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# Heart Transplantation

## ACC Middle East Conference

### Dubai UAE

*October 21, 2017*

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# ACC AHA HF Guideline

## Treatment Options for Stage D Heart Failure

### Cardiac transplantation

Evaluation for cardiac transplantation is indicated for carefully selected patients with stage D HF despite GDMT, device, and surgical management

|   |   |
|---|---|
| I | C |
|---|---|

### 7.4.6. Cardiac Transplantation: Recommendation

#### CLASS I

1. Evaluation for cardiac transplantation is indicated for carefully selected patients with stage D HF despite GDMT, device, and surgical management (680). (*Level of Evidence: C*)

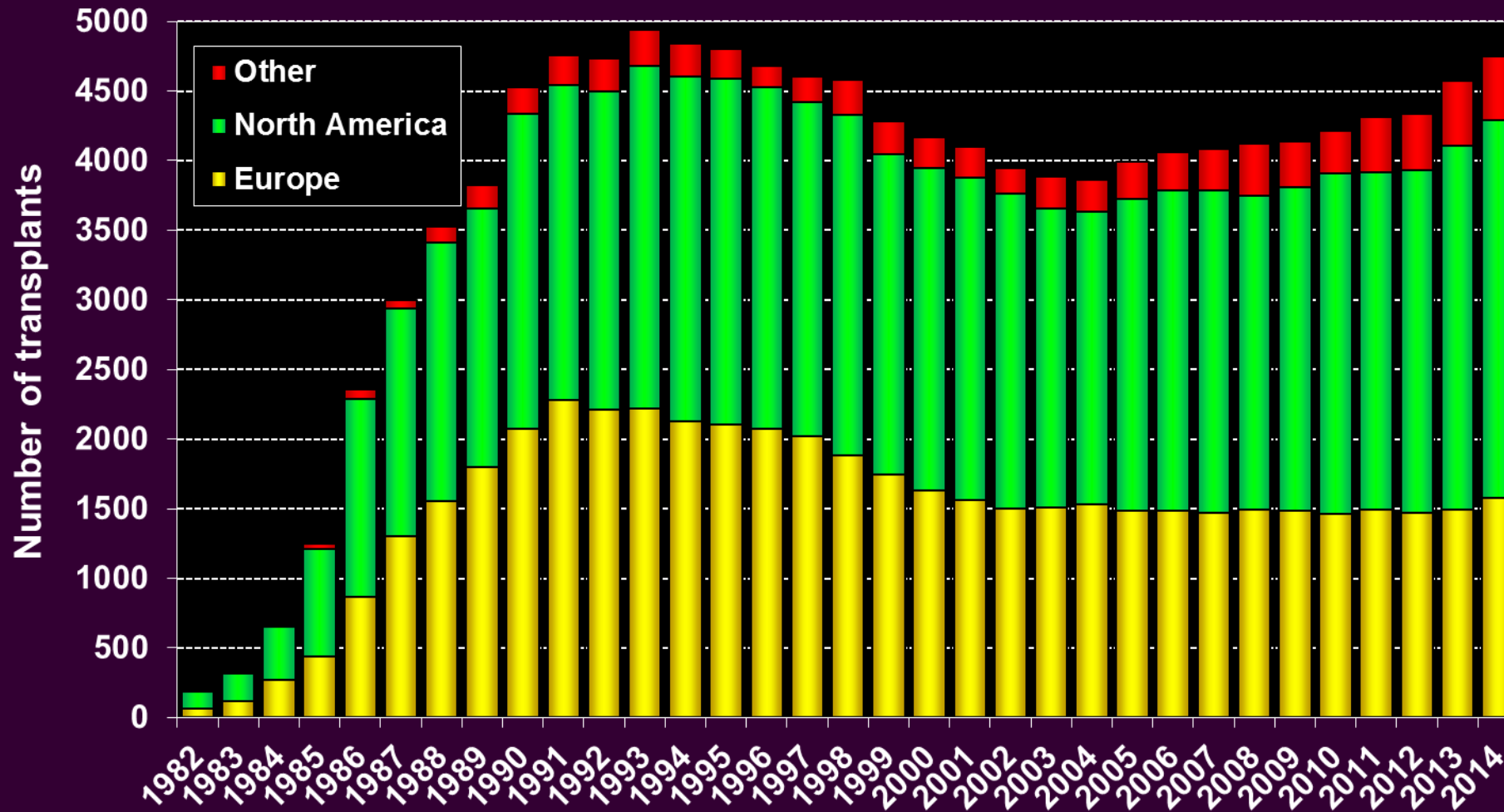
#### Survival

| 1 Year | 3 Year | 5 year |
|--------|--------|--------|
| 87.8%  | 78.5%  | 71.7%  |



# Adult and Pediatric Heart Transplants

## Number of Transplants by Year and Location



# UNOS

## United Network for Organ Sharing

Working together. Saving lives.

UNOS UNITED NETWORK FOR ORGAN SHARING

Transplantation Donation Policy Data Get Involved Careers About



True events inspire new awareness campaign

Watch it now

119,617 people waiting for a lifesaving transplant

Sign up to be a donor

Working together. Saving lives.

Our mission is to advance organ availability and transplantation to support patients through education, technology and policy development.

- Contracted to HHS
- Board reports to Secretary HHS
- Responsible for organ allocation
- Policy/Regulation
- Outcomes: SRTR public reported
- **1.2% of advanced HF population receive donor**



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# USA Geographic Variation in Waiting Time

## Transplantation Traffic — Geography as Destiny for Transplant Candidates

Peter A. Ubel, M.D.

N ENGL J MED 371;26 NEJM.ORG DECEMBER 25, 2014

Steve Jobs had a problem. He needed a liver transplant, but people in northern California, where he lived, waited more than 6 years on average before an organ became available. So he got himself listed at a second transplant center, one in Memphis, Tennessee, where average wait times were less than 3 months.<sup>1</sup>

revise the organ-allocation system so “neither place of residence nor place of listing shall be a major determinant of access to a transplant,”<sup>3</sup> the disparities persist.

The transplant community is considering rule revisions that would reduce these disparities by ensuring that organs are shared

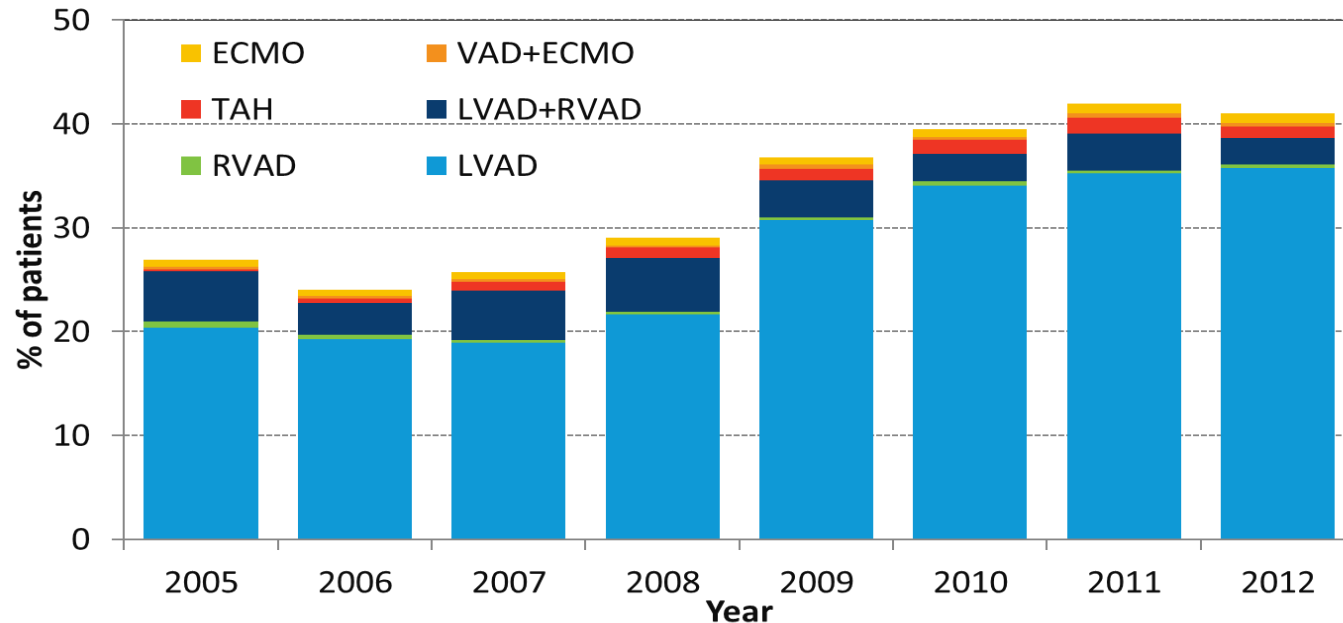
the current system, the United States is divided into 58 donation service areas (DSAs) in 11 regions. When a transplantable cadaveric liver, for example, becomes available, it’s offered to patients in the same DSA, with the sickest patients receiving priority. If there’s no suitable recipient in the DSA, the liver is offered within the

## Median Heart Waiting Time

|             |       |
|-------------|-------|
| USA         | 8 mo  |
| Los Angeles | 4 mo  |
| Cleveland   | 15 mo |



# Adults Bridged with MCS by Year & Device Type

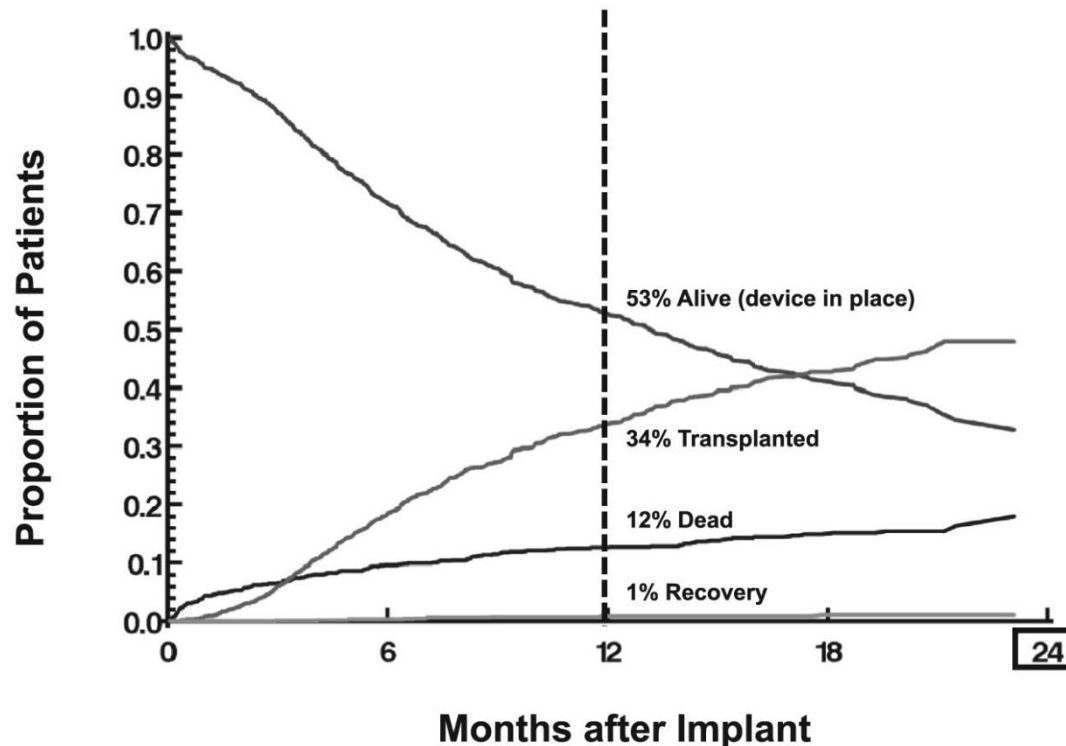


**In USA about HALF of all heart transplant recipients are on durable LVAD prior to transplant**

# Bridge to Transplant Outcomes 2015-2016

Intermacs Implants: June 2006 – December 2016, n=18987

BTT: Listed CFLVADs implants 2015-2016, n=1375



- 34% transplanted at 1 year
- 12% dead at 1 year
- 1% recovery
- 53% waiting

# Heart Transplant Outcomes

## ISHLT Registry

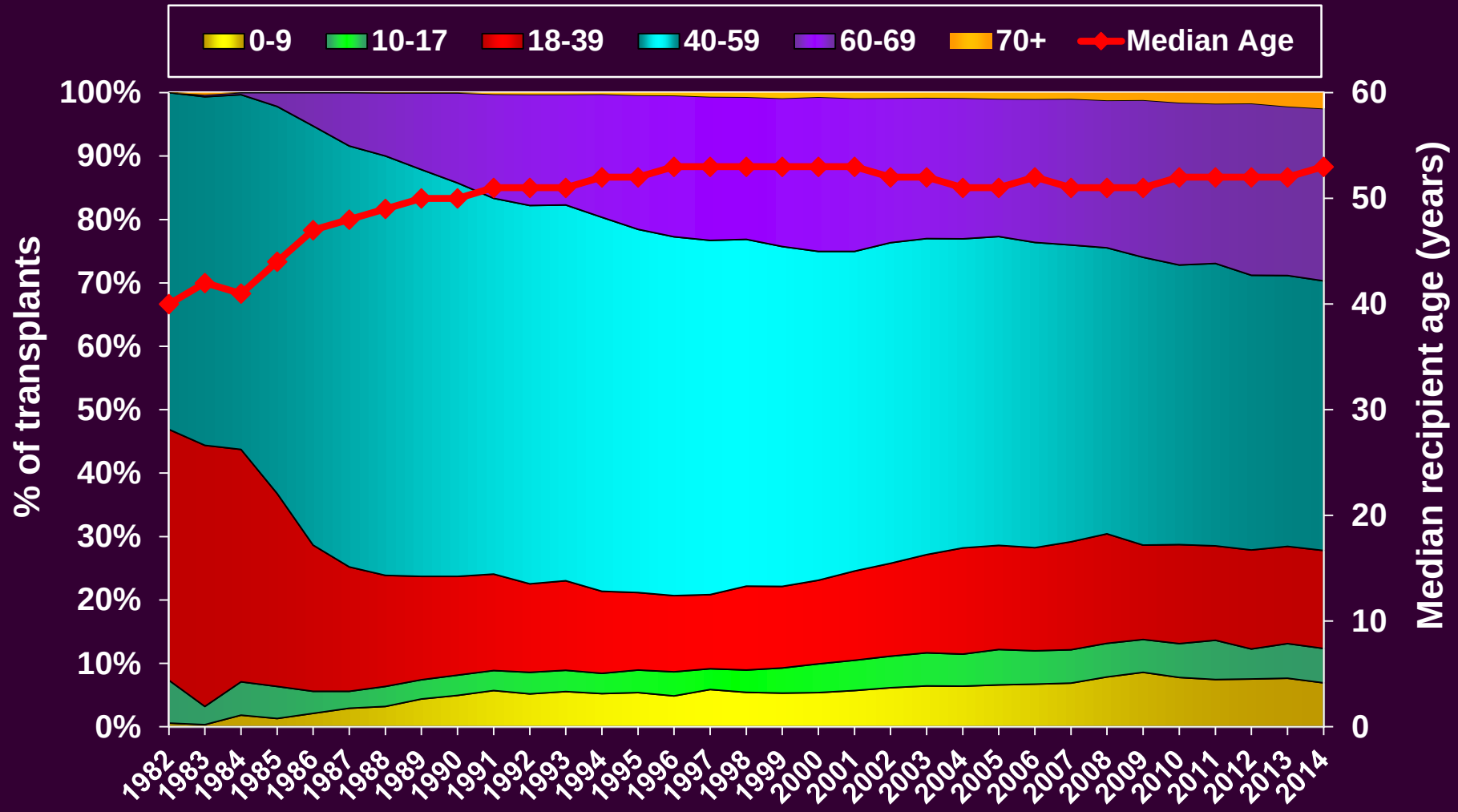
<https://www.isHLT.org/registries/slides.asp?slides=heartLungRegistry>



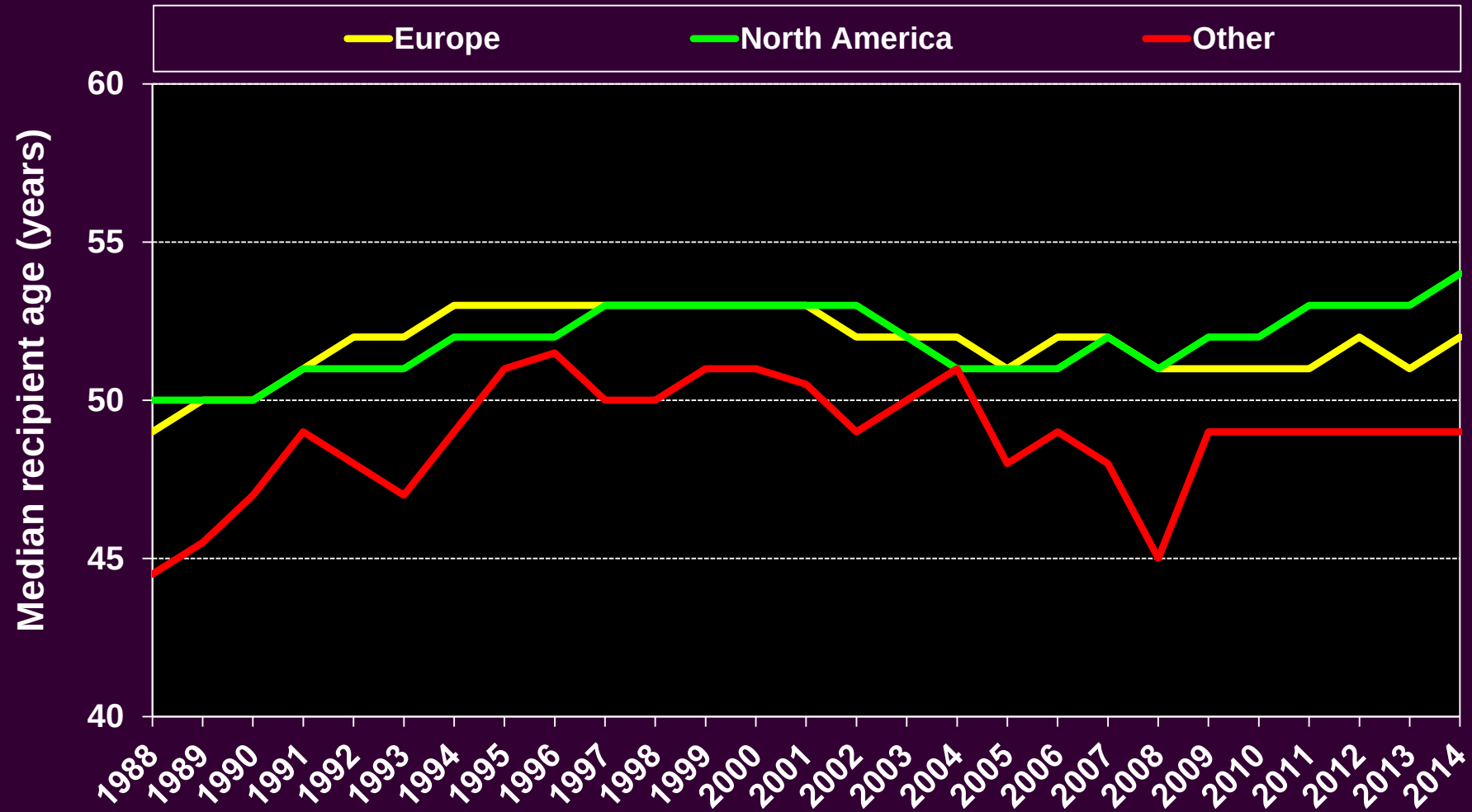
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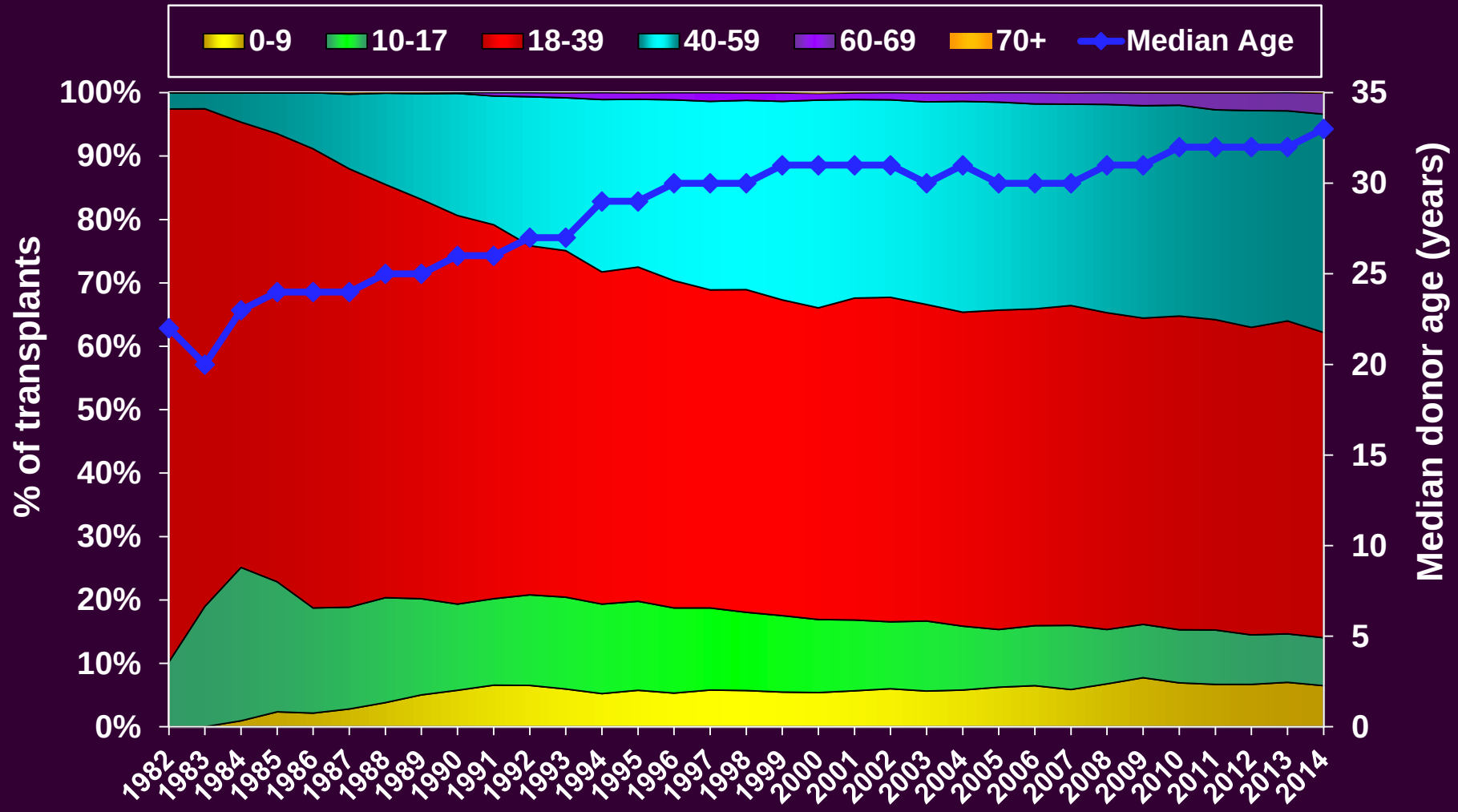
# Adult and Pediatric Heart Transplants Recipient Age by Year of Transplant



# Adult and Pediatric Heart Transplants Median Recipient Age by Location

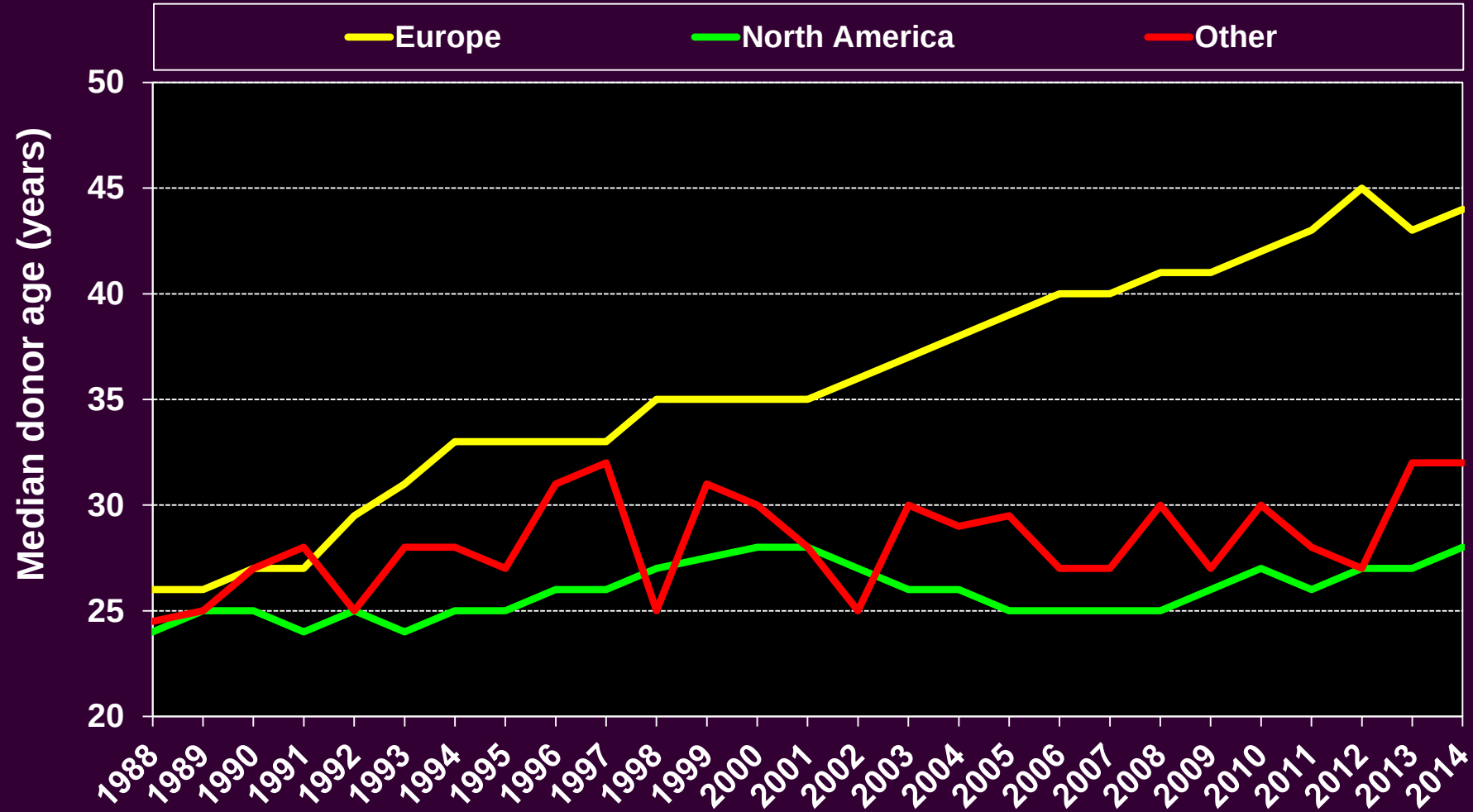


# Adult and Pediatric Heart Transplants Donor Age by Year of Transplant



# Adult and Pediatric Heart Transplants

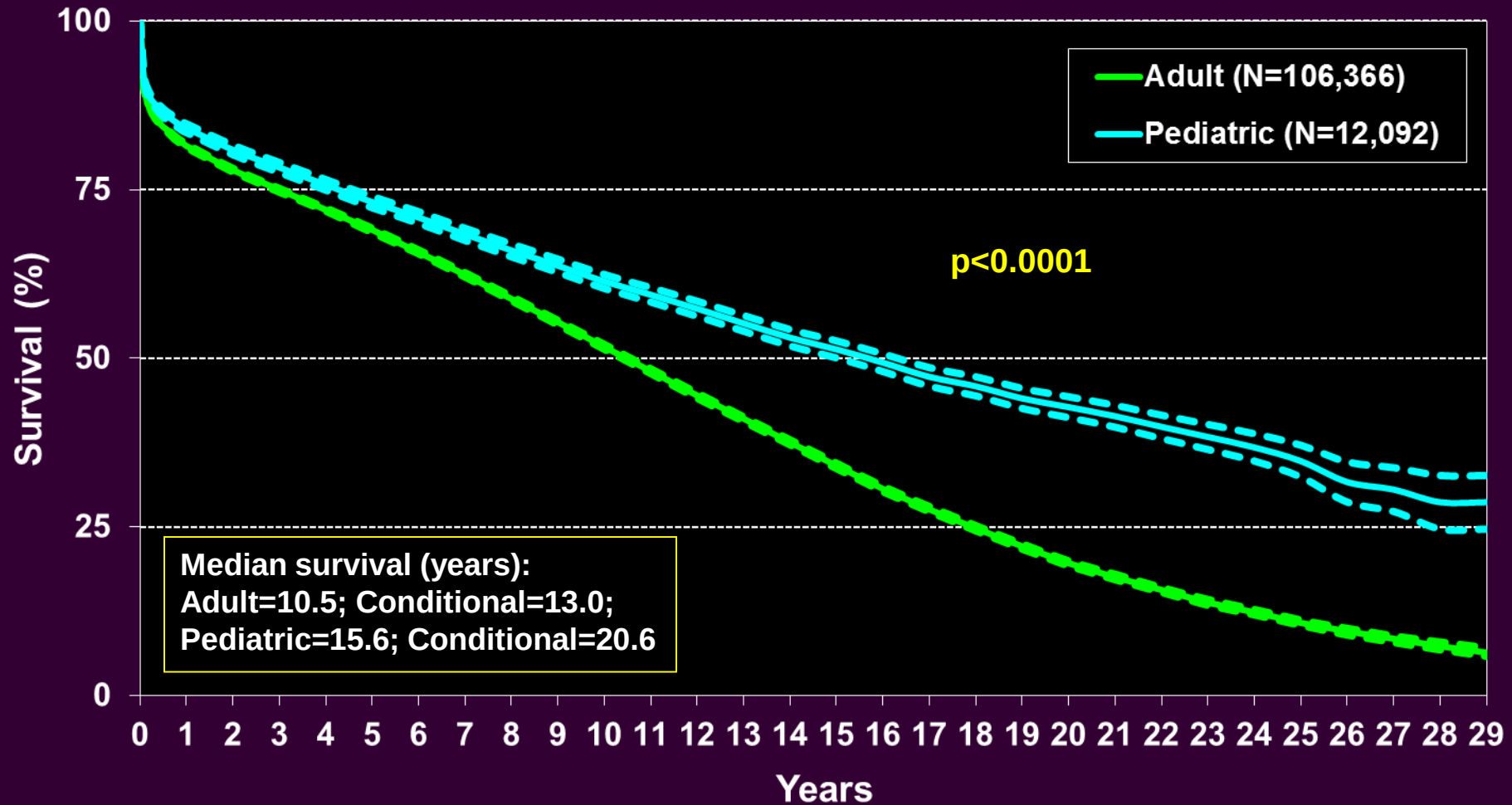
## Median Donor Age by Location



# Adult and Pediatric Heart Transplants

## Kaplan-Meier Survival by Age Group

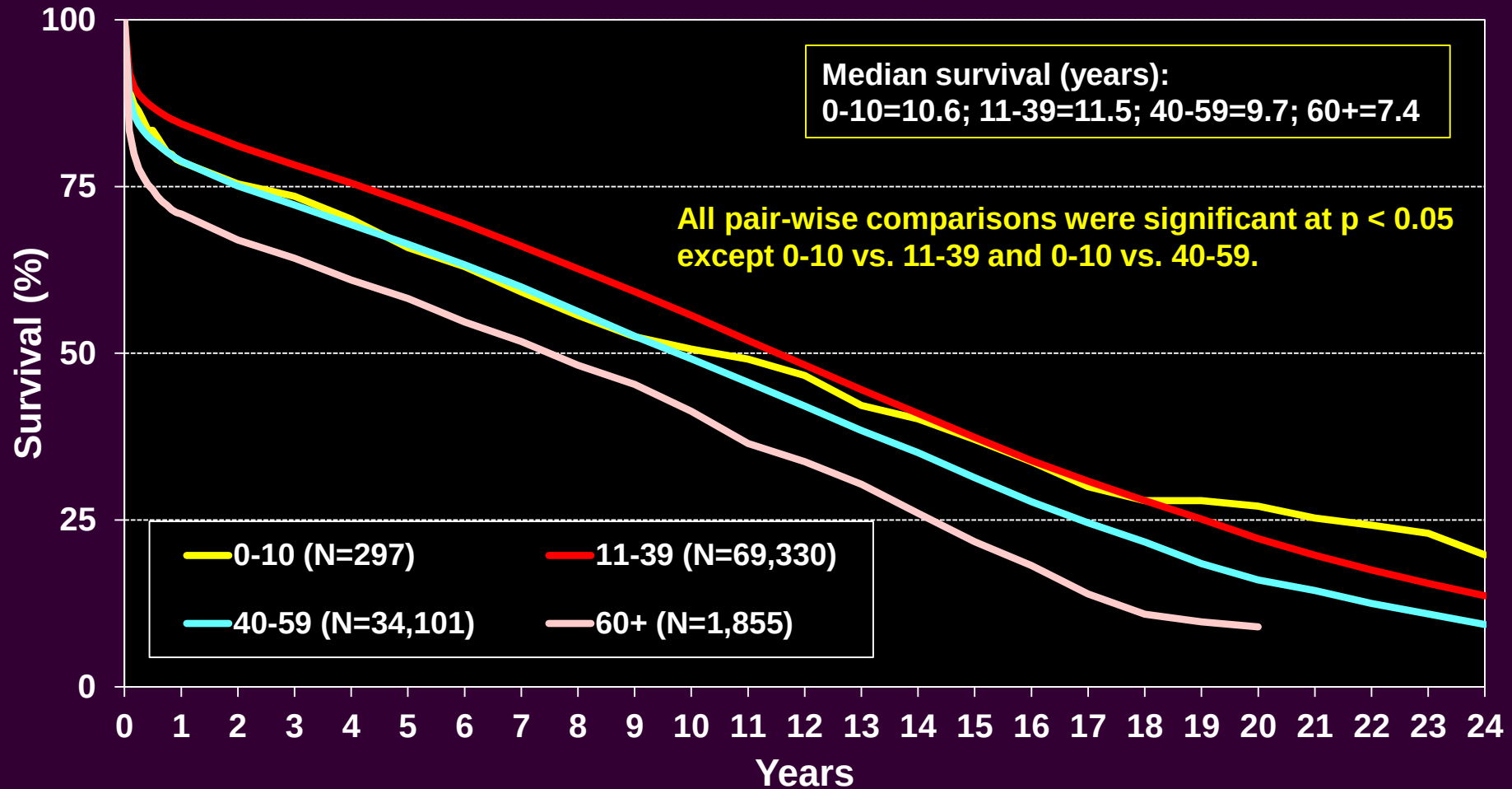
(Transplants: January 1982 – June 2015)



# Adult Heart Transplants

## Kaplan-Meier Survival by Donor Age Group

(Transplants: January 1982 – June 2015)

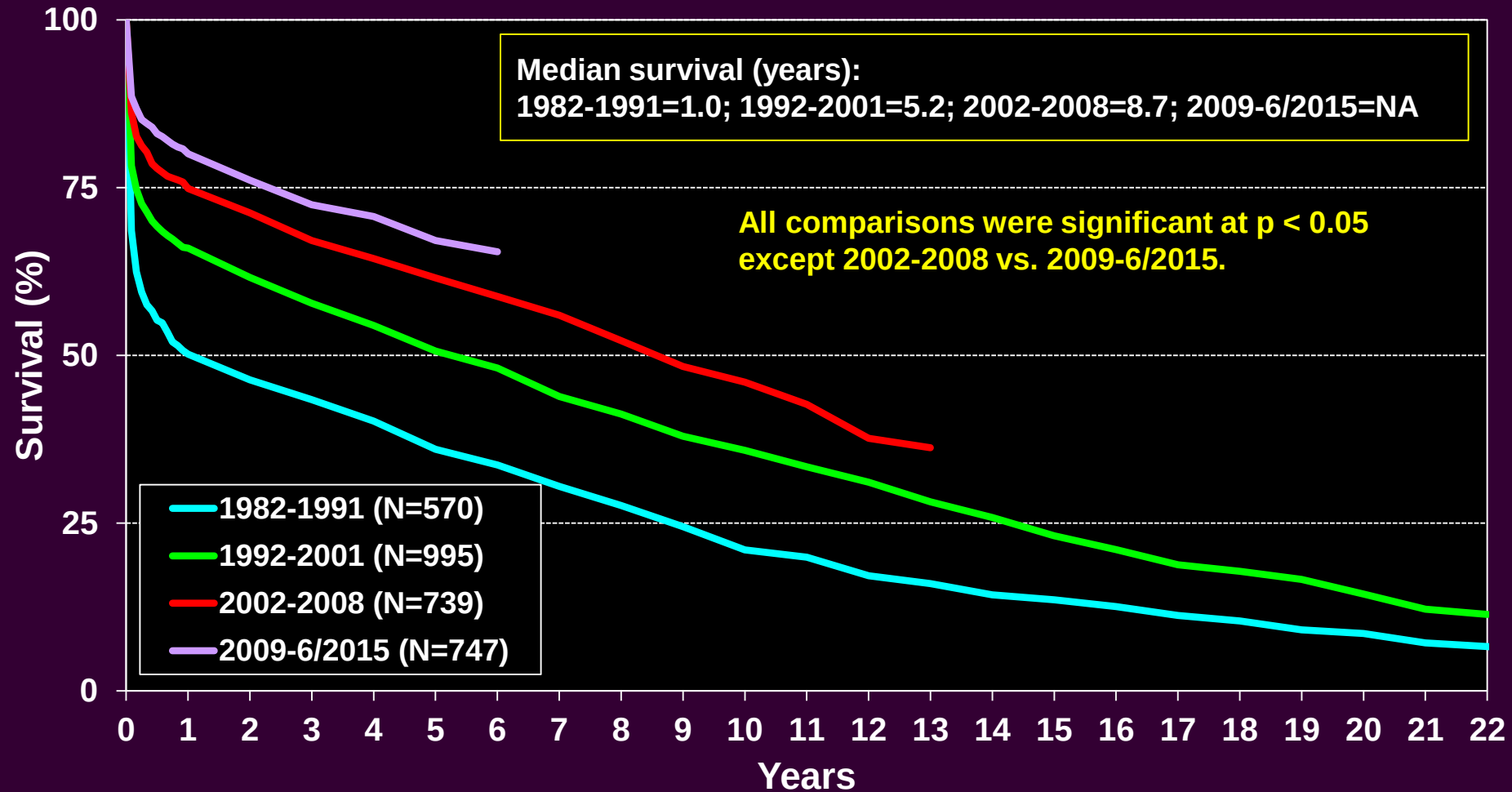




# Adult Heart Transplants

Kaplan-Meier Survival by Era (Transplants: January 1982 – June 2015)

## Diagnosis: Retransplant



# Adult Heart Transplants (2010-6/2015)

## Statistically Significant Risk Factors For 1 Year Mortality

### *Continuous Factors (see figures)*

Recipient age

Recipient creatinine

Recipient height

Height difference

PA systolic pressure

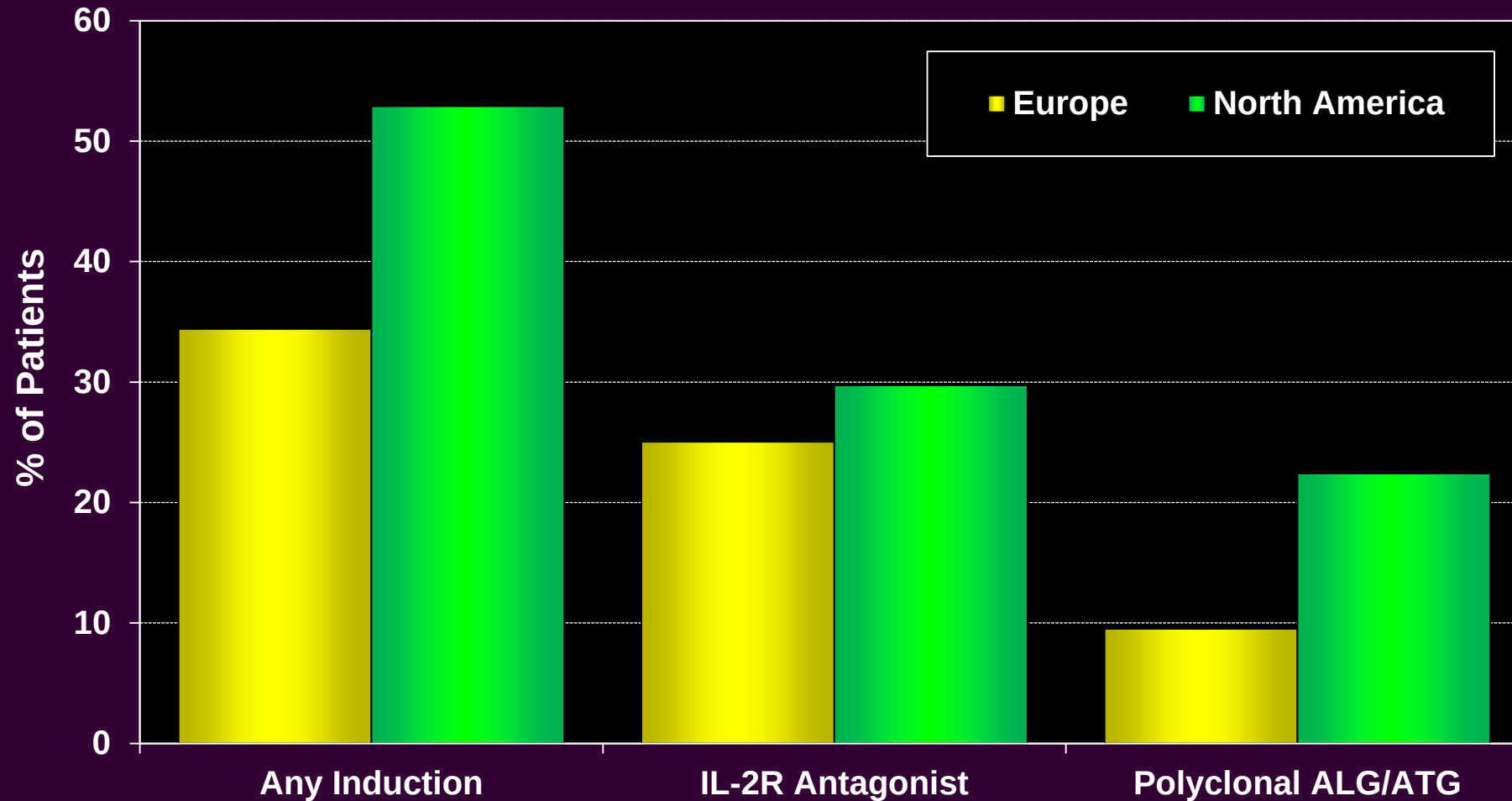
Transplant center volume

Total bilirubin

# Adult Heart Transplants

## Induction Immunosuppression by Location

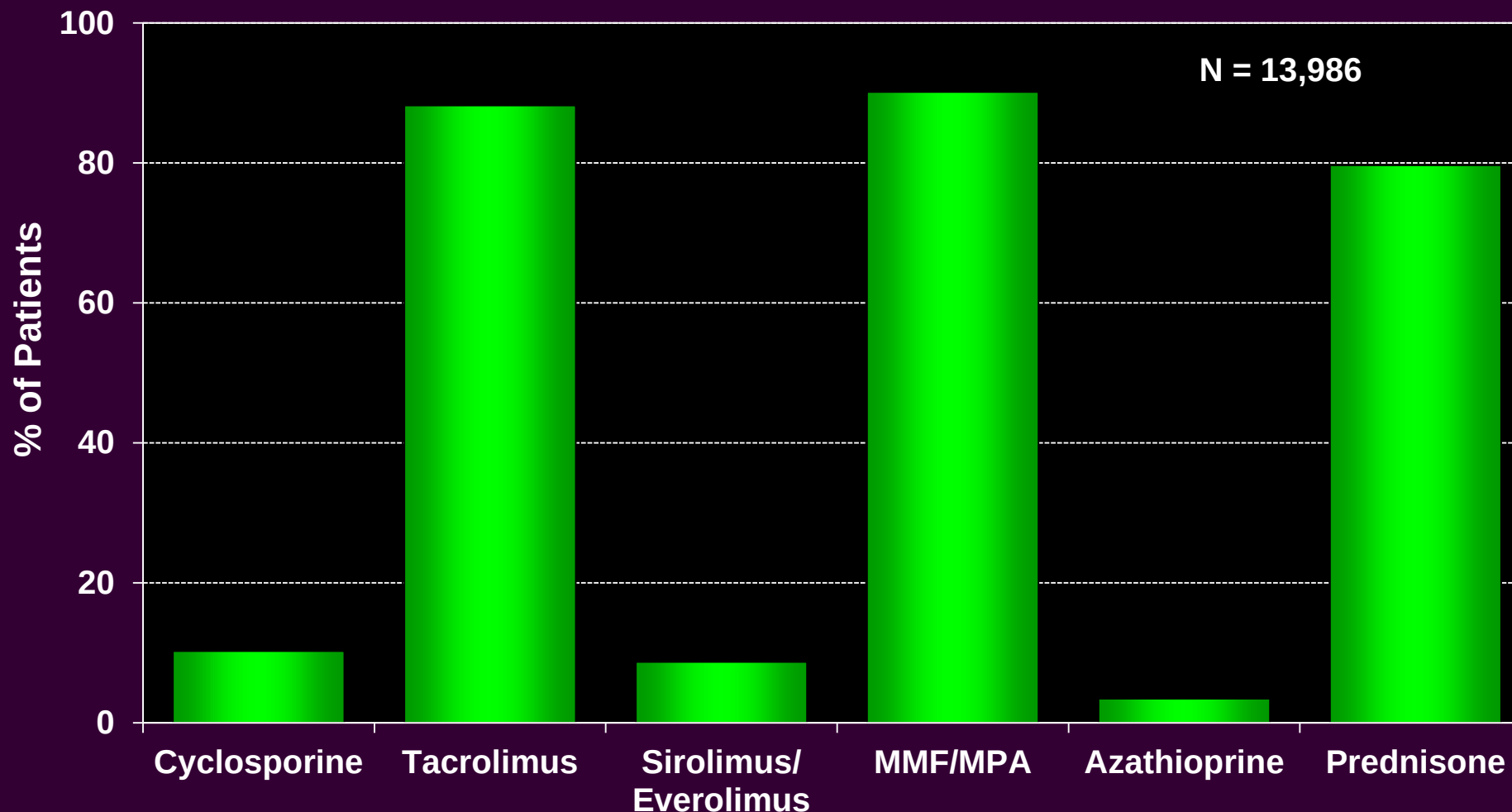
(Transplants: January 2009 – June 2016)



# Adult Heart Transplants

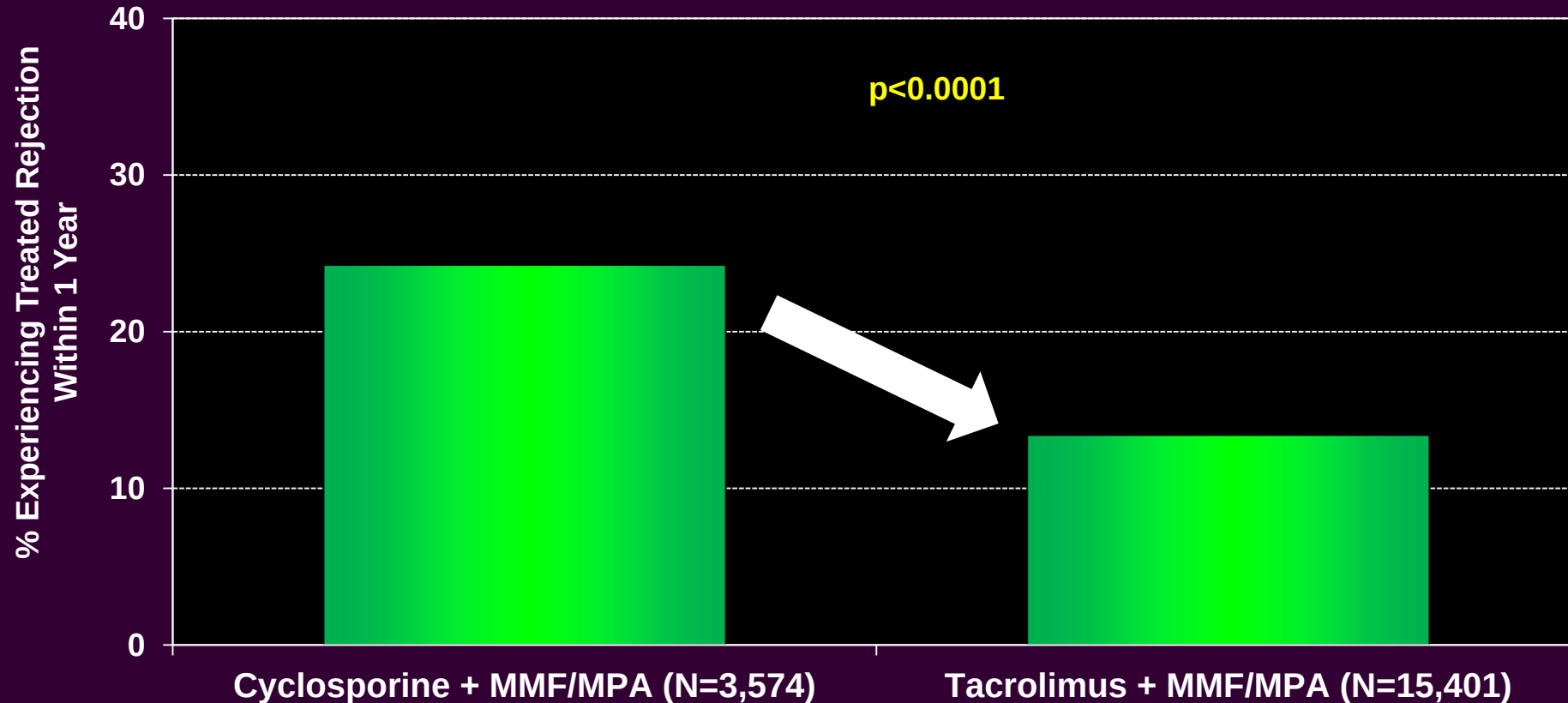
## Maintenance Immunosuppression at Time of 1 Year

### Follow-up (Follow-ups: January 2009 – June 2016)



# Adult Heart Transplants

% of Recipients Experiencing Treated Rejection Between Transplant Discharge and 1-Year Follow-Up by Maintenance Immunosuppression (Follow-ups: January 2005 – June 2016)

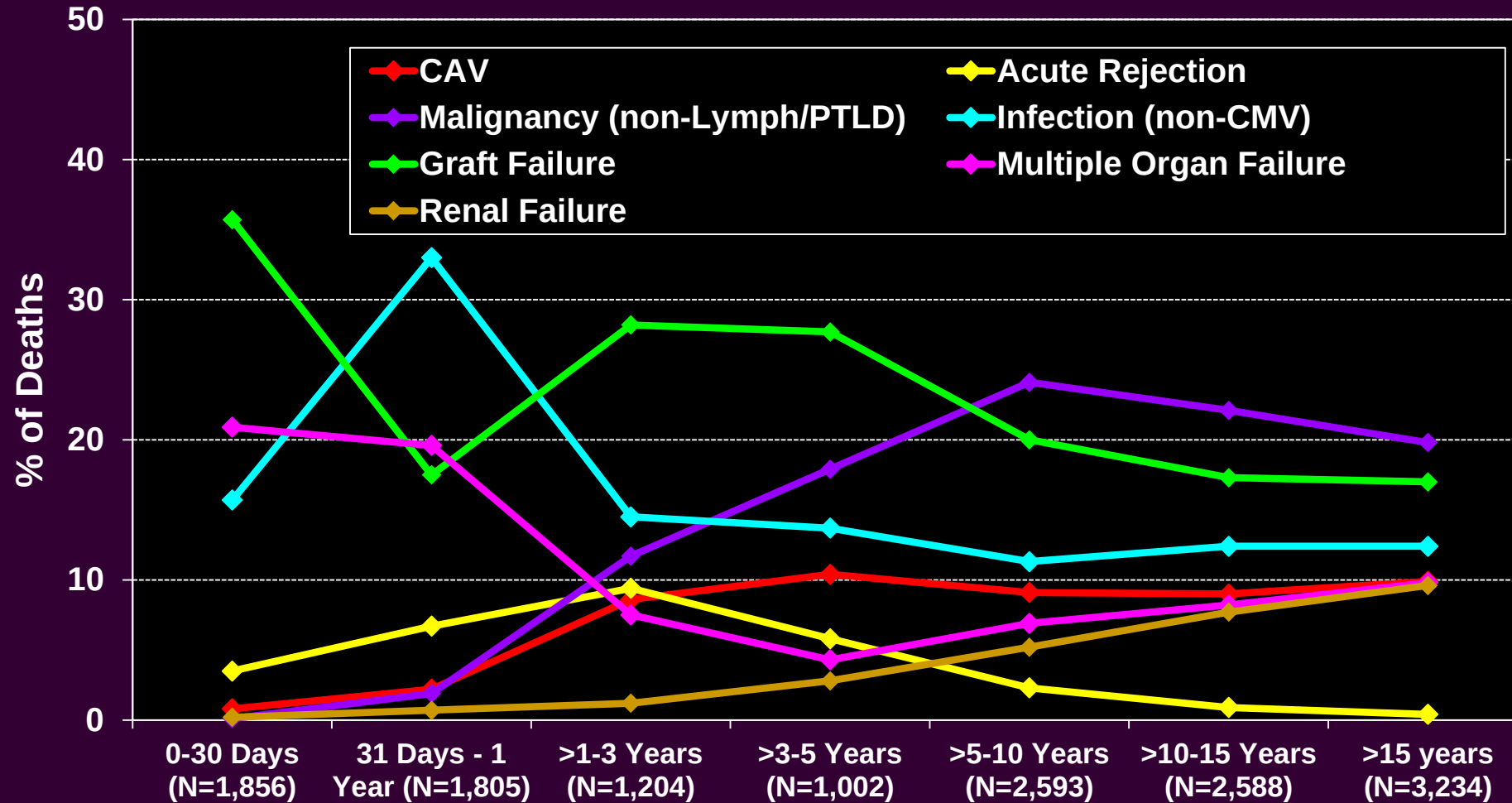


Analysis is limited to patients who were alive at the time of the follow-up.

Treated rejection = Recipient was reported to (1) have at least one acute rejection episode that was treated with an anti-rejection agent; or (2) have been hospitalized for rejection.

# Adult Heart Transplants

## Relative Incidence of Leading Causes of Death (Deaths: January 2009 – June 2016)



# Adult Heart Transplants

## Post Transplant Malignancy (Transplants: January 1994 – June 2015)

### Cumulative Morbidity Rates in Survivors

| Malignancy/Type                 |                          | 1-Year Survivors | 5-Year Survivors | 10-Year Survivors |
|---------------------------------|--------------------------|------------------|------------------|-------------------|
| No Malignancy                   |                          | 35,644 (94.8%)   | 19,728 (84.1%)   | 7,834 (72.3%)     |
| Malignancy (all types combined) |                          | 1,945 (5.2%)     | 3,736 (15.9%)    | 3,001 (27.7%)     |
| <i>Malignancy Type*</i>         | <i>Skin</i>              | 639 (1.7%)       | 2,228 (9.5%)     | 1,999 (18.4%)     |
|                                 | <i>Lymphoma</i>          | 198 (0.5%)       | 260 (1.1%)       | 196 (1.8%)        |
|                                 | <i>Other</i>             | 1,067 (2.8%)     | 1,458 (6.2%)     | 1,095 (10.1%)     |
|                                 | <i>Type Not Reported</i> | 41 (0.1%)        | 37 (0.2%)        | 17 (0.2%)         |

“Other” includes: prostate (11, 31, 19), adenocarcinoma (7, 2, 1), lung (6, 5, 1), bladder (2, 3, 0), Kaposi's sarcoma (0, 2, 0), breast (1, 4, 2), cervical (2, 3, 2), colon (2, 4, 3), and renal (2, 6, 1). Numbers in parentheses are those reported within 1 year, 5 years and 10 years, respectively.

\* Recipients may have experienced more than one type of malignancy so the sum of individual malignancy types may be greater than the total number with malignancy.



# Adult Heart Transplants

## Cumulative Morbidity Rates in Survivors within 1, 5 and 10 Years Post Transplant (Transplants: January 1994 – June 2015)

| Outcome                                                | Within<br><u>1 Year</u> | Total N with<br><u>known</u><br><u>response</u> | Within<br><u>5 Years</u> | Total N with<br><u>known</u><br><u>response</u> | Within<br><u>10 Years</u> | Total N<br>with <u>known</u><br><u>response</u> |
|--------------------------------------------------------|-------------------------|-------------------------------------------------|--------------------------|-------------------------------------------------|---------------------------|-------------------------------------------------|
| Renal Dysfunction                                      | 25.7%                   | (N=34,983)                                      | 51.1%                    | (N=19,655)                                      | 68.4%                     | (N=8,261)                                       |
| <i>Abnormal Creatinine <math>\leq</math> 2.5 mg/dl</i> | 17.2%                   |                                                 | 32.7%                    |                                                 | 39.2%                     |                                                 |
| <i>Creatinine &gt; 2.5 mg/dl</i>                       | 6.3%                    |                                                 | 13.8%                    |                                                 | 18.7%                     |                                                 |
| <i>Chronic Dialysis</i>                                | 1.9%                    |                                                 | 3.2%                     |                                                 | 6.7%                      |                                                 |
| <i>Renal Transplant</i>                                | 0.4%                    |                                                 | 1.4%                     |                                                 | 3.8%                      |                                                 |
| Diabetes*                                              | 22.2%                   | (N=37,659)                                      | 35.5%                    | (N=21,429)                                      | -                         |                                                 |
| Cardiac Allograft Vasculopathy                         | 7.8%                    | (N=34,438)                                      | 29.3%                    | (N=16,016)                                      | 47.4%                     | (N=5,468)                                       |

## Cardiac Allograft Vasculopathy

# Clinical Presentation

- Since denervated, ischemia is often silent
- New dyspnea
- New heart failure
- New wall motion abnormality
- Graft dysfunction/failure
- New arrhythmia (particularly AF)
- Sudden cardiac death

# CAV-Poor Prognostic Indicators

- Early post tx 1-2 yrs-- vasculitis
- Rapid rate of development
- CAV<sub>3</sub> (severe)
- Reduced LV ejection fraction
- Restrictive Physiology
- IVUS
  - Change in maximal intimal thickness at a specific site >0.5 mm in the 1st yr post tx
  - Change in percent atheroma volume year 1

# Cardiac Allograft Vasculopathy

## Treatment

- Palliative
  - Rapamycin/Everolimus
  - PCI
  - CABG (rare)
- Retransplant

## Everolimus Versus Mycophenolate Mofetil in Heart Transplantation: A Randomized, Multicenter Trial

**Table 4:** Results of the IVUS analysis of the evaluable patients in the IVUS substudy

| Change from baseline to month 12                   | Everolimus 1.5 mg (N = 88) | MMF 3 g (N = 101)    | p-Value <sup>1</sup> |
|----------------------------------------------------|----------------------------|----------------------|----------------------|
| Average MIT (mm)                                   |                            |                      | <0.001               |
| Mean                                               |                            |                      |                      |
| Median                                             |                            |                      |                      |
| Patient                                            |                            |                      | 0.018                |
| Patient                                            |                            |                      | 0.042                |
| Average                                            |                            |                      | 0.012                |
| Mean                                               |                            |                      |                      |
| Median                                             |                            |                      |                      |
| Average                                            |                            |                      | <0.001               |
| Mean ± SD                                          | 0.01 ± 0.02                | 0.03 ± 0.06          |                      |
| Median (min, max)                                  | 0.01 (−0.06, 0.09)         | 0.02 (−0.12, 0.33)   |                      |
| Normalized total intimal volume (mm <sup>3</sup> ) |                            |                      |                      |
| Mean ± SD                                          | 3.40 ± 8.75                | 11.44 ± 8.07         | 0.012                |
| Median (min, max)                                  | 2.58 (−34.69, 23.14)       | 6.39 (−23.60, 89.09) |                      |

Patients with CAV 12.5% vs 26.7% p=.018  
Azathioprine ~50%

Everolimus 1.5 mg with reduced CNI is non inferior to MMF at 12 months and reduces intimal proliferation in de novo heart transplant patients

# Heart Transplant Follow up



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# Post Heart Transplant Monitoring

- Historical approach is invasive:  
coronary angiography/IVUS  
endomyocardial biopsy
- Standard:
  - Cath yearly vs stress imaging
  - IVUS variable
  - 10-12 heart biopsies year 1



## The International Society of Heart and Lung Transplantation Guidelines for the care of heart transplant recipients

- **Class IIa:**
- Treadmill or dobutamine stress echocardiography and myocardial perfusion imaging may all be useful for the detection of CAV in HT recipients unable to undergo invasive evaluation. Non-invasive testing for CAV is technically possible in children.
- **Level of Evidence: B.**



# Gene-Expression Profiling for Rejection Surveillance after Cardiac Transplantation

- Management strategy of gene expression blood test and echo versus invasive biopsy
- Low risk heart transplant recipients > 6 months post transplant
- GEP non-inferior to invasive strategy
  - Feasible to reduce morbidity and number of heart biopsies



# Summary

- Heart transplantation is the “gold standard” treatment for Stage D advanced heart failure
- Survival and quality of life are excellent
  - Importance of donor and recipient selection
  - Improved immunotherapy
- Donor availability limits the impact as a therapy

