Developing a Risk Score in Heart Transplantation

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CEOT
CUTTING EDGE OF TRANSPLANTATION
RESOLVING THE ORGAN SHORTAGE
PRACTICE | POLICY | POLITICS
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Conflict of Interest Disclosure

- Grant Funding
  - NIH (NHLBI, R01)
  - American Heart Association

- CareDx, Inc: consultant, advisory board, speakers' bureau

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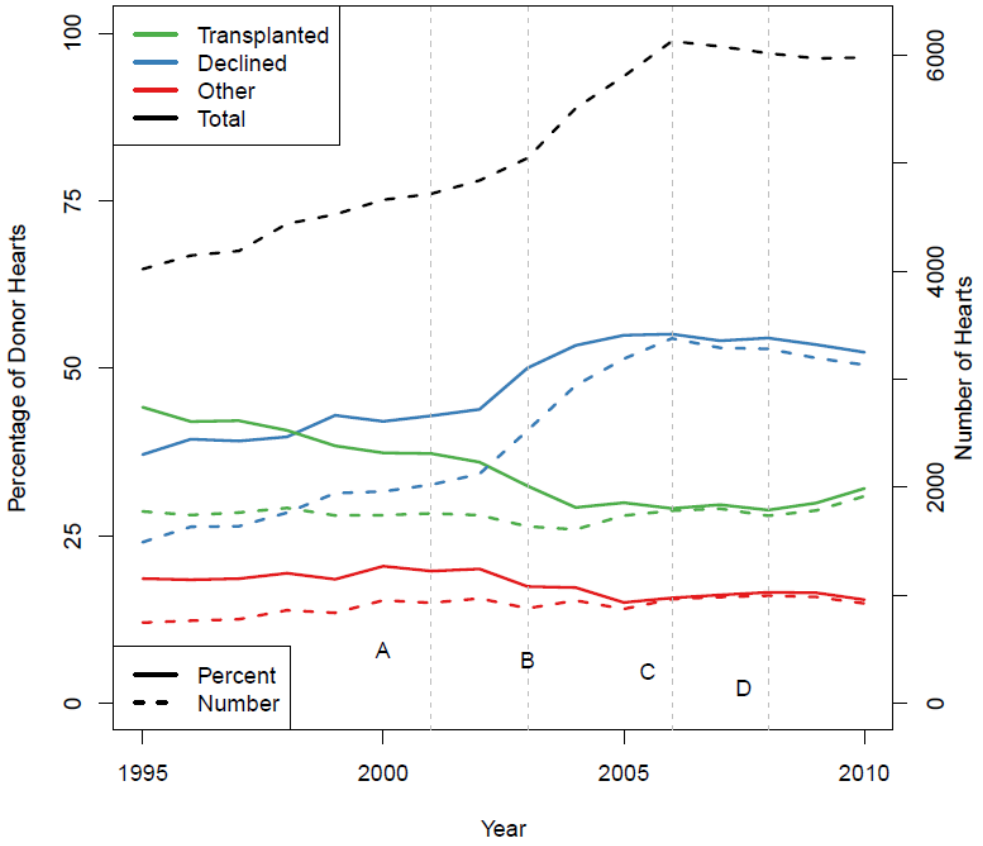
Decline in donor heart utilization nationwide



SRTR data 1995-2010,

All DNDD donors aged 14-70 years

- High: 44% in 1995
- Low: 29% in 2006
- Current: 32%

- Waiting time has increased by 3.5 months for status 1B and 9.3 months for status 2 recipients.

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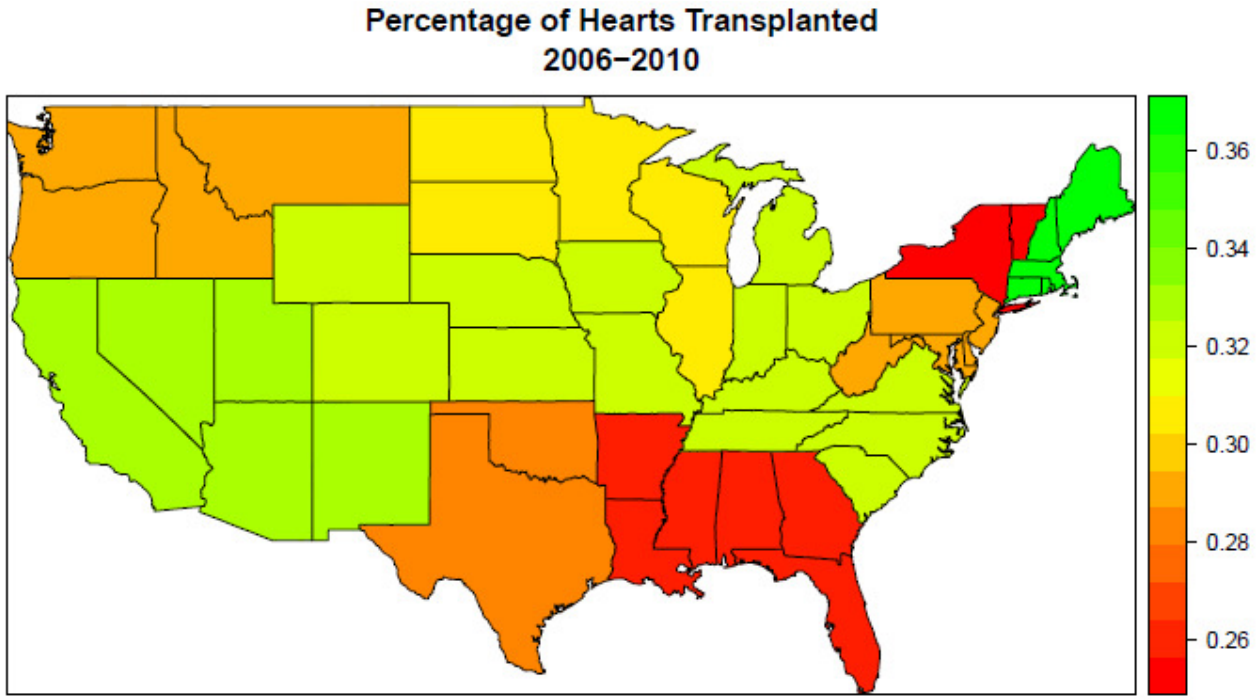
Regional variability in donor heart acceptance for transplant



Khush K, Am J Transplantation, 2015

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Advantages of having a risk score

- Tool that can be used “real time” for decision-making during an organ offer
- Applies evidence-based data, using donor and recipient risk factors, to predict transplant outcomes
- Standardize donor heart acceptance across the country
- Improve donor heart utilization

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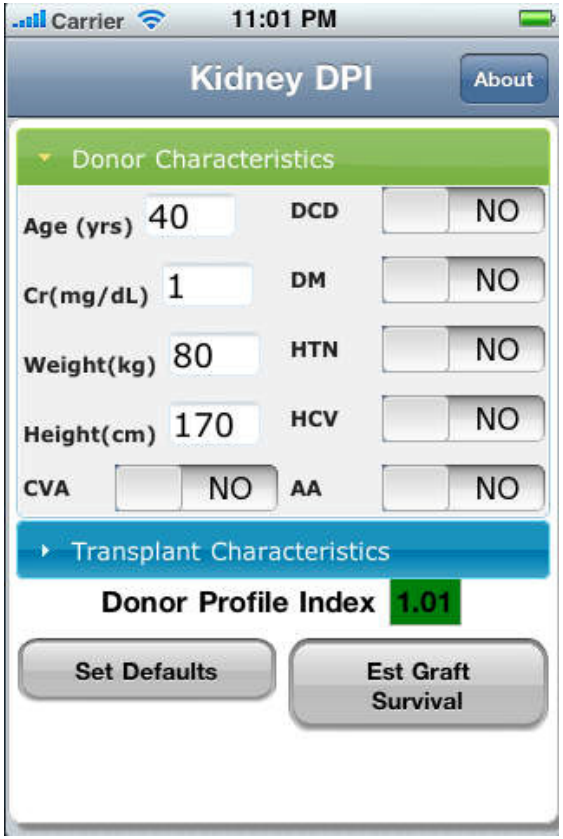
Kidney Donor Risk Index (KDRI)

- Real-time tool that combines donor risk factors to summarize the risk of graft failure after kidney transplant
- A donor with a KDPI of 80% has a higher expected risk of graft failure than 80% of all kidney donors recovered last year
- Launched on-line and as an app



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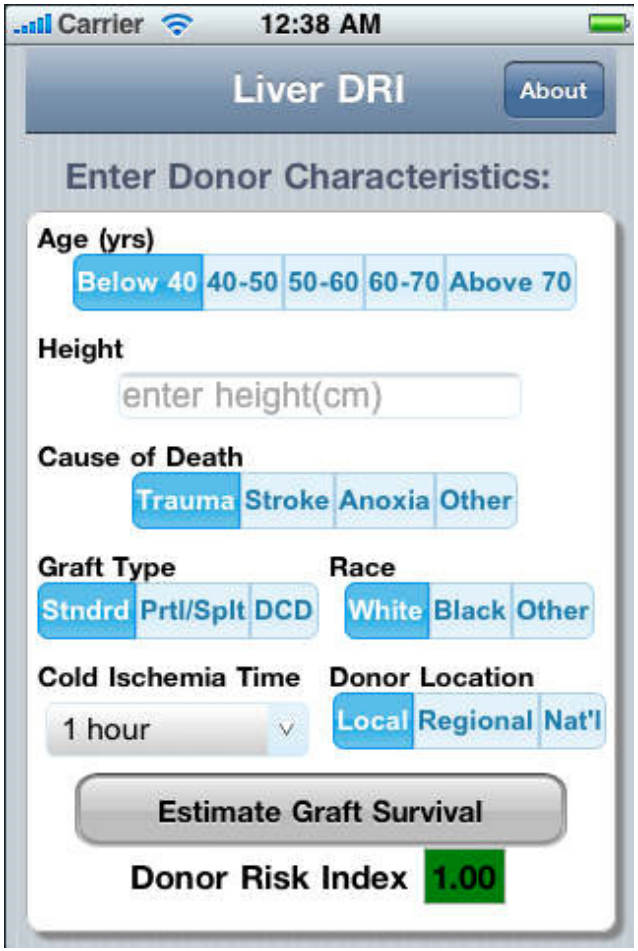
Liver Donor Risk Index (LDRI)



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How do we combine donor and recipient risk?

Low risk donor:
Low risk recipient

High risk donor:
High risk recipient

High risk donor:
Low risk recipient

Low risk donor:
High risk recipient

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High risk donor: High risk recipient

PRO

- Offer a heart that may have been discarded to a recipient who otherwise may not have been eligible for transplant
- Use “marginal” donor hearts for sickest patients, since they are likely to have a survival benefit, even though post-transplant outcomes may be sub-optimal

CON

- Transplanting a high-risk donor heart into a high-risk recipient may be considered an irresponsible accumulation of risk with a high likelihood of patient death after transplant.

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High risk donor: Low risk recipient

PRO

- Higher likelihood of graft survival

CON

- Placing our “best” candidates at a disadvantage?
- Reducing long-term survival

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Balancing Risk: Impact of Transplant Center Volume

Does institutional volume impact outcomes after HTx using marginal donor hearts?

- UNOS registry analysis, N=3200, 2000-2010
- Identified marginal donors (>90th percentile in Weiss donor risk index)
- Stratified into tertiles based on transplant center volume (<14, 14-25, >25)
- Examined post-transplant outcomes

Kilic, Ann Thorac Surg, 2012

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Impact of transplant center volume

Marginal vs. Standard Donors

- Recipients of marginal donor hearts were higher risk than recipients of standard donor hearts (IMPACT score 6.2 vs 5.6, $p<0.001$)
- A higher proportion of HTxs at high volume centers was performed using a marginal donor (high 22.4%, low 16.2%)
- High-volume centers had highest average donor risk index

Kilic, Ann Thorac Surg, 2012

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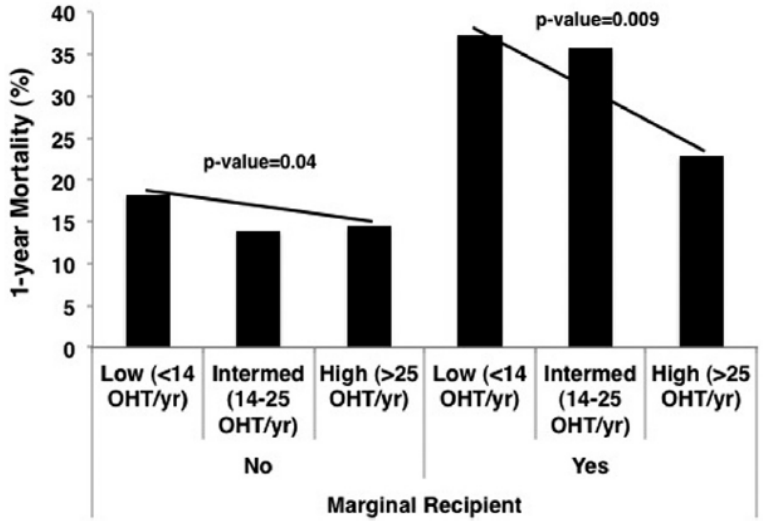
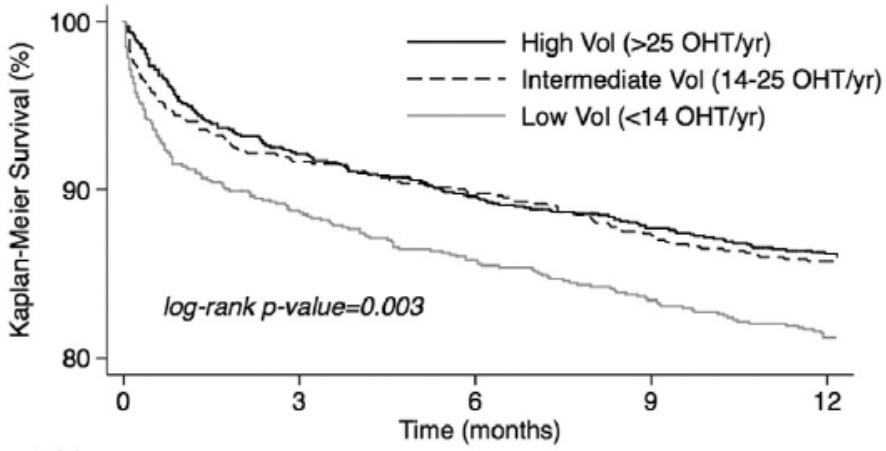
Impact of transplant center volume

Impact of center volume on 1-year mortality in marginal recipients





1-year survival

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Balancing Risk: Impact of transplant center volume

Conclusions

- Marginal donor heart transplants are more complex (higher donor risk, higher recipient risk, higher complication rates)
- Transplant center experience plays an important role
  - Experienced personnel
  - Experience selecting marginal hearts (e.g. older donors with short ischemic time)
  - Standardized clinical pathways
  - Dedicated ICU and ancillary staff

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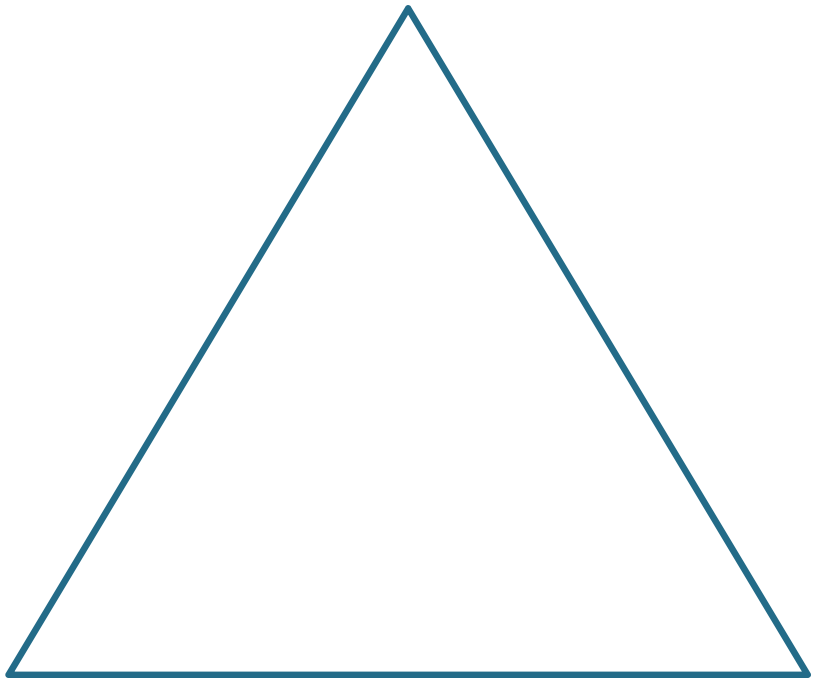
Balancing Risk



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Looking forward

- High-risk transplants should ideally be performed at high-volume centers.
- Introduction of a risk stratification scheme may prevent penalizing centers that transplant higher risk donors and recipients by accounting for case mix in quality and reimbursement measures.
- Rigorous, high-quality data required to develop a real-time risk score incorporating donor- and recipient-specific variables are lacking

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Donor Heart Study

Evidence-Based Evaluation and Acceptance of Donor Hearts for Transplantation

- Funded by National Institutes of Health
- 5-year prospective study
- 5,000 potential heart donors

PI: Kiran Khush, Stanford

Co-I: Darren Malinoski, OHSU

Co-I: Jonathan Zaroff, KPSF

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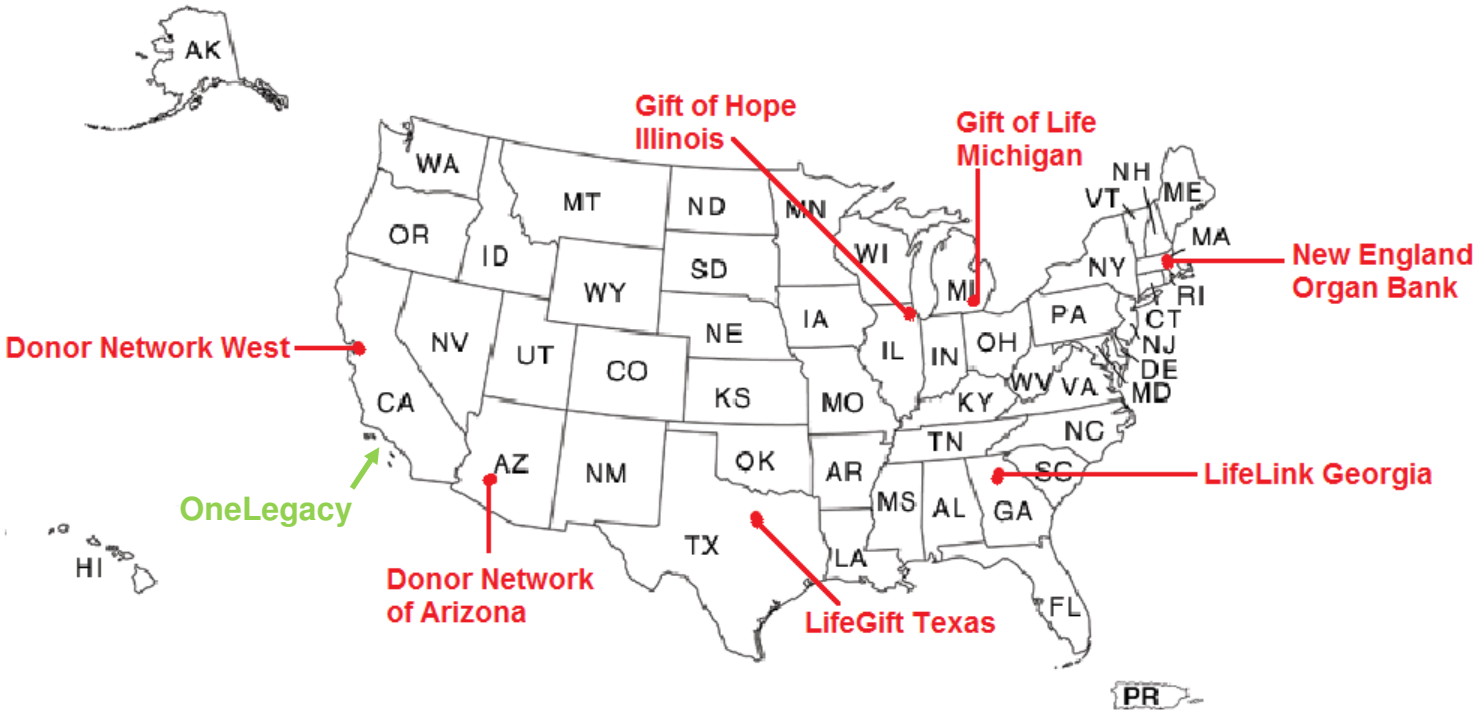
Donor Heart Study

7 participating high-volume OPOs representing 6 UNOS regions



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Donor Heart Study

Aim 1: To collect systematic data on cardiac structure and function in a nationally-representative cohort of potential heart donors

- Serial ECG, TnI, BNP during donor management
- Serial TTEs in donors with LV dysfunction (EF<50%) with core interpretation
- Data collection on donor heart acceptance

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Donor Heart Study

Aim 1: To collect systematic data on cardiac structure and function in a nationally-representative cohort of potential heart donors

Study Databases

- Stanford REDCap
- DMG Web Portal

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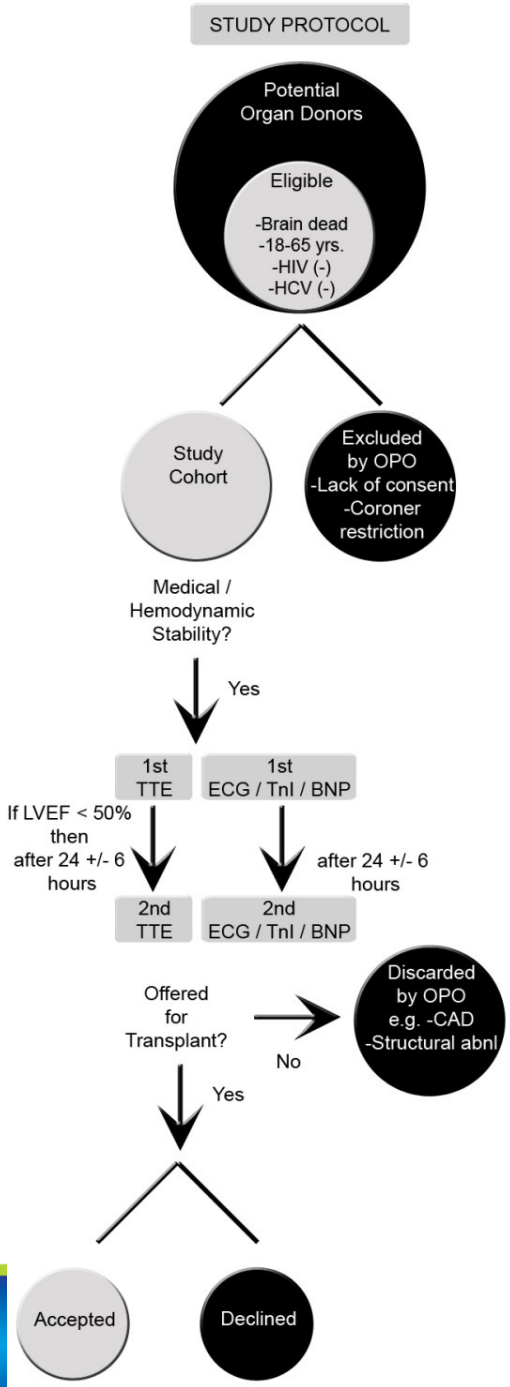
STUDY PROTOCOL
Potential Organ Donors
Eligible
-Brain dead
-18-65 yrs.
-HIV (-)
-HCV (-)
Study Cohort
Excluded by OPO
-Lack of consent
-Coroner restriction
Medical / Hemodynamic Stability?
Yes
1st TTE
1st ECG / TnI / BNP
If LVEF < 50% then after 24 +/- 6 hours
after 24 +/- 6 hours
2nd TTE
2nd ECG / TnI / BNP
Offered for Transplant?
No
Discarded by OPO
e.g. -CAD
-Structural abnl
Yes
Accepted
Declined

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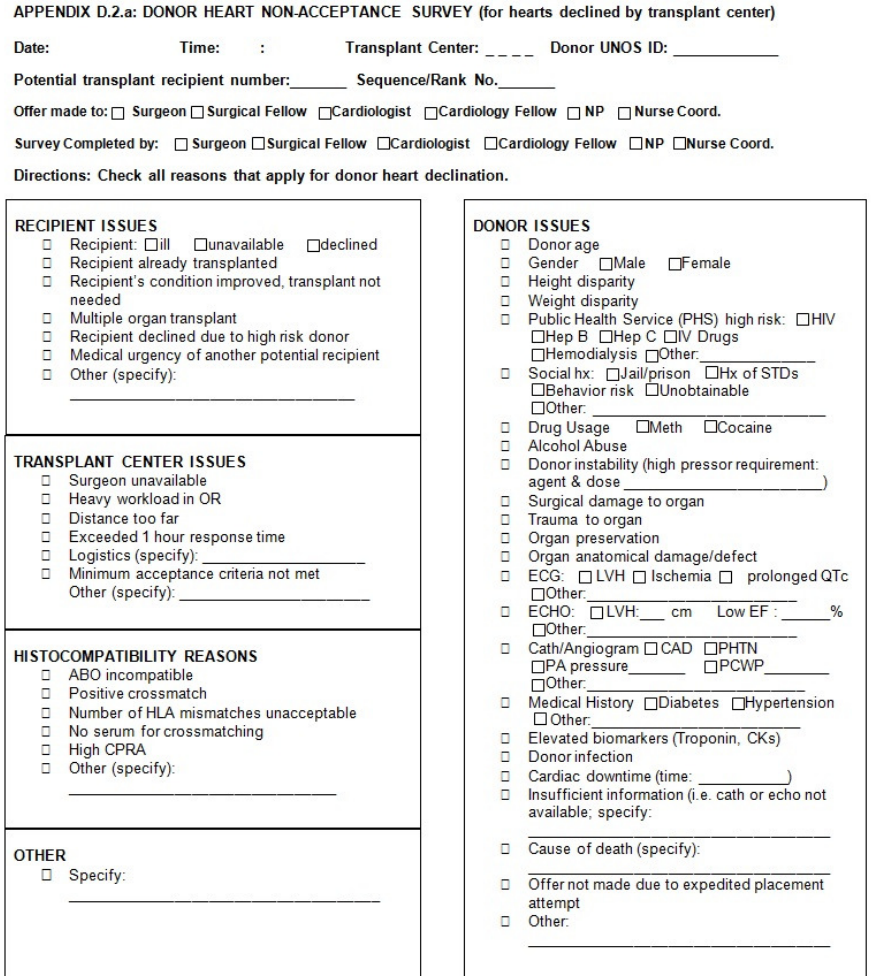
Donor Heart Study

Aim 2: To collect real-time detailed data on reasons for donor heart non-acceptance



APPENDIX D.2.a: DONOR HEART NON-ACCEPTANCE SURVEY (for hearts declined by transplant center)

Date: **Time:** : **Transplant Center:** _ _ _ _ **Donor UNOS ID:** _____

Potential transplant recipient number:_____ **Sequence/Rank No.**_____

Offer made to: ☐ Surgeon ☐ Surgical Fellow ☐ Cardiologist ☐ Cardiology Fellow ☐ NP ☐ Nurse Coord.

Survey Completed by: ☐ Surgeon ☐ Surgical Fellow ☐ Cardiologist ☐ Cardiology Fellow ☐ NP ☐ Nurse Coord.

Directions: Check all reasons that apply for donor heart declination.

RECIPIENT ISSUES

- ☐ Recipient: ☐ ill ☐ unavailable ☐ declined
- ☐ Recipient already transplanted
- ☐ Recipient's condition improved, transplant not needed
- ☐ Multiple organ transplant
- ☐ Recipient declined due to high risk donor
- ☐ Medical urgency of another potential recipient
- ☐ Other (specify): _____

TRANSPLANT CENTER ISSUES

- ☐ Surgeon unavailable
- ☐ Heavy workload in OR
- ☐ Distance too far
- ☐ Exceeded 1 hour response time
- ☐ Logistics (specify): _____
- ☐ Minimum acceptance criteria not met
  Other (specify): _____

HISTOCOMPATIBILITY REASONS

- ☐ ABO incompatible
- ☐ Positive crossmatch
- ☐ Number of HLA mismatches unacceptable
- ☐ No serum for crossmatching
- ☐ High CPRA
- ☐ Other (specify): _____

OTHER

- ☐ Specify: _____

DONOR ISSUES

- ☐ Donor age
- ☐ Gender ☐ Male ☐ Female
- ☐ Height disparity
- ☐ Weight disparity
- ☐ Public Health Service (PHS) high risk: ☐ HIV ☐ Hep B ☐ Hep C ☐ IV Drugs ☐ Hemodialysis ☐ Other:_____
- ☐ Social hx: ☐ Jail/prison ☐ Hx of STDs ☐ Behavior risk ☐ Unobtainable ☐ Other: _____
- ☐ Drug Usage ☐ Meth ☐ Cocaine
- ☐ Alcohol Abuse
- ☐ Donor instability (high pressor requirement: agent & dose _____)
- ☐ Surgical damage to organ
- ☐ Trauma to organ
- ☐ Organ preservation
- ☐ Organ anatomical damage/defect
- ☐ ECG: ☐ LVH ☐ Ischemia ☐ prolonged QTc ☐ Other:_____
- ☐ ECHO: ☐ LVH:___ cm Low EF : _____% ☐ Other:_____
- ☐ Cath/Angiogram ☐ CAD ☐ PHTN ☐ PA pressure_____ ☐ PCWP_____ ☐ Other:_____
- ☐ Medical History ☐ Diabetes ☐ Hypertension ☐ Other:_____
- ☐ Elevated biomarkers (Troponin, CKs)
- ☐ Donor infection
- ☐ Cardiac downtime (time: _____)
- ☐ Insufficient information (i.e. cath or echo not available; specify: _____
- ☐ Cause of death (specify): _____
- ☐ Offer not made due to expedited placement attempt
- ☐ Other: _____

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Donor Heart Study

Aim 3: To develop clinical tools to assist transplant centers with real-time decisions about donor heart acceptance

- Risk models for recipient outcomes, given donor and recipient characteristics at the time of an organ offer

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Sample Donor Heart Report

Donor Characteristics:

Age	Gender	Cause of Death
45	Male	Stroke

Donor Health:

Hypertension	Diabetes	Coronary Artery Disease
No	Yes	No

Echo Results:

Ejection Fraction	Regional Wall Motion Abnormalities	Left Ventricular Hypertrophy
58%	No	Yes

A heart with these characteristics has been transplanted **83%** of the time. **97%** of patients with a similar heart survive at least 30 days and **92%** survive 1 year. It is expected that you would have to wait on average **6 months** to be offered a more desirable heart.

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Study Goals

- Standardized data collection on donor characteristics nationwide
- To study prevalence and reversibility of cardiac dysfunction after brain death
- To identify biomarkers that define organ quality
- Detailed examination of current donor heart acceptance practices
- To identify donor predictors of recipient outcomes
- To develop tools that can be used real-time in decision making for donor heart acceptance

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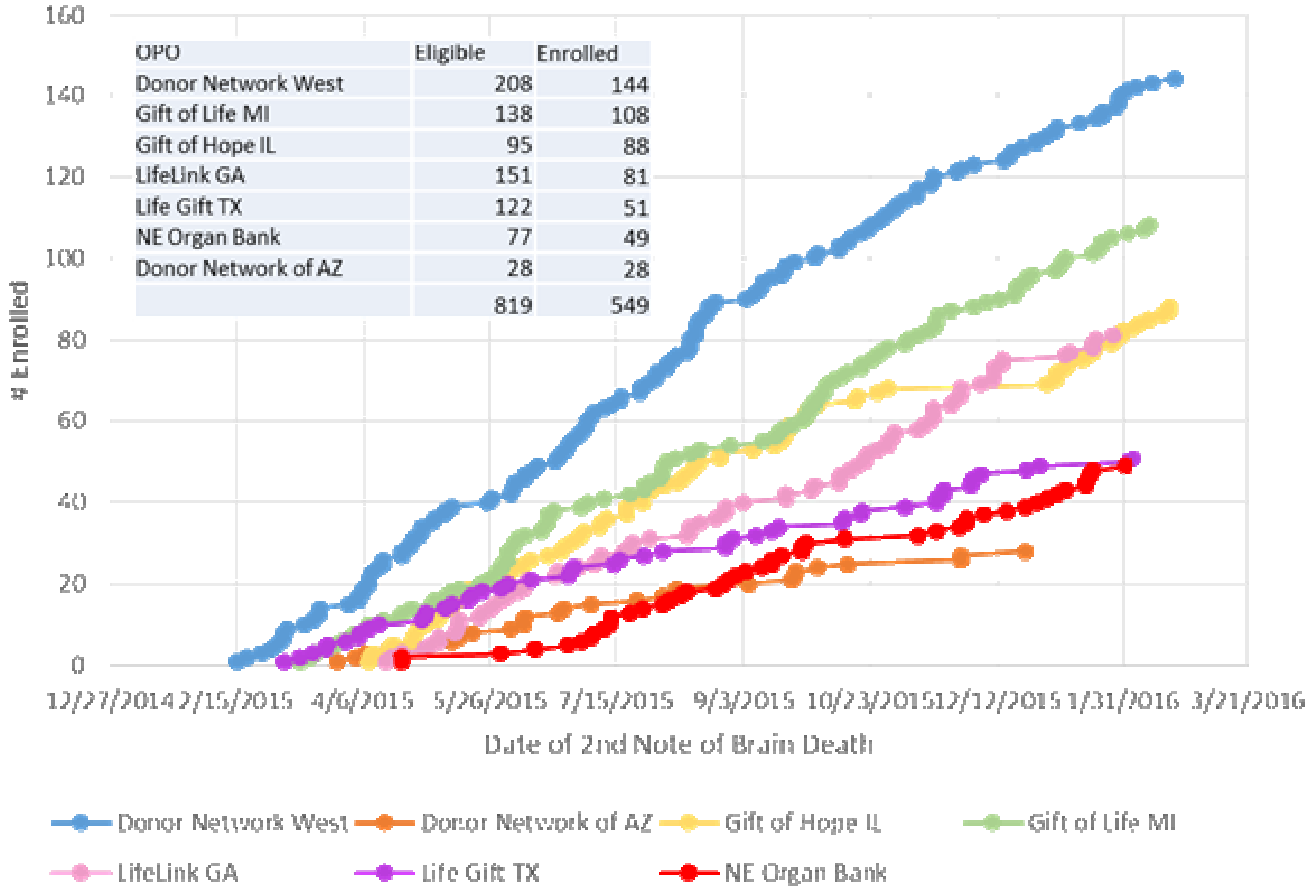
Donor Heart Study

Enrollment v. Time

OPO	Eligible	Enrolled
Donor Network West	208	144
Gift of Life MI	138	108
Gift of Hope IL	95	88
LifeLink GA	151	81
Life Gift TX	122	51
NE Organ Bank	77	49
Donor Network of AZ	28	28
	819	549



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Thank you

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