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Disparities in donor heart acceptance between the USA and Europe: clinical implications

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Abstract

Background and Aims Given limited evidence and lack of consensus on donor acceptance for heart transplant (HT), selection practices vary widely across HT centres in the USA. Similar variation likely exists on a broader scale—across countries and HT systems—but remains largely unexplored. This study characterized differences in heart donor populations and selection practices between the USA and Eurotransplant—a consortium of eight European countries—and their implications for system-wide outcomes.

Methods Characteristics of adult reported heart donors and their utilization (the percentage of reported donors accepted for HT) were compared between Eurotransplant ($n = 8714$) and the USA ($n = 60\,882$) from 2010 to 2020. Predictors of donor acceptance were identified using multivariable logistic regression. Additional analyses estimated the impact of achieving Eurotransplant-level utilization in the USA amongst donors of matched quality, using probability of acceptance as a marker of quality.

Results Eurotransplant reported donors were older with more cardiovascular risk factors but with higher utilization than in the USA (70% vs. 44%). Donor age, smoking history, and diabetes mellitus predicted non-acceptance in the USA and, by a lesser magnitude, in Eurotransplant; donor obesity and hypertension predicted non-acceptance in the USA only. Achieving Eurotransplant-level utilization amongst the top 30%–50% of donors (by quality) would produce an additional 506–930 US HTs annually.

Conclusions Eurotransplant countries exhibit more liberal donor heart acceptance practices than the USA. Adopting similar acceptance practices could help alleviate the scarcity of donor hearts and reduce waitlist morbidity in the USA.

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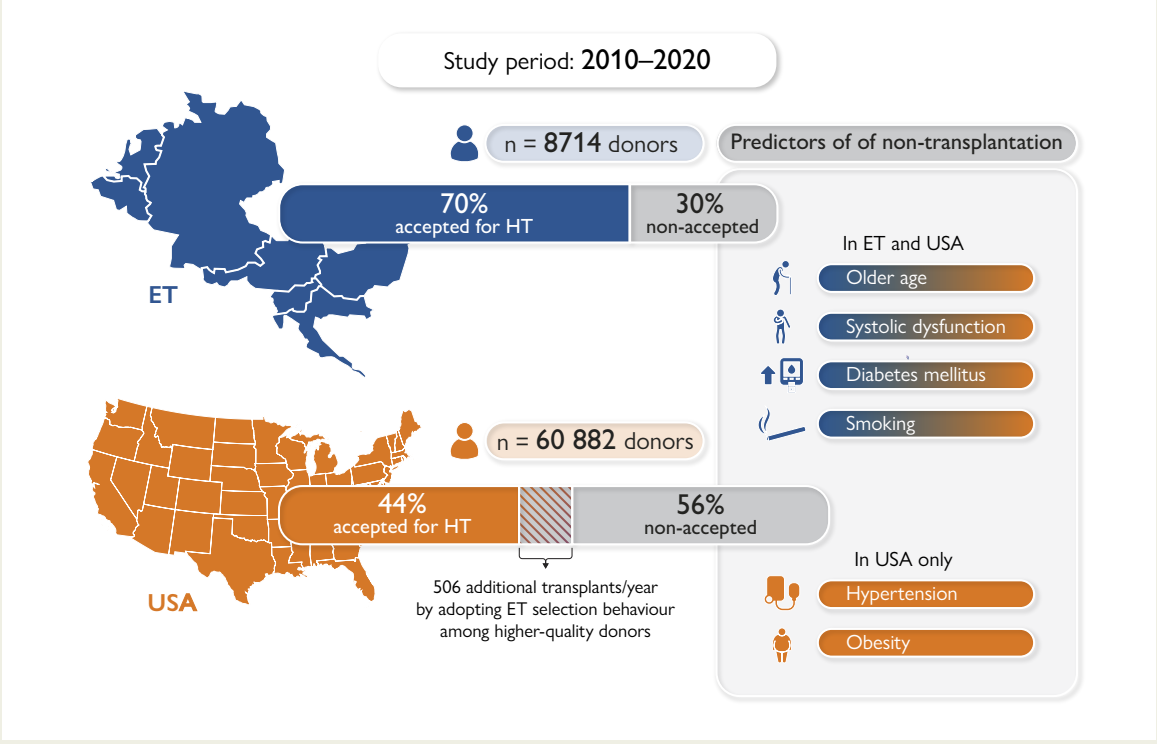
Structured Graphical Abstract

Key Question
How do heart transplant donor populations and selection practices differ between the USA and Eurotransplant, and what are the implications for system-wide outcomes?

Key Finding
Eurotransplant donors were older and had more cardiovascular risk factors than those in the USA. In addition, a greater percentage of Eurotransplant donor candidates were accepted. Achieving Eurotransplant-level utilization among the top 30% of donors would have produced an additional 506 USA heart transplants annually.

Take Home Message
Eurotransplant countries exhibit more liberal donor heart acceptance practices than the USA. Adopting similar acceptance practices could help alleviate the scarcity of donor hearts and reduce waitlist morbidity in the USA.



Eurotransplant countries exhibit more liberal donor heart acceptance practices than the USA. Adopting similar acceptance practices could help alleviate the scarcity of donor hearts in the USA. ET, Eurotransplant; HT, heart transplant.

Keywords Heart transplant • Risk factors • Donor selection • Health policy • Heart failure • Comparative study

Introduction

Heart transplant (HT) remains the treatment of choice for advanced heart failure, with median survival improving over time and now approaching 13 years.[1] Due to the growing population burden of heart failure, combined with a scarcity of donors, hundreds of patients die annually whilst waiting for a transplant in the USA alone.[2] Responses to the donor shortage have included (i) increased use of mechanical circulatory support (MCS), either as a 'bridge to' or in lieu of transplant, and (ii) expansion of the pool of heart donors to include those with older age and other putative risk factors.[3]

Using higher-risk donor hearts for transplant entails a 'trade-off'—the benefit of more transplants done with shorter wait times, with the potential risk of poorer post-transplant outcomes. Exactly which donor risk factors impact post-transplant outcomes remains poorly understood. Observational studies consistently show an association of donor age,[4,5] hypertension,[6,7] smoking,[7–9] and coronary artery disease[10,11] with adverse recipient outcomes such as mortality and graft failure. However, for other donor characteristics such as diabetes mellitus[5,7,12–14] and left ventricular dysfunction,[15–18] the evidence is mixed and even contradictory.

Concern for these potential risks has constrained donor pool expansion in the USA, where both median donor age and donor heart utilization (percentage of potential hearts used for transplant) are in decline; these trends signal increasingly conservative donor heart selection.[12,19] The opposite trends are present in Eurotransplant (ET), a consortium of eight central European countries that share organs for transplant, where

reported donor utilization rates and the median age of those used for HT (44 years, vs. 31 in the USA) are higher and increasing over time.[20,21]

These figures suggest that ET donor heart acceptance practices are more 'liberal' than in the USA; however, this presumption overlooks other possible explanations. For example, if the ET potential donor pool has a lower co-morbidity burden, then using a higher percentage for HT—including those of older age—would be a rational (but not necessarily more liberal) strategy. Differences in donor cause of death—and the much lower prevalence of drug overdose in the ET[22]—could also produce donor pools of disparate age profiles; if so, ET's use of older donors may stem from necessity. A related possibility is that, due to greater experience with donors of older age, ET centres give greater weight to other factors when performing a donor risk assessment.

This study aimed to identify differences in donor heart acceptance practices between the USA and ET. Specifically, we compared the USA and ET in terms of (i) the potential donor pool, by age and other risk factors, (ii) donor heart utilization, before and after adjustment for donor risk, and (iii) donor-level predictors of acceptance for transplant. We then asked: 'What if the USA adopted the same donor utilization practices as ET?' and estimated subsequent increases in USA HT volume that would occur. Together, our analyses can help inform rational donor heart selection practices in the USA, ET, and other transplant systems worldwide.

Methods

Study population and data source

We used data from both (i) the ET registry, which consists of data voluntarily reported by transplant centres within its eight member countries (Austria, Belgium, Croatia, Germany, Hungary, Luxembourg, the Netherlands, and Slovenia), and (ii) the US-based Scientific Registry for Transplant Recipients (SRTR). Our study sample consisted of all adult (age ≥ 18 years) potential heart donors recovered from 1 January 2010 to 31 December 2020 in ET or the USA.

We defined a potential donor in ET as any donor designated as a potential heart donor when reported to the ET registry; being reported to ET as a potential heart donor is a pre-requisite to being offered to centres for potential use for HT. The SRTR data set includes no explicit 'potential heart donor' designation. To construct a comparable sample, we defined a potential donor in the USA as any with both (i) at least one solid organ recovered for transplant and (ii) an echocardiogram performed during donor management. We excluded donation after circulatory death (DCD) donors, because utilization of such donors for HT was in its infancy during the study period and thus felt to be highly non-representative.

The donor utilization rate was calculated as the percentage of potential donors that are used for HT. This calculated rate is sensitive to how a potential donor is defined, which differs by cohort as detailed above. Accordingly, we performed a sensitivity analysis in which we applied a more stringent set of criteria to define a potential donor in the US cohort. These stringent US criteria defined potential heart donors as those meeting the above criteria (i.e. at least one solid organ recovered for transplant, echocardiogram performed) who also had at least one heart offer made to a transplant centre. A visual comparison of how potential donors were defined in the base case and sensitivity analyses is shown in Supplementary data online, *Figure S1*.

For consistency with preferred terminology used within ET, we refer to potential donors defined above as 'reported' donors throughout this manuscript, acknowledging that this includes donors both used and not used for HT.

Donor-level covariates

We limited our analysis to donor characteristics available in both the SRTR and ET registries. We further defined 'high cardiovascular disease (CVD) risk' by the presence of age ≥ 50 years, diabetes mellitus, and/or two or more of the following: (i) age 40–49 years, (ii) hypertension, and (iii) smoking history. 'No CVD risk' was defined by the absence of any of the above characteristics. Along with these CVD risk factors, other donor-level covariates included obesity (defined as body mass index ≥ 30 kg/m^2), history of alcohol abuse, and abnormal left ventricular ejection fraction (LVEF < 50%). Whilst echocardiography results were available for nearly all donors, coronary angiogram findings and reported cause of death were often incomplete and lacked a consistent language or format. Thus, despite their likely clinical importance, neither factor was considered in our analysis.

Whilst a quantified LVEF was consistently available in SRTR, this was not the case in the ET registry. Eurotransplant echocardiography reports were provided in a free text format with a variable level of detail. Thus, for the ET cohort, we employed the following sequential algorithm to define 'abnormal LVEF'.

(1) If LVEF is quantified, designate those with LVEF < 50% as abnormal.
(2) If global contractility or systolic function are described qualitatively, designate those described as 'reduced' (or the equivalent) as abnormal.
(3) If left ventricular regional wall motion is described qualitatively, designate those with hypokinesis or akinesis in two or more myocardial segments and/or the anterior or anterolateral wall as abnormal.
(4) If fractional shortening is quantified, designate those with fractional shortening < 25% as abnormal.

Systolic function was designated as 'missing' when it could not be characterized based on any of the above criteria.

Analyses

The primary outcome in our analysis is donor heart utilization for transplant. We calculated utilization in both ET and the USA over the study period, employing two different definitions for US potential donors as detailed above. We further compared donor utilization by calendar year, individual country within ET, and donor characteristics. Univariate linear regression was used to assess temporal trends in donor utilization and in the annual volumes of potential donors and transplants. The chi-squared test was used to identify donor factors associated with utilization, using $P < .05$ as the threshold for statistical significance.

We performed multivariable logistic regression to estimate the independent associations of donor characteristics with utilization for HT. We accounted for missing donor covariates using multiple imputations, with 50 imputed data sets. We first fit separate models for the US and ET cohorts and present the odds ratios (ORs) from each model. We then fit a model using both cohorts combined, which included a cohort indicator variable (i.e. 'Europe') and interaction terms between cohort and each donor-level covariate.

Subsequent analyses estimated the impact of adopting ET-level utilization on transplant volume in the USA. Our approach is summarized in Supplementary data online, *Figure S2* and detailed as follows. First, the results of the ET-specific logistic regression model were used to estimate the odds of utilization for each potential donor in both the USA and ET—this odds estimate was used as a measure of donor quality. Then, within the ET sample only, potential donors were grouped into deciles of donor quality. The lowest and highest odds of utilization amongst ET donors in each decile were used to define a quality range by decile. Finally, potential donors in the USA were assigned to a decile based on which quality range contained their predicted odds of utilization. This methodology produces equal (10%) proportions of ET donors in each quality decile but unequal proportions of US donors by quality decile.

We then calculated ET-level utilization by quality decile—the percentage of ET donors in each decile that were used for transplant. Multiplying ET-level utilization by the number of US donors in each quality decile produced an estimate of US transplant volume, by quality decile, in the hypothetical scenario wherein the USA adopts ET-level utilization behaviour.

The rationale for this overall approach is to control for differences in quality between the US and ET donor pools.

We felt that a scenario in which the USA adopts ET-level utilization across all quality deciles would be implausible. Instead, we posited scenarios in which the USA adopts ET-level utilization only above a specified threshold of donor quality (e.g. for the top decile, top three deciles, or top five deciles). We then calculated hypothetical transplant volume in the USA, overall and separately by calendar year and quality decile. To provide qualitative context, we identified the specific donor with the median value of quality amongst US donors in each decile; these were labelled the 'median' donor by decile.

Analyses were conducted using SAS version 9.4 and Microsoft Excel 2016. Some of the data reported here have been supplied by the Minneapolis Medical Research Foundation as the contractor for SRTR. The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy of or interpretation by the SRTR or the US government.

Results

Over the entire study period (2010–20), 69.7% ($n = 6076$) of 8714 potential donors in the ET were utilized for transplant. The donor utilization rate was lower in the USA over the same period (44.1%; 26 852 of 60 882 potential donors). As shown in *Figure 1*, the annual number of both potential donors and transplants increased significantly over time in the USA ($P < .001$ for both trends), but neither exhibited a significant temporal trend in ET. Utilization rates increased significantly over the study period in ET (from 67% in 2010 to 76% in 2020; $P = .01$ for trend) and simultaneously decreased in the USA (47%–40%; $P = .002$ for trend). When applying stringent criteria (detailed in Methods) to define potential donors, the calculated US donor utilization rate remained lower than in ET (45.7%; 26 852 of 58 819 potential donors in 2010–20).

The age distribution of both reported donors and those accepted for transplant differed significantly between ET and the USA (*Figure 2A*). Younger donors (aged 18–34 years) comprised 40.2% of reported donors and 59.7% of those used for HT in the USA, but only 22.3% of reported donors and 27.1% of those used for HT in ET. Utilization rates were significantly lower in the USA for every age category. At the highest age range (≥60 years), ET utilized 42.8% ($n = 446$) of 1021 reported donors, whilst only 3.2% ($n = 120$) in this oldest age group were utilized for HT in the USA.

The ET and USA reported donor pools had different risk factor profiles, as shown in *Figure 2B* and further detailed in Supplementary data online, *Table 1*. The prevalence of smoking (46% in ET vs. 20% in USA) and hypertension (41% vs. 31%) were significantly higher amongst ET-reported donors, but obesity (13% in ET vs. 33% in USA) and abnormal LVEF (5% vs. 16%) were less prevalent in ET. Rates of diabetes mellitus (~10%) and alcohol abuse (~20%) were similar in both cohorts. Eurotransplant had a higher prevalence of donors classified as high CVD risk (49% vs. 31% in the USA) and fewer with no CVD risk (16% vs. 31%; as defined in Methods). Utilization rates were consistently higher in ET (vs. USA) when donors were stratified by any of the above characteristics ($P < .01$ for all comparisons).

The distribution of selected risk factors and their overlap amongst donors used for HT are visualized separately by cohort (*Figure 3A* and *B*). Consistent with the above findings, a significantly greater proportion in the USA (60%) were aged < 40 with no risk factors (vs. only 22% in ET). Risk factors overlap to a greater extent in ET (vs. USA). For example, a majority of 40+-year-old donors in the USA

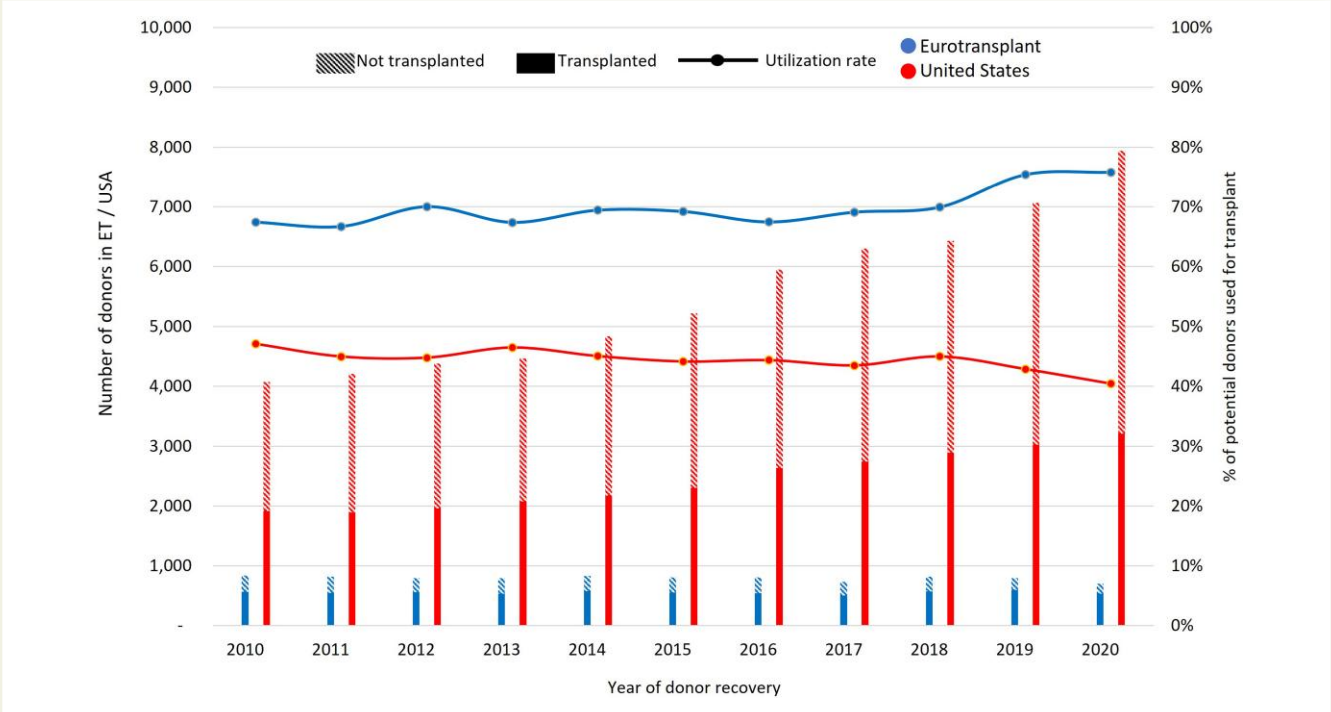


Figure 1 Time trends in donor volume and utilization (2010–20) in Eurotransplant and the USA. Shown are a number of potential donors used for heart transplant (solid bars) and not used for heart transplant (dashed bars), by cohort and year. A different scale (see *y*-axis labels at left) is used for Eurotransplant and USA donor volume to facilitate comparison. Utilization rate by cohort and year (lines) is calculated as (number of donors used for heart transplant/total number of potential donors).

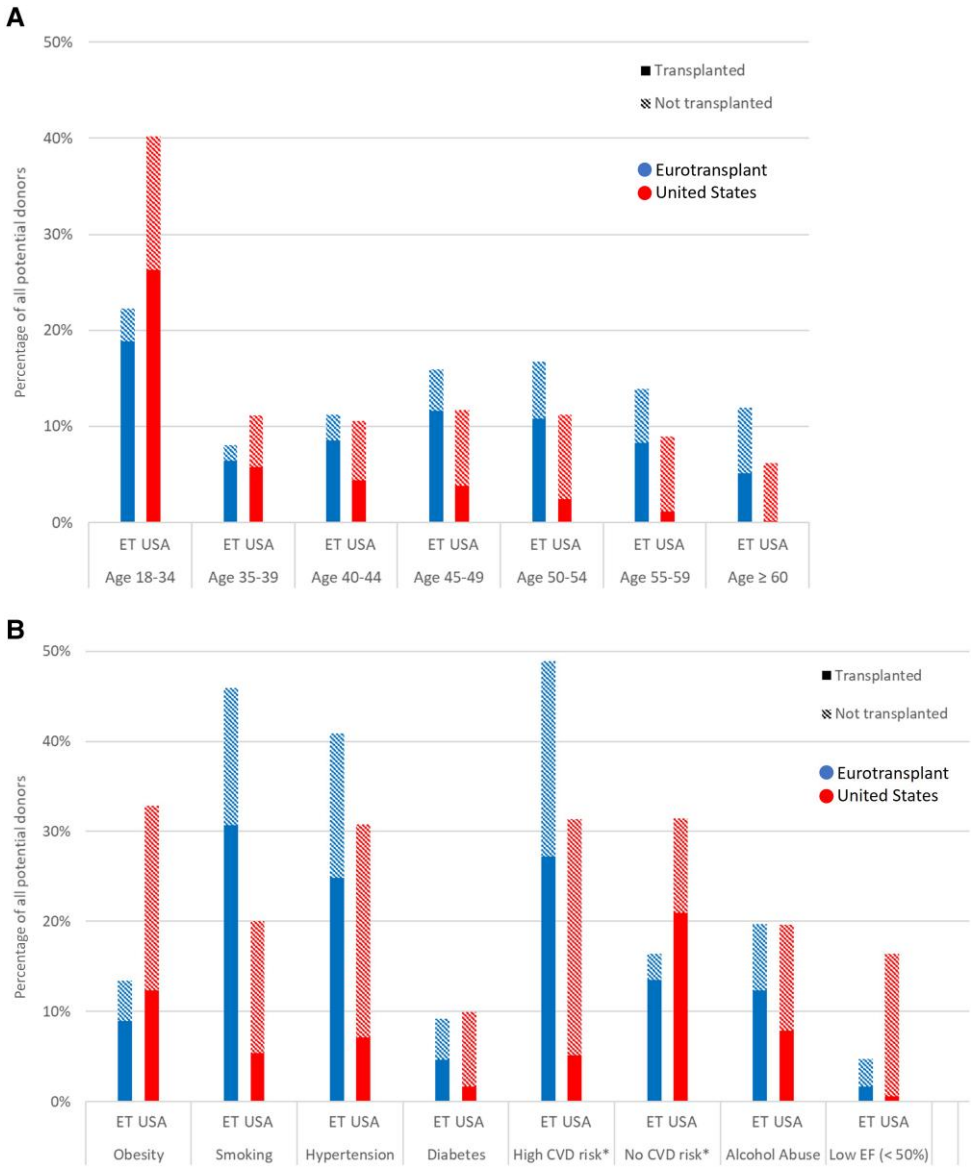


Figure 2 Comparison of (*A*) donor age distribution and (*B*) risk factors amongst potential heart donors in Eurotransplant vs. USA. Shown are number of potential donors used for heart transplant (solid bars) and not used for heart transplant (dashed bars) amongst donors with each listed characteristic. 'High cardiovascular disease risk' refers to the presence of age ≥ 50 years, diabetes mellitus, and/or two or more of the following: (i) age 40–49 years, (ii) hypertension, and (ii) smoking history. 'No cardiovascular disease risk' refers to the absence of any of these characteristics. ET, Eurotransplant.

have no accompanying risk factor; in contrast, most 40+-year-old donors in ET have an accompanying LVEF < 50% and/or other CVD risk factor. When comparing non-transplanted donors in ET vs. USA (*Figure 3C* and *D*), these differences (in the prevalence of risk factors and their overlap) are less pronounced.

Adjusted associations between donor characteristics and utilization —based on separate logistic regression models performed for each cohort—are shown in *Figure 4*. All donor characteristics in the model had either negative or null associations with utilization (i.e. decreased the likelihood of utilization or had no effect). Most donor characteristics had similar direction of effect when comparing utilization between ET and the USA. For example, the seven covariates with the lowest odds ratios were consistent in both ET and the USA; these included blood type AB (with type O as referent group), abnormal LVEF, and five of the age range variables (from 'age 40–44' to 'age ≥ 60'). Other blood type variables, smoking history (OR 0.90 in ET vs. 0.85 in USA; $P < .001$ for both), and alcohol abuse (OR 0.93 vs. 0.98; $P > .05$ for both) had similar effect sizes in both cohorts.

Other characteristics exhibited qualitatively different effects by cohort. Both obesity and hypertension had no effect in ET (OR = 1.01 and 0.99, respectively) but significantly reduced the likelihood of utilization in the USA (OR = 0.86 and 0.72, respectively). Diabetes mellitus (OR 0.90 in ET vs. 0.70 in the USA) and female sex (OR 0.74 vs. 0.62) also reduced the likelihood of utilization to a greater extent in the USA than in ET. Finally, calendar year had a significant positive effect (OR = 1.05 for each 1-year increment) in ET; this indicates that, after adjusting for any changes

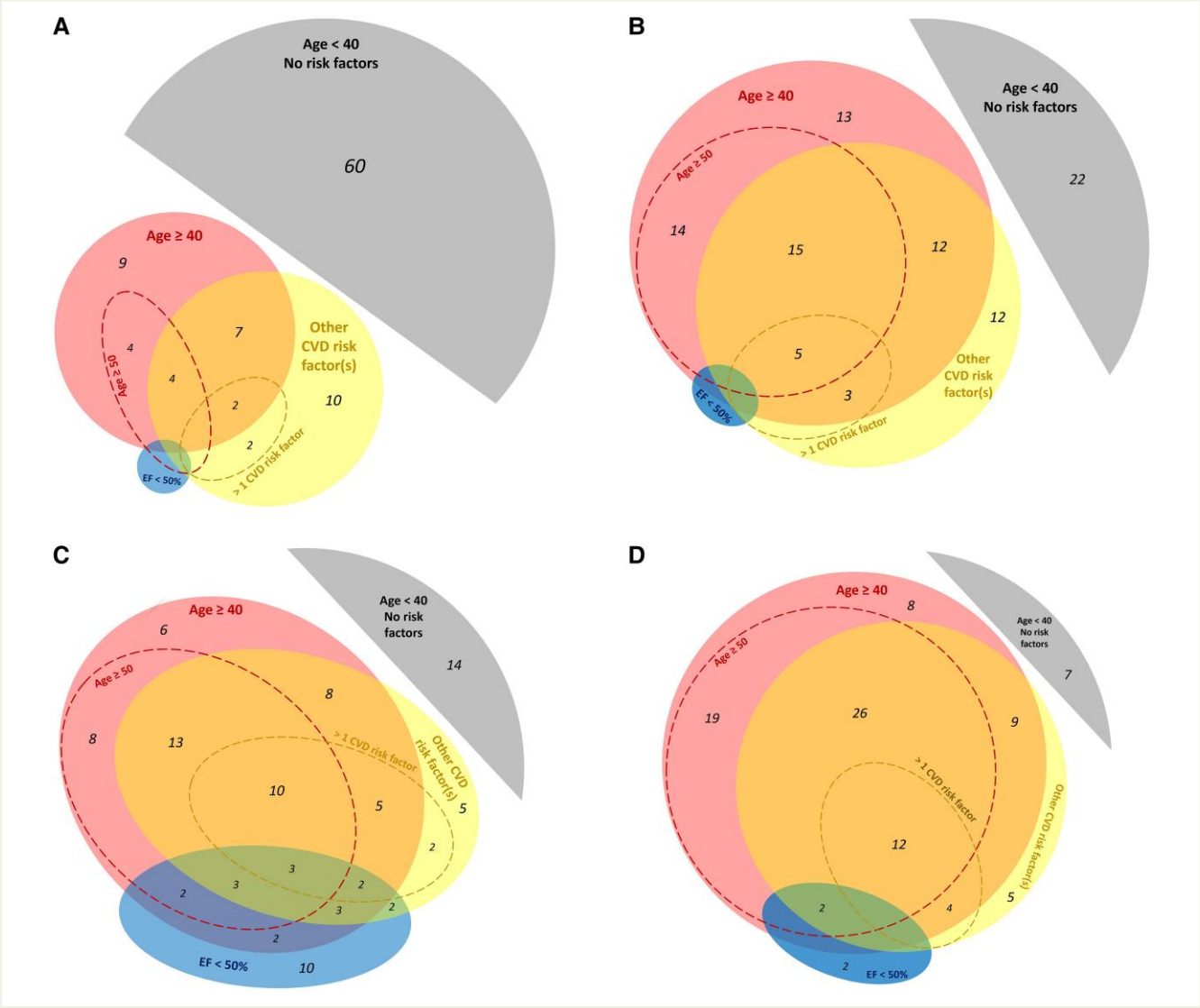


Figure 3 Profile of potential donors, by cohort and use for heart transplant (vs. discard). Potential donor subsets include (*A*) donors used for heart transplant in the USA, (*B*) donors used for heart transplant in Eurotransplant, (*C*) donors not used for heart transplant in the USA, and (*D*) donors not used for heart transplant in Eurotransplant. Numeric labels and the size of each region represent the proportion of donors with a given characteristic (or combination of characteristics). These labels are omitted for regions representing ≤ 1% of donors. 'Other cardiovascular disease risk factors' refer to include hypertension, smoking, and diabetes mellitus. CVD, cardiovascular disease; EF, ejection fraction.

in donor characteristics, ET centres became more likely to utilize a given donor heart for transplant over time. The opposite effect of the calendar year was noted in the US cohort (OR = 0.97), confirming that US centres were increasingly conservative over time. The above differences in covariate effect size by cohort were all statistically significant, as assessed by interaction terms in the 'combined' model (further detailed in Methods with results shown in Supplementary data online, *Table S2*).

Figure 5 shows the average annual number of potential and actual donors, by cohort and quality decile. As detailed in Methods, quality was defined as the predicted odds of utilization for transplant based on the 'Europe-only' multivariable logistic regression model. In both cohorts, utilization consistently increased with each decile increment in donor quality. Utilization was significantly higher in ET than in the USA at all donor quality deciles; this difference in cohorts was most pronounced in the lowest quality decile (36% in ET vs. 1.3% in the USA). Utilization rates converged somewhat with increasing donor quality, and the difference between cohorts was least pronounced amongst donors in the highest quality decile (90% in ET vs. 81% in the USA).

Also shown in *Figure 5* (separately for each donor quality decile) is the hypothetical increase in transplant volume if the USA matched utilization levels seen in ET. For instance, if the USA matched ET-level utilization amongst the top 10% of donors, this would have produced an additional 101 transplants per year (averaged over the entire study period). Matching ET-level utilization amongst the highest three and five deciles of donor quality would have produced 506 and 930 additional US transplants per year, respectively.

Transplant volume by year, in hypothetical scenarios where the USA matched ET-level utilization for varying subsets of potential donors, is shown in *Figure 6*. Matching ET-level utilization for only the top 10% of donors produces a relatively modest increase in US transplant

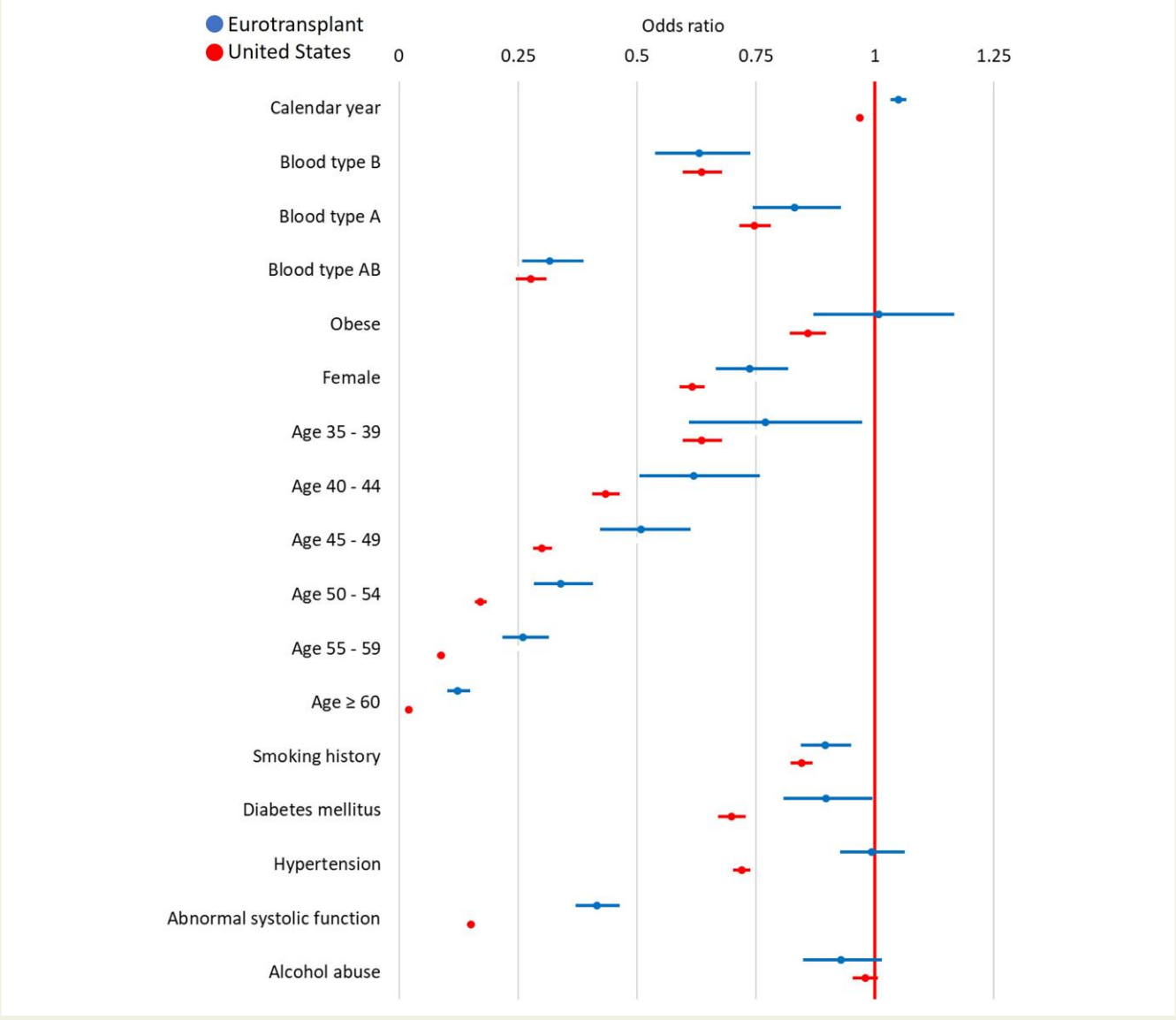


Figure 4 Multivariable associations of donor characteristics with utilization for transplant, in Eurotransplant and the USA. Results are obtained from separate logistic models performed for the Eurotransplant and US cohorts, with use for heart transplant (vs. discard) as the dependent variable.

volume. When this scenario is expanded to include broader subsets of donors (i.e. top 30%, top 50%), there is a progressive increase in estimated US transplant volume. By the end of the study period (2020), estimates of US transplant volume under these 'broader' scenarios match or exceed the number of new HT listings in the same year.

Discussion

Our study is the largest to date comparing HT donor characteristics and selection behaviour across countries or continents and is the first such comparison between the USA and ET. We found that over the past decade, the ET potential donor pool was significantly older with a greater overall cardiovascular risk profile. Eurotransplant has utilized a consistently higher proportion of these reported donors for HT; their higher utilization was evident even after adjusting for donor risk factors. As a result, the vast majority (78%) of ET HTs utilize donors with age ≥ 40 years and/or another cardiovascular risk factor. In contrast, the majority (60%) of transplanted US donors are under 40 years old with no risk factors.

We found that this utilization disparity is partly attributable to the greater weight that US (vs. ET) centres ascribe to certain donor 'risk factors'. Obesity and hypertension, for example, significantly reduced the likelihood of accepting a donor for transplant in the USA—but had no such influence in ET. We show that the system-wide implications of such conservative donor selection in the USA are profound. Under a hypothetical scenario where the USA matched ET-level utilization for just the top 30%–50% of donors (in terms of quality), this would have resulted in an additional 506–930 HTs per year—enough to meet the demand amongst all newly listed candidates in the current era (*Structured Graphical Abstract*).

Given a limited evidence base and lack of consensus guidelines around donor heart selection, the practice variation we observe is not surprising and potentially instructive. It shows that the concept of the 'marginal' donor is a relative one and that the reported 'shortage'

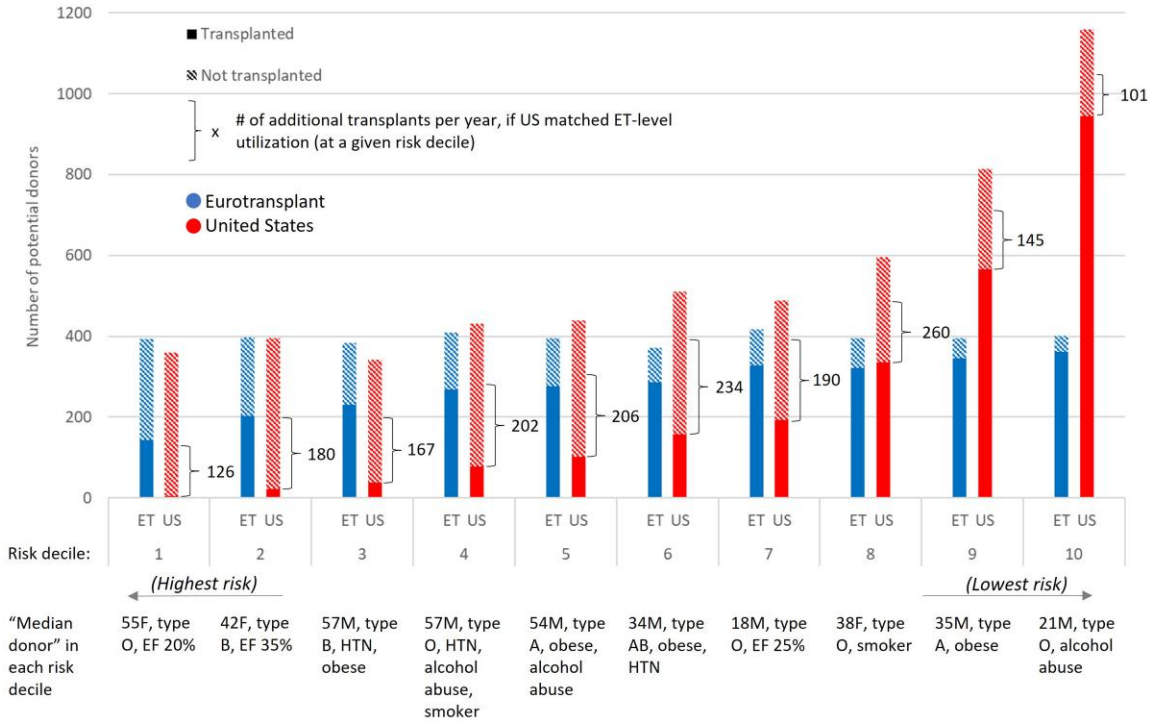


Figure 5 Estimated impact of adopting Eurotransplant-level utilization behaviour on annual heart transplant volume in the USA, by level of donor risk. Shown are a number of potential donors used for heart transplant (solid bars) and not used for heart transplant (dashed bars), by cohort, amongst donors in a given quality decile (as defined in Methods). Adjacent numeric labels (in brackets) denote the estimated number of additional transplants per year in the USA, in the hypothetical scenario where USA adopts ET-level utilization amongst donors in a given quality decile. 'Median donor' refers to the specific donor with the median value of quality amongst US donors in each decile. EF, ejection fraction; ET, Eurotransplant; HT, heart transplant; HTN, hypertension.

of viable heart donors in the USA may be a misnomer.[23] That 'marginal' donors (e.g. those with age > 50 years, ± other risk factors) have been regularly used in ET for over a decade suggesting that this 'ET utilization model' is at least worthy of consideration, alongside other strategies to reduce the 'supply–demand gap' in US heart transplantation. The alternatives—including broader geographic sharing facilitated by *ex vivo* perfusion[24] and the expanded use of DCD,[25] hepatitis C (HCV) positive,[26] and even porcine donors[27]—each carry their own costs and potential risks. The 'ET model' may be a low-tech, less 'exciting' option; but comparing our findings with those of prior DCD- and HCV-related analyses suggests that it would have a much greater system-wide impact at lower economic cost.[25,26]

We suspect that the observed regional disparity in donor utilization at least partly stems from differences in the underlying pool of potential donors. Prior analyses indicate that the devastating opioid epidemic has contributed to an increase in size—and decrease in average age—of the US donor pool.[22] Further studies are needed to characterize the (likely many) other epidemiological, cultural, and policy-driven reasons why the ET donors are older and scarcer. As donor pool composition likely drives donor selection behaviour, we suspect that ET centres might be similarly conservative to US centres if such a large number of younger donors were available to them. In the future, rising demand for HT and policy efforts to reduce drug overdose and other preventable causes of death could increase the scarcity of (particularly younger) donors in the USA. Should this occur, our findings suggest that by adopting the 'ET model', the USA could satisfy the demand for HT without a rise in wait times or waitlist morbidity.

A key question is how these disparities in donor utilization might impact graft survival and other post-transplant outcomes. Observational evidence shows an association between older donor age and lower post-transplant survival,[5] suggesting a downside to the 'ET model'. The degree to which this association is causal remains uncertain. In the absence of randomized trials (likely infeasible), future observational studies comparing post-transplant outcomes in high vs. low utilization settings may help characterize this downside. Critically, any signal towards worse post-transplant outcomes might be outweighed by the benefits of higher donor utilization—in the form of decreased pre-transplant wait times and associated morbidity. These benefits will vary by context and are perhaps most pronounced for sicker candidates facing long wait times but smaller for low-acuity candidates in regions with a relative surplus of donors.

Inevitably, any attempts to weigh the risks (i.e. worse post-transplant outcomes) against the benefits (i.e. decreased pre-transplant morbidity) of a high-utilization strategy will be subject to uncertainty. This uncertainty must be acknowledged but does not justify an exclusive focus on the risks with a disregard of the benefits. Yet the current US regulatory environment—which uses post-transplant survival as the primary metric to rate HT programs—incentivizes such risk aversion in the context of donor selection.[28] In light of these incentives, low donor utilization in the USA could be seen as rational and expected. Even if the 'ET model' was shown to produce net benefit by some holistic metric (e.g. 'post-listing survival'), its adoption in the USA would likely require revision to existing regulatory incentives.

Other practical limitations to applying the 'ET model' in the USA must be acknowledged. First, greater obesity rates could make the

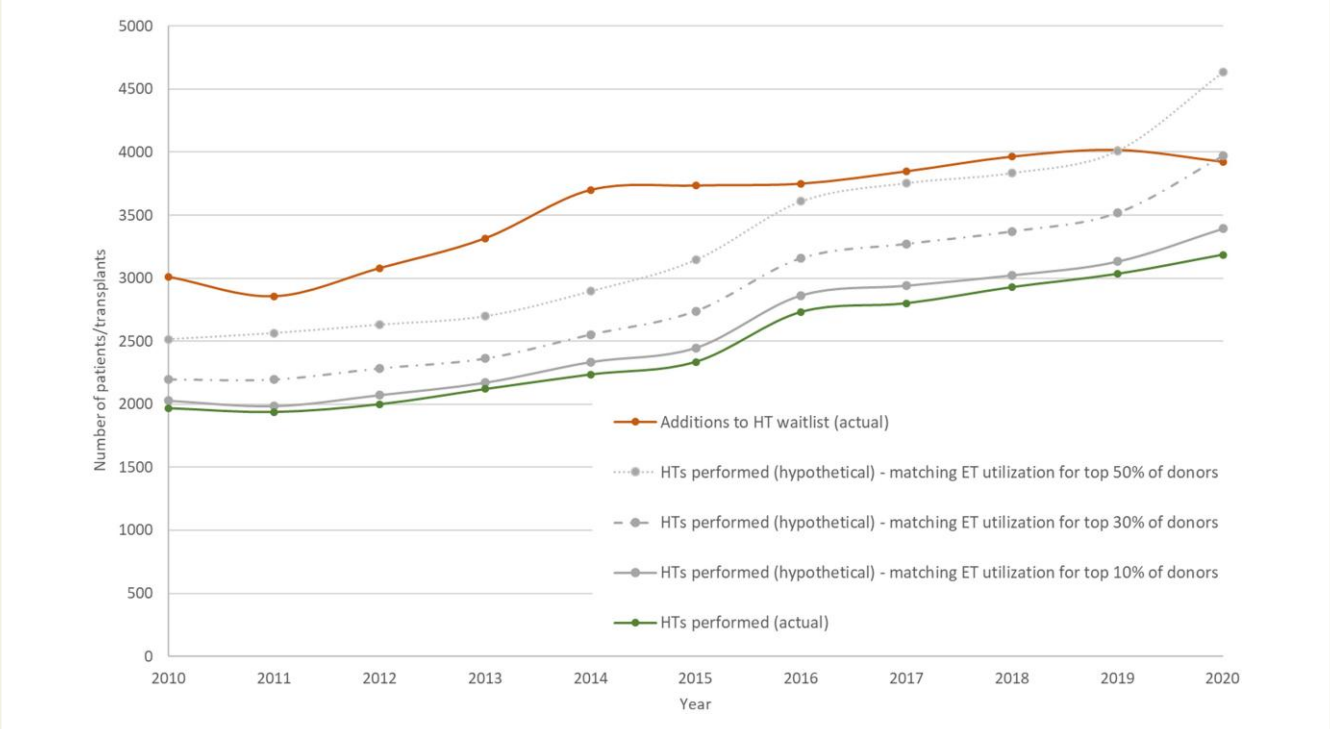


Figure 6 Transplant volume by year, in hypothetical scenarios where the USA matched ET-level utilization for varying subsets of potential donors (2010–2020). Shown is the progressive increase in transplant volume that would have resulted if the USA had achieved ET-levels of utilization among the top 10%, 30%, and 50% (in terms of donor quality) of potential donors.

average USA donor more 'difficult to match' by predicted heart mass, thus rendering the use of some otherwise viable donor hearts infeasible. Another key constraint on utilization is geography; ET member countries have a combined area 686 000 km^2—roughly the size of Texas, but with nearly five times its population. This higher density gives ET a natural advantage in identifying a suitable (and nearby) recipient for all viable donor hearts. Achieving ET-level utilization in the USA would likely require broader geographic sharing than in current practice. Newer modes of donor heart preservation and transport, such as normothermic *ex vivo* perfusion,[29] could make this feasible, but their cost-effectiveness warrants further study.

In light of these practical constraints, our hypothetical scenarios in which the USA matches ET-level utilization for a subset of higher-quality donors are merely illustrative, not a concrete policy prescription. A more realistic scenario might be partial US adoption of the 'ET model', producing an increase of ~230 additional transplants annually. A prior simulation-based analysis suggests such an increase in HT volume would have a significant impact on pre-transplant outcomes, including ~50 fewer deaths and ~130 fewer de-listings due to clinical deterioration per year.[26]

Other limitations of our study should be acknowledged. The eight ET member countries should not be assumed to represent all of Europe, in terms of donor characteristics and utilization. Whilst we find significant temporal trends in both US and ET donor utilization from 2010 to 2020, we would not conclude that ET and US utilization rates will continue to 'diverge' in the future; policy and epidemiologic changes could arrest these temporal trends. As with any registry-based analysis, ascertainment of donor risk factors is subject to imprecision. Moreover, the nine donor covariates included in our study do not fully capture all aspects of donor quality. Other characteristics that predict utilization and (possibly) outcomes—such as coronary angiography results, drug use, and cause of death[12]—were either unavailable in the ET registry or not amenable to analysis (i.e. reported in free text format, in varying languages, and with variable completeness). If US donors have a more adverse profile in terms of these unmeasured risk factors, then adjusting for these in our analysis would have narrowed the apparent gap between US and ET utilization.

Our estimates of utilization—and of the disparity in utilization between the USA and ET—are sensitive how the potential donor pool is defined. Reasonable definitions might range from 'all donors actively evaluated and offered for HT' to the more expansive 'all deceased persons with consent for organ donation'. Due to limitations of available registry data, we could not apply the exact same definition to both US and ET cohorts—a limitation that could bias our estimate of the gap between US and ET donor utilization.

To assess the extent of potential bias, we performed a sensitivity analysis in which the US potential donor definition was intentionally stringent—further limited to the pool of donors that were actually offered for HT. Note that our ET definition is also inclusive of all donors offered for HT and further includes those who were reported to ET as potential donors but ultimately not offered for HT. Even after applying this more stringent definition to the US cohort, we find that its utilization rate remains much lower than in ET.

Regardless of how potential donors are defined and how large the numerical difference in utilization rates, one key finding is beyond dispute—donors used for HT in ET are significantly older with a higher risk factor burden. The average donor used for HT in ET would likely be considered 'marginal' by many US centres. Such conservative donor

selection results in an apparent 'shortage' of heart donors in the USA—which could turn into a surplus if the 'ET model' of donor utilization were applied. These observations present a serious challenge to the US *status quo*, in which most potential donor hearts are discarded despite persistently high wait times and waitlist morbidity. Further analyses weighing the risks and benefits of the 'ET model'—in terms of pre- and post-transplant outcomes—will be needed to safely increase donor utilization in the USA and can also help refine donor selection in ET itself.

Supplementary Data

Supplementary data are available at *European Heart Journal* online.

Declarations

Disclosure of Interest

All authors declare no disclosure of interest for this contribution.

Data Availability

No data were generated or analysed for or in support of this paper.

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Ethical Approval

Ethical approval was not required.

Pre-registered Clinical Trial Number

Not applicable.

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