Trends and Innovations in Organ Transplantation: Focus on Thoracic

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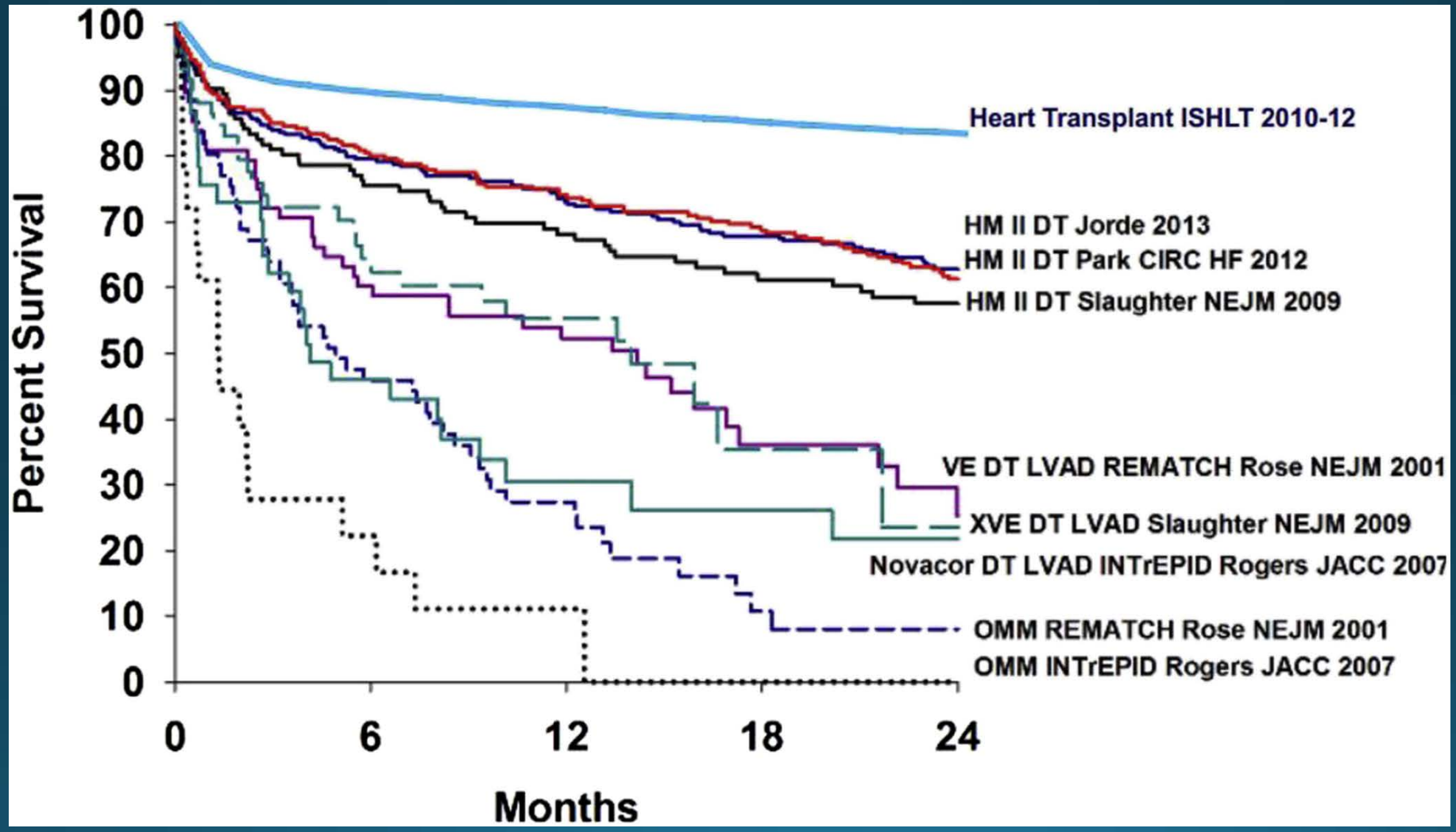
Objectives

- Identify trends in thoracic organ transplantation and discuss disparities in donor organ availability and organ allocation
- Describe the cost of organ transplantation and strategies to improve cost efficiency
- Discuss innovations that have potential to improve donor organ availability
- State trends and advances in organ transplantation

Survival in Advanced Heart Failure



J Am Coll Cardiol. 2014;63(17):1758-1760. doi:10.1016/j.jacc.2014.02.531

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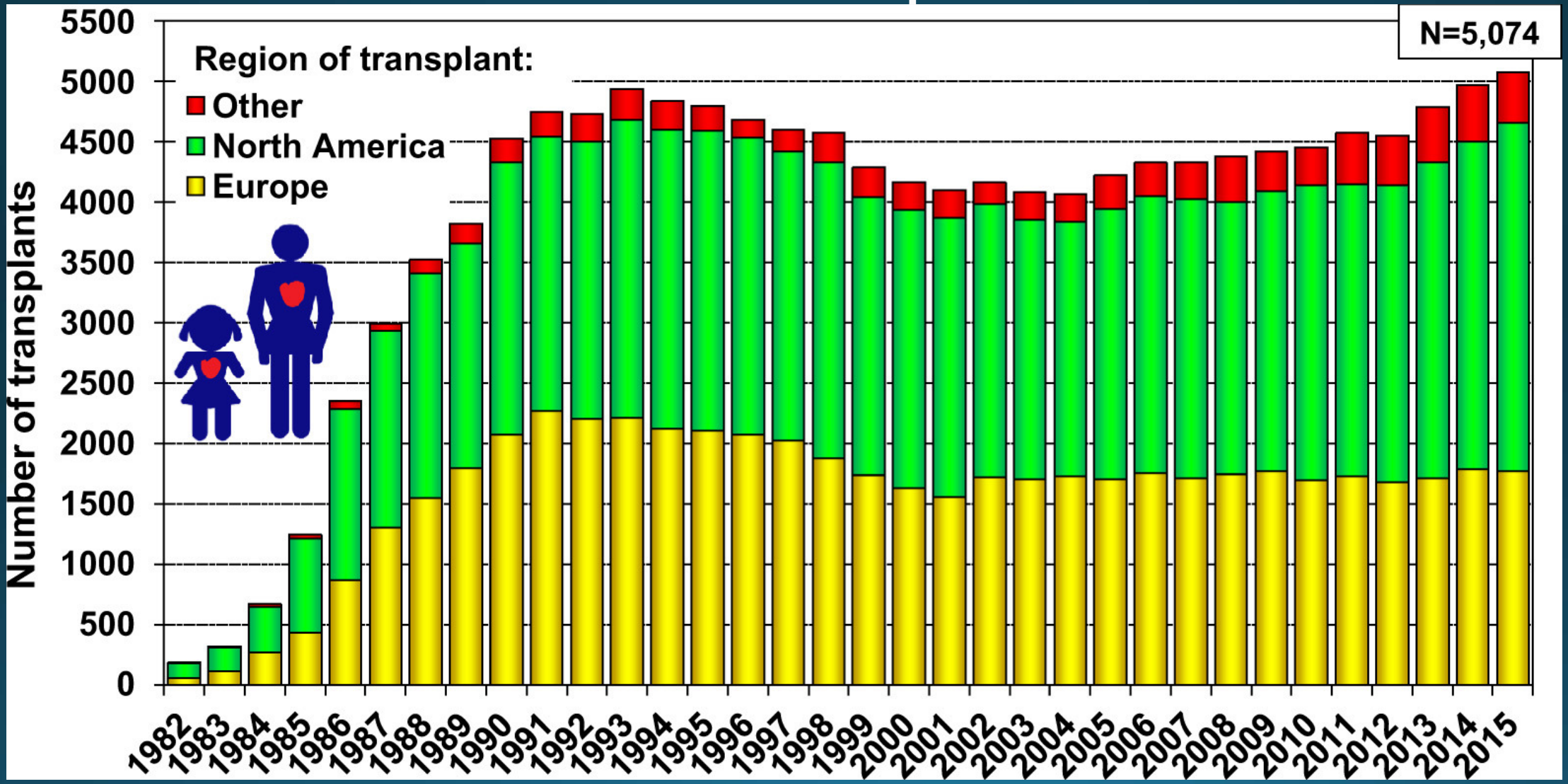
Transplant is a Limited Resource and the Gold Standard:

- 3,191 people received a heart transplant in the United States in 2016 (most ever in one year)
- ~3,800 people listed the same year
- Median survival of 12 years, 13-14 years if patient survives the first year
- Trend towards many more listed patients supported with Mechanical Circulatory Support (MCS)
  - 5.1% in 2005
  - 31% in 2015
- Improving survival with MCS
  - Evolving field
  - Has not reached a point of clinical equipoise with OHT

Heart Transplants



The Journal of Heart and Lung Transplantation 2017 36, 1037-1046DOI: (10.1016/j.healun.2017.07.019)

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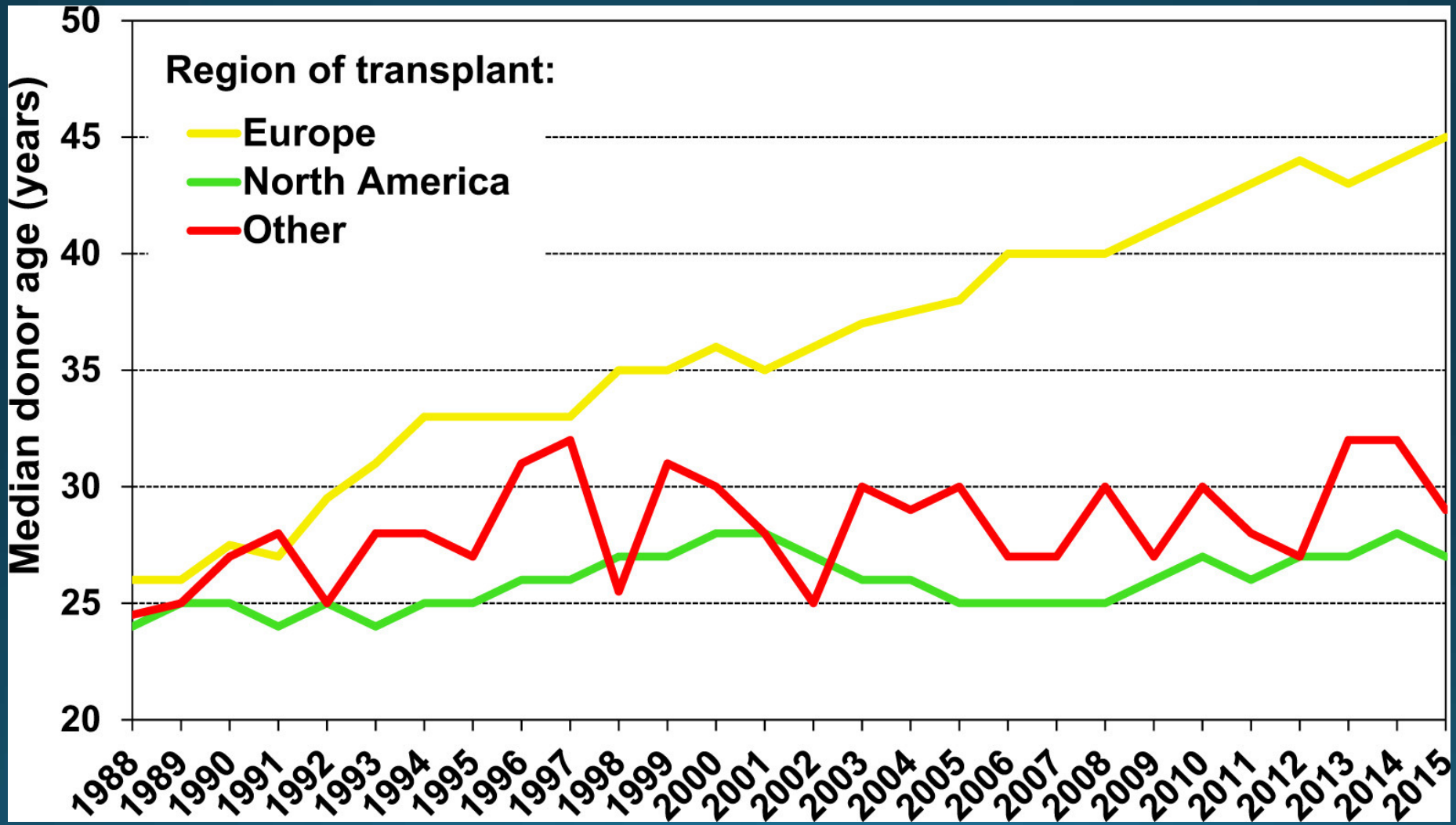
Heart Trends

- Recipient and Donor ages continues to increase
  - There is a need!
- Number of combined organ transplants (Heart-kidney and Heart Liver) are increasing. Now account for 4% of total heart transplant volume
- ~50% of pts are transplanted with bridge MCS. This has increased significantly since mid 2000's and is now leveling off
- Adult post transplant survival continues to gradually improve
- MCS does not appear to dramatically adversely effect post OHT survival (with the exception of VA ECMO)

Median Donor Age: Heart Transplant



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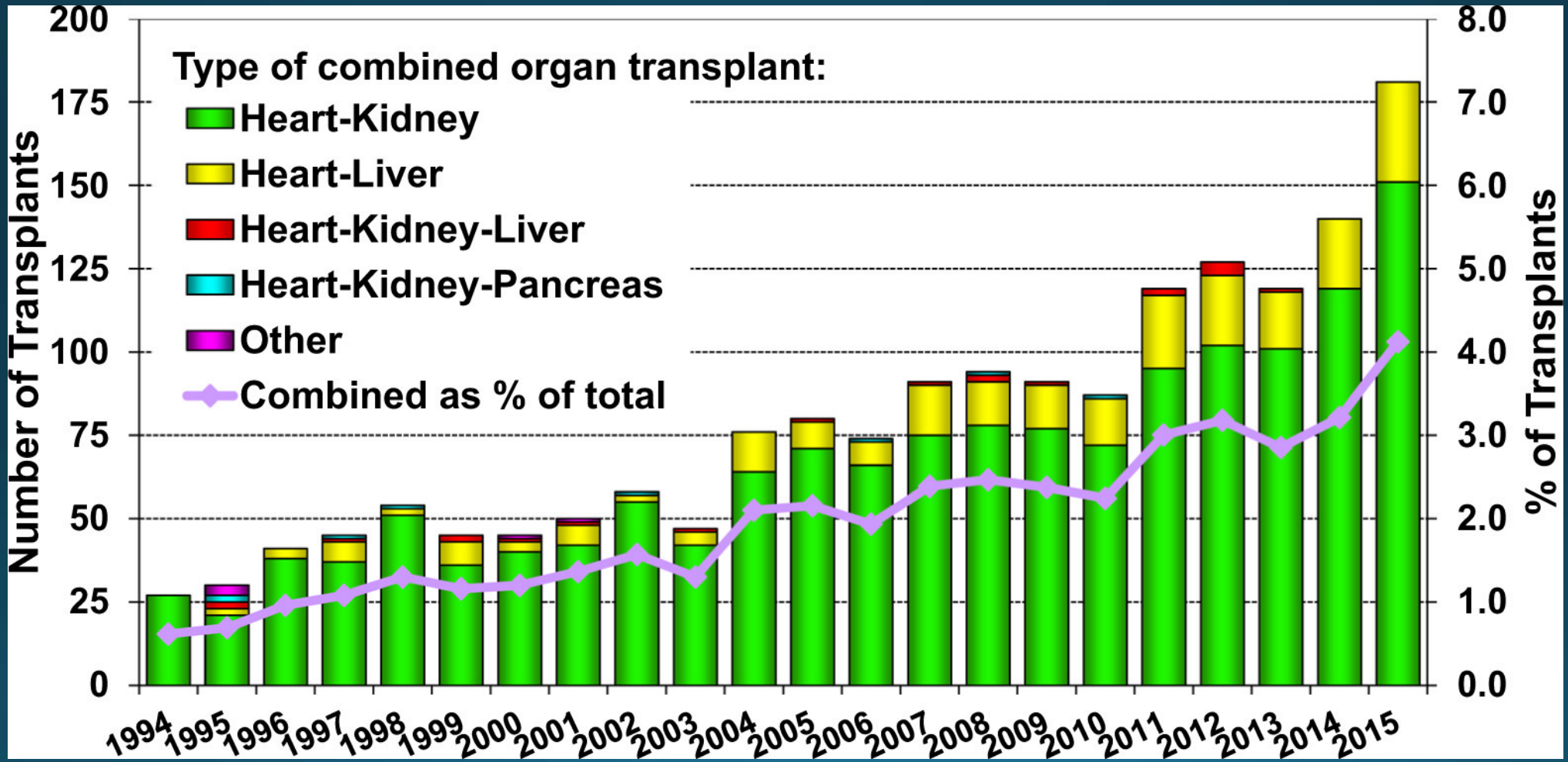
Combined Organ Transplants



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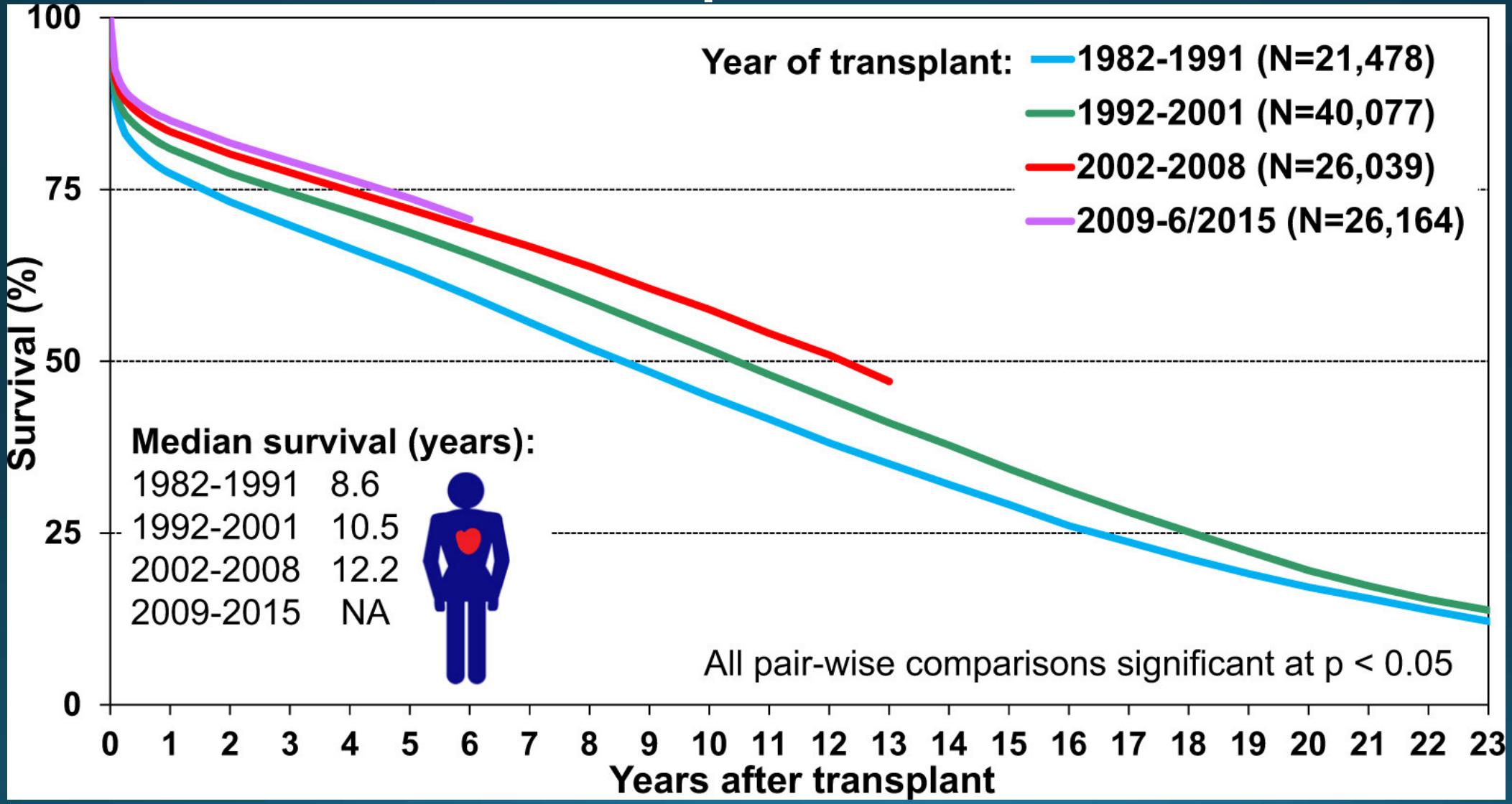
Heart Transplant Survival



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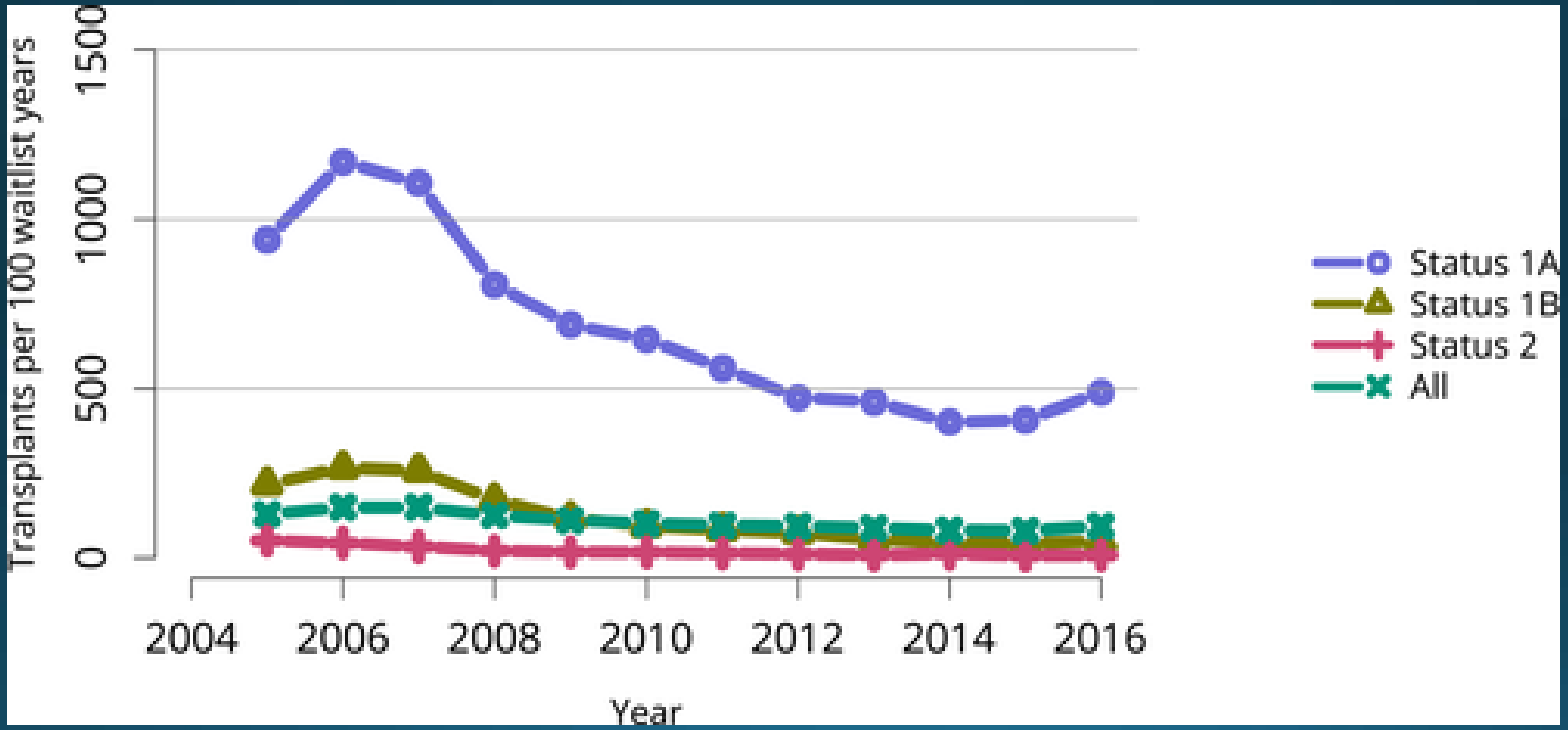
Heart Transplants per Waitlist Years
Are We Meeting the Need?



OPTN/SRTR 2016 Annual Data Report: Heart, Volume: 18, Issue: S1, Pages: 291-362, First published: 02 January 2018, DOI: (10.1111/ajt.14561)

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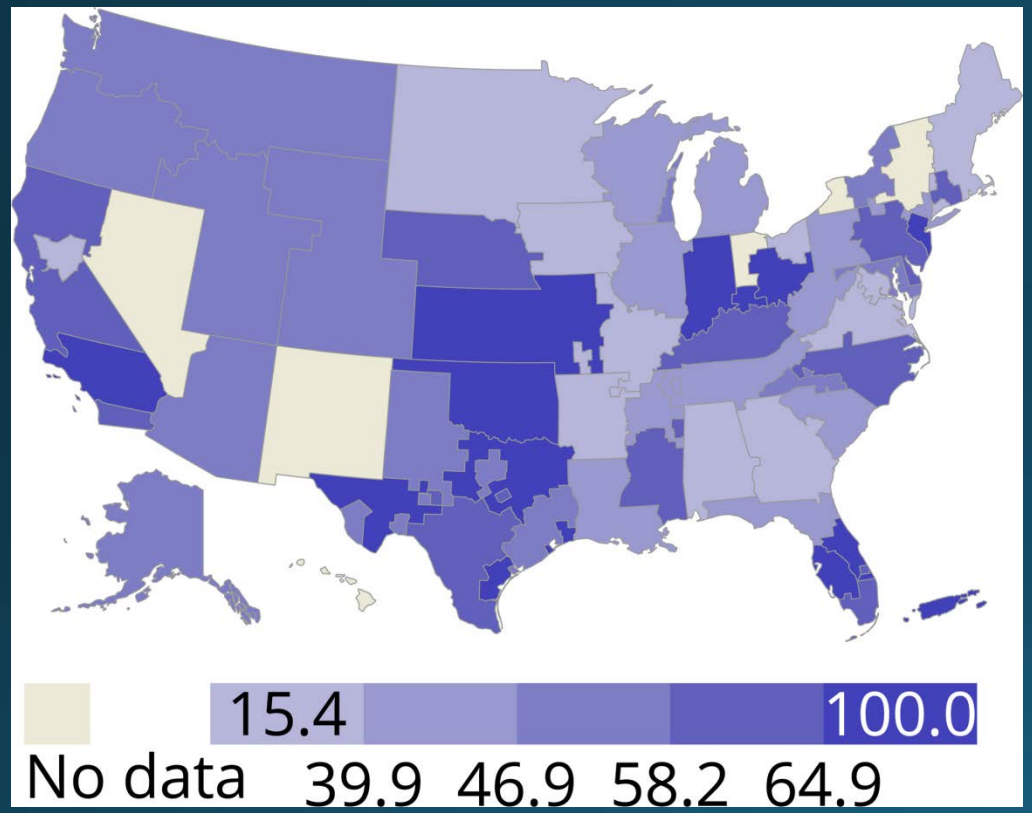
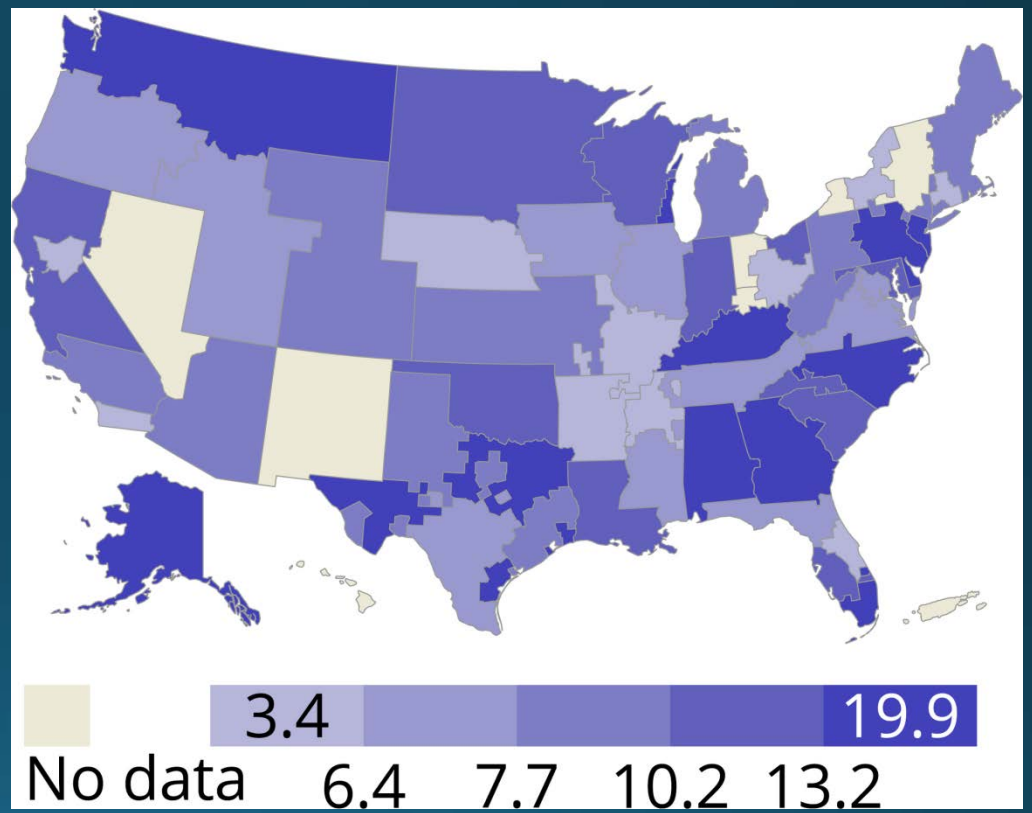
Cardiac Organ Allocation Disparities

- **Cardiac:** Current Cardiac Allocation system (changes 10/18/18) is geographically inequitable and was deemed not to be in keeping with OPTN rule of equitable organ sharing
- **Cardiac:** The current geographic sharing scheme favors less urgent candidates in the local DSA rather than more urgent candidates who may be as close as 25 miles away from the donor but are in Zone A
- Disparities in organ donation by geographic region partially related differences in culture and public perception of organ donation
- Some OPO's more aggressive than others

Percentage of adults who underwent deceased donor heart transplant within 1 year of listing in 2015 by DSA.



Pretransplant mortality rates among adults waitlisted for heart transplant in 2015-2016, by DSA. Mortality rates are computed as the number of deaths per 100 patient-years of waiting in the given year.



Why do these discrepancies exist?

OPTN/SRTR 2016 Annual Data Report: Heart, Volume: 18, Issue: S1, Pages: 291-362, First published: 02 January 2018, DOI: (10.1111/ajt.14561)

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What can be done to close the GAP?

- Increase # Donors
  - Age
  - Hepatitis C Virus
  - Geographical redistribution
  - Formalize "alternate list"/Standardized donor criteria to avoid Intercenter variability (Donor Score)
  - Education for Organ Donation
- Decrease number patients on the waitlist
  - Exclude advanced age?
  - Exclude based upon comorbidities: evidence driven? "Being more strict"
- Improve survival of MCS so that it approaches that of transplant
- Most Importantly: we need more evidenced based studies to guide us!

New Heart Allocation Status

Adult Heart Allocation Criteria for Medical Urgency Status

OPTN | UNOS

Details of extensive criteria requirements outlined in policy

Status 1

- VA ECMO
- Non-dischargeable, surgically implanted, non-endovascular biventricular support device
- MCSD with life-threatening ventricular arrhythmia

Status 2

- Non-dischargeable, surgically implanted, non-endovascular LVAD
- IABP
- V-tach / V-fib, mechanical support not required
- MCSD with device malfunction/mechanical failure
- TAH, BiVAD, RVAD, or VAD for single ventricle patients
- Percutaneous endovascular MCSD

Status 3

- Dischargeable LVAD for discretionary 30 days
- Multiple inotropes or single high-dose inotrope with continuous hemodynamic monitoring
- VA ECMO after 7 days; percutaneous endovascular circulatory support device or IABP after 14 days
- Non-dischargeable, surgically implanted, non-endovascular LVAD after 14 days
- MCSD with one of the following:
  - device infection
  - hemolysis
  - pump thrombosis
  - right heart failure
  - mucosal bleeding
  - aortic insufficiency

Status 4

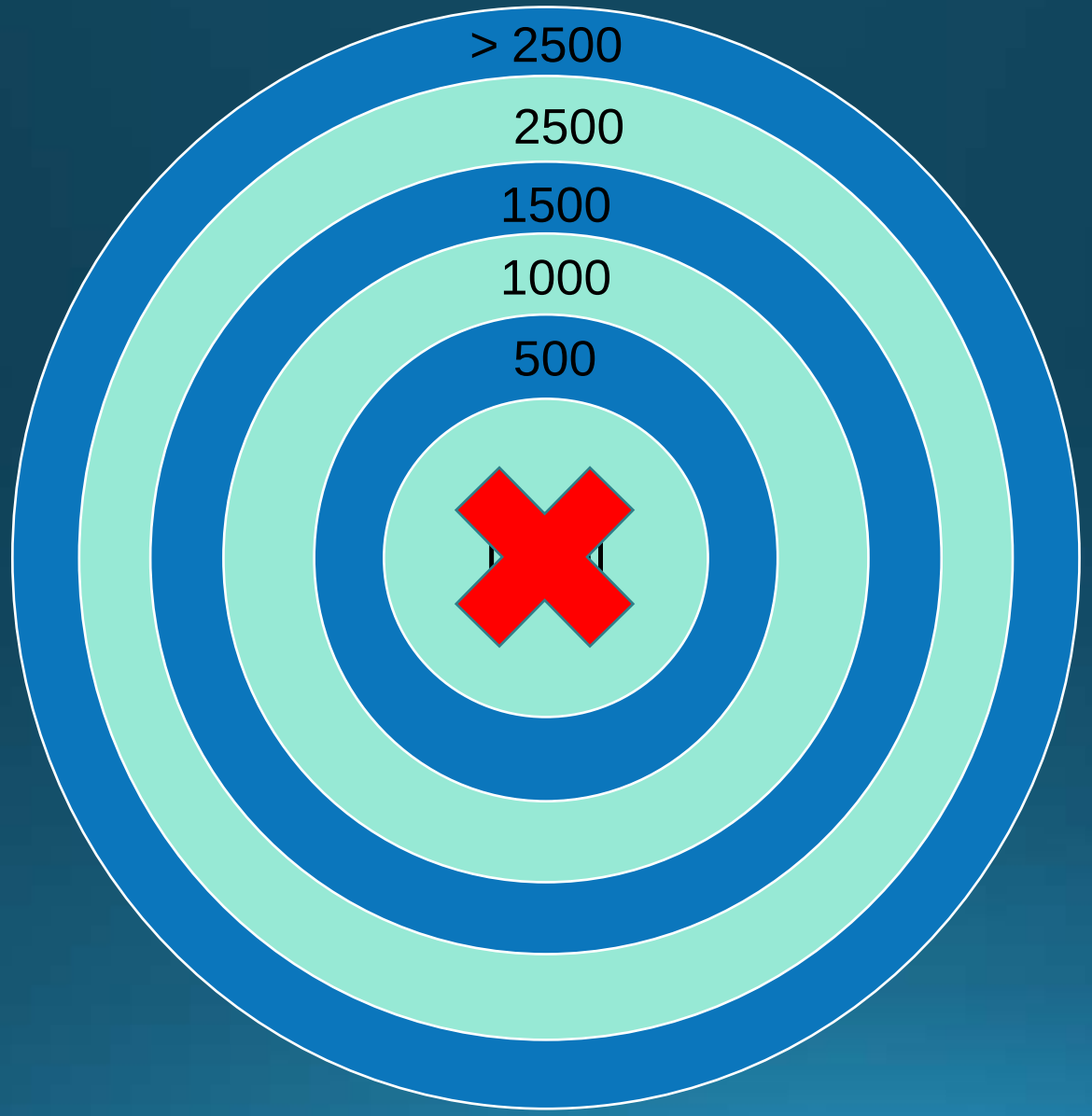
- Dischargeable LVAD without discretionary 30 days
- Inotropes without hemodynamic monitoring
- Retransplant
- Diagnosis of one of the following:
  - congenital heart disease (CHD)
  - ischemic heart disease with intractable angina
  - hypertrophic cardiomyopathy
  - restrictive cardiomyopathy
  - amyloidosis

No more 1A, 1B, Status 2!

Heart Geographic Distribution

New Heart Allocation policy starting October 18th, 2018

1) Change from 3 to 6 status groups
2) Expands “local” geographic distribution to a 500 mile radius from the donor
3) Goal is to decrease waitlist mortality and to have more equitable sharing of organs



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ELSEVIER

The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

Early outcomes using hepatitis C–positive donors for cardiac transplantation in the era of effective direct-acting anti-viral therapies

Kelly H. Schlendorf, MD, Sandip Zalawadiya, MD, Ashish S. Shah, MD, Mark Wigger, MD, Chan Y. Chung, MD, Sarah Smith, MSN, APRN, Matthew Danter, MD, Chun W. Choi, MD, Mary E. Keebler, MD, D. Marshall Brinkley, MD, Suzanne Brown Sacks, MD, Henry Ooi, MD, Roman Perri, MD, Joseph A. Awad, MD, Samuel Lewis, RN, BSN, Rachel Hayes, MSN, APRN, Heather O'Dell, MSN, APRN, Callie Darragh, MSN, APRN, Alicia Carver, PharmD, Cori Edmonds, PharmD, Shelley Ruzevich-Scholl, RN, and JoAnn Lindenfeld, MD

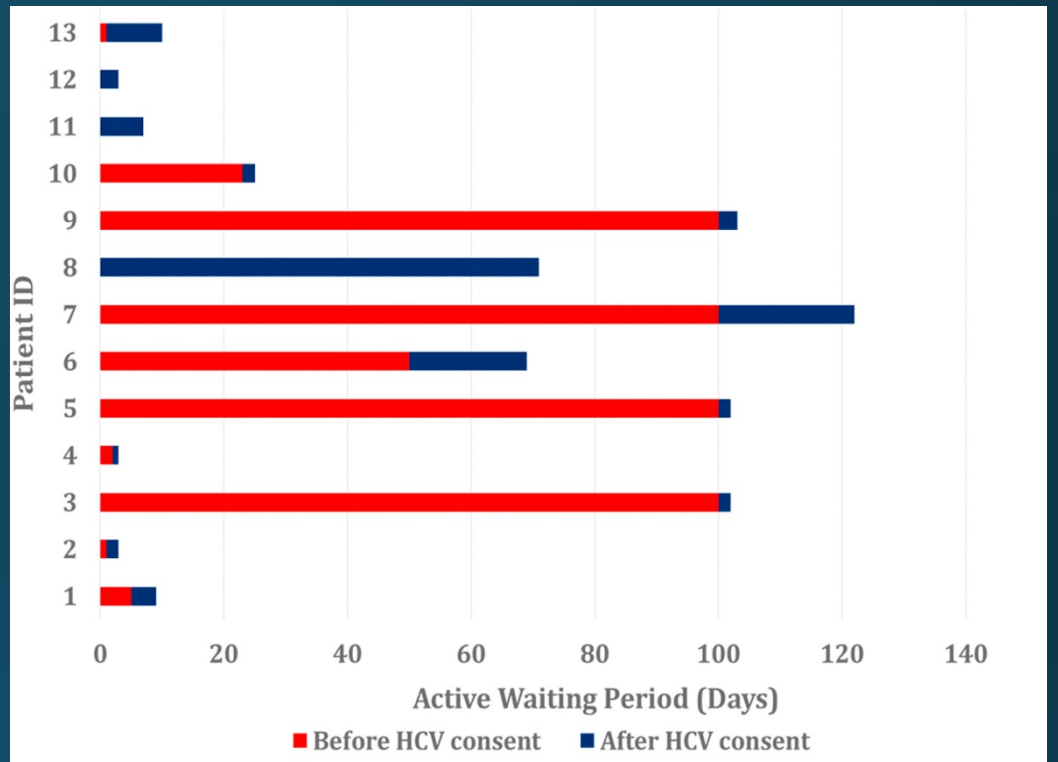
From the Section of Heart Failure and Cardiac Transplantation, Vanderbilt University Medical Center, Nashville, Tennessee, USA.

Major advances in treatment of Hepatitis C Virus

Transplant Nephrology has embraced HCV + donors with robust results

Evolving area of investigation of other solid organ transplants to potentially expand the donor pool.

Partially related to opioid crisis



Patient ID	1	2	3*	4	5*	6	7*	8	9*	10	11	12	13
Status 2 before HCV Consent	0	0	0	1	0	0	13	0	0	0	0	0	0
Status 1B before HCV Consent	1	1	202	0	266	50	2043	0	644	9	0	0	0
Status 1A before HCV Consent	4	0	0	1	5	0	30	0	37	14	0	0	1
Total active days before HCV consent	5	1	202	2	271	50	2086	0	681	23	0	0	1
Status 2 after HCV Consent	0	0	0	0	0	0	0	71	0	0	0	0	0
Status 1B after HCV consent	0	1	0	0	0	1	22	0	0	0	0	0	0
Status 1A after HCV Consent	4	1	2	1	2	18	0	0	3	2	7	3	9
Total active days after HCV consent	4	2	2	1	2	19	22	71	3	2	7	3	9

The Journal of Heart and Lung Transplantation 2018 37, 763-769DOI: (10.1016/j.healun.2018.01.1293)

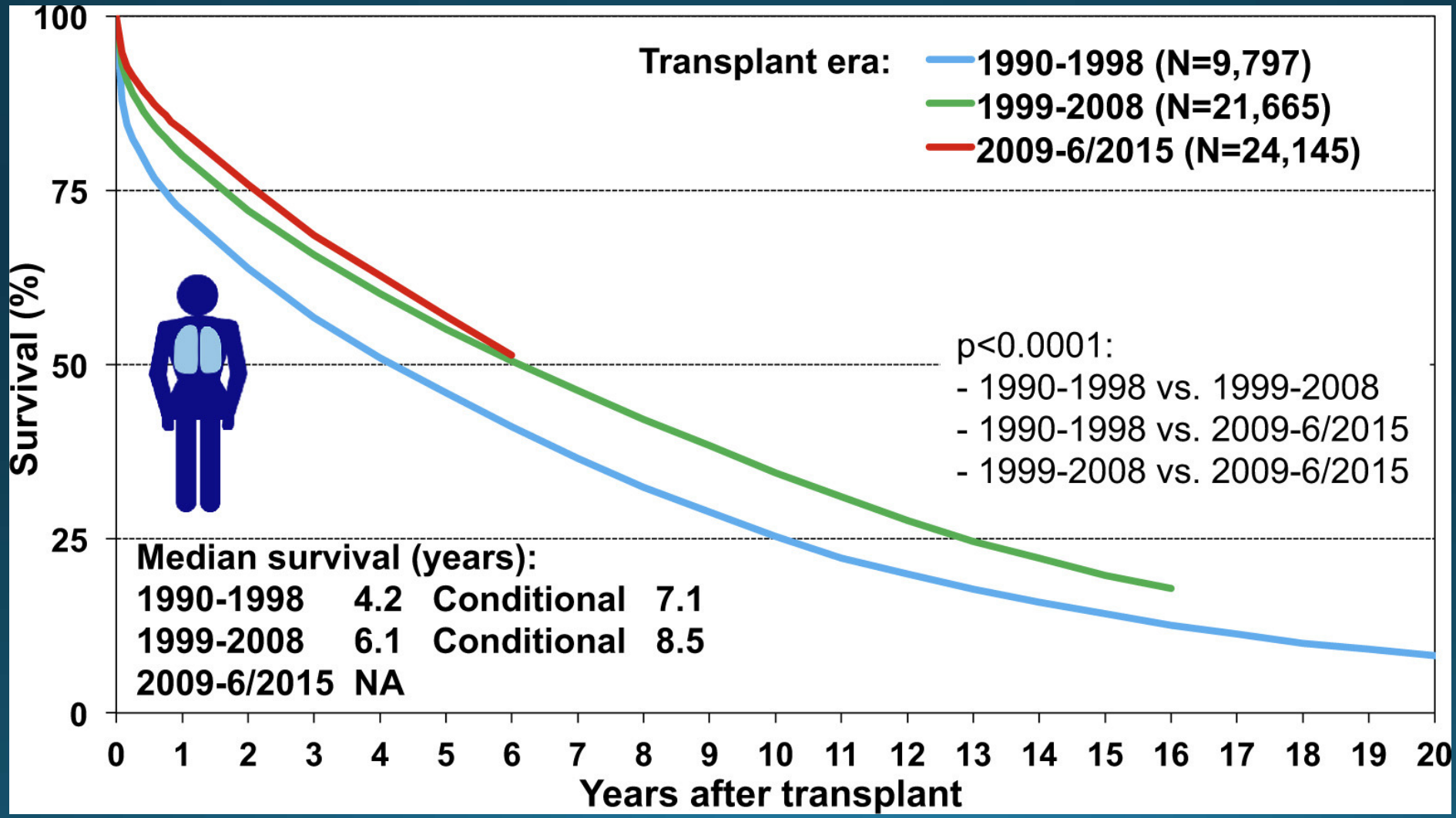
Lung

- 2345 Lung transplant performed in 2016
- In 2016 candidates >65yo accounted for 26.6% of waitlist compared to 11.2% in 2007
- Proportion represented by diagnosis groups A-D remained stable over past 2 yrs:
  - A 33% : Obstructive Lung Disease (COPD, emphysema)
  - B 5.1%: Pulmonary Vascular disease (Idiopathic Pulmonary Hypertension)
  - C 12.3%: Cystic Fibrosis and Immune Deficiency Disorders
  - D 50.1%: Restrictive Lung Disease (Idiopathic Pulmonary Fibrosis)
- Median LAS at transplant has remained relatively stable

Lung

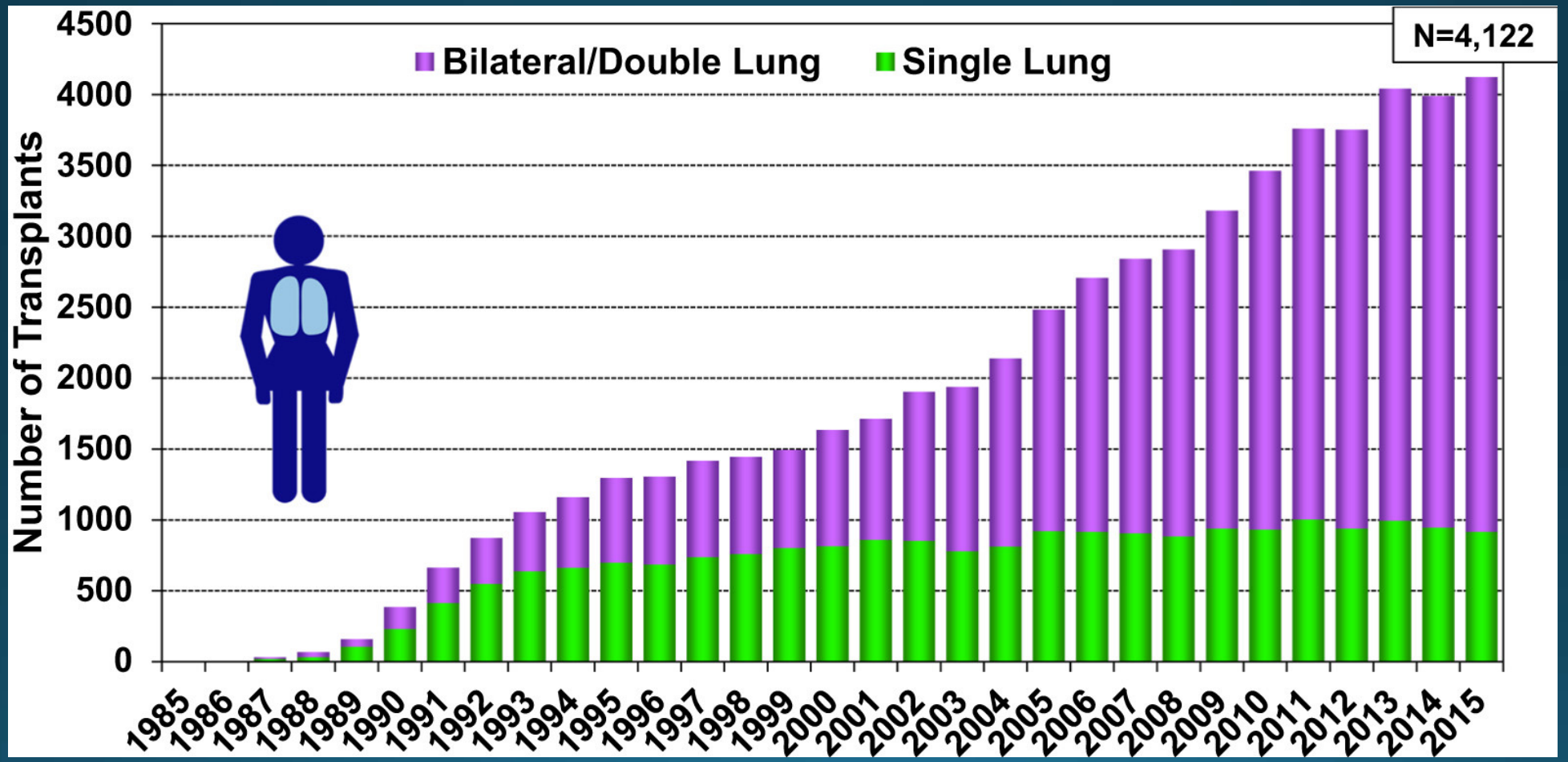
- Median wait time across all groups was 2.9 months
- Median survival is 6 years and is 8 years if pt survives the first year post transplant
- Increased use of
  - ECMO 2.3- 5.8%
  - DCD 1.0%-4.0% (increased use of EVLP)
  - ExViVO
- Bilateral Lung transplants continue to increase as a proportion of overall Lung transplants ~75%

Lung Transplant Survival



The Journal of Heart and Lung Transplantation 2017 36, 1047-1059DOI: (10.1016/j.healun.2017.07.016)

Lung Transplants by Type



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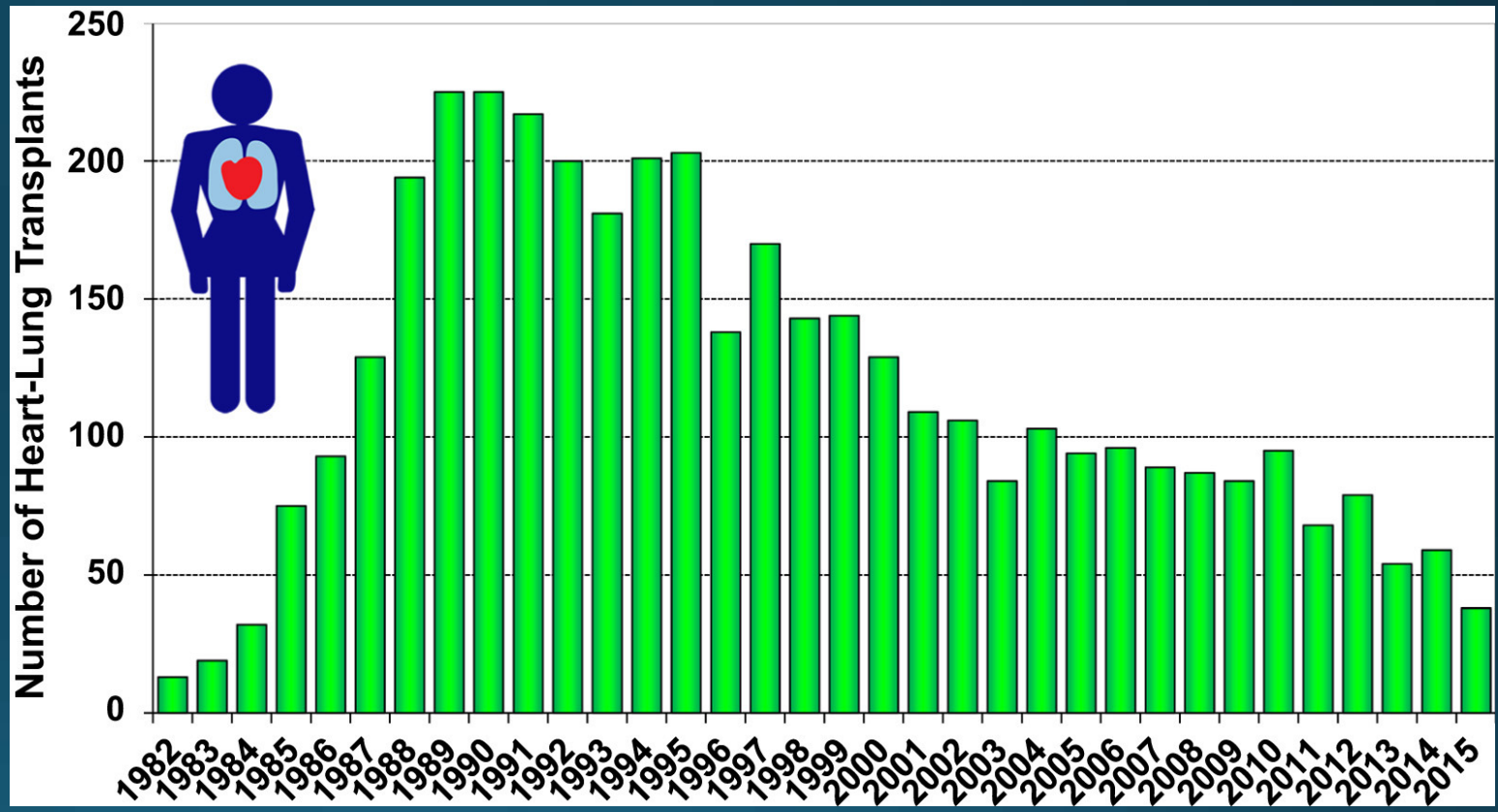
Heart-Lung Transplantation

-Declining volumes since 1989 (225) to 2015 (38)

-Most common indication is Pulmonary Hypertension (66%) of cases

- High short term mortality.
- Median survival is 10.3 years if pt survives the first year post transplant (conditional survival)
- Costs of $2.6 Million/transplant
- Most recipients are < 50yo



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What are the Estimated Cost for Transplant?

Heart Transplant

- Overall: 1.4M
- 30 days pre: 40K
- Procurement: 80K
- Hospitalization: 890K
- MD services: 90K
- 180 days post: 225K
- Rx and Appts: 35K

Lung Transplant (Single/Double)

- Overall: 860K/1.19M
- 30 days pre: 28K/39K
- Procurement: 106K/128K
- Hospitalization: 475K/680K
- MD services: 48K/69K
- 180 days post: 163K/227K
- Rx and Appts: 40K/50K

Combined Heart Kidney $2.5 million, Combined Heart Lung $2.6 million

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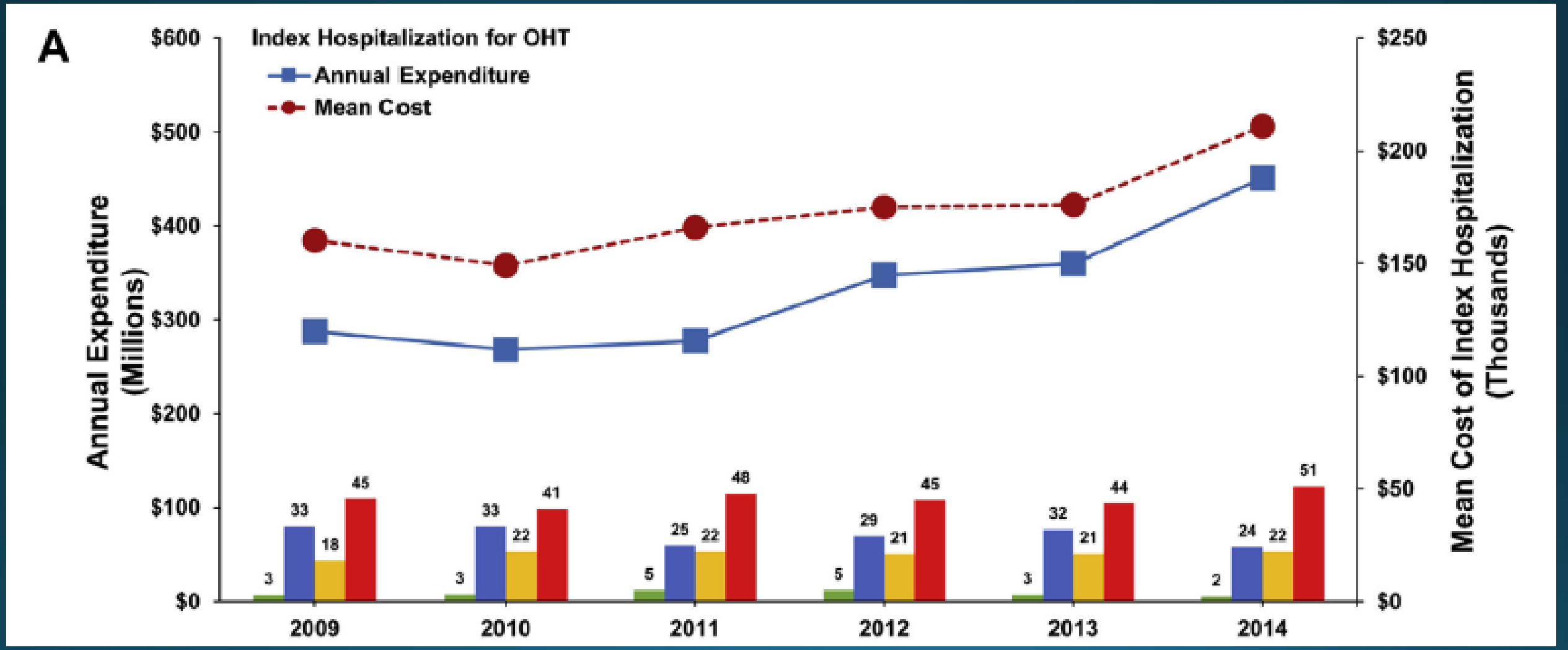
Costs

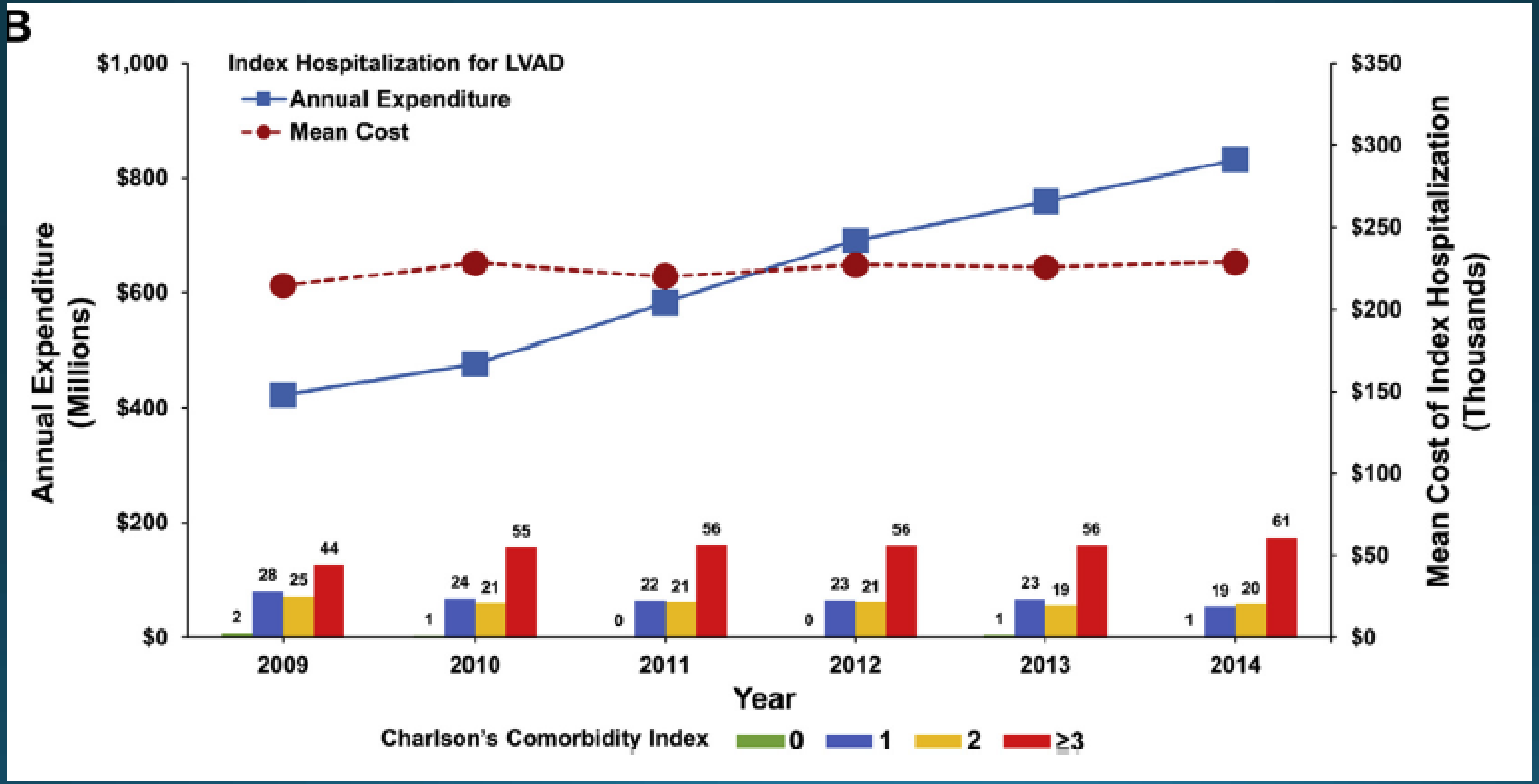
- Heart Transplant and LVAD account for estimated $1.25 billion in costs for Medicare and Medicaid patients.
  - Increased from $688 million in 2009
- 55% of all OHT and LVAD implants/hospitalizations are funded by Medicare
- Cuts to Medicare could adversely effect Medicare beneficiaries
- Transplant Medicine is of high public importance
- We are seeing increased utilization of therapies that work
- Portion of the population with advanced organ disease continues to increase…. So with the overall costs of the treatment for these diseases just based upon volume assuming reimbursement remains stable.
- The $ pie is only so large

Heart Transplant Costs



Patel, N, et al. J Am Coll Cardiol HF 2018;6:424-32

LVAD Costs



Patel, N, et al. J Am Coll Cardiol HF 2018;6:424-32

How Do We Decrease Costs?

- We live in a world where we are told we always need to decrease costs
- I think we should strive to become more efficient and continue to advance the field of solid organ transplant and the therapies and strategies that help us get there while being cost conscious
- Solid organ transplant is a unique therapy. A gift from one human to another
- Most cost efficient centers are high volume centers. High volume centers also have the best outcomes
- Should we funnel transplant patients to high volume centers/ centers of excellence?
  - We need to be data driven and strike a balance between cost efficiency and center accessibility for patients: this balance varies significantly based upon geography

Future of Transplant

- Personalized medicine using genomics and molecular science to customize treatments to optimize outcomes
- Better understanding of both acute and chronic rejection processes
- Potential non-invasive surveillance for rejection (no biopsies for cardiac patients)
  - donor derived cell-free DNA, microRNA, and messenger RNA.
  - Biochemical serum assays measuring gene expression profiling
- Growth in immuno-biology and the development of more effective therapeutic antibody pharmacological treatments
- Inducing donor tolerance to recipient through immuno-modulation
- Continued advances in MCS to further BTT and BTC

Future of Transplant

- Enhanced geographical sharing
  - May be further enhanced by advances in ex vivo preservation
- Possibility of donation after cardiac death (DC D)
- Xenotransplantation: many challenges
- With new technologies will come new challenges. It is a very exciting time in Thoracic Transplant

Thank You

Questions?

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