

**State of the Science in Solid Organ Transplantation and Disability  
System and Clinical Challenges**

**Consequences for Health and Function  
in Adult Heart Transplant Recipients**

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# Consequences for Health and Function in Adult Heart Transplant Recipients

## Presentation outline

- How sick is the Patient at transplant?
- Patient survival
- Morbidity factors contributing to patient outcomes
- Functional status and return to work
- Summary

## Indications for Heart Transplant

### How sick is the Patient at Transplant?

#### Indications for heart transplantation

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The ACC/AHA guidelines include the following indications for cardiac transplantation

- Refractory cardiogenic shock requiring intra-aortic balloon pump counterpulsation or left ventricular assist device (LVAD);
- Cardiogenic shock requiring continuous intravenous inotropic therapy (i.e., dobutamine, milrinone, etc.);
- Peak  $\text{VO}_2$  ( $\text{VO}_{2\text{max}}$ ) less than 10 mL/kg per min;
- NYHA class of III or IV despite maximized medical and resynchronization therapy;
- Recurrent life-threatening left ventricular arrhythmias despite an implantable cardiac defibrillator, antiarrhythmic therapy, or catheter-based ablation;
- End-stage congenital HF with no evidence of pulmonary hypertension;
- Refractory angina without potential medical or surgical therapeutic options.

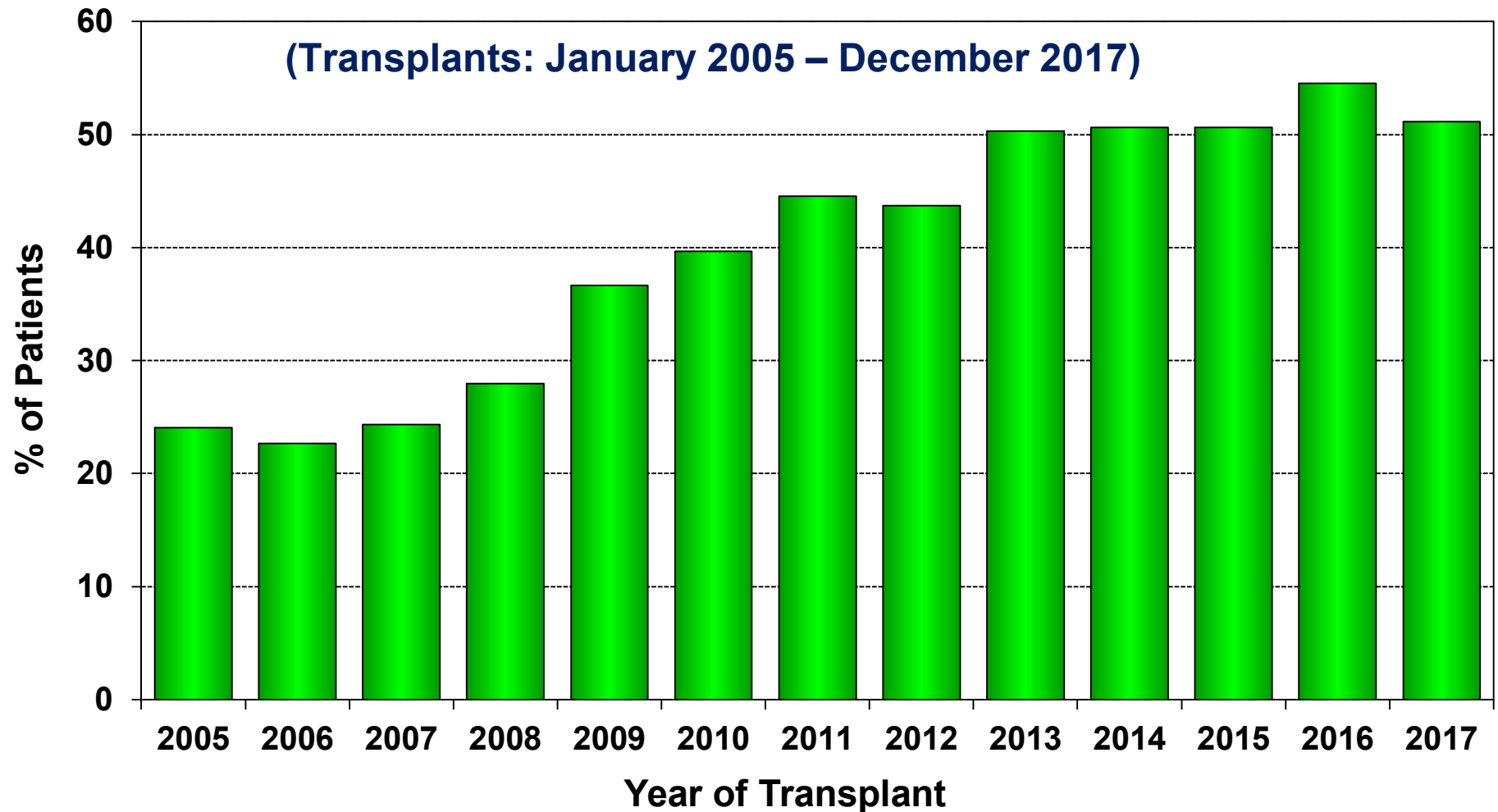
# Adult Heart Transplants

## Recipient Diagnosis

Diagnosis	1992-2000 (N = 37,794)	2001-2009 (N = 33,625)	2010-6/2018 (N = 36,883)
Congenital Heart Disease	1.7%	2.7%	3.1%
Hypertrophic Cardiomyopathy	1.1%	2.7%	3.4%
Ischemic Cardiomyopathy	45.1%	39.2%	32.4%
Non-Cardiomyopathy	44.1%	46.1%	50.8%
Restrictive Cardiomyopathy	1.2%	2.3%	3.5%
Retransplant	2.6%	2.9%	2.8%

# Adult Heart Transplants

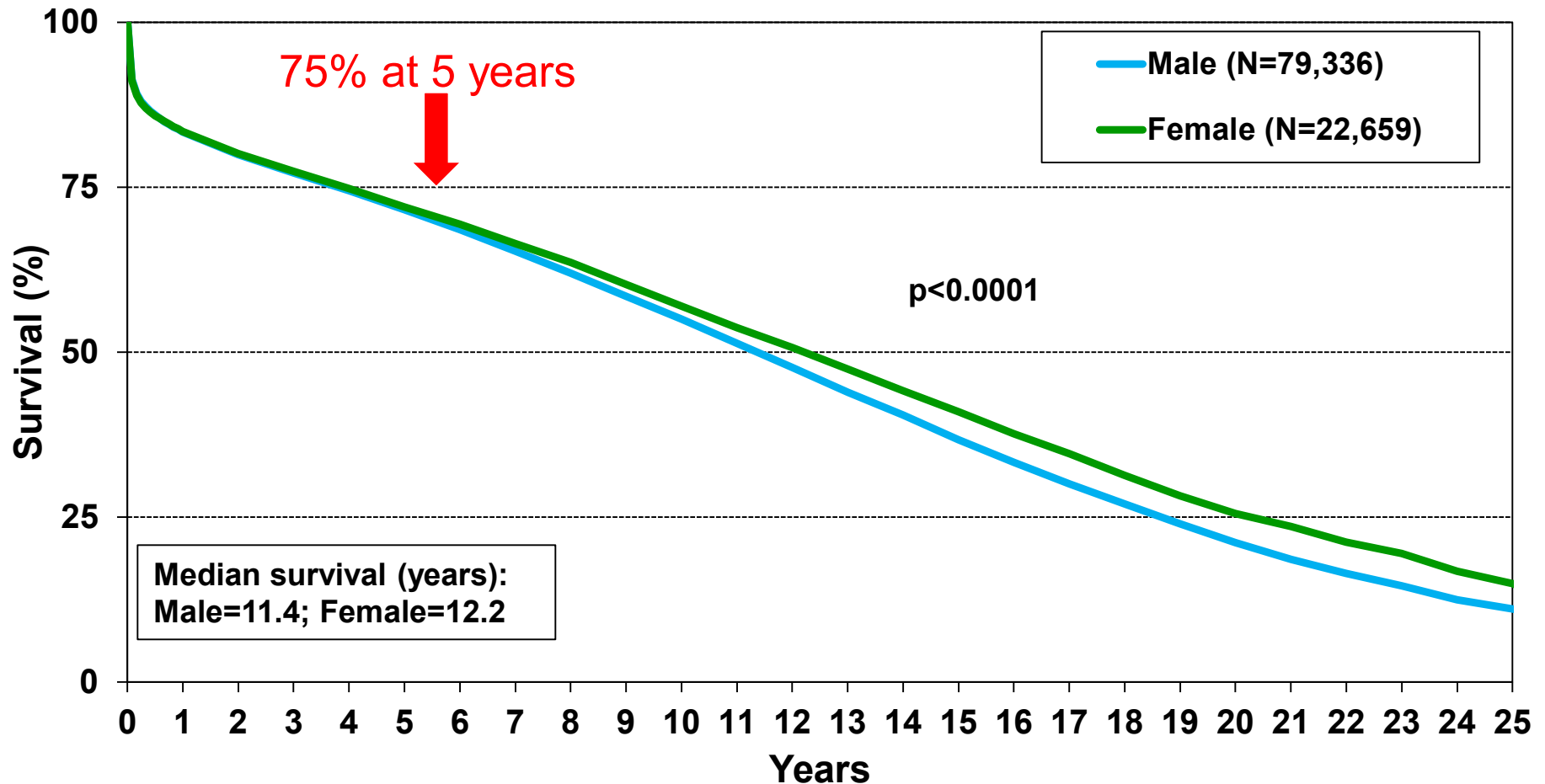
## % of Patients Bridged with Mechanical Circulatory Support\*



# Adult Heart Transplants

## Kaplan-Meier Survival by Recipient Sex

(Transplants: January 1992 – June 2017)



# Adult Heart Transplants

## Causes of Deaths: January 1995 – June 2018

Cause of Death	31 Days - 1 Year (N=5,980)	3-5 Years (N=3,630)	5-10 Years (N=9,441)	>15 Years (N=5,695)
Infection, Non-CMV	1,904 (31.8%)	394 (10.9%)	1,023 (10.8%)	702 (12.3%)
Graft Failure	1,052 (17.6%)	884 (24.4%)	1,838 (19.5%)	944 (16.6%)
Acute Rejection	474 (7.9%)	171 (4.7%)	176 (1.9%)	29 (0.5%)
Cardiac Allograft Vasculopathy	190 (3.2%)	449 (12.4%)	1,153 (12.2%)	598 (10.5%)
Malignancy (non-PTLD)	137 (2.3%)	712 (19.6%)	2,081 (22.0%)	1,103 (19.4%)
PTLD	57 (1.0%)	105 (2.9%)	305 (3.2%)	121 (2.1%)

# Adult Heart Transplants (2012-6/2017)

## Statistically Significant Risk Factors

### For 1 Year Mortality

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- Recipient age (years)
- Recipient creatinine (mg/dL)
- Recipient BMI (kg/m<sup>2</sup>)
- Donor-recipient predicted heart mass match (%)
- Donor age (years)
- Ischemic time (hours)
- Recipient bilirubin (mg/dl)

### For 5 Year Mortality Conditional on Survival to 1 Year

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- Recipient age (years)
- Recipient creatinine (mg/dL)
- Recipient transpulmonary gradient (mmHg)
- Donor age (years)
- Recipient BMI (kg/m<sup>2</sup>)
- Recipient diabetes(30%)
- Recipient & donor cigarette history (45%)



# Adult Heart Transplants

## Cumulative Morbidity Rates in Survivors within 1, 5 and 10

Years Post Transplant: January 1995 – June 2017)

Outcome	Within <u>1 Year</u>	Total N with <u>known</u> <u>response</u>	Within <u>5 Years</u>	Total N with <u>known</u> <u>response</u>	Within <u>10 Years</u>	Total N with <u>known</u> <u>response</u>
Severe Renal Dysfunction <sup>1</sup>	6.7%	(N=39,544)	15.7%	(N=22,462)	22.3%	(N=9,195)
<i>Creatinine &gt; 2.5 mg/dl</i>	5.1%		12.2%		14.3%	
<i>Chronic Dialysis</i>	1.5%		2.9%		6.0%	
<i>Renal Transplant</i>	0.1%		0.6%		2.0%	
Diabetes <sup>2</sup>	20.0%	(N=39,834)	33.8%	(N=22,720)	-	
Cardiac Allograft Vasculopathy	7.7%	(N=36,774)	29.0%	(N=17,392)	46.8%	(N=5,962)

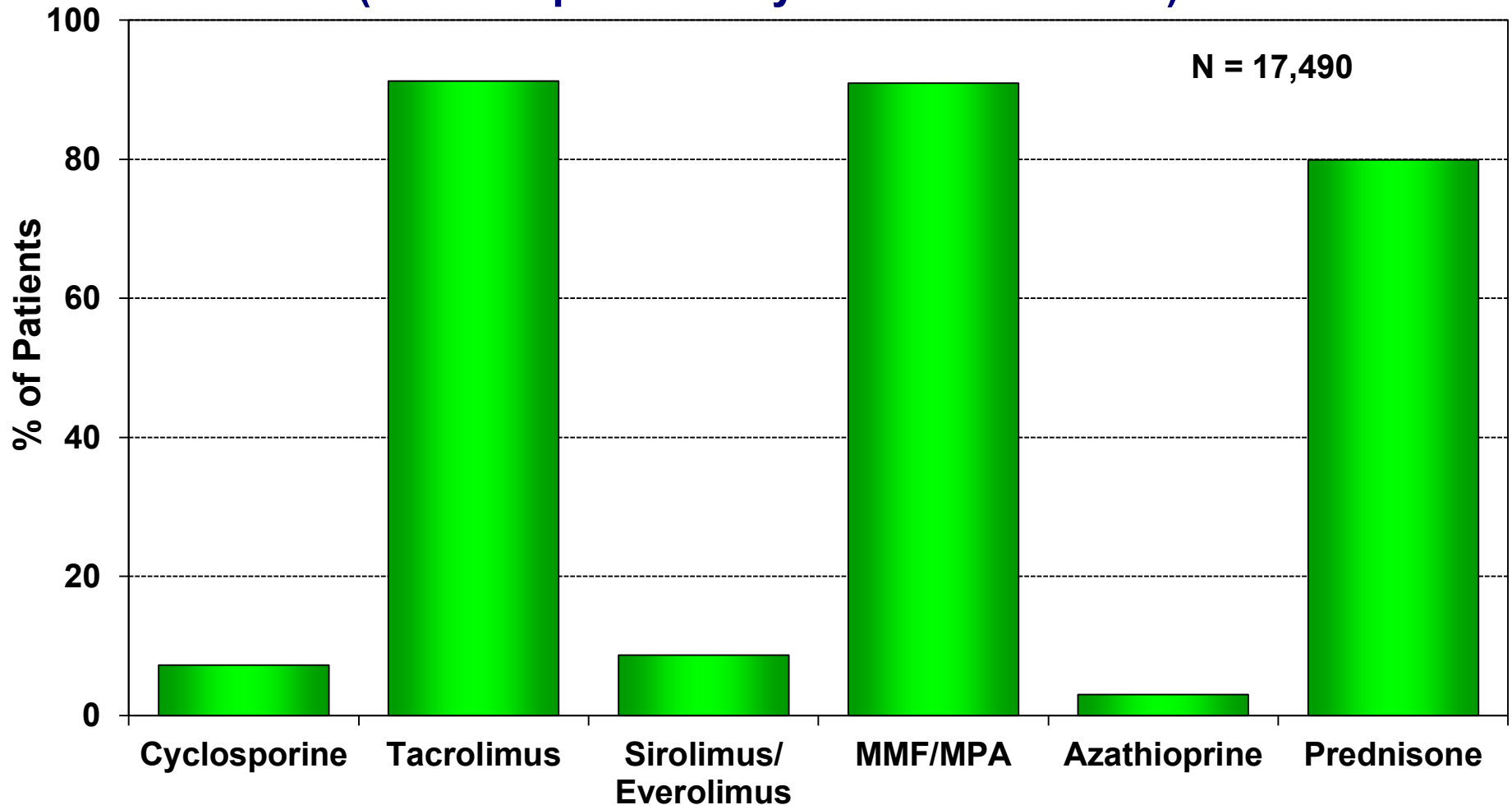
<sup>1</sup> Severe renal dysfunction = Creatinine > 2.5 mg/dl (221 µmol/L), dialysis, or renal transplant

<sup>2</sup> Data are not available 10 years post-transplant.

# Adult Heart Transplants

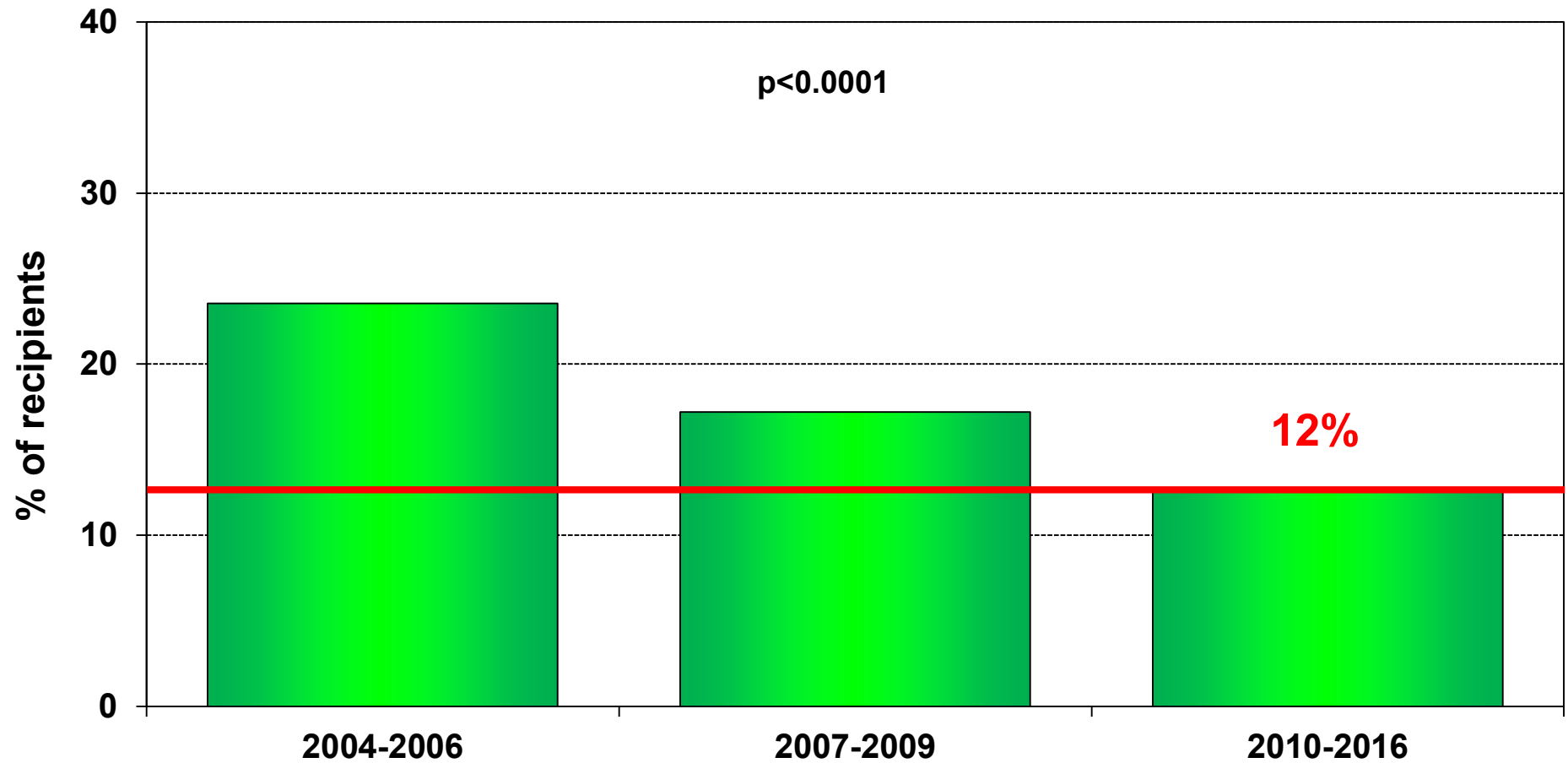
## Maintenance Immunosuppression at Year-1

(Follow-ups: January 2010 – June 2018)



# Adult Heart Transplants

## % of Recipients Experiencing Treated Rejection during Year-1 by Transplant Era

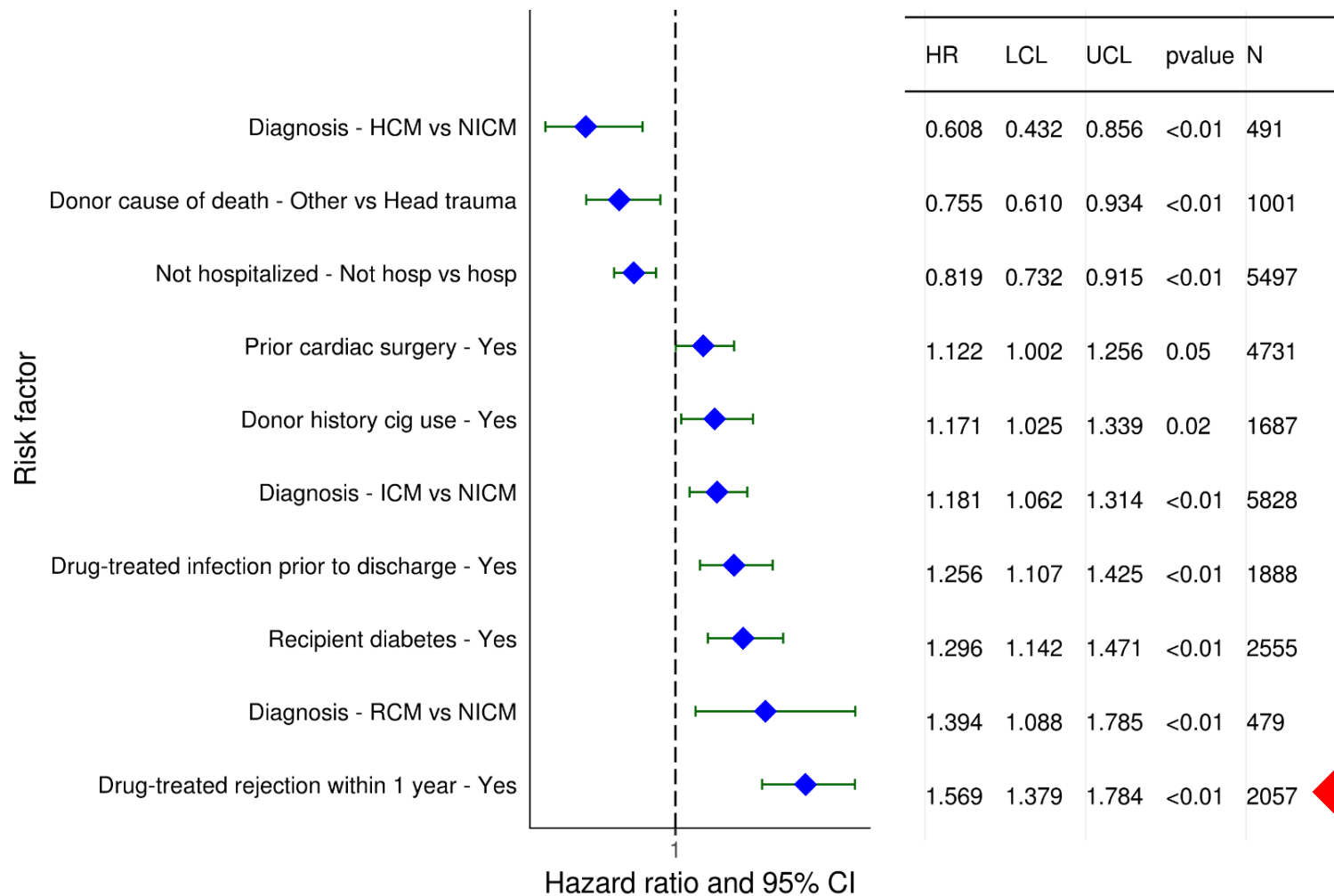


Analysis is limited to patients who were alive at the time of the follow-up.

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 (2008-6/2013)

## Risk Factors For 5 Year Mortality Conditional on Survival to 1 Year; 95% Confidence Limits

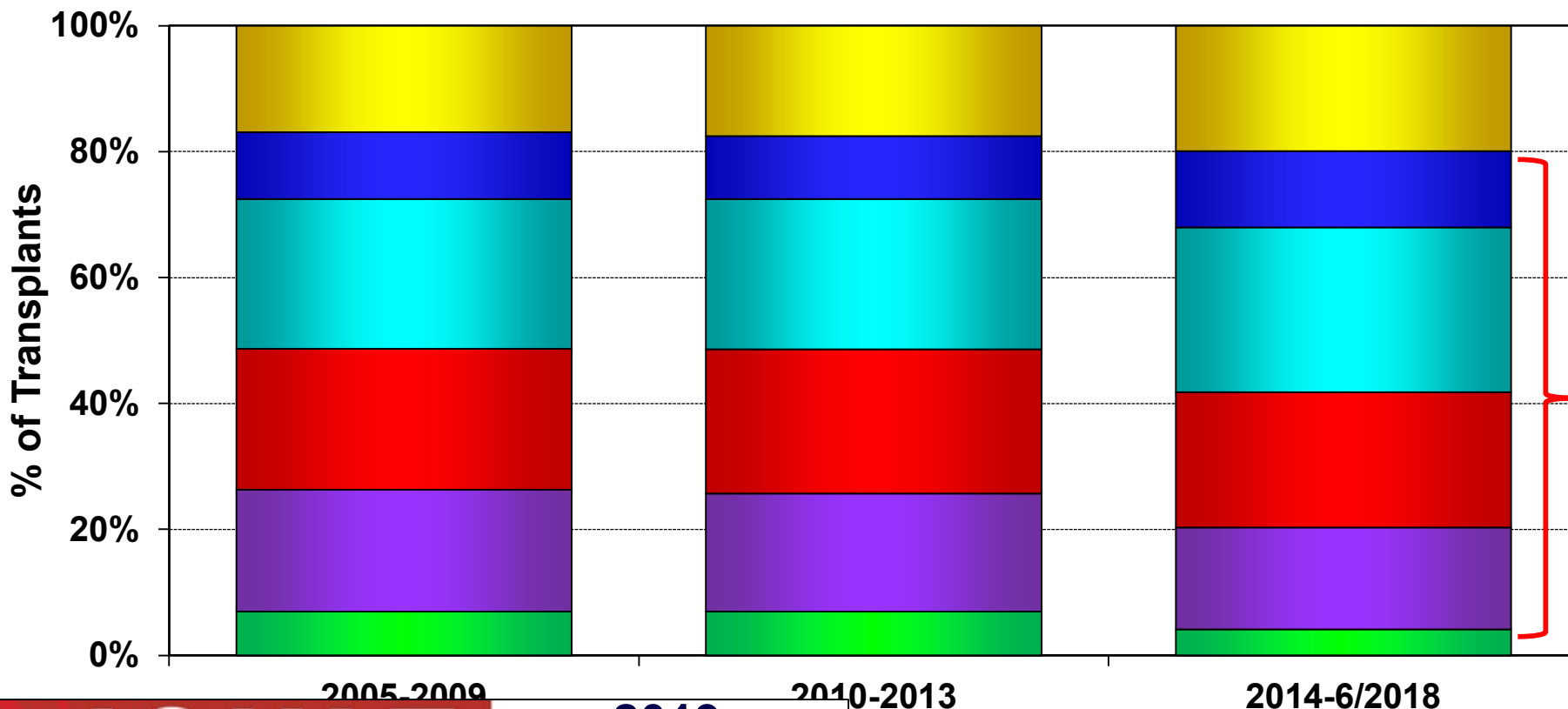


# Adult Heart Transplants Length of Stay by Era:

## 80% Stay $\leq$ 22 days

(Transplants: January 2005 – 6/2018)

0-7 days 8-10 days 11-14 days 15-21 days 22-28 days 29+ days



2005-2009

2010-2013

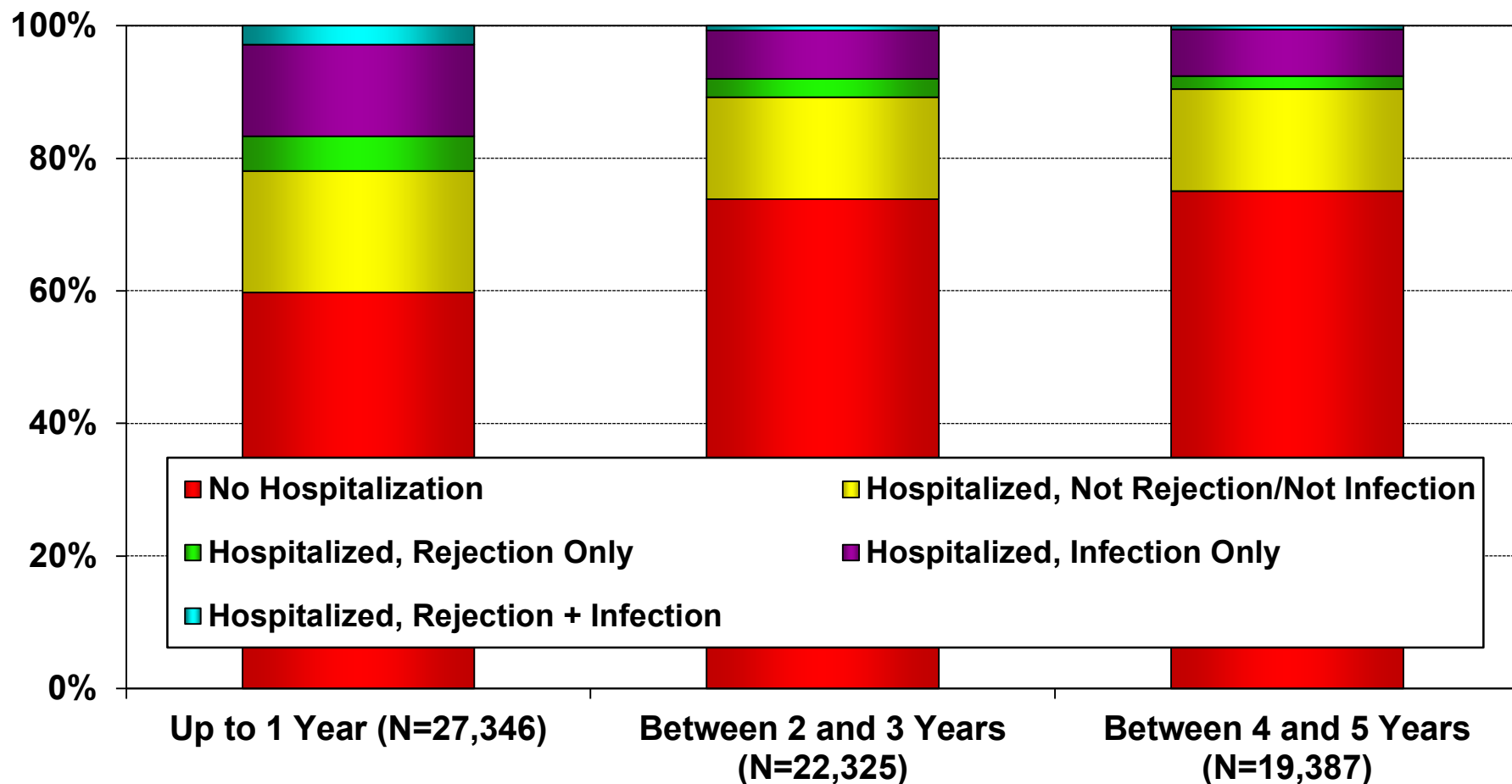
2014-6/2018

2019

# Adult Heart Transplants

## Rehospitalization Post Transplant of Surviving Recipients

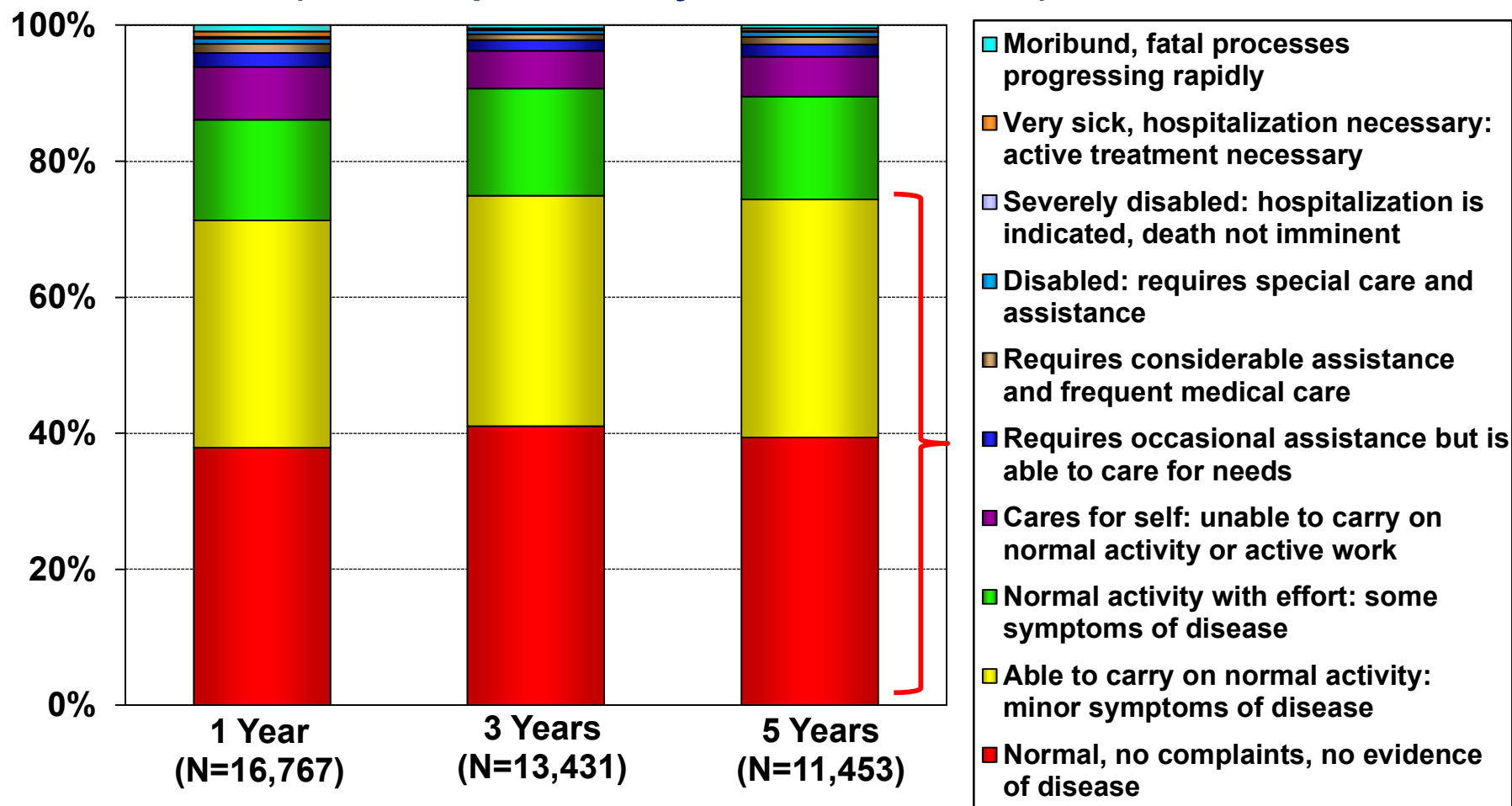
(Follow-ups: January 2005 – June 2018)



# Adult Heart Transplants Functional Status of Surviving Recipients by Karnofsky Score

**75% Able to Carry out Normal Activity**

(Follow-ups: January 2010 – June 2018)

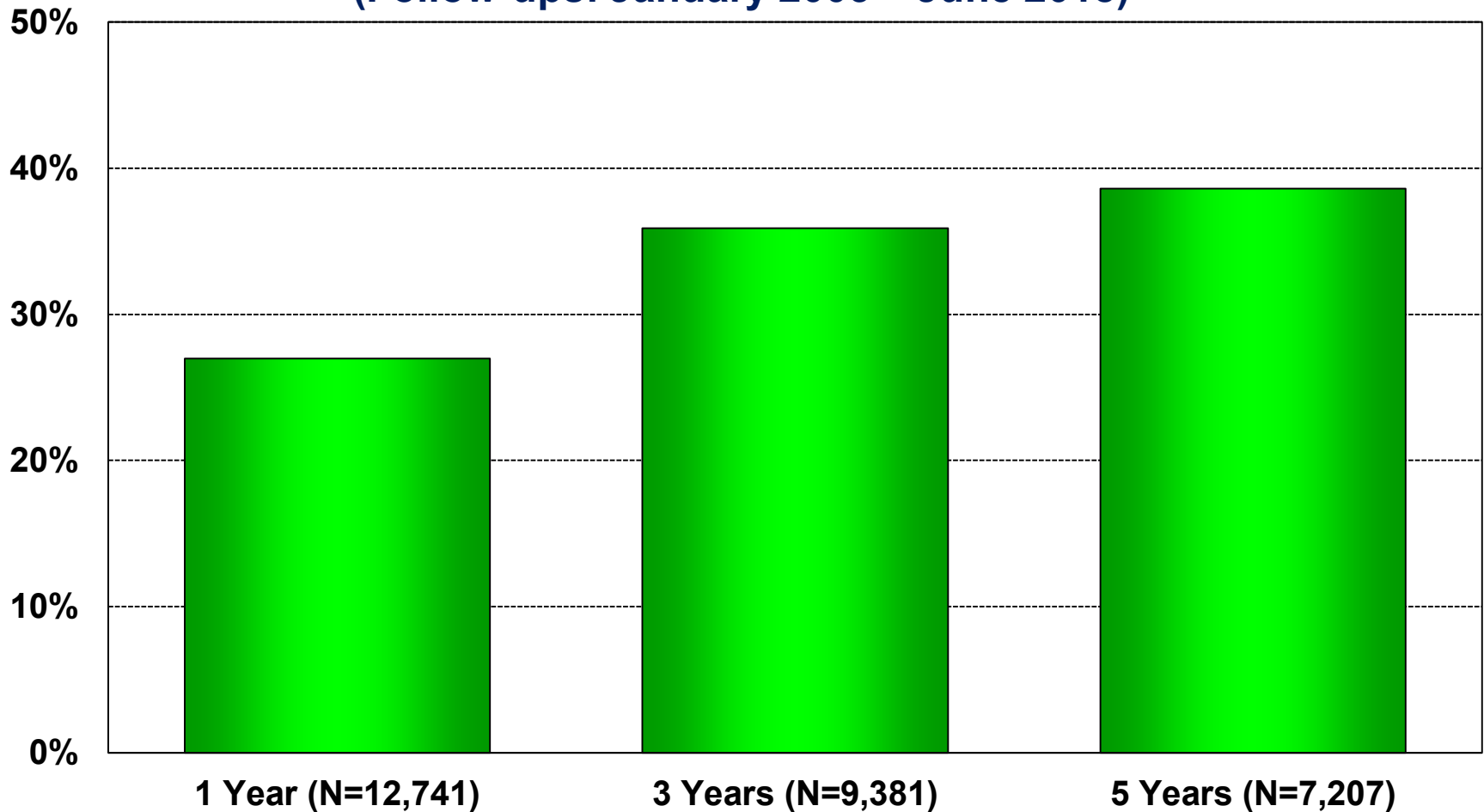


# Adult Heart Transplants

## Surviving Recipients Working Post-Transplant

Age at Follow-up: 25-60 Years

(Follow-ups: January 2005 – June 2018)





Clinical Factors	Summary
Functional Severity at Transplant	<ul style="list-style-type: none"> <li>Refractory heart failure: cardiogenic shock; requiring mechanical device; or continuous inotropic support</li> <li>NYHA class III or IV despite maximum medical Rx and resynchronization</li> <li>Recurrent life-threatening arrhythmia despite implantable defibrillator</li> <li>End-stage congenital Heart disease</li> </ul>
Patient survival	<ul style="list-style-type: none"> <li>Median overall survival: 11.6 Years. Year-1 - 95%; Year 5: 75%; Year 10: 50%</li> </ul>
Pre-transplant risk factors for disability and survival	<ul style="list-style-type: none"> <li>Donor: age, cigarette history; donor/recipient heart mass (mismatch); ischemic time</li> <li>Recipient: age, creatinine; diabetes; bilirubin; body mass index (BMI); transpulmonary gradient</li> </ul>
Diagnosis leading to transplant	<ul style="list-style-type: none"> <li>Ischemic Cardiomyopathy (32%); non-ischemic CM (51%)</li> </ul>
Post-transplant risk factors for disability and survival	<ul style="list-style-type: none"> <li>Acute rejection; diabetes; BMI, renal dysfunction; cardiac transplant vasculopathy (CAV); malignancy; infection</li> </ul>
Functional Status by Karnofsky Score (% patients Normal Activity)	<ul style="list-style-type: none"> <li>75% patients can carry out normal activity</li> </ul>
Employment post-transplant	<ul style="list-style-type: none"> <li>30% patients are working by Year-1; 35% by Year-3; 40% by year-5</li> </ul>
Rehospitalization Post Transplant	<ul style="list-style-type: none"> <li>60-75% of patient will not be re-hospitalized</li> </ul>