1186 (4.5)	229 (2.4)	957 (5.8)
B	3568 (13.6)	1110 (11.4)	2458 (14.8)
O	11663 (44.3)	5191 (53.5)	6472 (39.0)
Diabetes (%)			
None	19036 (72.3)	6776 (69.8)	12260 (73.8)
History of diabetes 0-5 years	559 (2.1)	208 (2.1)	351 (2.1)
History of diabetes 6-10 years	6171 (23.4)	2455 (25.3)	3716 (22.4)
History of diabetes > 10 years	62 (0.2)	31 (0.3)	31 (0.2)
History of diabetes unknown years	382 (1.5)	176 (1.8)	206 (1.2)
Unknown history of diabetes	110 (0.4)	60 (0.6)	50 (0.3)
History of cigarette use (%)			
Unknown	237 (0.9)	165 (1.7)	72 (0.4)
No	14035 (53.3)	4988 (51.4)	9047 (54.5)
Yes	12048 (45.8)	4553 (46.9)	7495 (45.1)
Prior cardiac surgery at listing (%)			
No	14761 (56.1)	5397 (55.6)	9364 (56.4)
Unknown	1567 (6.0)	474 (4.9)	1093 (6.6)
Yes	9992 (38.0)	3835 (39.5)	6157 (37.1)
Days as status 1A (median [IQR])	7.00 [0.00, 31.00]	0.00 [0.00, 25.00]	12.00 [0.00, 33.00]
Days as status 1B (median [IQR])	21.00 [0.00, 130.00]	29.00 [0.00, 210.00]	19.00 [0.00, 98.00]
Days as status 2 (median [IQR])	0.00 [0.00, 60.00]	1.00 [0.00, 247.00]	0.00 [0.00, 13.00]
Total days on waiting list (median [IQR])	154.00 [43.00, 423.00]	357.00 [139.00, 771.75]	90.00 [27.00, 247.00]
Age at listing (median [IQR])	54.00 [43.00, 62.00]	54.00 [44.00, 62.00]	54.00 [43.00, 62.00]
Race (%)			
White	17412 (66.2)	6344 (65.4)	11068 (66.6)
Black	5693 (21.6)	2286 (23.6)	3407 (20.5)
Hispanic	2130 (8.1)	762 (7.9)	1368 (8.2)
Asian	768 (2.9)	212 (2.2)	556 (3.3)
Native American/Alaska Native	87 (0.3)	35 (0.4)	52 (0.3)
Native Hawaiian/other Pacific Islander	81 (0.3)	23 (0.2)	58 (0.3)
Multiracial	149 (0.6)	44 (0.5)	105 (0.6)
Height (in cm) at removal/current time (median [IQR])	175.00 [167.60, 180.30]	175.30 [167.60, 182.90]	172.70 [165.10, 180.30]

Candidate characteristics	Overall	Not transplanted	Transplanted
Weight (in kg) at removal/current time (median [IQR])	82.10 [69.00, 95.30]	85.70 [72.60, 99.80]	80.30 [67.60, 93.00]
BMI at removal/current time (median [IQR])	27.10 [23.60, 30.80]	28.10 [24.40, 32.00]	26.50 [23.10, 30.20]
Hypertension (%)			
No	16611 (63.1)	6046 (62.3)	10565 (63.6)
Unknown	3662 (13.9)	1326 (13.7)	2336 (14.1)
Yes	6047 (23.0)	2334 (24.0)	3713 (22.3)

BMI: body mass index; IQR: interquartile range

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Table 2:

Donor characteristics

Donor characteristic	Overall	Not transplanted	Transplanted
N	28083	12403 (44.2)	15680 (55.8)
Number of offers (median [IQR])	9.00 [2.00, 31.00]	26.00 [10.00, 59.00]	3.00 [1.00, 10.00]
BMI (median [IQR])	26.56 [23.37, 30.68]	26.79 [23.40, 31.39]	26.35 [23.33, 30.17]
Age in years (median [IQR])	36.00 [25.00, 47.00]	44.00 [32.00, 52.00]	31.00 [23.00, 42.00]
Height in cm (median [IQR])	172.70 [165.10, 180.00]	170.00 [162.60, 177.80]	175.00 [167.60, 182.00]
Weight in kg (median [IQR])	80.00 [68.30, 93.00]	78.30 [66.55, 92.40]	80.35 [70.00, 93.00]
Serum sodium (median [IQR])	148.00 [142.00, 154.00]	148.00 [142.00, 153.00]	148.00 [142.00, 154.00]
BUN (median [IQR])	15.00 [10.00, 23.00]	16.00 [11.00, 24.00]	14.00 [10.00, 22.00]
Creatinine (median [IQR])	1.00 [0.80, 1.40]	1.00 [0.80, 1.50]	1.00 [0.80, 1.40]
Total bilirubin (median [IQR])	0.70 [0.50, 1.10]	0.70 [0.40, 1.10]	0.70 [0.50, 1.20]
Male (%)	17470 (62.2)	6414 (51.7)	11056 (70.5)
Cause of death (%)			
Anoxia	6482 (23.1)	3156 (25.4)	3326 (21.2)
Other	658 (2.3)	307 (2.5)	351 (2.2)
Cerebrovascular/stroke	8804 (31.3)	5302 (42.7)	3502 (22.3)
Head trauma	11951 (42.6)	3551 (28.6)	8400 (53.6)
CNS tumor	188 (0.7)	87 (0.7)	101 (0.6)
Race (%)			
White	18136 (64.6)	8053 (64.9)	10083 (64.3)
Black	4505 (16.0)	2000 (16.1)	2505 (16.0)
Hispanic	4395 (15.7)	1793 (14.5)	2602 (16.6)
Asian	645 (2.3)	358 (2.9)	287 (1.8)
Native American/Alaska Native	144 (0.5)	61 (0.5)	83 (0.5)
Native Hawaiian/other Pacific Islander	43 (0.2)	23 (0.2)	20 (0.1)
Multiracial	215 (0.8)	115 (0.9)	100 (0.6)
Blood type (%)			
O	13684 (48.7)	5543 (44.7)	8141 (51.9)
A	10073 (35.9)	4564 (36.8)	5509 (35.1)
AB	928 (3.3)	591 (4.8)	337 (2.1)
B	3398 (12.1)	1705 (13.7)	1693 (10.8)
History of cigarette use (%)			
No	22132 (78.8)	8819 (71.1)	13313 (84.9)
Unknown	375 (1.3)	204 (1.6)	171 (1.1)
Yes	5576 (19.9)	3380 (27.3)	2196 (14.0)
Hypertension (%)			
No	20961 (74.6)	7844 (63.2)	13117 (83.7)
Unknown	198 (0.7)	107 (0.9)	91 (0.6)

Donor characteristic	Overall	Not transplanted	Transplanted
Yes	6924 (24.7)	4452 (35.9)	2472 (15.8)
Diabetes (%)			
None	26093 (92.9)	11047 (89.1)	15046 (96.0)
History of diabetes 0-5 years	802 (2.9)	505 (4.1)	297 (1.9)
History of diabetes 6-10 years	341 (1.2)	250 (2.0)	91 (0.6)
History of diabetes > 10 years	501 (1.8)	367 (3.0)	134 (0.9)
History of diabetes unknown years	188 (0.7)	142 (1.1)	46 (0.3)
Unknown history of diabetes	158 (0.6)	92 (0.7)	66 (0.4)
Cocaine use (%)			
No	22634 (80.6)	9821 (79.2)	12813 (81.7)
Unknown	611 (2.2)	281 (2.3)	330 (2.1)
Yes	4838 (17.2)	2301 (18.6)	2537 (16.2)
History of myocardial infarction (%)			
No	27612 (98.3)	12079 (97.4)	15533 (99.1)
Unknown	276 (1.0)	185 (1.5)	91 (0.6)
Yes	195 (0.7)	139 (1.1)	56 (0.4)
Pre-recovery steroids (%)			
No	7030 (25.0)	3164 (25.5)	3866 (24.7)
Unknown	34 (0.1)	21 (0.2)	13 (0.1)
Yes	21019 (74.8)	9218 (74.3)	11801 (75.3)
Pre-recovery thyroxine-T4 (%)			
No	7377 (26.3)	3269 (26.4)	4108 (26.2)
Unknown	20 (0.1)	11 (0.1)	9 (0.1)
Yes	20686 (73.7)	9123 (73.6)	11563 (73.7)
Public Health Service high risk (%)			
No	23786 (84.7)	10370 (83.6)	13416 (85.6)
Unknown	50 (0.2)	23 (0.2)	27 (0.2)
Yes	4247 (15.1)	2010 (16.2)	2237 (14.3)
History of heavy alcohol use (2+ drinks/day) (%)			
No	22534 (80.2)	9719 (78.4)	12815 (81.7)
Unknown	488 (1.7)	215 (1.7)	273 (1.7)
Yes	5061 (18.0)	2469 (19.9)	2592 (16.5)
Left ventricular ejection fraction (%)			
> 50	24397 (86.9)	9706 (78.3)	14691 (93.7)
50 or less	3374 (12.0)	2410 (19.4)	964 (6.1)
Unknown	312 (1.1)	287 (2.3)	25 (0.2)
Donor/Recipient weight ratio (median [IQR])	-	-	0.99 [0.87, 1.16]
Donor/Recipient weight mismatch (%)	-	-	348 (2.2)
Donor/Recipient identical blood type (%)	-	-	13330 (85.0)

Donor characteristic	Overall	Not transplanted	Transplanted
Donor/Recipient sex mismatch (%)	-	-	3969 (25.3)
Cold ischemic time (%)			
4 or more hours	-	-	3355 (21.4)
< 4 hours	-	-	11960 (76.3)
Unknown	-	-	365 (2.3)

BMI: body mass index, BUN: blood urea nitrogen, CNS: central nervous system; IQR: interquartile range

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Table 3A:Top 15 characteristics most predictive of *offer* acceptance

Characteristic	Standardized Coefficient	Rank (importance)
Candidate days waiting	-1.130	1
Candidate days on status 1B	-1.065	2
Donor age	-0.785	3
Candidate days on status 2	-0.606	4
Candidate days on status 1A	-0.501	5
Candidate BMI	-0.386	6
Donor/Candidate weight ratio	-0.359	7
Donor LV EF		8
>50%	0.341	
50%	-0.270	
Unknown	-0.061	
Candidate blood type		9
O	0.330	
A	-0.164	
AB	-0.124	
B	0.000	
Donor weight	0.327	10
Candidate cigarette use		11
Yes	-0.005	
No	0.000	
Unknown	0.312	
Candidate weight	0.293	12
Candidate height	-0.290	13
Candidate/Donor weight mismatch	-0.275	14
Donor height	0.260	15

LV: left ventricular, EF: ejection fraction, BMI: body mass index

Table 3B:Top 15 characteristics most predictive of *organ* acceptance

Characteristic	Standardized Coefficient	Rank (importance)
Donor age	-0.710	1
Donor LV EF		2
> 50%	0.588	
50%	0.000	
Unknown	-0.108	
Donor height	0.262	3
Donor cause of death		4
Head trauma	0.179	
Anoxia	-0.018	
Other	-0.006	
Cerebrovascular/stroke	0.000	
CNS tumor	0.005	
Donor PHS risk factors		5
Yes	-0.166	
No	0.000	
Unknown	0.000	
Donor hypertension		6
Yes	-0.166	
No	0.010	
Unknown	0.000	
Donor blood type		7
O	0.139	
A	0.000	
AB	-0.161	
B	-0.071	
Donor history of cigarette use		8
Yes	-0.103	
No	0.022	
Unknown	0.000	
Donor race		9
Multiracial	-0.087	
White	0.012	
Native Hawaiian/Pacific Islander	-0.024	
Asian	-0.014	
Native American/Alaska Native	-0.009	
Black	-0.010	
Hispanic	0.000	

Characteristic	Standardized Coefficient	Rank (importance)
Donor BUN	-0.071	10
Donor history of MI		11
Yes	-0.003	
No	0.066	
Unknown	0.000	
Donor history of diabetes		12
Yes, > 10 years	-0.065	
Yes, 6-10 years	-0.057	
Yes, 0-5 years	0.000	
Yes, unknown years	-0.029	
Unknown	0.030	
No	0.061	
Donor sex		13
Male	0.062	
Female	-0.044	
Donor BMI	0.054	14
Donor total bilirubin	-0.033	15

LV: left ventricular, EF: ejection fraction, MI: myocardial infarction, CNS: central nervous system; BUN: blood urea nitrogen, PHS: public health service; BMI: body mass index

Table 3C:Top 15 characteristics most predictive of *organ sequence number* at acceptance

Characteristic	Standardized Coefficient	Rank (importance)
Recipient days waiting	-0.329	1
Recipient days on status 2	0.316	2
Center volume		3
Very low	0.000	
Low	-0.044	
Medium	-0.002	
High	0.316	
Donor blood type		4
O	0.208	
AB	-0.031	
A	0.000	
B	0.000	
Cold ischemic time		5
4 hours	0.182	
< 4 hours	-0.131	
Unknown	0.000	
Recipient age at listing	0.175	6
Donor age	0.158	7
Recipient blood type		8
O	0.000	
AB	-0.155	
A	0.000	
B	-0.104	
Donor height	-0.137	9
Donor BMI	0.128	10
Donor cause of death		11
Head trauma	-0.127	
CNS tumor	0.045	
Anoxia	0.022	
Cerebrovascular/stroke	0.000	
Other	0.000	
Donor race		12
Hispanic	-0.117	
Asian	-0.030	
White	0.000	
Native Hawaiian/Pacific Islander	-0.010	
Black	0.000	

Characteristic	Standardized Coefficient	Rank (importance)
Multiracial	-0.010	
Native American/Alaska Native	-0.013	
Recipient hypertension		13
Yes	0.000	
No	0.000	
Unknown	-0.113	
Recipient and Donor identical blood type		14
Yes	-0.084	
No	0.070	
Donor cocaine use		15
Yes	0.082	
No	0.000	
Unknown	0.000	

BMI: body mass index; CNS: central nervous system

Table 3D:

Top 15 characteristics most predictive of mortality or re-transplantation within 30 days

Characteristic	Standardized Coefficient	Rank (importance)
Cold ischemic time		1
< 4 hours	-0.066	
4 hours	0.000	
Unknown	0.160	
Recipient height	-0.127	2
Recipient cigarette use		3
Yes	0.000	
No	0.000	
Unknown	0.088	
Recipient prior cardiac surgery		4
Yes	0.082	
No	-0.030	
Unknown	0.000	
Donor cocaine use		5
Yes	0.074	
No	0.000	
Unknown	-0.036	
Donor PHS high risk		6
Yes	0.029	
No	-0.049	
Unknown	0.000	
Recipient race		7
Hispanic	0.000	
Asian	0.047	
White	0.000	
Native Hawaiian/Pacific Islander	0.000	
Black	0.000	
Multiracial	0.044	
Native American/Alaska Native	0.000	
Recipient diabetes		8
Yes, > 10 years	0.000	
Yes, 6-10 years	0.000	
Yes, 0-5 years	0.000	
Yes, unknown years	0.000	
No	0.000	
Unknown	0.033	
Donor last serum sodium	-0.029	9

Characteristic	Standardized Coefficient	Rank (importance)
Donor hypertension		10
Yes	0.000	
No	-0.028	
Unknown	0.013	
Donor blood type		11
O	0.000	
AB	0.027	
A	0.000	
B	0.000	
Recipient weight	-0.023	12
Center volume		13
Very low	0.000	
Low	0.000	
Medium	0.000	
High	-0.019	
Recipient hypertension		14
Yes	0.000	15
No	-0.013	
Unknown	0.000	

PHS: public health service

Table 3E:

Top 15 characteristics most predictive of mortality or re-transplantation within 1 year

Characteristic	Standardized Coefficient	Rank (importance)
Recipient days on status 1B	0.043	1
Donor cocaine use		2
Yes	0.000	
No	0.000	
Unknown	-0.036	
Donor hypertension		3
Yes	0.000	
No	-0.032	
Unknown	0.001	
Donor race		4
Hispanic	0.000	
Asian	0.000	
White	0.000	
Native Hawaiian/Pacific Islander	-0.010	
Black	0.028	
Multiracial	0.000	
Native American/Alaska Native	0.000	
Donor diabetes		5
Yes, > 10 years	-0.027	
Yes, 6-10 years	0.000	
Yes, 0-5 years	0.010	
Yes, un known years	0.000	
No	0.000	
Unknown	0.000	
Recipient diabetes		6
Yes, > 10 years	0.000	
Yes, 6-10 years	0.025	
Yes, 0-5 years	-0.022	
Yes, unknown years	0.000	
No	0.000	
Unknown	0.000	
Center volume		7
Very low	0.000	
Low	0.000	
Medium	0.022	
High	0.000	
Recipient sex		8

Characteristic	Standardized Coefficient	Rank (importance)
Male	-0.021	
Female	0.020	
Donor cause of death		9
Head trauma	0.000	
CNS tumor	0.000	
Anoxia	0.013	
Cerebrovascular/stroke	-0.004	
Other	0.021	
Recipient cigarette use		10
Yes	0.000	
No	0.008	
Unknown	-0.013	
Center access rate	0.013	11
Recipient hypertension		12
Yes	0.013	
No	0.000	
Unknown	0.000	
Cold ischemic time		13
< 4 hours	0.000	
4 hours	0.013	
Unknown	-0.006	
Recipient race		14
Hispanic	0.000	
Asian	0.000	
White	0.000	
Native Hawaiian/Pacific Islander	0.000	
Black	0.000	
Multiracial	0.011	
Native American/Alaska Native	0.000	
Donor creatinine	-0.009	15

CNS: central nervous system