How Well Do Organ Allocation Policies Correlate to Models – A Case Study

Michael M. Givertz, MD
Medical Director, Heart Transplant and Mechanical Circulatory Support
Brigham and Women's Hospital
Professor of Medicine
Harvard Medical School

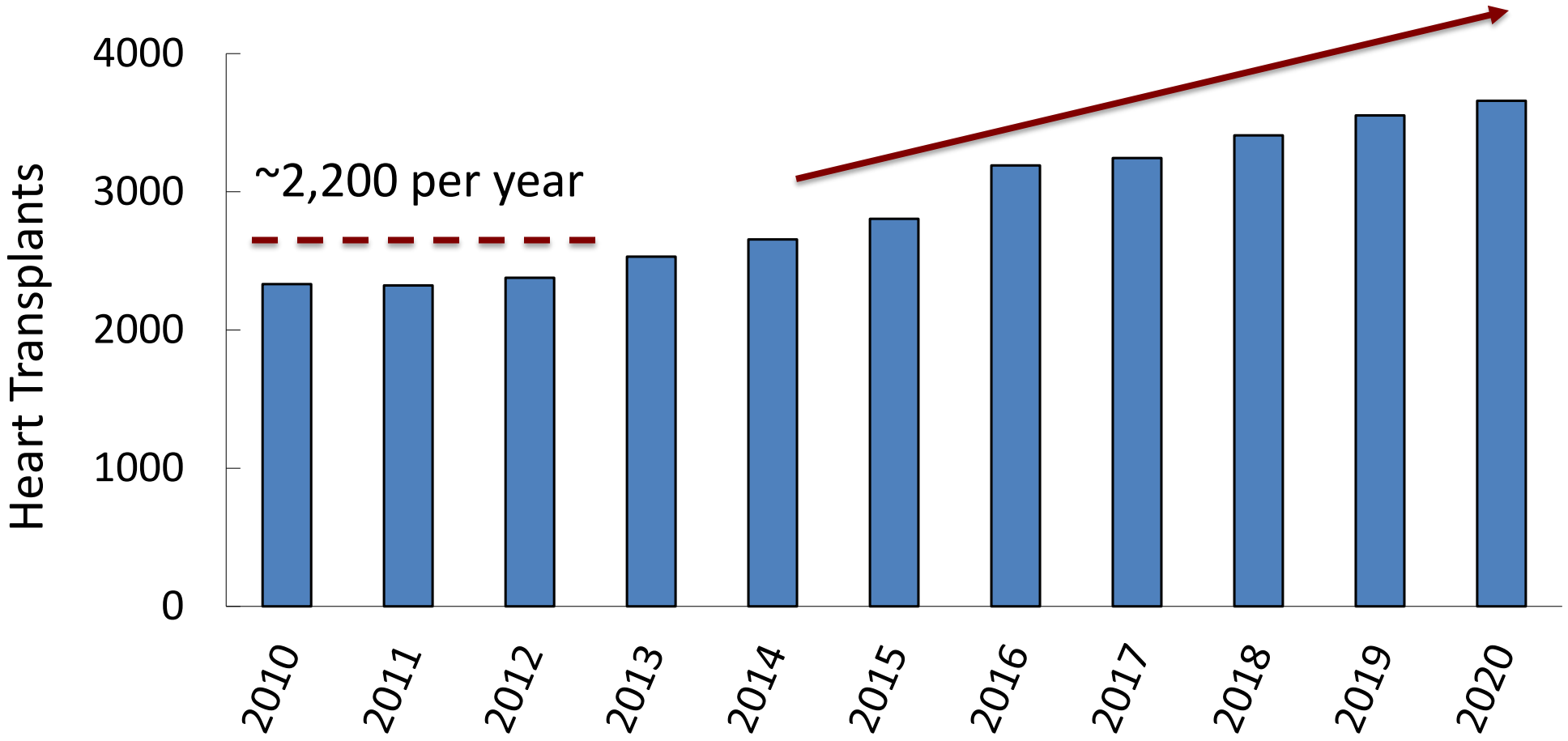
BWH BRIGHAM AND WOMEN'S HOSPITAL | Heart & Vascular Center |

HARVARD MEDICAL SCHOOL

Mass General Brigham


1.
Idea
2.
Problem
Analysis
3.
Project
Approval
4.
Evidence
Gathering
5.
Public
Comment
Approval
6.
Public
Comment
7.
Pending
Board
Approval
8.
Board
Approval
9.
Implementation
10.
Post
Implementation
Review
OPTN
Policy
Development
Process

Let's Start with the Good News

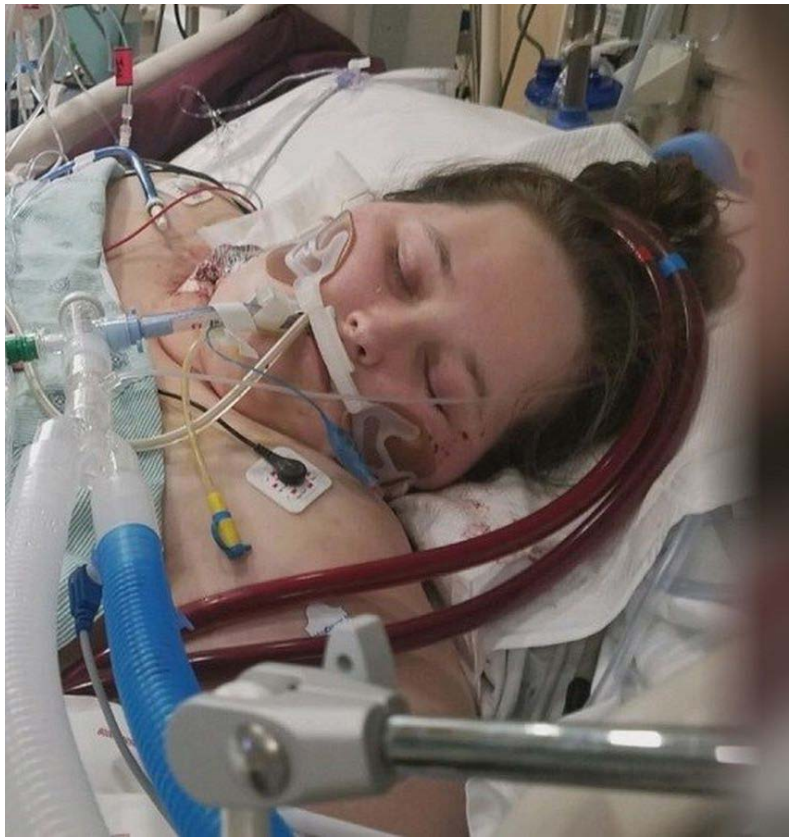


http://optn.transplant.hrsa.gov

The Problem (Circa 2015)

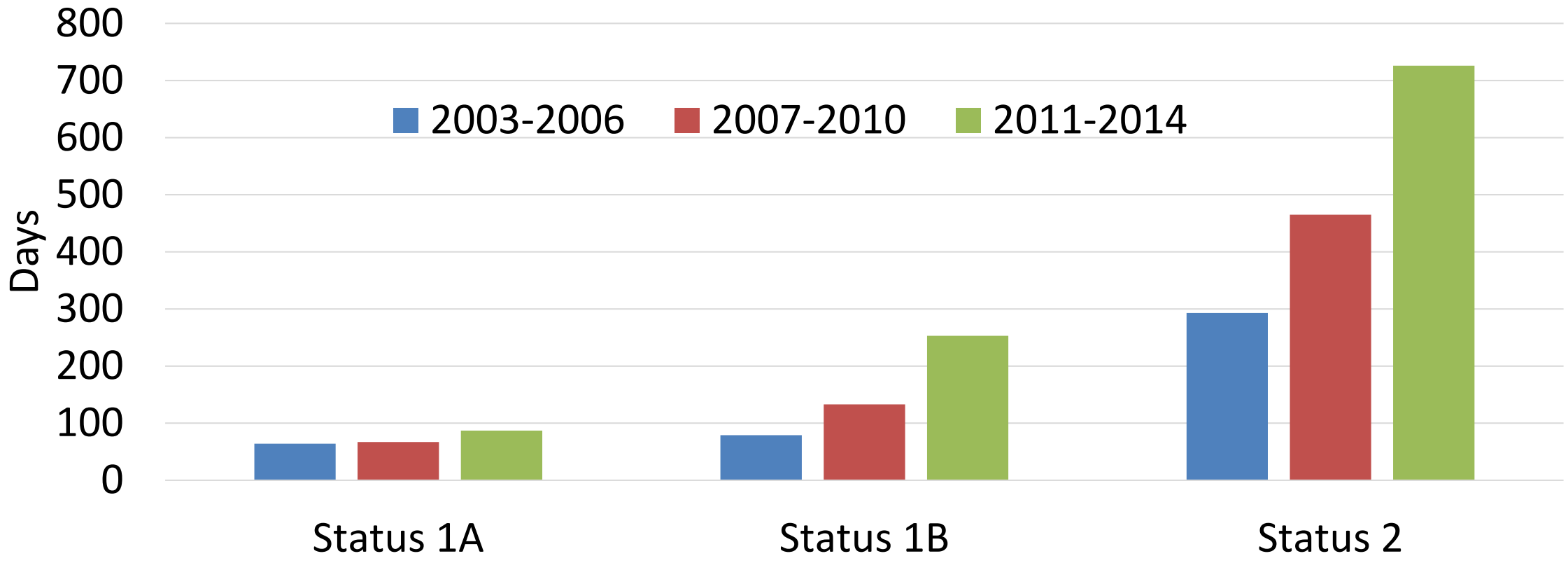
VAD with driveline infection

PA catheter on inotrope

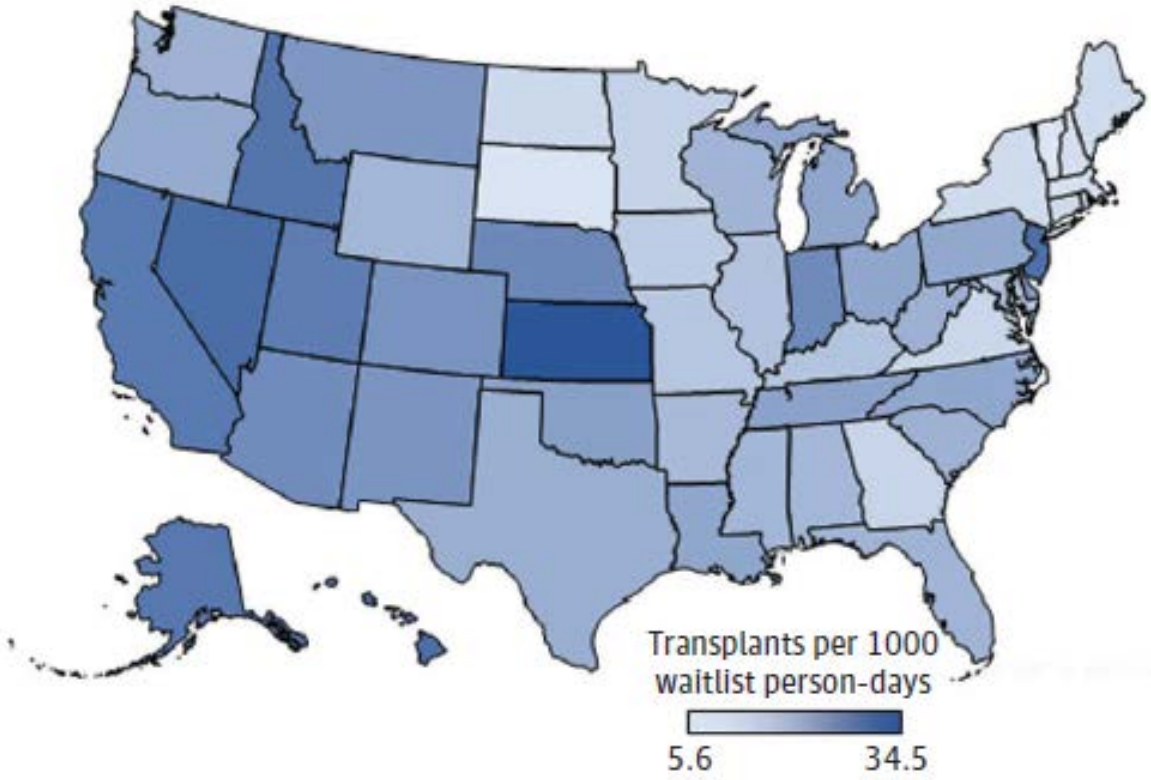


VA ECMO

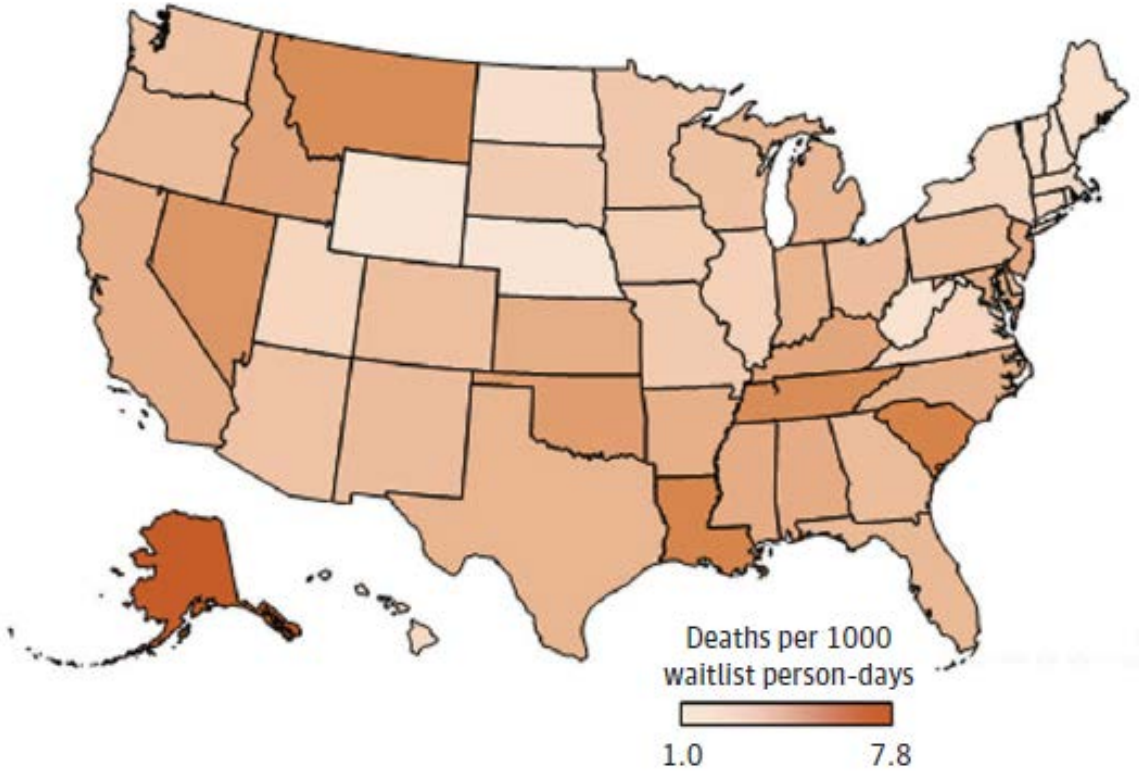
Median Waitlist Times



Transplant Rates



Waitlist Mortality



Akintoye et al., JAMA Network Open 2020;3:e2028459

UNOS Revised Donor Heart Allocation

Primary Aims:

- Reduce waitlist mortality by better stratification of sickest patients
- Enhance geographic sharing to improve organ distribution equity
- Reflect increased use of (and complications related to) durable LVADs

Secondary Aims:

- Reduce exception requests

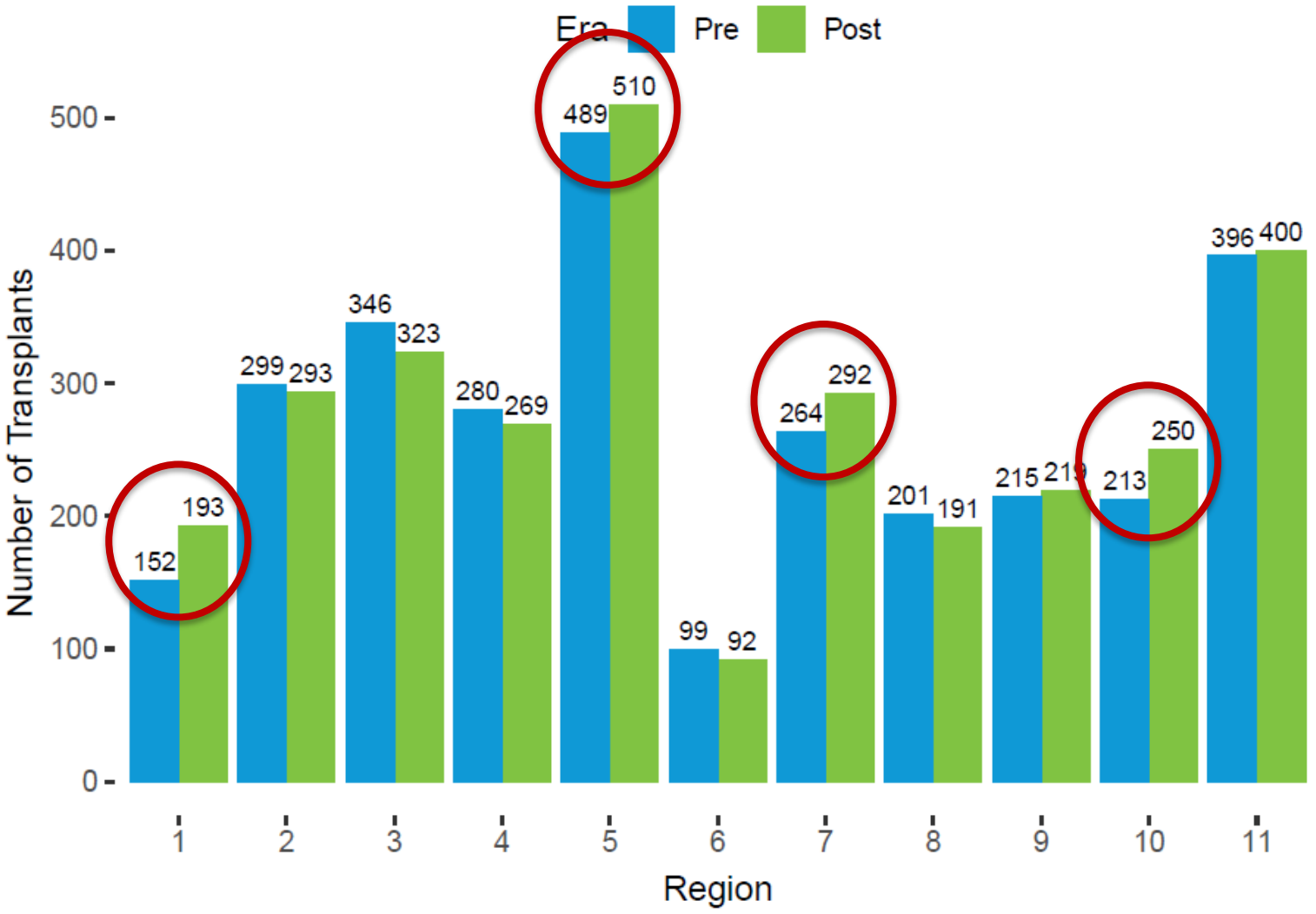
Revised Heart Allocation

Status	Criteria
1	VA-ECMO Non-dischargeable BIVADs MCS with life-threatening VT
2	Dischargeable BIVAD, TAH Non-dischargeable LVAD IABP or percutaneous MCS
3	Dischargeable LVAD for 30 days (discretionary) Inotropes and PA catheter VA-ECMO > 7 days, percutaneous IABP or MCS > 14 days VAD with complication
4	Stable LVAD Inotropes without PAC Other: re-transplant, ACHD, HCM, amyloid
5	Dual organ transplant
6	All others

Status 1A

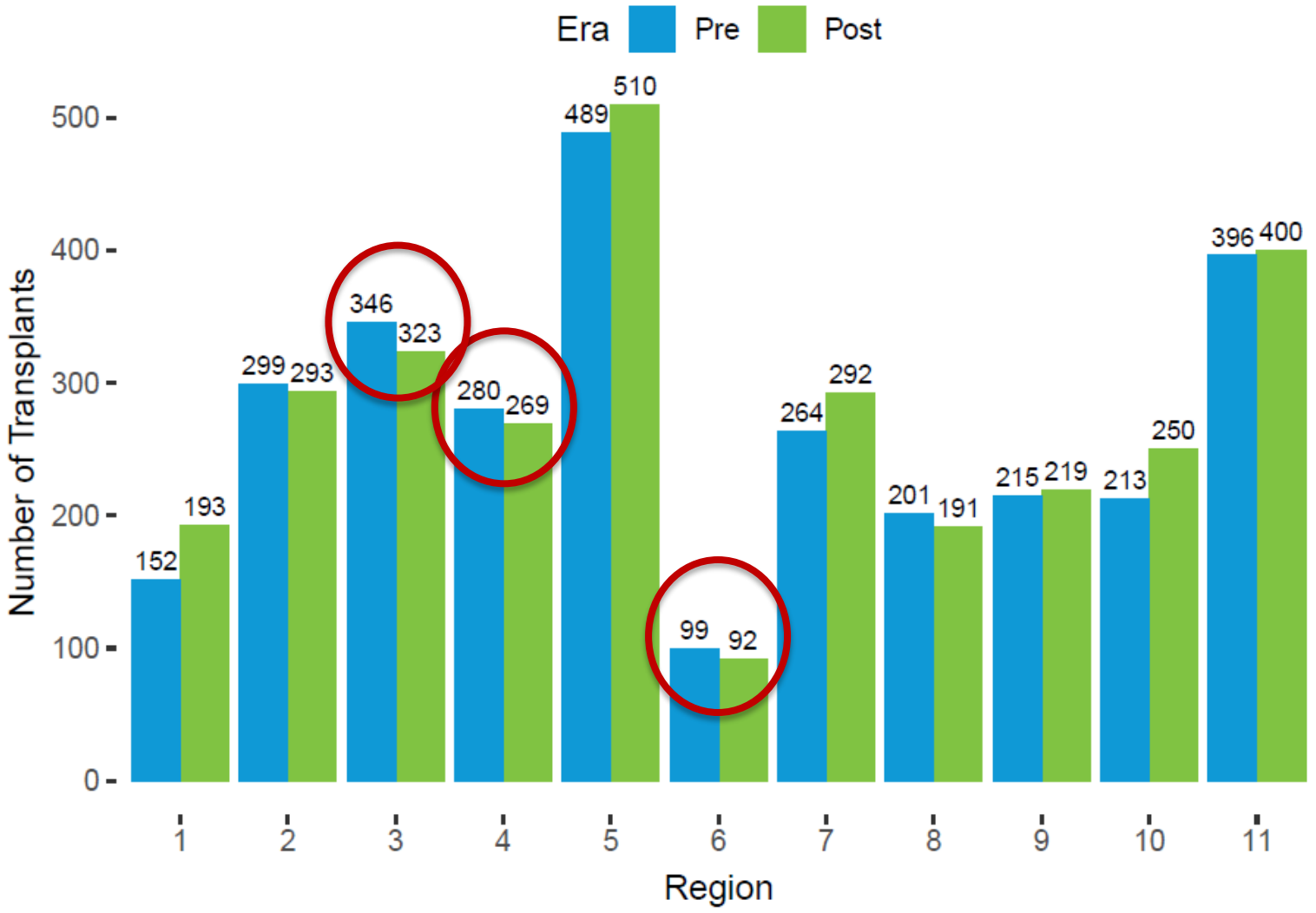
https://optn.transplant.hrsa.gov

Transplants by Region



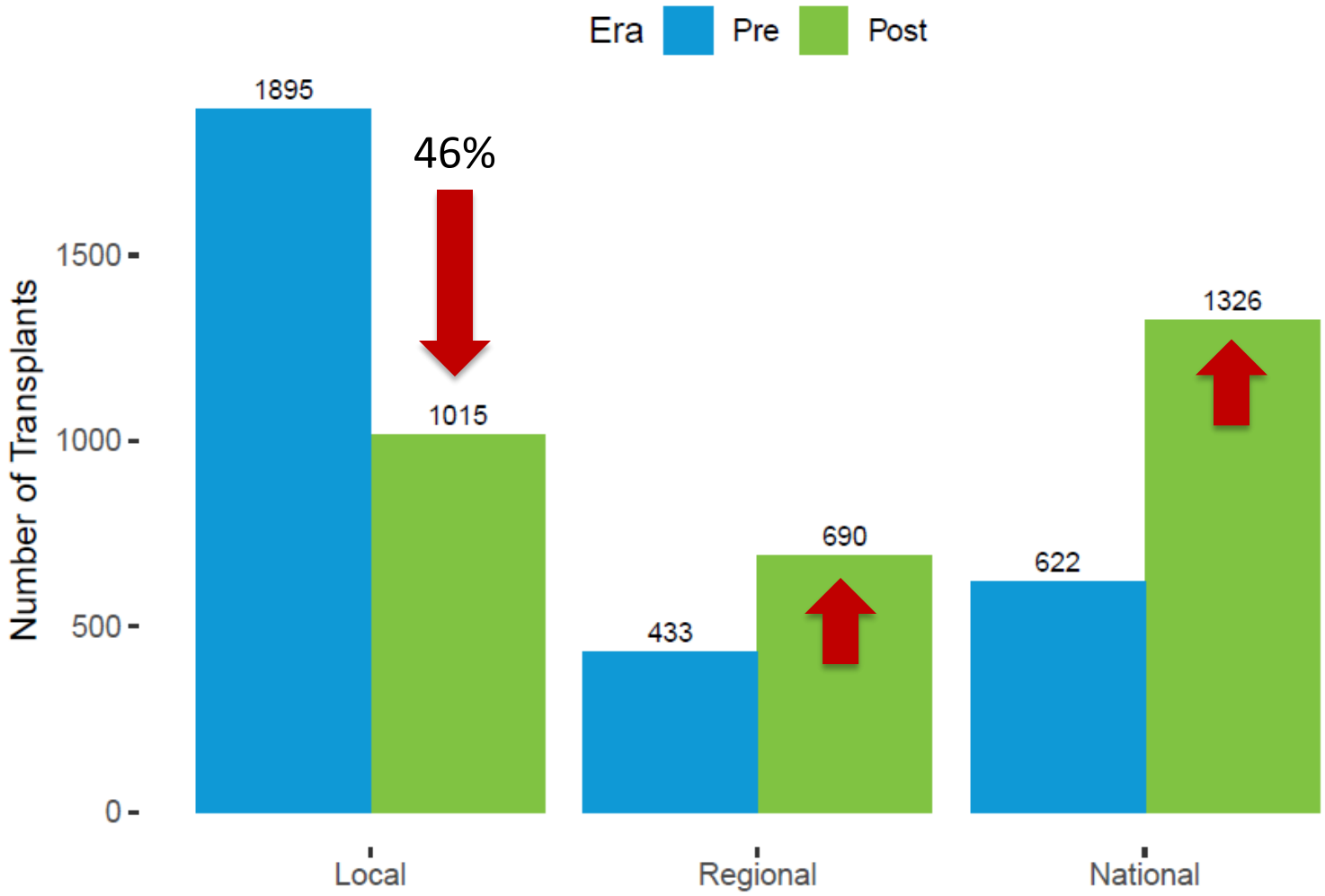
OPTN Thorac Committee Report, February 27, 2020

Transplants by Region



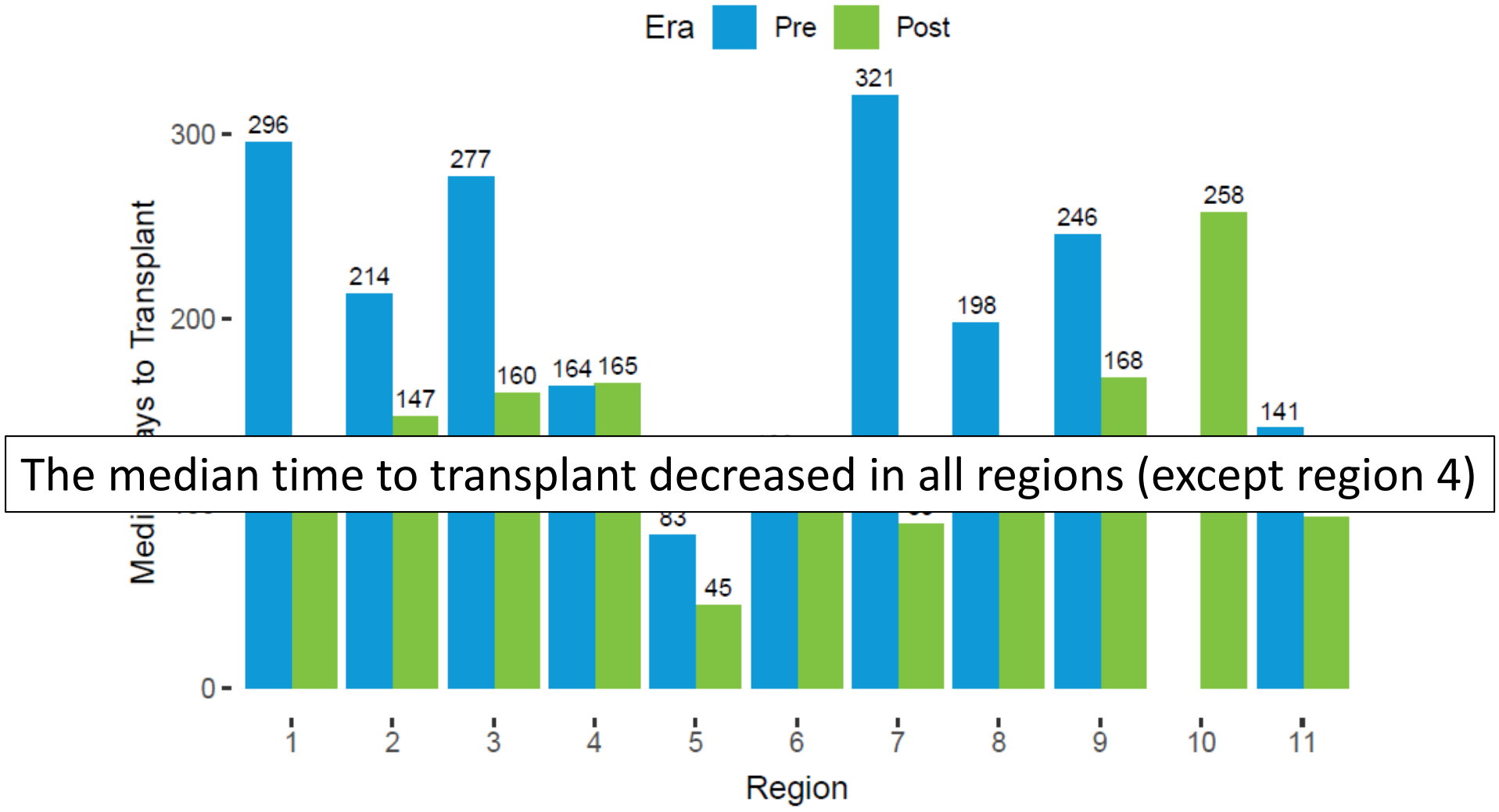
OPTN Thorac Committee Report, February 27, 2020

Transplants by Share Type



OPTN Thorac Committee Report, February 27, 2020

Median Days Waiting Before Transplant

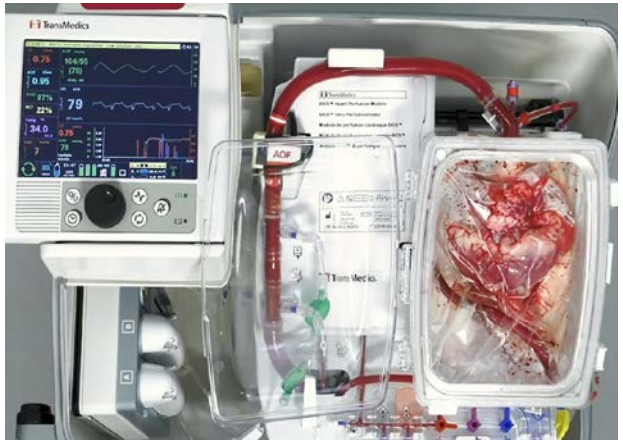


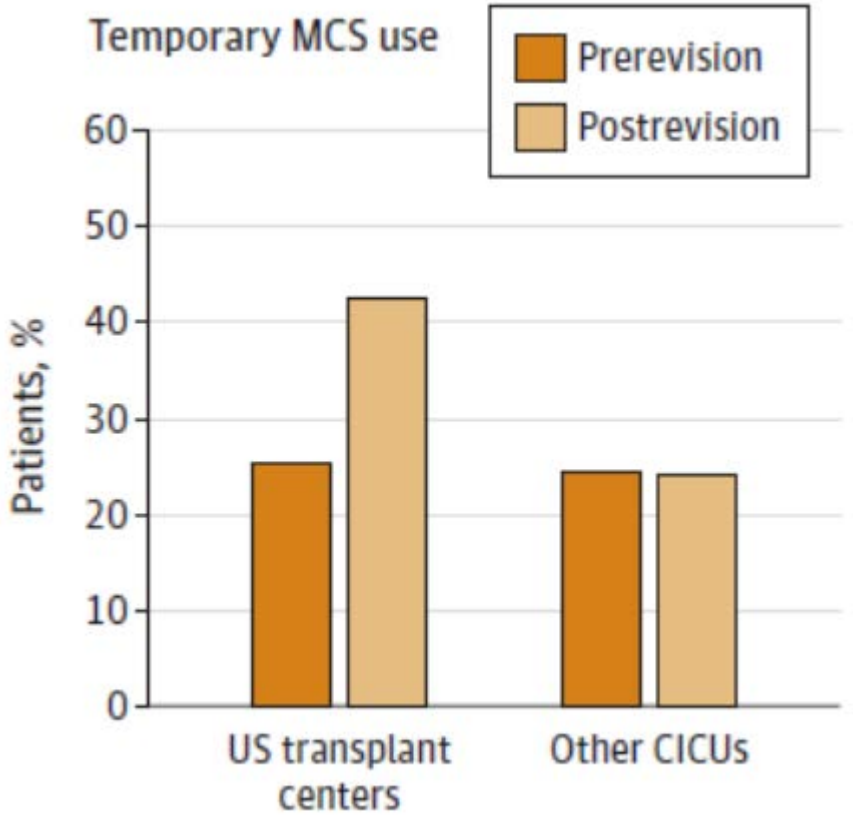
The median time to transplant decreased in all regions (except region 4)

OPTN Thorac Committee Report, February 27, 2020

Unintended Consequences

- ↑ Use of temporary MCS
- ↓ Use of durable LVAD
- ↓ Volume at (already) low-volume centers
- ↑ Distance traveled and ischemic time
  - new markets for innovative organ transport





Varshney et al., JAMA Cardiol 2020;5:703

BUT…

- What about waitlist mortality and post-transplant survival?

Similar Data, Discrepant Findings

Study	Cogswell JHLT	Kilic CIRC	Jawitz JACC HF	Goff AJT	Trevidi ASAIO J
Study period	2015–2019	2018–2019	2015–2019	2017–2019	2016–2019
Primary outcome	Mortality or retransplant	Mortality	Mortality or retransplant	Mortality	Mortality
Statistical analyses	K-M analysis Cox regression Propens. match	K-M analysis	K-M analysis	K-M analysis	K-M analysis
Post-transplant survival					
Waitlist mortality					

Varshney et al., J Heart Lung Transplant 2020;39:1191

Similar Data, Discrepant Findings

Study	Cogswell JHLT	Kilic CIRC	Jawitz JACC HF	Goff AJT	Trevidi ASAIO J
Study period	2015–2019	2018–2019	2015–2019	2017–2019	2016–2019
Primary outcome	Mortality or retransplant	Mortality	Mortality or retransplant	Mortality	Mortality
Statistical analyses	K-M analysis Cox regression Propens. match	K-M analysis	K-M analysis	K-M analysis	K-M analysis
Post-transplant survival	↓ at 6 mos (unadjusted)	↓ at 6 mos (unadjusted)	No difference (adjusted)	No difference (unadjusted)	↓ at 6 mos (unadjusted)
Waitlist mortality					

Varshney et al., J Heart Lung Transplant 2020;39:1191

Similar Data, Discrepant Findings

Study	Cogswell JHLT	Kilic CIRC	Jawitz JACC HF	Goff AJT	Trevidi ASAIO J
Study period	2015–2019	2018–2019	2015–2019	2017–2019	2016–2019
Primary outcome	Mortality or retransplant	Mortality	Mortality or retransplant	Mortality	Mortality
Statistical analyses	K-M analysis Cox regression Propens. match	K-M analysis	K-M analysis	K-M analysis	K-M analysis
Post-transplant survival	↓ at 6 mos (unadjusted)	↓ at 6 mos (unadjusted)	No difference (adjusted)	No difference (unadjusted)	↓ at 6 mos (unadjusted)
Waitlist mortality	↓	↓	Not reported	No change	Not reported

Varshney et al., J Heart Lung Transplant 2020;39:1191

Disparate Analyses and Potential Biases

- Different analytical cohorts
  - Different inclusion/exclusions
  - Different temporal definition of “prior” system
  - Immortal time/survivor bias
- Violation of non-informative censoring assumption
  - Varying follow-up times
  - Ascertainment bias
- Risk adjustment prone to biases
  - Model building, covariate selection

Varshney et al., J Heart Lung Transplant 2020;39:1191

Where Do We Go from Here?

- Longer follow-up
  - Account for time-dependent changes in clinical decision making
  - Greater numbers, narrower confidence intervals
- Stratification by exception status
- Account for sicker pre-transplant patient phenotype
  - Higher expected mortality
  - Preserved (or possibly improved) observed mortality
- Include post-transplant survival in subsequent modeling
  - Balance competing risks to best utilize organs (i.e., maximize benefit)

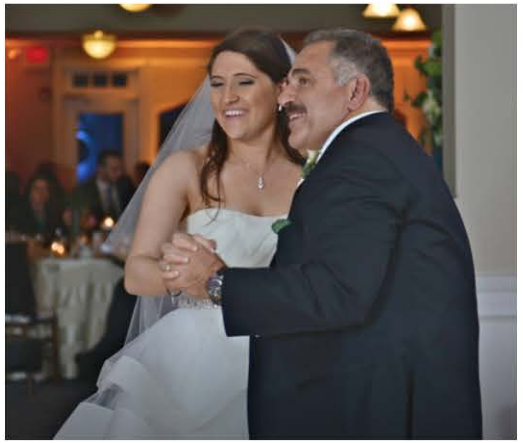
Heart Transplant Community: Looking Forward

- Commit to critical review of future investigations and being open to re-revising donor heart allocation policy to ensure:
  - Unintended consequences are addressed
  - Patient outcomes are not compromised
- Develop metrics of expected changes in care processes, post-transplant mortality, and other outcomes before widespread policy change
- Recognize that post-transplant outcomes are influenced by other concomitant changes (expanding donor pools, advancements in MCS)

The consequences of our actions are so complicated, so diverse, that predicting the future is a very difficult business indeed.
—J.K. Rowling, British Novelist (1965–present)

You can't always get what you want...But if you try sometimes, well, you might find you get what you need.
—Mick Jagger, English singer, songwriter (1943–present)

Everything Possible



BRIGHAM AND WOMEN'S HOSPITAL
| Heart & Vascular Center |

Thank you for your attention…

Michael M. Givertz, MD
(617) 525-7052
mgivertz@bwh.harvard.edu

Life. Giving. Breakthroughs.

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL