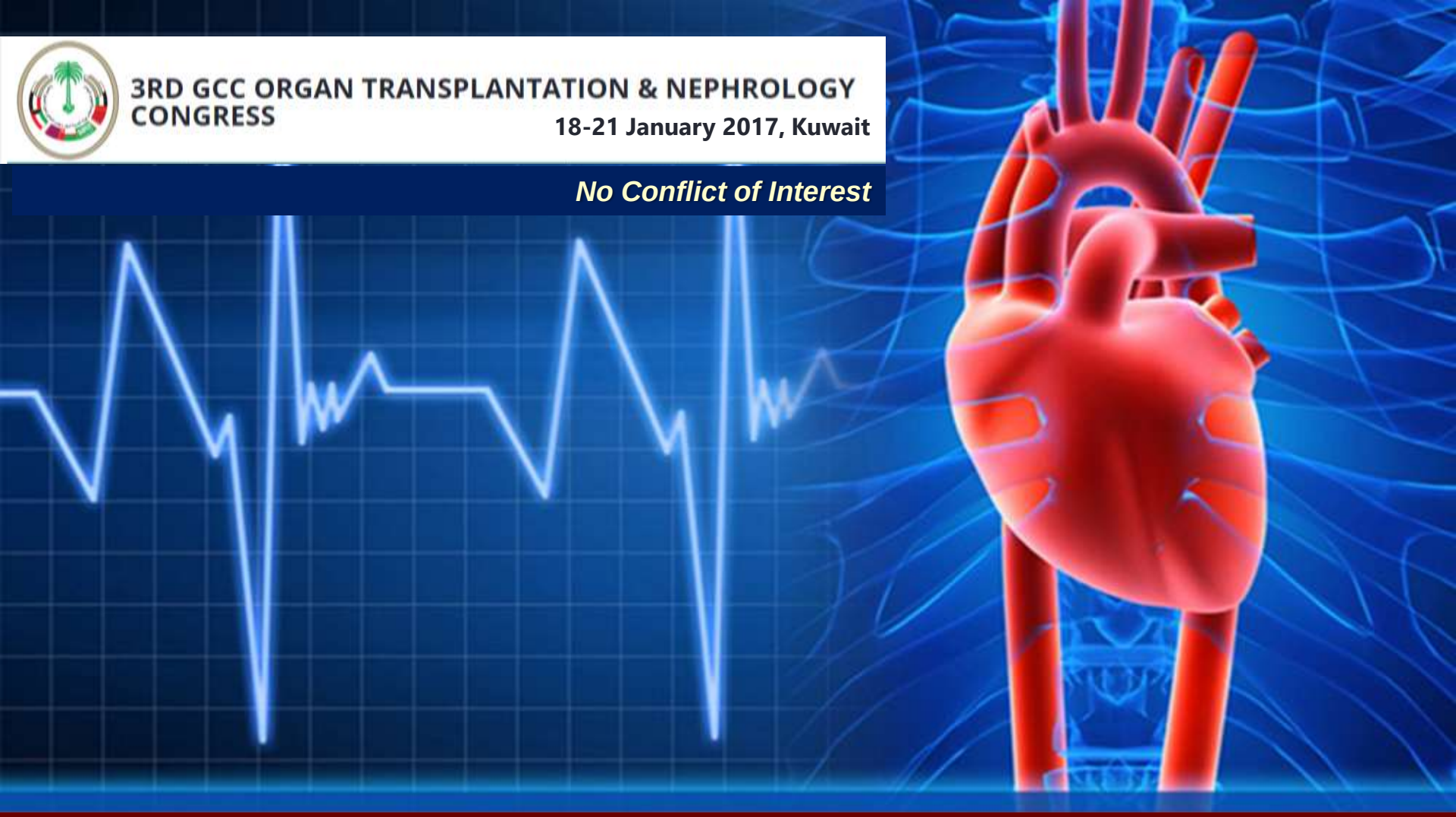
3RD GCC ORGAN TRANSPLANTATION & NEPHROLOGY CONGRESS

18-21 January 2017, Kuwait

No Conflict of Interest



UPDATES IN HEART TRANSPLANTATION

Jehad AlBuraiki, MD

- HISTORIC BACKGROUND
- INDICATIONS
- IMMUNOSUPPRESSION
- OUTCOME
  - Survival
  - Morbidities
  - Functional Status
- CONCLUSION

UPDATES IN HEART TRANSPLANTATION

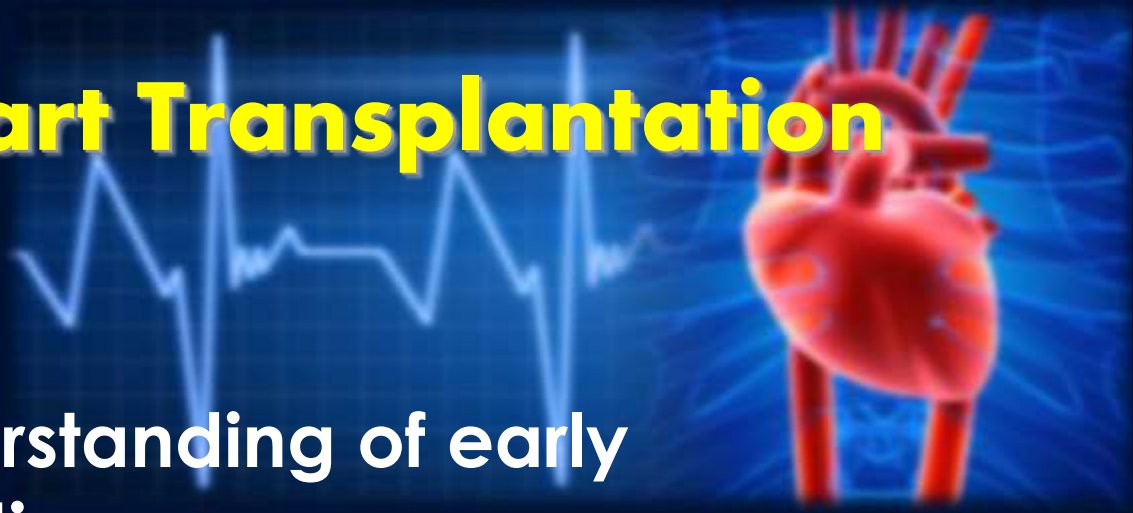
No Conflict of Interest


wedding garters . . .
Stuttafords
The Cape Argus
CITY LATE
CAPE TOWN, MONDAY, DECEMBER 4, 1967
PRICE 4c
WONDOSOL
Patient's condition 'first class', Groote Schuur doctors say
CRISIS AFTER 7 DAYS
MAN WITH A NEW HEART
Three years' work on 'op'
Louw tells of key factor in heart transplant
Thirty-two hours after his historic heart transplant in Groote Schuur Hospital, Mr. Louis Washkansky is maintaining his satisfactory condition. Dr. J. G. Burger, Medical Superintendent of the hospital, said this afternoon that the 55-year-old patient's condition was unchanged since this morning.
THE critical part in the heart transplantation would be in about a week's time, Prof. I. H. Louw, head of the Department of Surgery at the University of Cape Town Medical School, said today.
Crucial time
Round the clock
They will miss
Woman had no chance of survival
By a Staff Reporter
MR. LOUIS WASHKANSKY, whose life expectancy
DAVIS CUP: SPAIN WINS. REPORT Page 2
DAVIS CUP CONTEST
Other pages

On December 3, 1967, a heart from a cadaver was successfully transplanted into a 54 year old man whose heart was irreparably damaged by repeated myocardial infarction.

C.N. Barnard, South African Medical Journal, 1967;41:1271-1274

Updates in Heart Transplantation

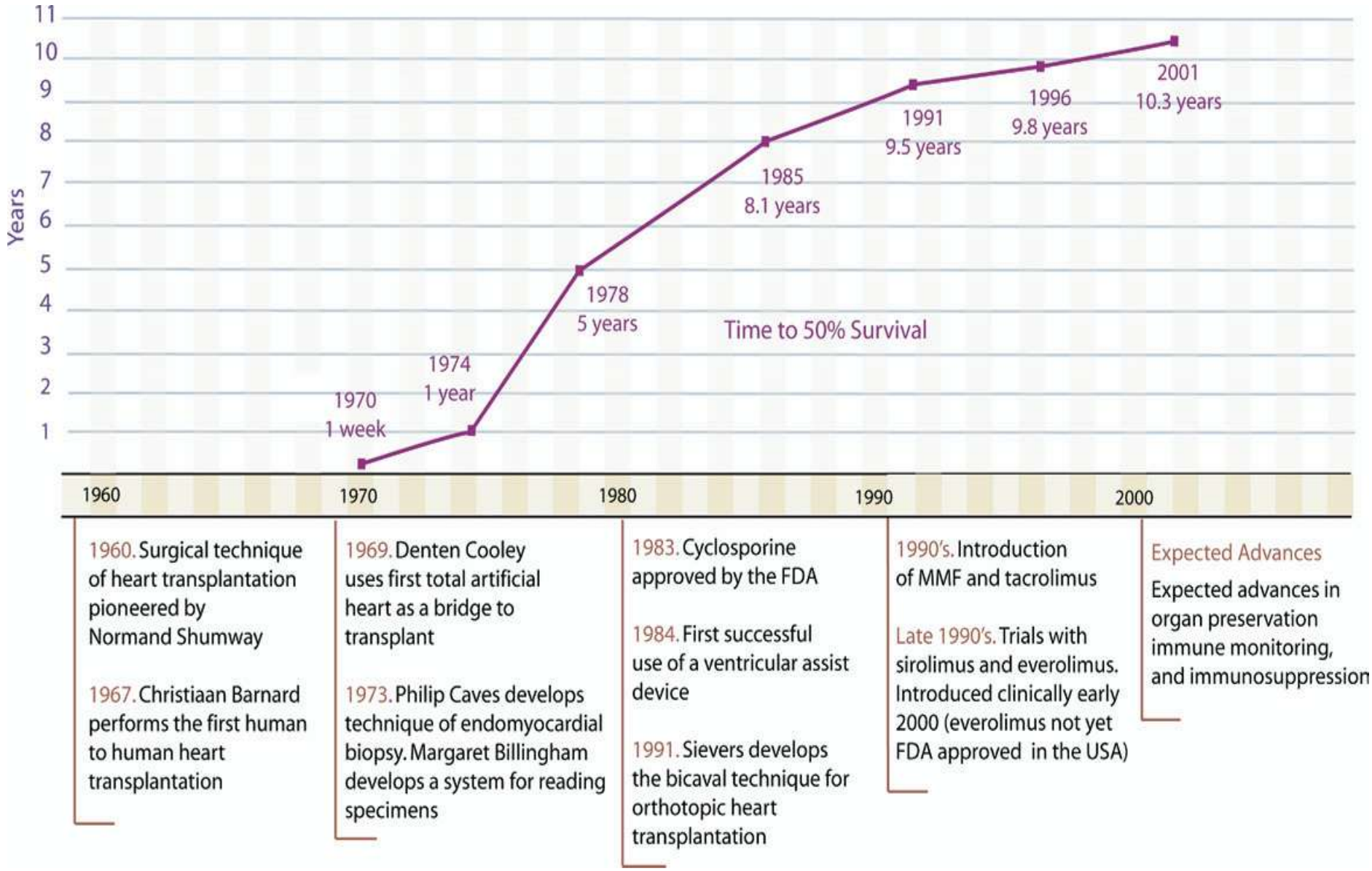


- Inadequate understanding of early postop complications

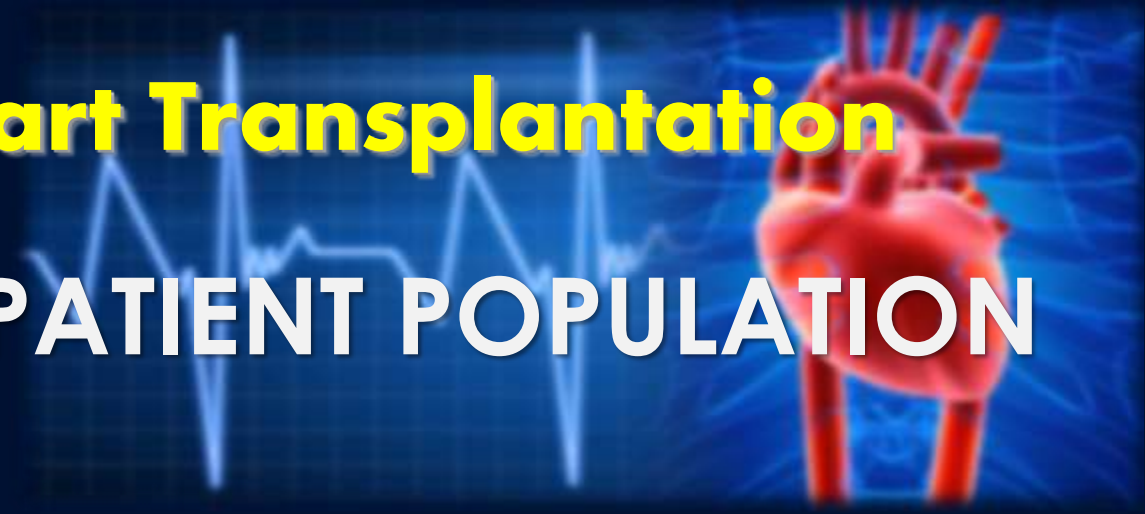
- Lack of tools to address
  a) Acute rejection
  b) Opportunistic infections
  c) Allograft Vasculopathy

Updates in Heart Transplantation

- Refinement of donor and Recipient Selection
- Advances in Immunosuppression
- Advances in Surgical Technique
- Prevention and Treatment of Infection


Years
11
10
9
8
7
6
5
4
3
2
1
1970
1 week
1974
1 year
1978
5 years
1985
8.1 years
1991
9.5 years
1996
9.8 years
2001
10.3 years
Time to 50% Survival
1960
1970
1980
1990
2000
1960. Surgical technique of heart transplantation pioneered by Normand Shumway
1967. Christiaan Barnard performs the first human to human heart transplantation
1969. Denten Cooley uses first total artificial heart as a bridge to transplant
1973. Philip Caves develops technique of endomyocardial biopsy. Margaret Billingham develops a system for reading specimens
1983. Cyclosporine approved by the FDA
1984. First successful use of a ventricular assist device
1991. Sievers develops the bicaval technique for orthotopic heart transplantation
1990's. Introduction of MMF and tacrolimus
Late 1990's. Trials with sirolimus and everolimus. Introduced clinically early 2000 (everolimus not yet FDA approved in the USA)
Expected Advances
Expected advances in organ preservation immune monitoring, and immunosuppression

Updates in Heart Transplantation

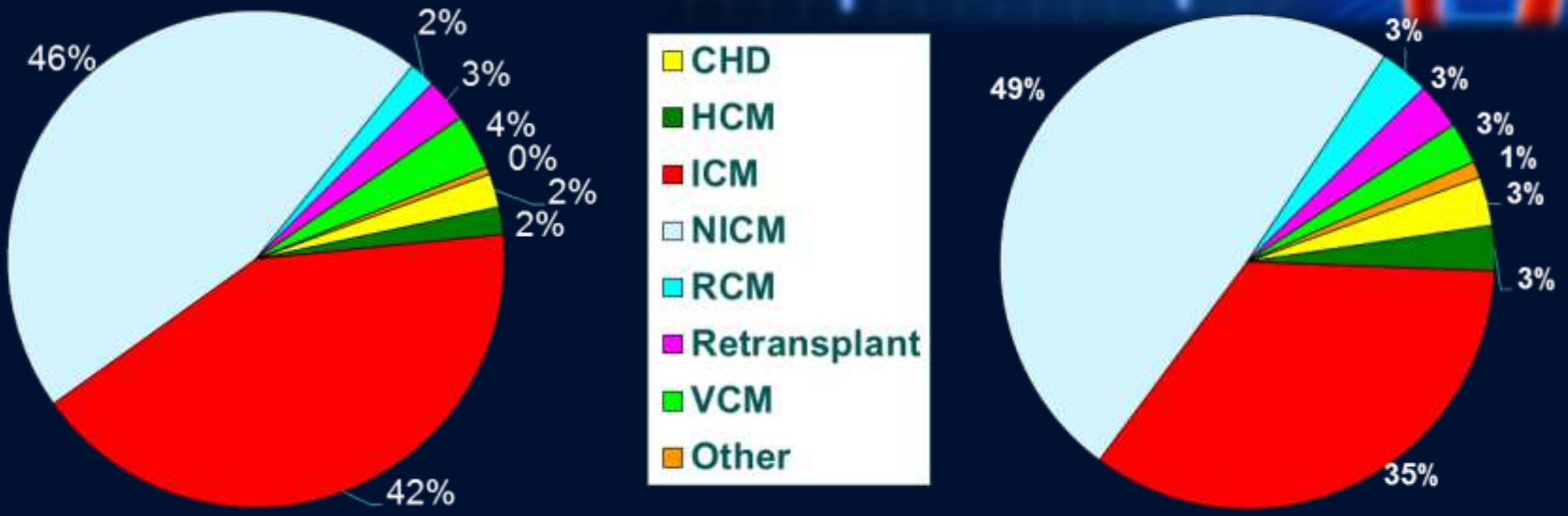


CHANGING PATIENT POPULATION

- Older patients
- Patients with complex congenital heart disease
- Patients requiring mechanical circulatory support as bridge to transplant
- Increased number of re-transplant candidates

INDICATIONS

Adult Heart Transplants
Diagnosis

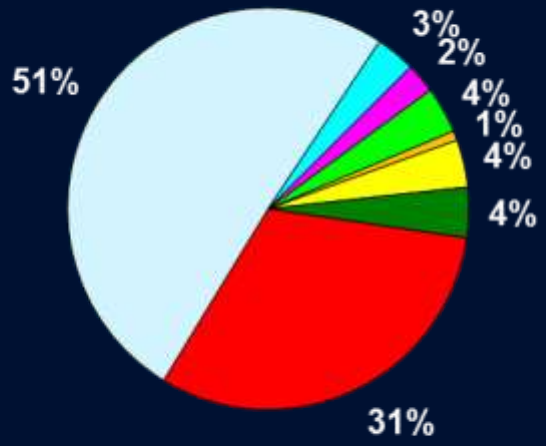


1/1982 – 6/2015

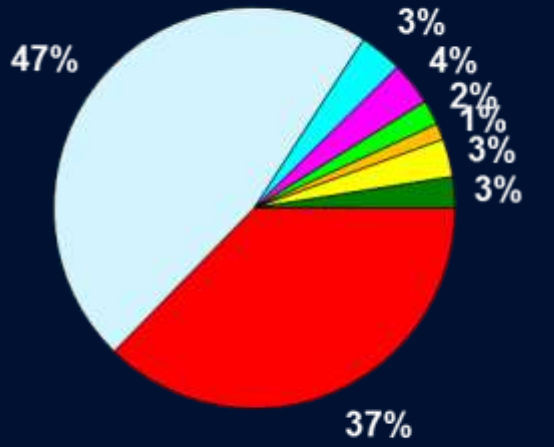
1/2009 – 6/2015

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2016
JHLT. 2016 Oct; 35(10): 1149-1205

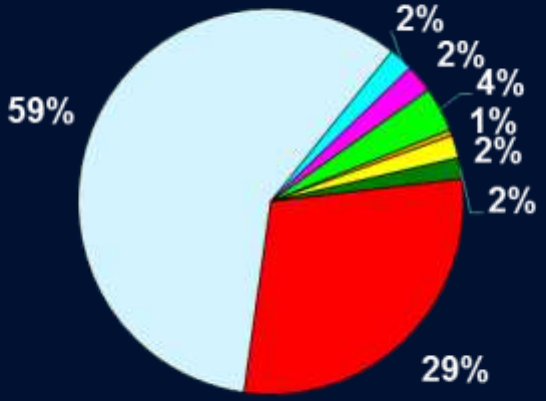
Adult Heart Transplants
Diagnosis by Location
(Transplants: January 2009 – June 2015)



Europe



North America



Other

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2016
JHLT. 2016 Oct; 35(10): 1149-1205

Adult Heart Transplants
Donor and Recipient Characteristics

	1992-2003 (N = 48,388)	2004-2008 (N = 17,666)	2009-6/2015 (N = 24,474)	p-value
Recipient age (years)	54.0 (28.0 - 65.0)	53.0 (24.0 - 66.0)	54.0 (25.0 - 68.0)	<0.0001
Donor age (years)	32.0 (15.0 - 54.0)	34.0 (16.0 - 56.0)	35.0 (17.0 - 57.0)	<0.0001
Donor and recipient age difference (years)	-19.0 (-43.0 - 8.0)	-16.0 (-43.0 - 12.0)	-16.0 (-43.0 - 12.0)	<0.0001
Recipient weight (kg)	76.0 (53.1 - 103.0)	78.0 (53.5 - 107.5)	80.0 (54.0 - 108.9)	<0.0001
Recipient height (cm)	174.0 (157.0 - 188.0)	175.0 (157.5 - 188.0)	174.5 (157.5 - 188.0)	0.0091
Recipient BMI	25.1 (19.1 - 32.8)	25.8 (19.3 - 34.2)	26.3 (19.5 - 34.8)	<0.0001
Donor weight (kg)	75.0 (53.0 - 104.0)[1]	78.3 (56.0 - 110.0)	80.0 (56.7 - 114.0)	<0.0001
Donor height (cm)	175.0 (157.0 - 188.0)[1]	175.3 (160.0 - 190.0)	175.0 (157.5 - 189.0)	<0.0001
Donor BMI	24.4 (19.0 - 33.3)[1]	25.2 (19.8 - 35.4)	25.8 (19.9 - 37.0)	<0.0001

Continuous factors are expressed as median (5th – 95th percentiles)

[1] Based on 4/1994-2003 transplants.

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2016
JHLT. 2016 Oct; 35(10): 1149-1205

Adult Heart Transplants
Donor and Recipient Characteristics

	1992-2003 (N = 48,388)	2004-2008 (N = 17,666)	2009-6/2015 (N = 24,474)	p-value
Recipient/donor gender (% male)	80.1%/ 68.6%	77.3%/ 70.2%	74.9%/ 68.3%	<0.0001/ 0.0001
Male recipient/ female donor	20.7%	17.2%	16.4%	<0.0001
Female recipient/ male donor	9.2%	10.1%	9.9%	0.0005
Recipient/donor diabetes mellitus	14.8%[1]/ 1.6%[1]	23.0%/ 2.5%	26.0%/ 3.4%	<0.0001/ <0.0001
Recipient prior history of dialysis	3.3%[1]	4.1%	4.6%	<0.0001
Recipient amiodarone use	24.1%[1]	28.8%	33.8%	<0.0001
Recipient/donor cigarette history	- / 36.2%[1]	49.3%[2]/ 23.8%	45.7%/ 15.9%	<0.0001/ <0.0001
Recipient/donor hypertension	35.2%[1]/ 11.0%[1]	42.6%/ 12.4%	51.1%/ 15.2%	<0.0001/ <0.0001
Recipient prior cardiac surgery	-	40.0%[2]	50.3%	<0.0001
Recipient peripheral vascular disease	3.6%[1]	3.1%	3.1%	0.0103
Recipient previous malignancy	3.9%[1]	6.0%	8.2%	<0.0001
Recipient COPD	3.3%[1]	3.6%	5.1%	<0.0001
Ischemic time (hours)	3.0 (1.4 - 4.9)	3.3 (1.6 - 5.1)	3.2 (1.5 - 5.1)	<0.0001

(Cont'd) Continuous factors are expressed as median (5th – 95th percentiles)

[1] Based on 4/1994-2003 transplants.
[2] Based on 7/2004-2008 transplants.

Adult Heart Transplants
Donor and Recipient Characteristics

	1992-2003 (N = 48,388)	2004-2008 (N = 17,666)	2009-6/2015 (N = 24,474)	p-value
Most recent PRA > 10%[1]				
Overall	7.7%	11.5%[2]	13.5%[3]	<0.0001
Class I	-	12.5%[4]	15.8%[5]	<0.0001
Class II	-	8.5%[4]	11.5%[5]	<0.0001
Creatinine at time of transplant (mg/dL)	1.2 (0.7 - 2.4)	1.2 (0.7 - 2.4)	1.2 (0.7 - 2.3)	<0.0001
Pulmonary vascular resistance (Wood units)	2.1 (0.2 - 6.1)[6]	2.1 (0.0 - 5.7)	2.1 (0.0 - 5.5)	<0.0001
HLA Mismatches				
0-2	4.3%	4.0%	3.9%	
3-4	40.4%	39.7%	38.4%	0.0001
5-6	55.2%	56.3%	57.7%	

(Cont'd) Continuous factors are expressed as median (5th – 95th percentiles)

[1] PRA was collected as a single percentage outside of US. Until mid-2004 PRA was collected in US as a single percentage. After this date, PRA was collected separately for Class I and Class II.

[2] Based on US 1/2004-6/2004 transplants and non-US 2004-2008 transplants.
[3] Based on non-US transplants.
[4] Based on US 7/2004-2008 transplants.
[5] Based on US transplants.
[6] Based on 4/1994-2003 transplants.

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2016
JHLT. 2016 Oct; 35(10): 1149-120

Adult Heart Transplants
Donor and Recipient Characteristics

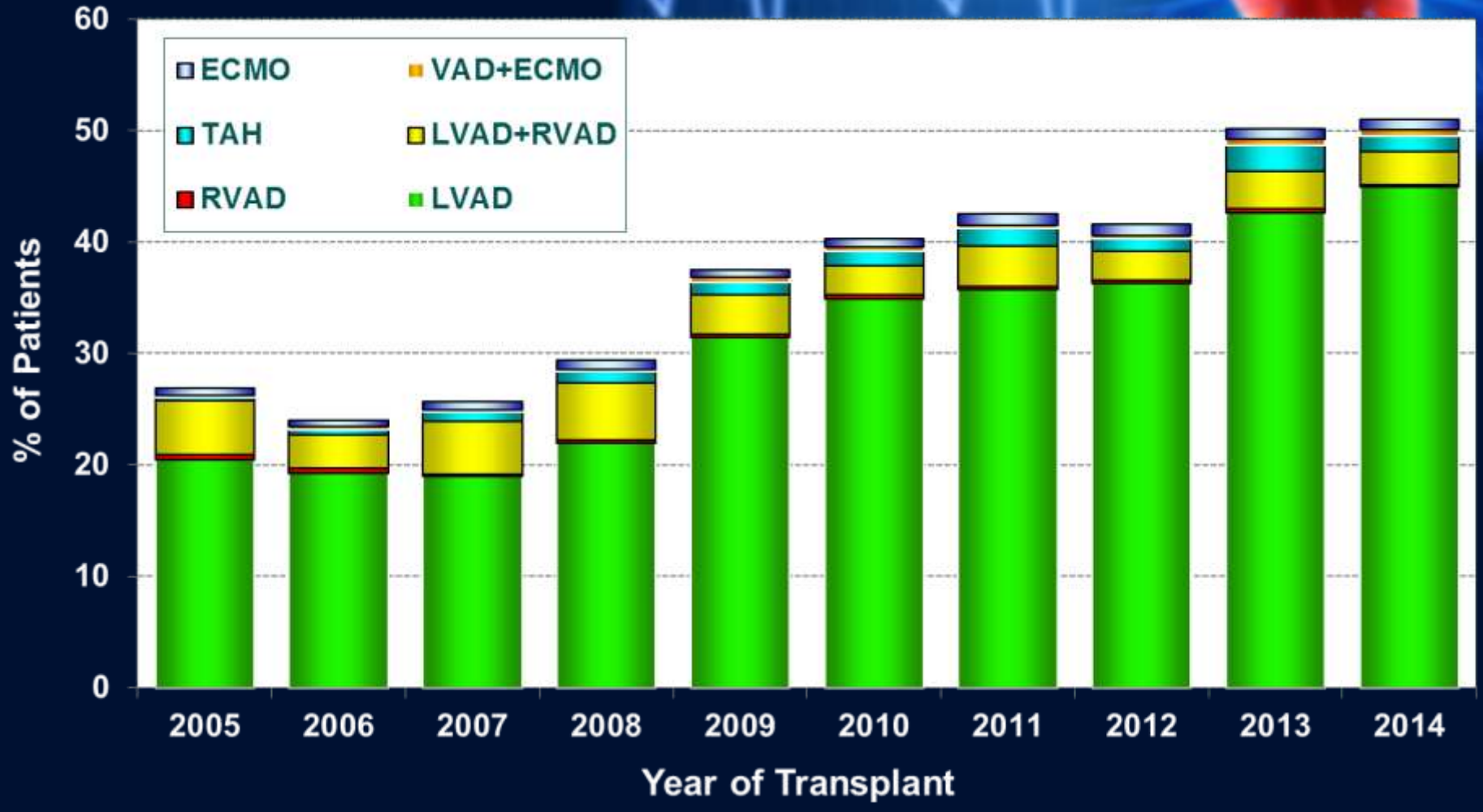
	1992-2003 (N = 48,388)	2004-2008 (N = 17,666)	2009-6/2015 (N = 24,474)	p-value
Pre-operative support (multiple items may be reported)				
Hospitalized at time of transplant	59.0%	46.4%	44.1%	<0.0001
On IV inotropes	54.6%[1]	44.6%	39.4%	<0.0001
Ventilator	3.3%	3.0%	2.1%	<0.0001
IABP	6.4%	7.0%	6.4%	0.1497
Mechanical circulatory support	22.2%[2]	26.0%	44.7%	<0.0001
LVAD	20.1%[2]	22.2%	38.1%	<0.0001
RVAD	-	4.4%[3]	3.2%	<0.0001
TAH	0.5%[2]	0.5%	1.4%	<0.0001
ECMO	0.3%[4]	0.9%	1.3%	<0.0001

(Cont'd)

[1] Based on 4/1994-2003 transplants.
[2] Based on 11/1999-2003 transplants.
[3] Based on 2005-2008 transplants.
[4] Based on 5/1995-2008 transplants.

Adult Heart Transplants

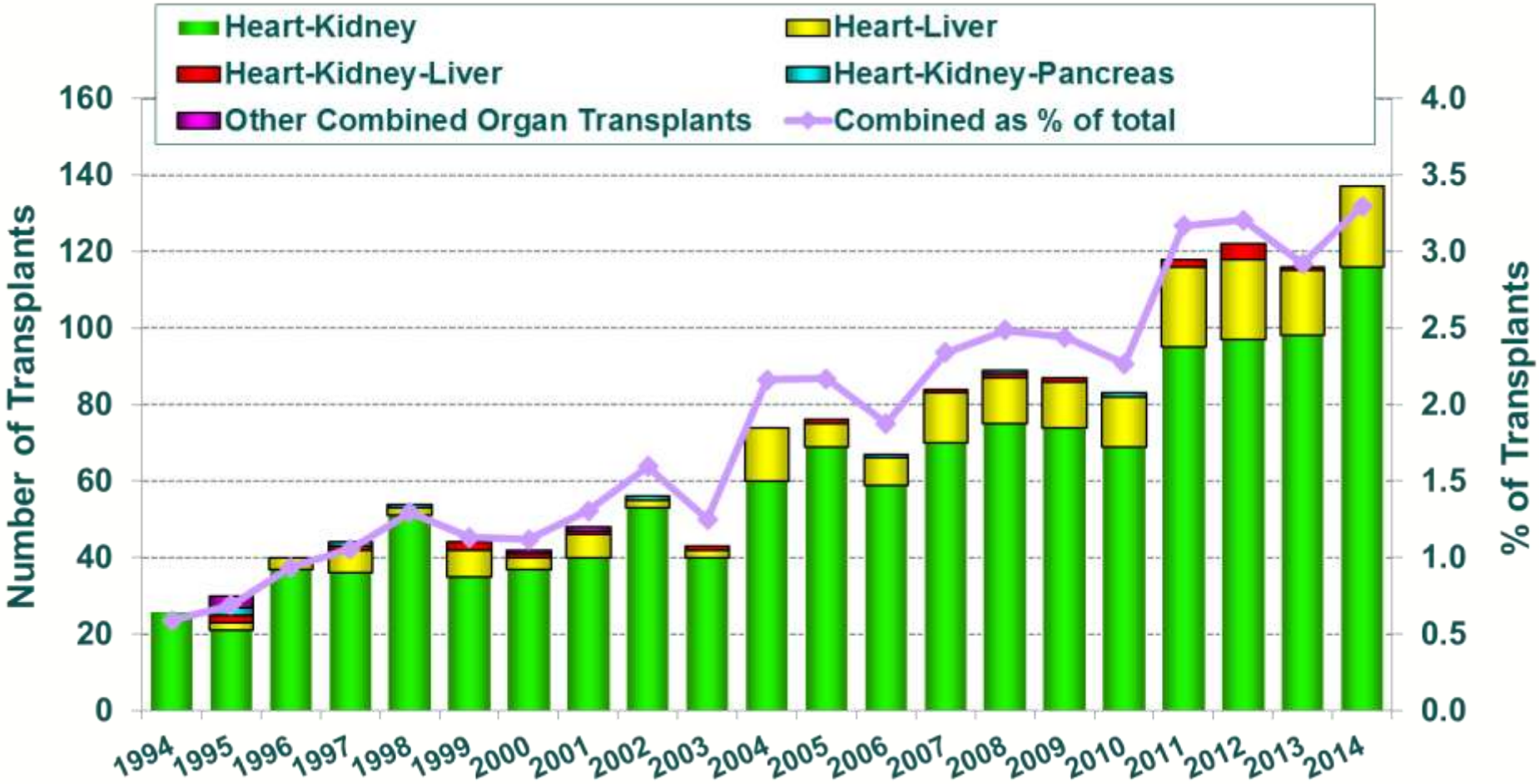
% of Patients Bridged with Mechanical Circulatory Support* by Year and Device Type



ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2016
JHLT. 2016 Oct; 35(10): 1149-120

* LVAD, RVAD, TAH, ECMO

Adult Heart Transplants
Number and % of Combined Organ Transplants Reported by Year and Type of Transplant



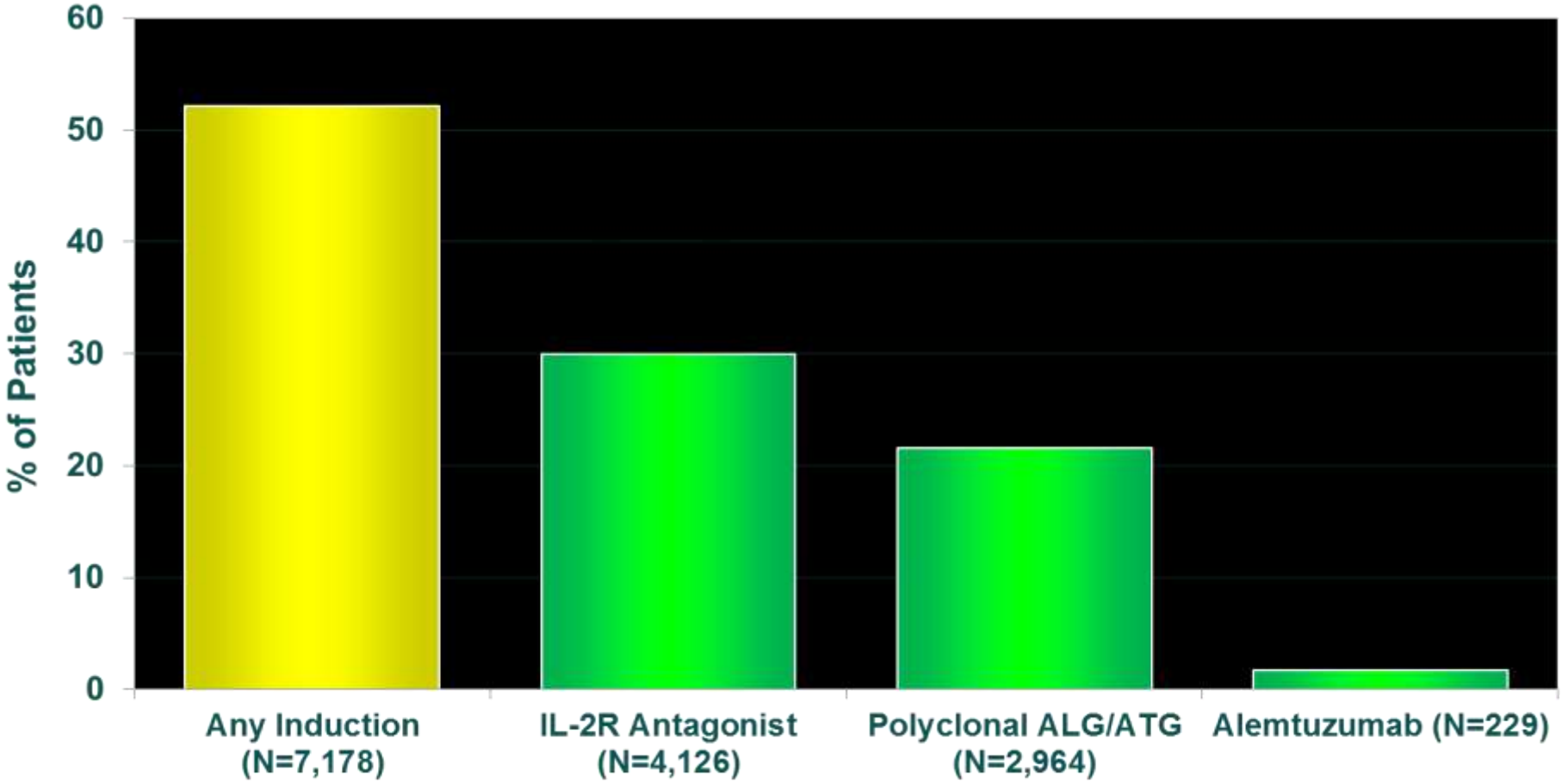
ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

2016

JHLT. 2016 Oct; 35(10): 1149-120

IMMUNOSUPPRESSION PROTOCOL

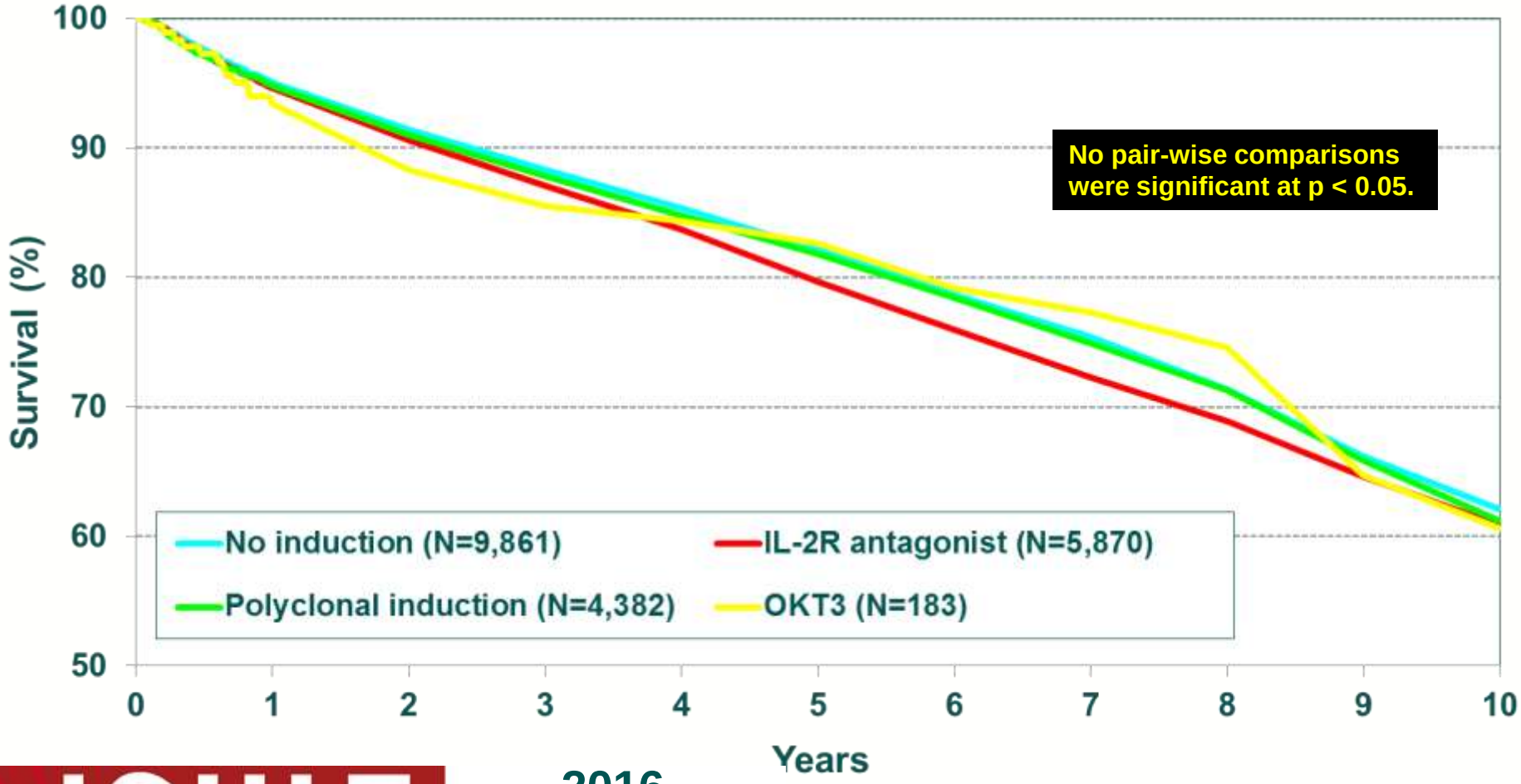
Adult Heart Transplants
Induction Immunosuppression
(Transplants: January 2009 – June 2015)



Analysis is limited to patients who were alive at the time of the discharge.

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2016
JHLT. 2016 Oct; 35(10): 1149-120

Adult Heart Transplants
Kaplan-Meier Survival by Induction Type
Conditional on Survival to 14 Days
(Transplants: January 2004 – June 2014)

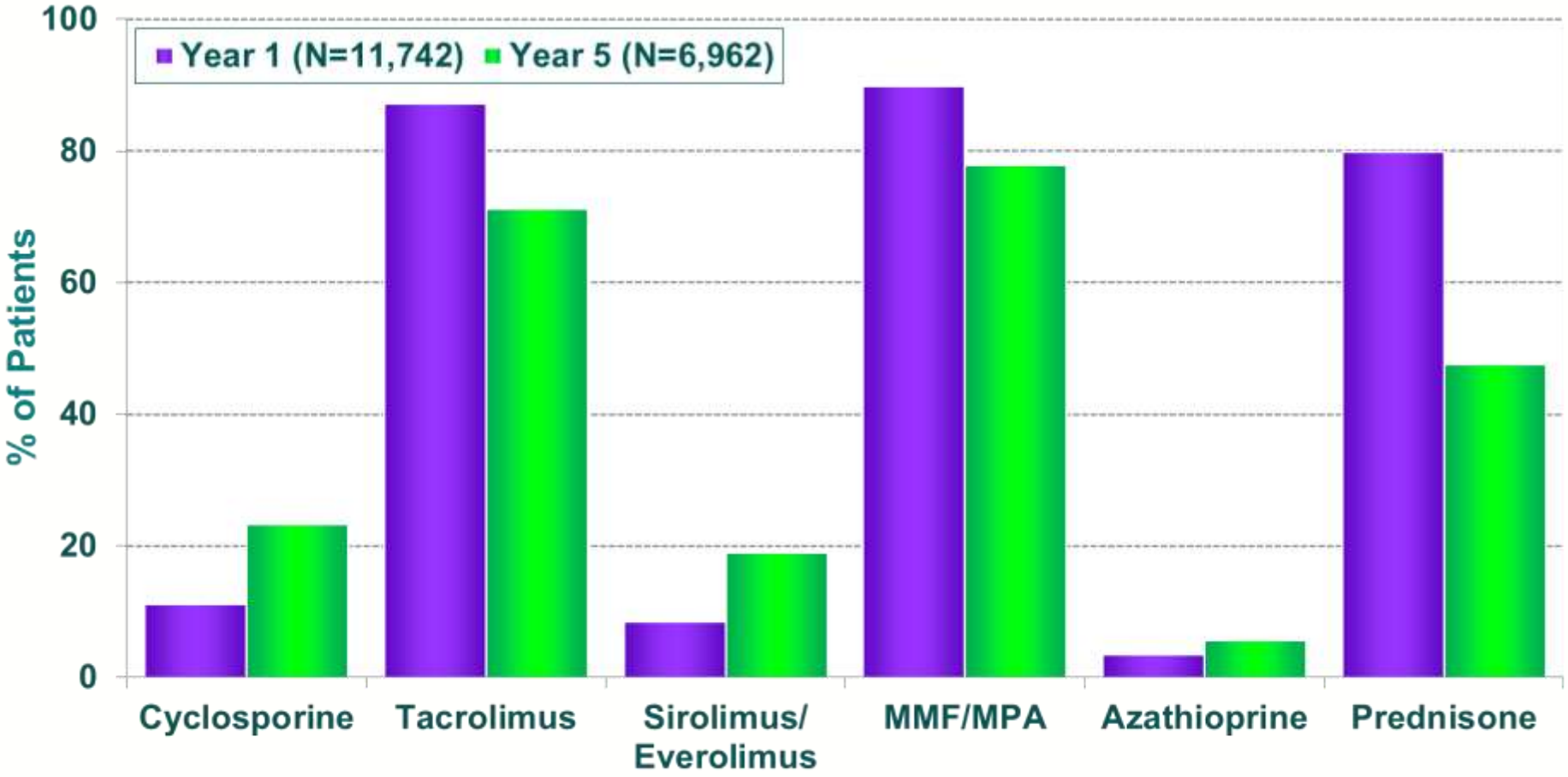


ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

2016

JHLT. 2016 Oct; 35(10): 1149-1205

Adult Heart Transplants Maintenance Immunosuppression at Time of Follow-up (Follow-ups: January 2009 – June 2015)



NOTE: Different patients are analyzed in Year 1 and Year 5.

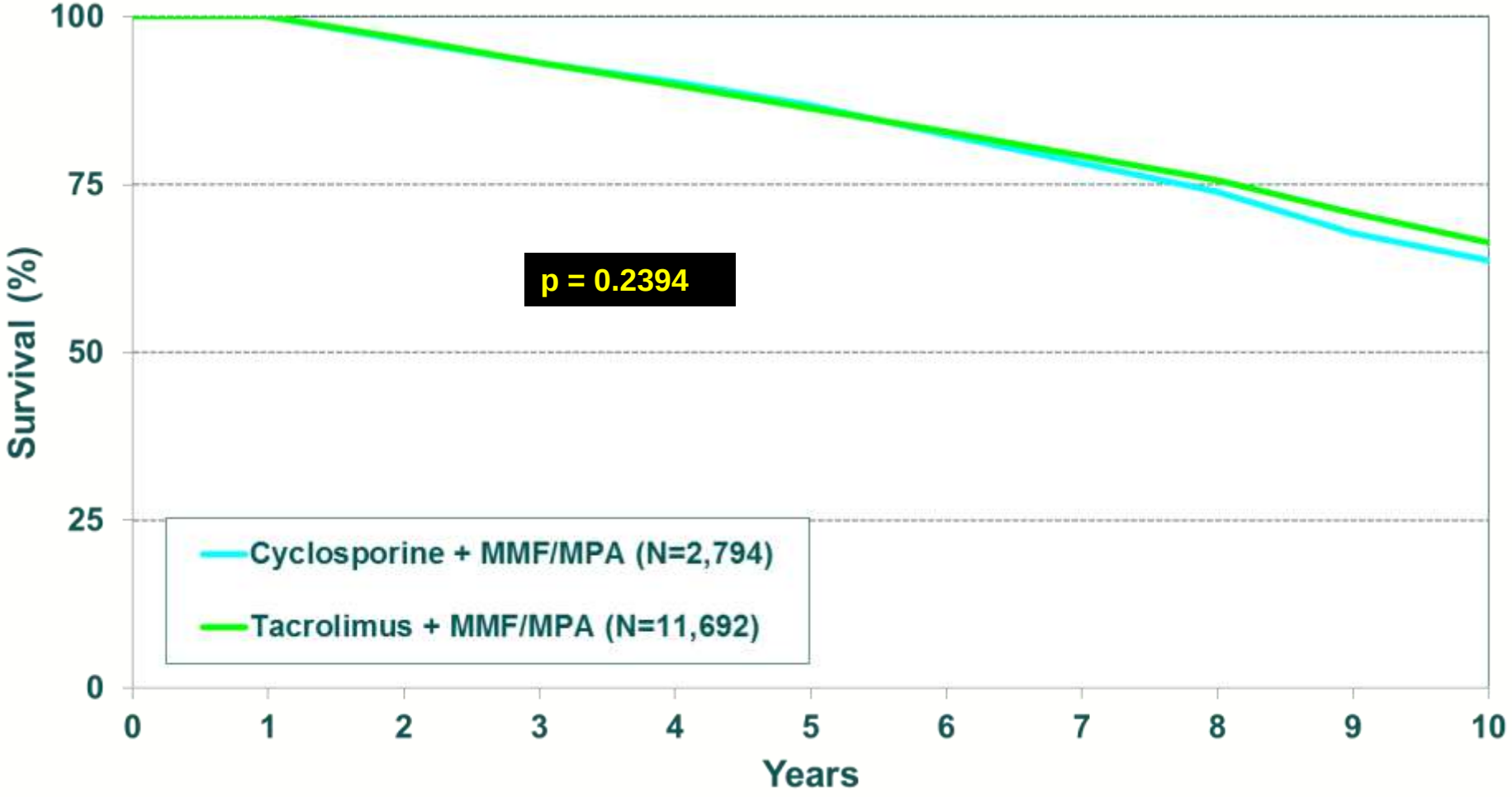
Analysis is limited to patients who were alive at the time of the follow-up.

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2016
JHLT. 2016 Oct; 35(10): 1149-1205

Adult Heart Transplants

Kaplan-Meier Survival by Maintenance Immunosuppression at 1 year (Transplants: January 2004 – June 2014)

Conditional on Survival to 1 Year



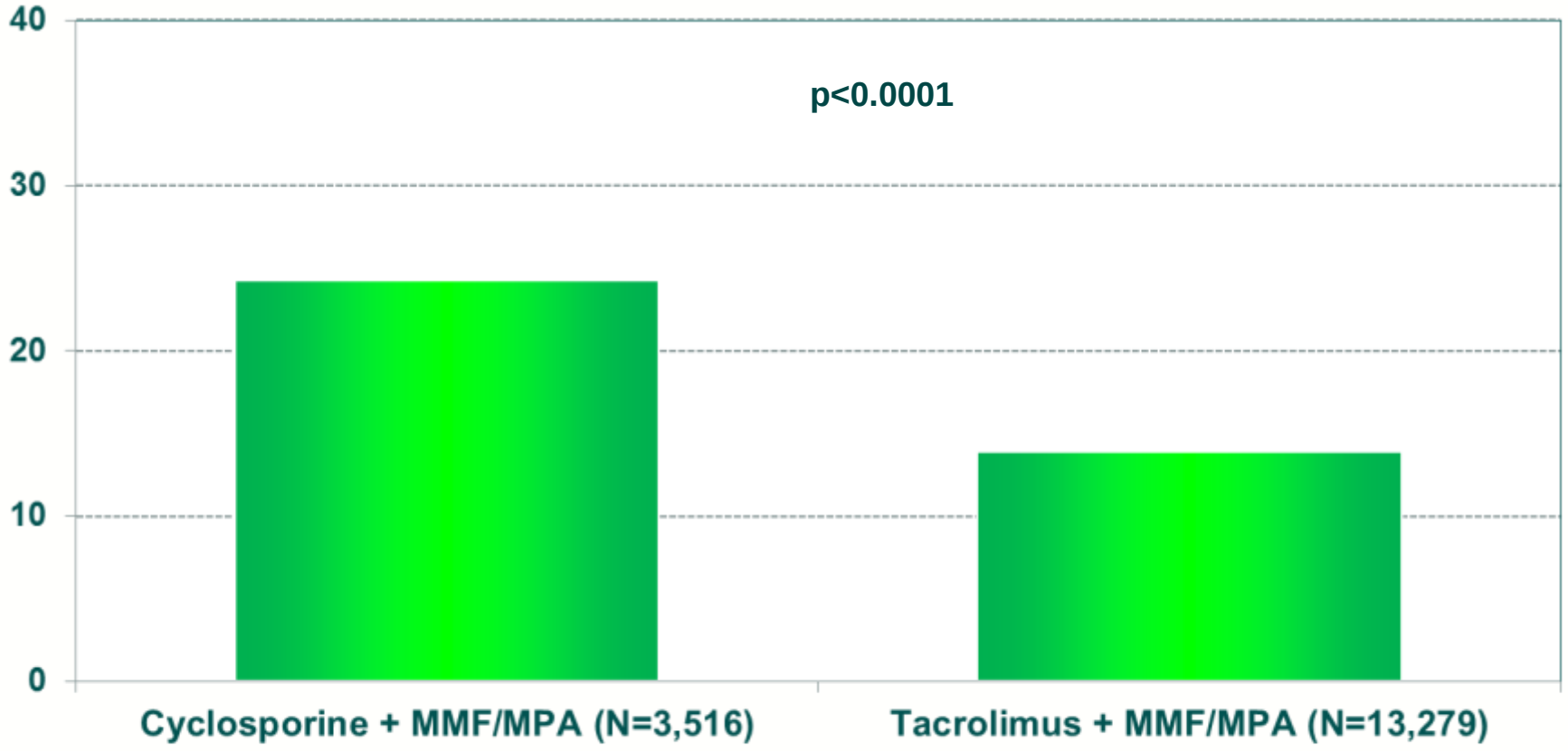
2016

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

JHLT. 2016 Oct; 35(10): 1149-1205

Adult Heart Transplants

% of Recipients Experiencing *Treated* Rejection Between Transplant Discharge and 1-Year Follow-Up by Maintenance Immunosuppression (Follow-ups: January 2005 – June 2015)



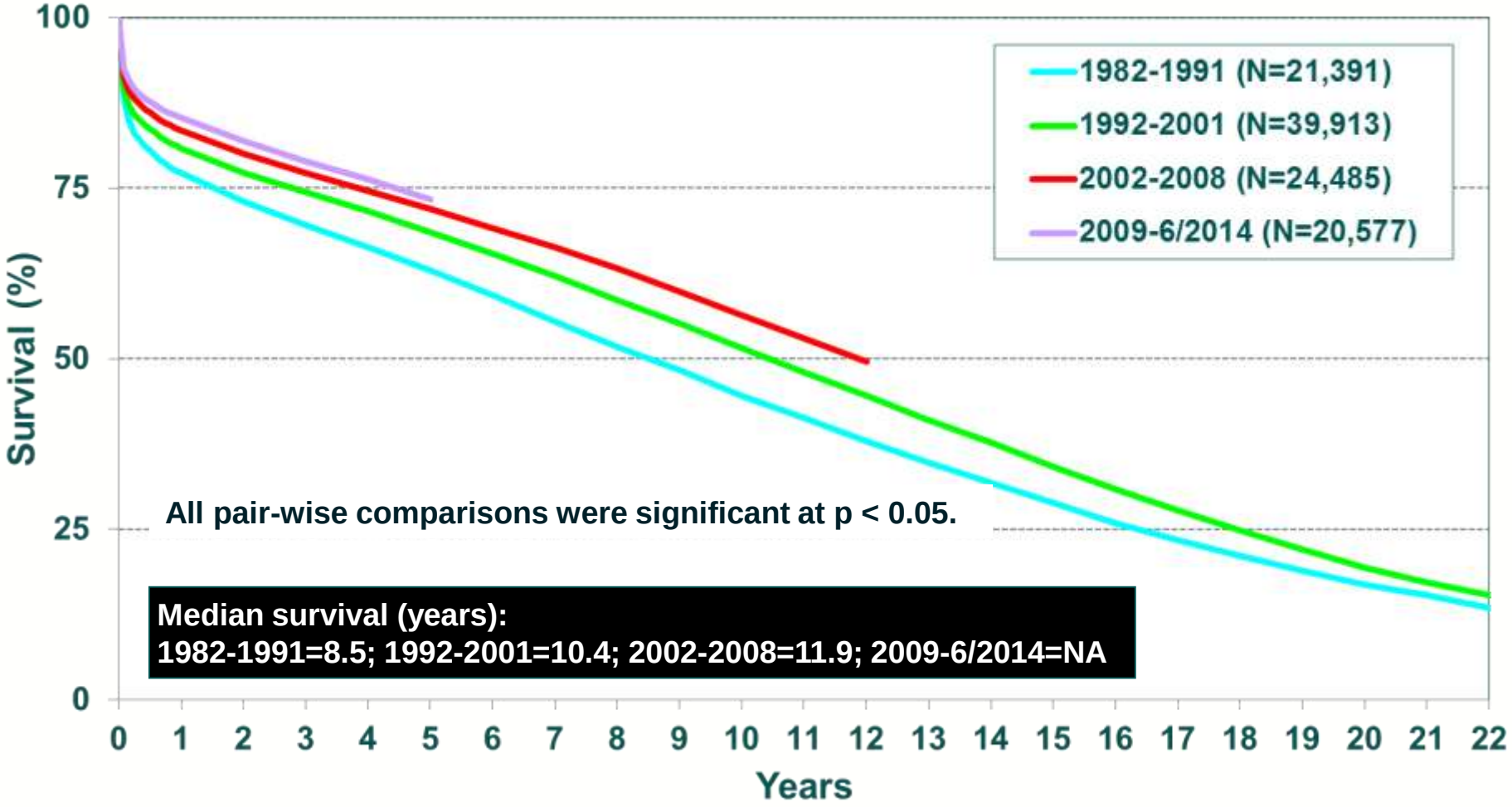
Analysis is limited to patients who were alive at the time of the follow-up.

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.

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2016
JHLT. 2016 Oct; 35(10): 1149-1205

OUTCOME: SURVIVAL

Adult Heart Transplants
Kaplan-Meier Survival by Era
(Transplants: January 1982 – June 2014)



2016

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

JHLT. 2016 Oct; 35(10): 1149-1205

Adult Heart Transplants (2009-6/2014)

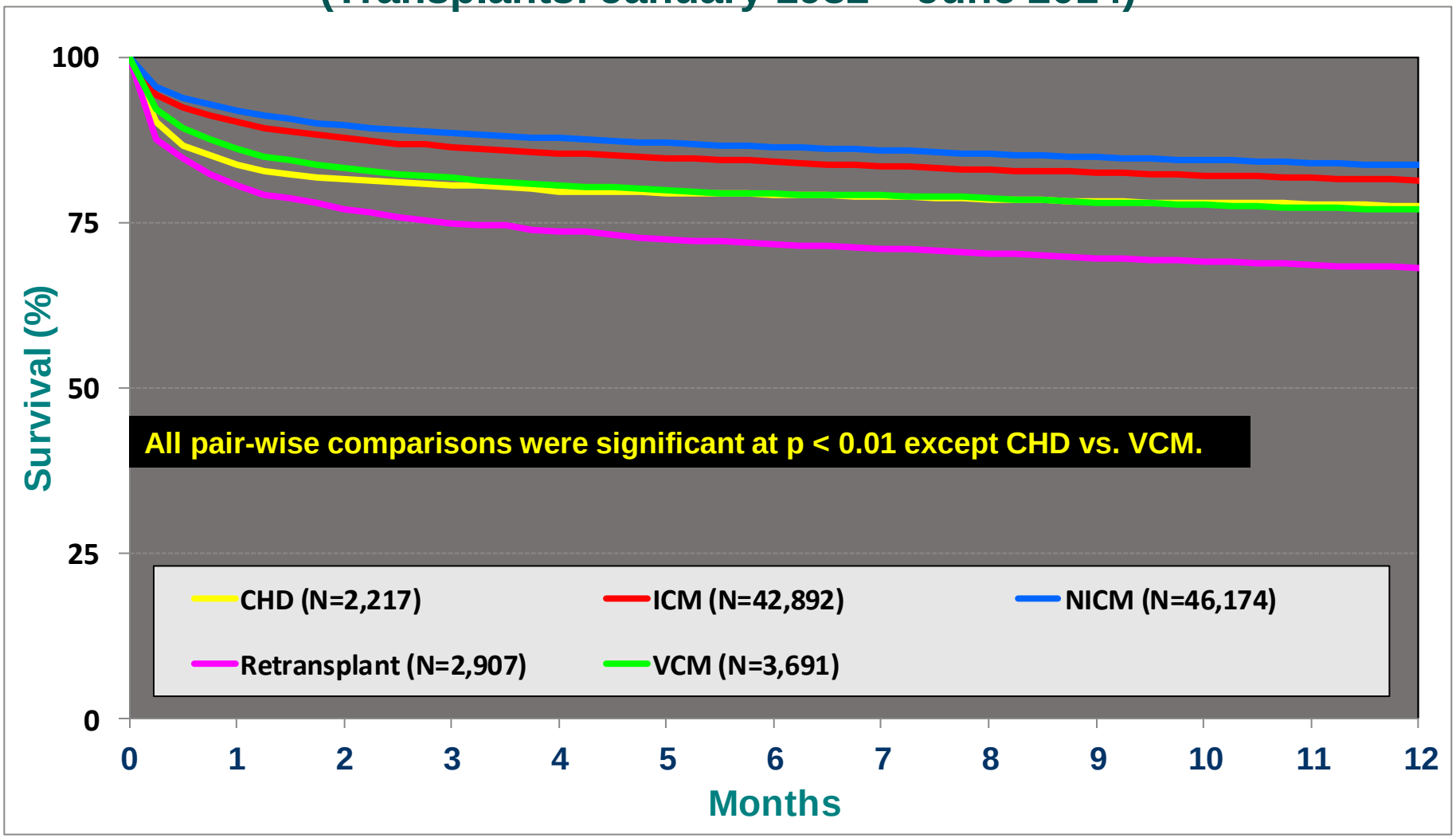
Risk Factors For 1 Year Mortality

Continuous Factors

- Recipient age
- Recipient creatinine
- Donor height
- Transplant center volume
- Donor age
- Ischemia time
- Recipient BSA
- Recipient total bilirubin

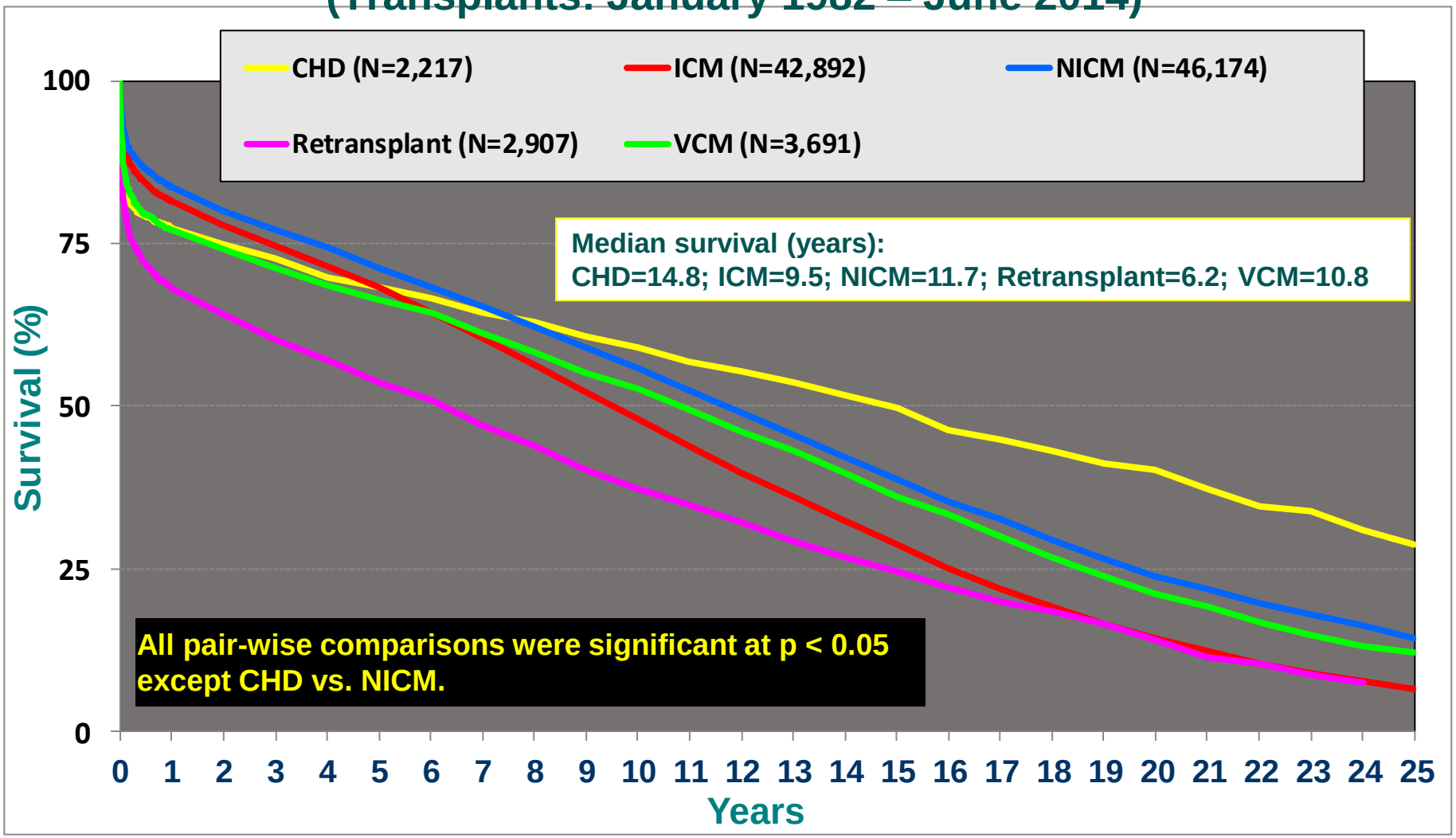
ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2016
JHLT. 2016 Oct; 35(10): 1149-1205

Adult Heart Transplants
Kaplan-Meier Survival Within 1 Year by Diagnosis
(Transplants: January 1982 – June 2014)



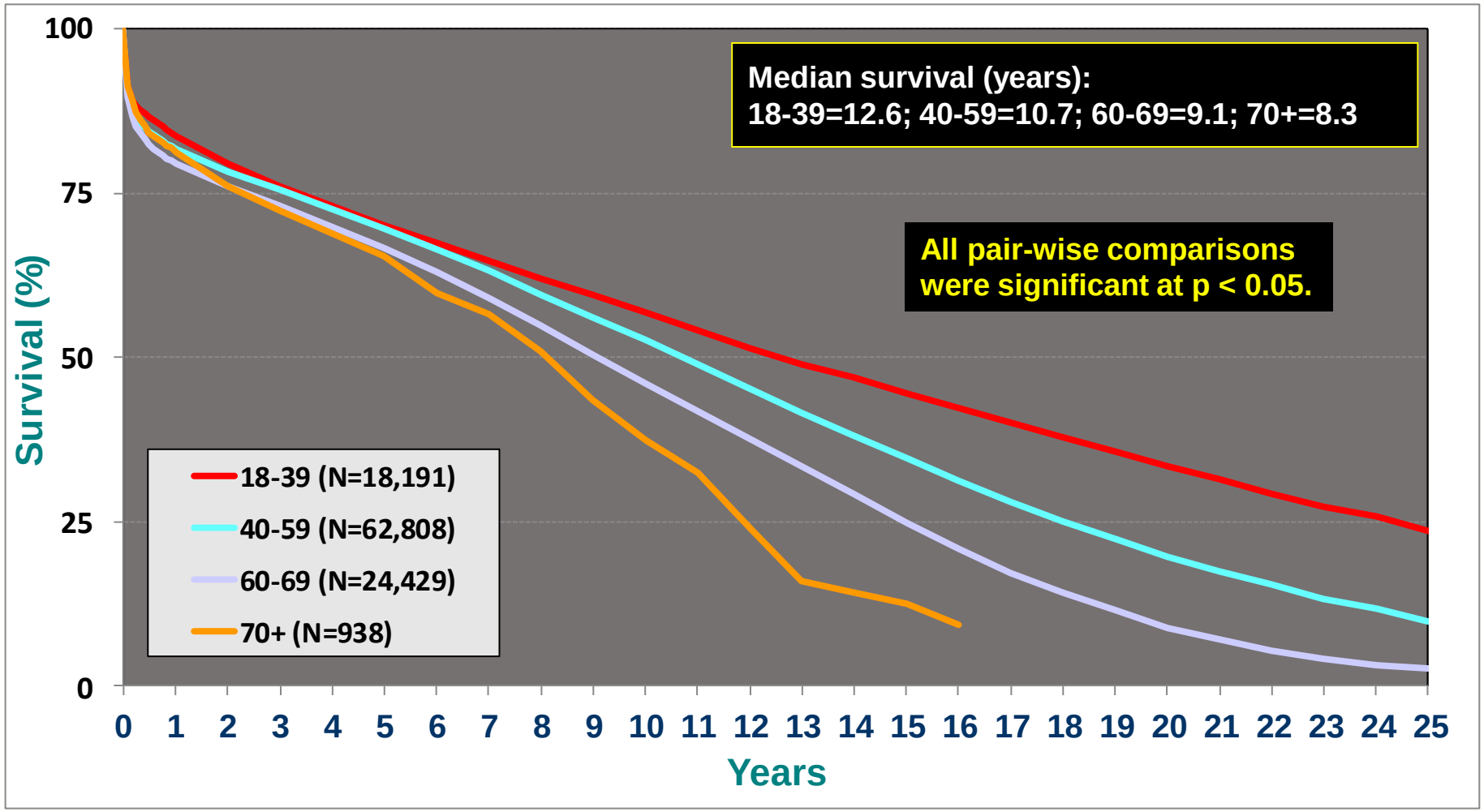
ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2016
JHLT. 2016 Oct; 35(10): 1149-1205

Adult Heart Transplants
Kaplan-Meier Survival by Diagnosis
(Transplants: January 1982 – June 2014)



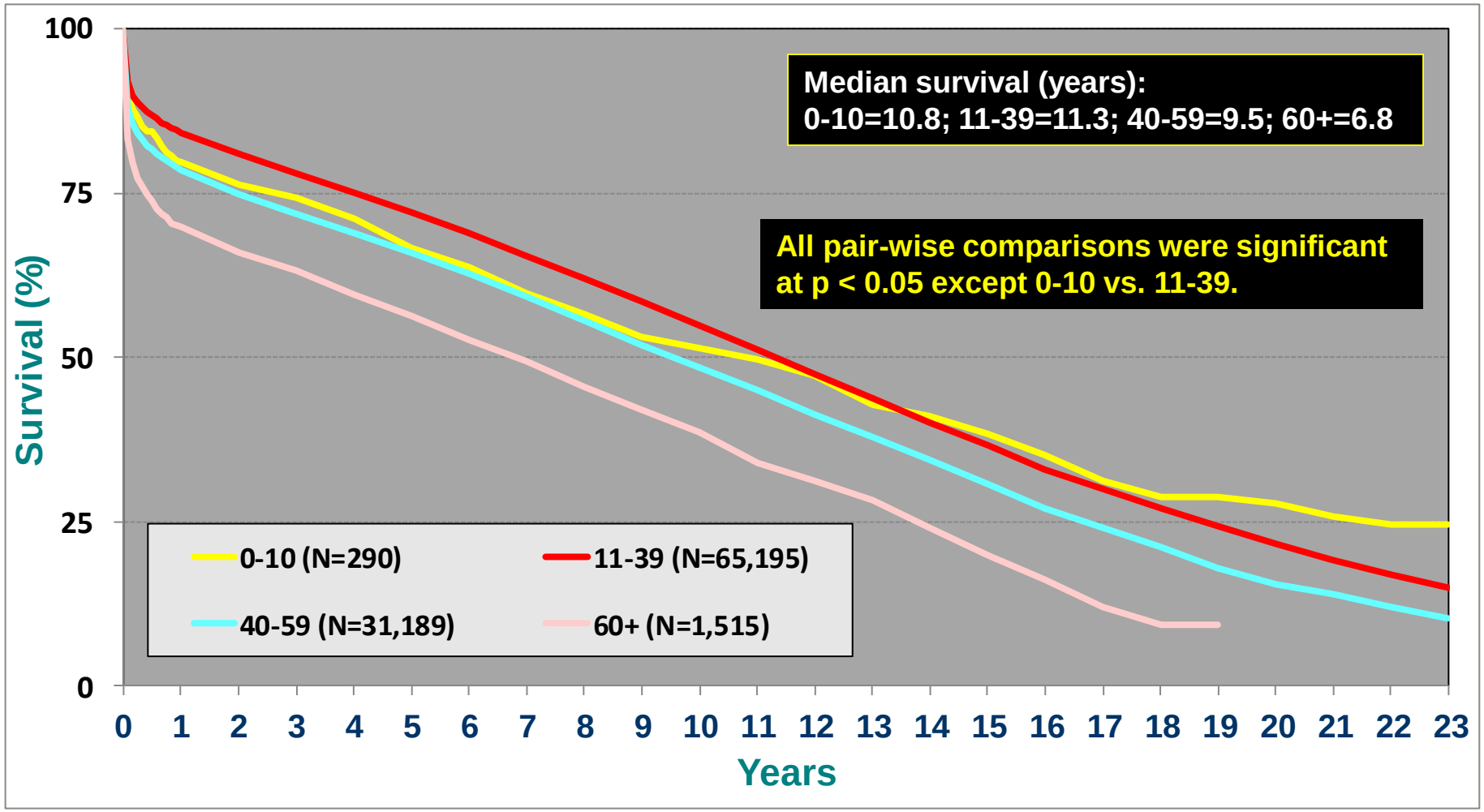
ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2016
JHLT. 2016 Oct; 35(10): 1149-1205

Adult Heart Transplants
Kaplan-Meier Survival by Age Group
(Transplants: January 1982 – June 2014)



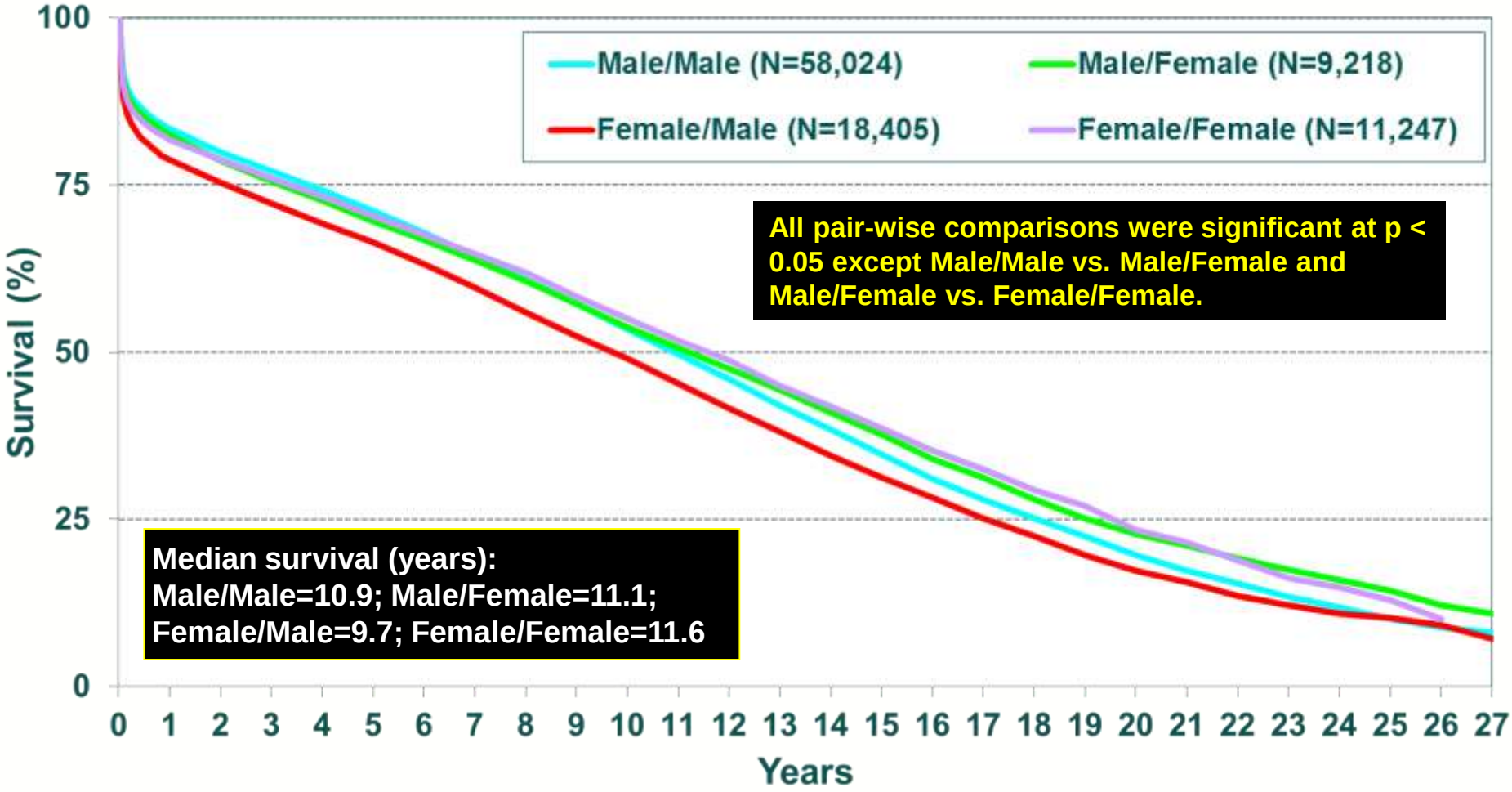
ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2016
JHLT. 2016 Oct; 35(10): 1149-1205

Adult Heart Transplants
Kaplan-Meier Survival by Donor Age Group
(Transplants: January 1982 – June 2014)



ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2016
JHLT. 2016 Oct; 35(10): 1149-1205

Adult Heart Transplants
Kaplan-Meier Survival by Donor/Recipient Gender
(Transplants: January 1982 – June 2014)



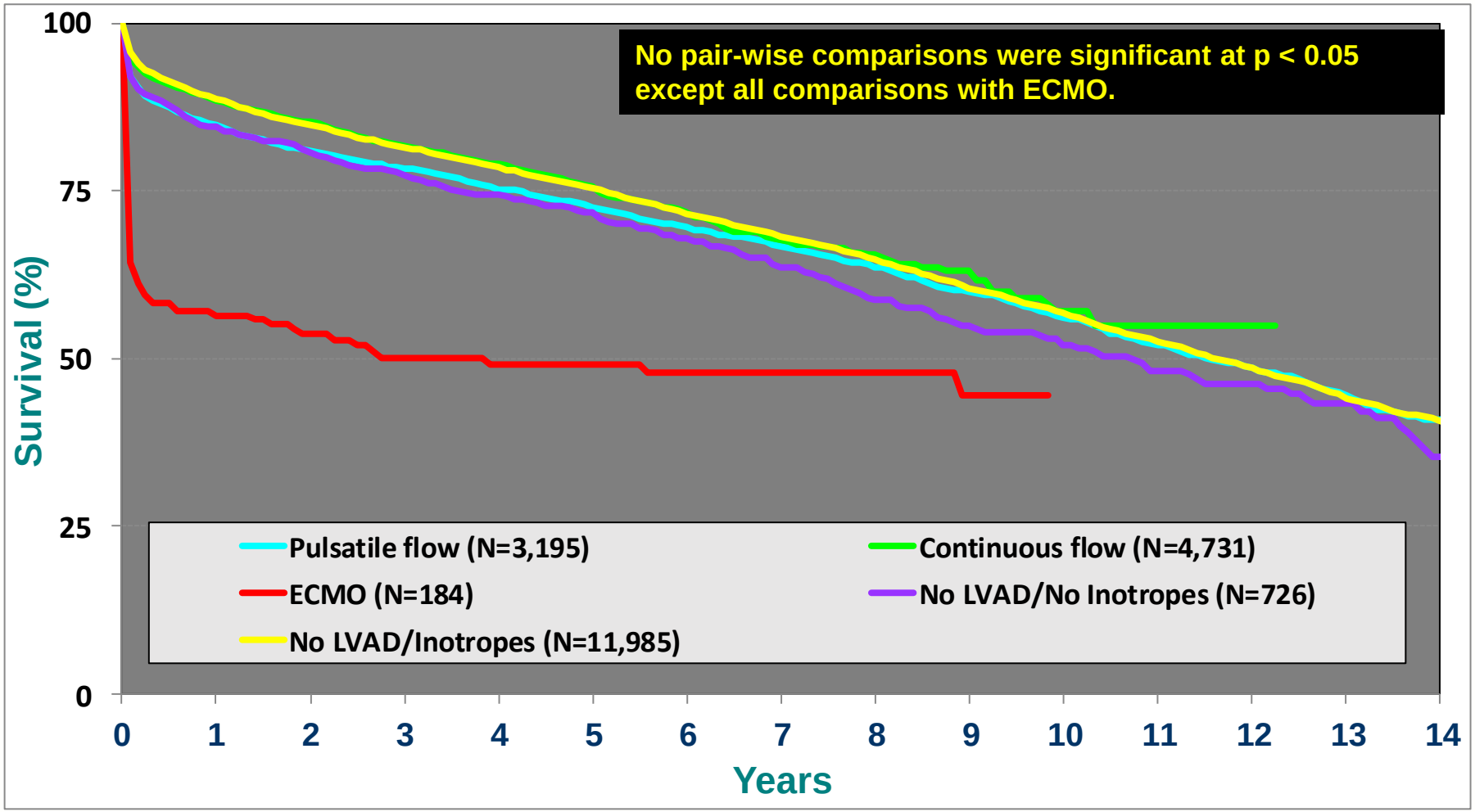
ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

2016

JHLT. 2016 Oct; 35(10): 1149-1205

Adult Heart Transplants

Kaplan-Meier Survival by Pre-Transplant Mechanical Circulatory Support Use (Transplants: January 1999 – June 2014)



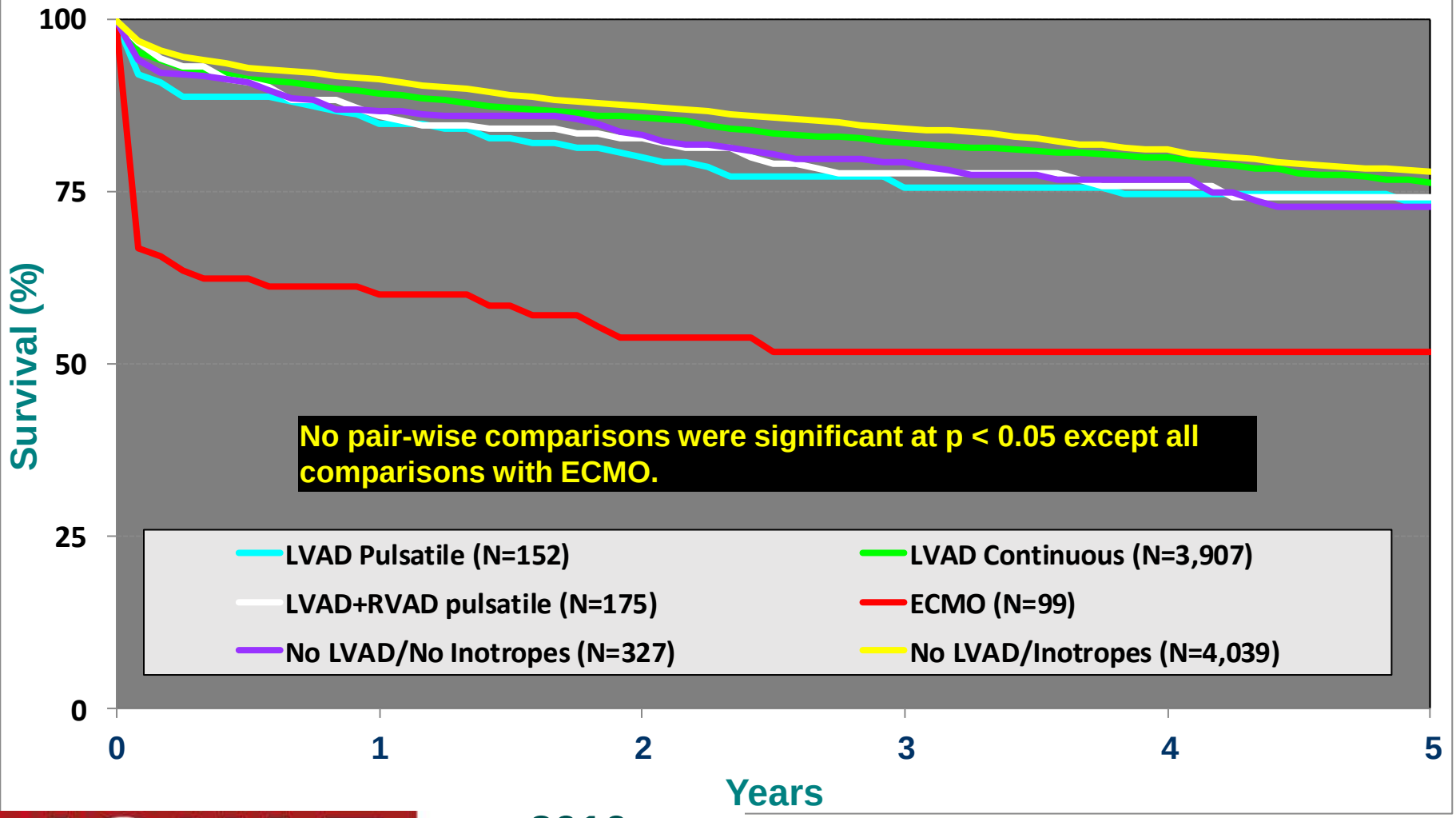
ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

2016

JHLT. 2016 Oct; 35(10): 1149-1205

Adult Heart Transplants

Kaplan-Meier Survival by Pre-Transplant Mechanical Circulatory Support Use (Transplants: January 2009 – June 2014)

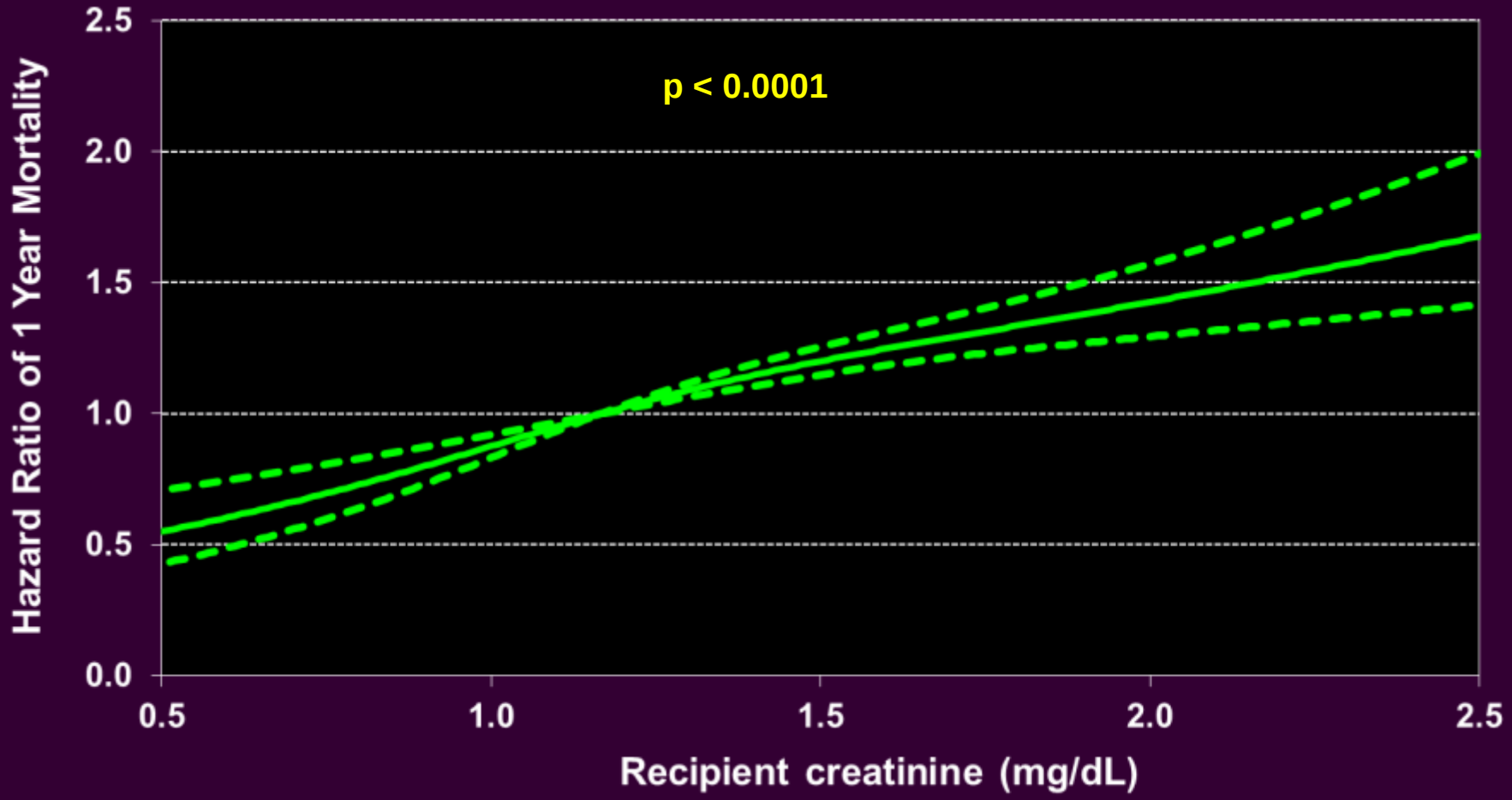


2016

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

JHLT. 2016 Oct; 35(10): 1149-1205

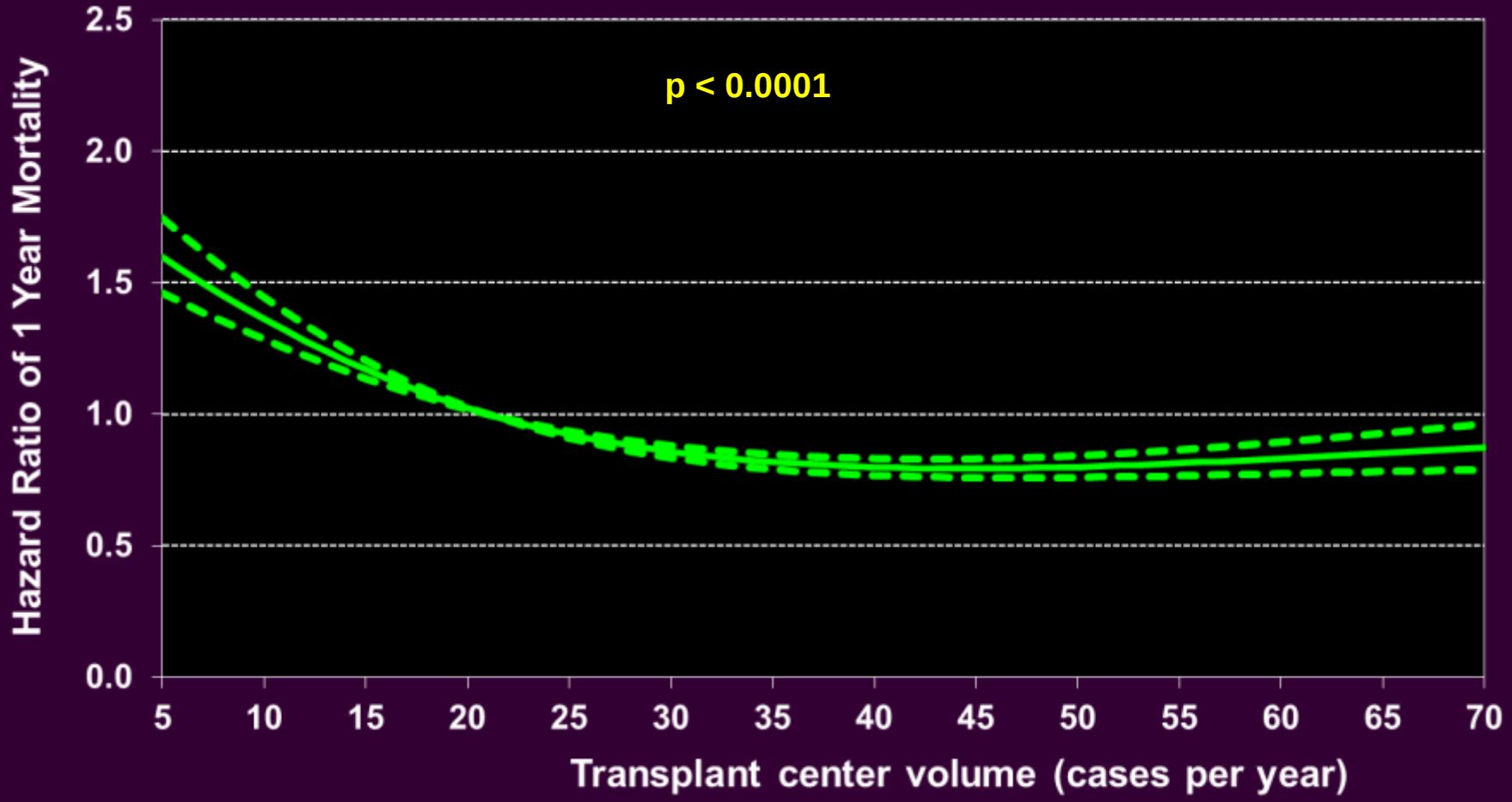
Adult Heart Transplants (2009-6/2014)
Risk Factors For 1 Year Mortality with 95% Confidence Limits
Recipient creatinine



(N = 19,948)

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2016
JHLT. 2016 Oct; 35(10): 1149-1205

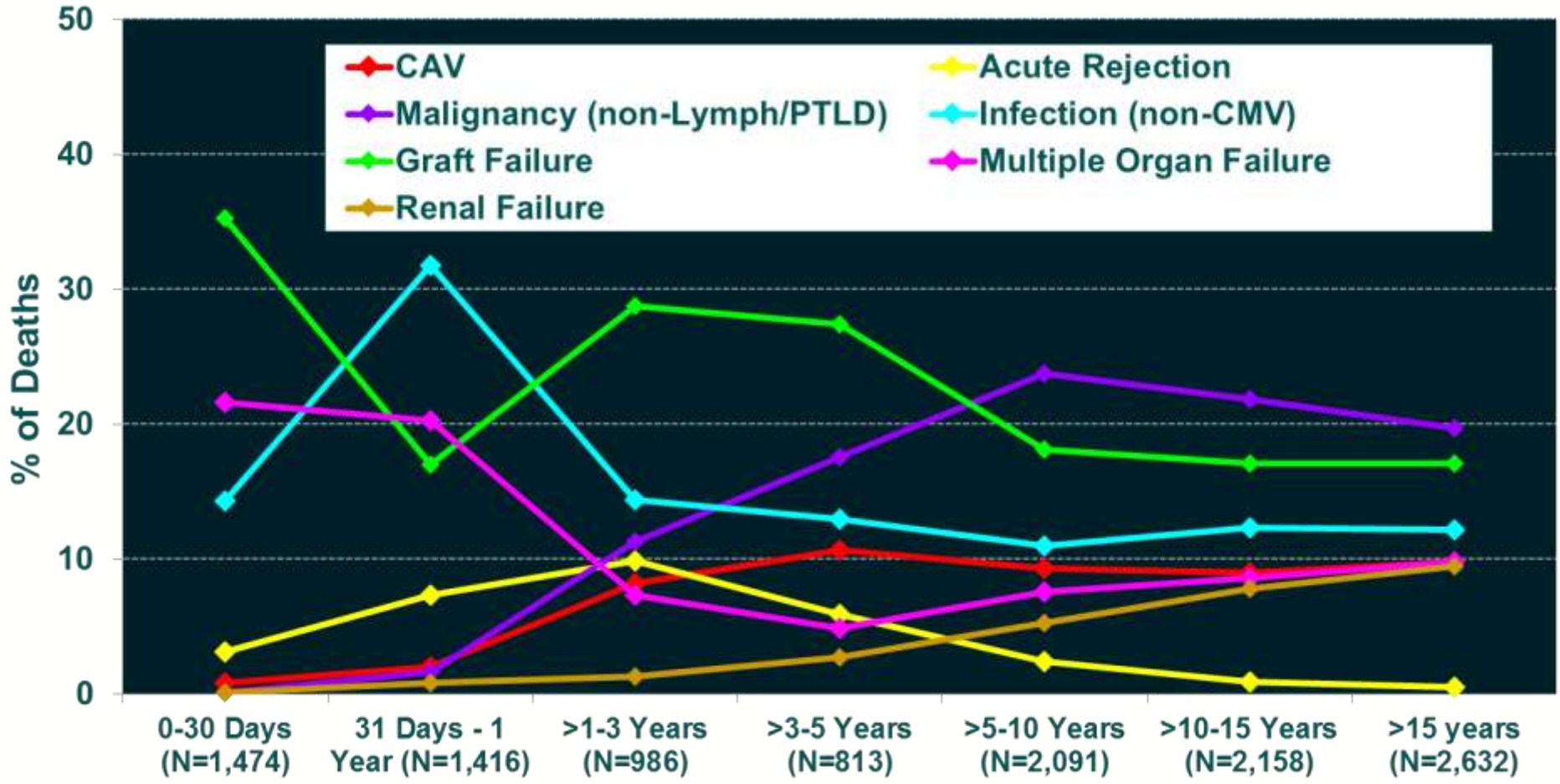
Adult Heart Transplants (2009-6/2014)
Risk Factors For 1 Year Mortality with 95% Confidence Limits
Transplant center volume



(N = 19,948)

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2016
JHLT. 2016 Oct; 35(10): 1149-1205

Adult Heart Transplants
Relative Incidence of Leading Causes of Death
(Deaths: January 2009 – June 2015)



ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

2016

JHLT. 2016 Oct; 35(10): 1149-1205

Since only leading causes of death are shown, the sum of percentages for each time period is less than 100%.

OUTCOME: MORBIDITY

Adult Heart Transplants

Cumulative Morbidity Rates in Survivors within 1, 5 and 10 Years Post Transplant (Transplants: January 1994 – June 2014)

Outcome	Within 1 Year	Total N with known response	Within 5 Years	Total N with known response	Within 10 Years	Total N with known response
Hypertension*	70.8%	(N=31,161)	90.9%	(N=15,499)	-	
Renal Dysfunction	25.4%	(N=34,723)	50.9%	(N=19,546)	68.0%	(N=8,142)
Abnormal Creatinine ≤ 2.5 mg/dl	*17.3%*		*32.8%*		*39.5%*	
Creatinine > 2.5 mg/dl	*6.1%*		*13.7%*		*18.6%*	
Chronic Dialysis	*1.7%*		*3.0%*		*6.2%*	
Renal Transplant	*0.3%*		*1.3%*		*3.7%*	
Hyperlipidemia*	59.9%	(N=32,371)	87.6%	(N=17,082)	-	
Diabetes*	23.3%	(N=35,391)	36.6%	(N=19,975)	-	
Cardiac Allograft Vasculopathy	7.8%	(N=32,292)	29.4%	(N=14,808)	47.6%	(N=4,944)

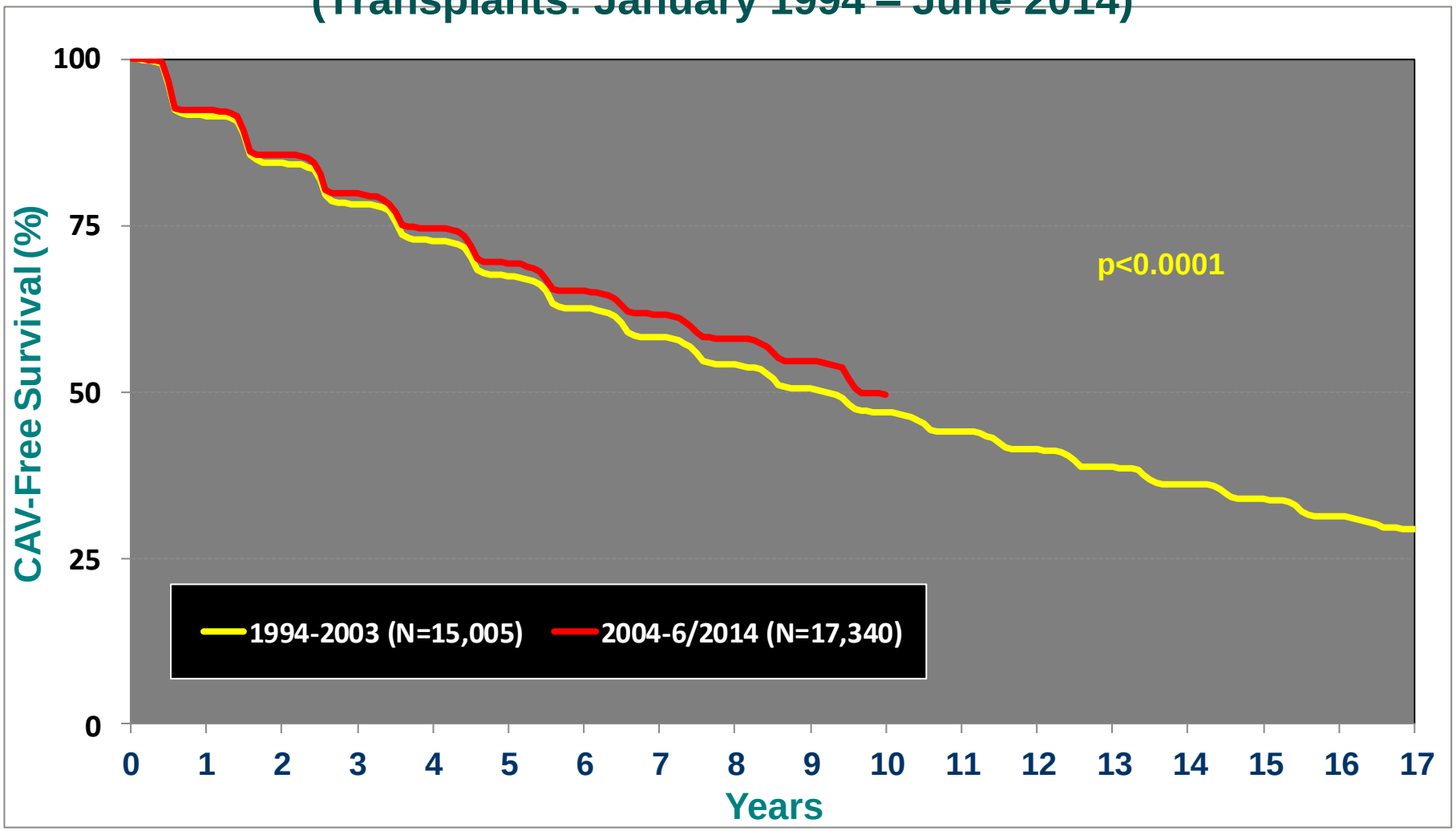
ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2016
JHLT. 2016 Oct; 35(10): 1149-1205

* Data are not available 10 years post-transplant.

Adult Heart Transplants

Cardiac Allograft Vasculopathy-Free Survival by Era

(Transplants: January 1994 – June 2014)



ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

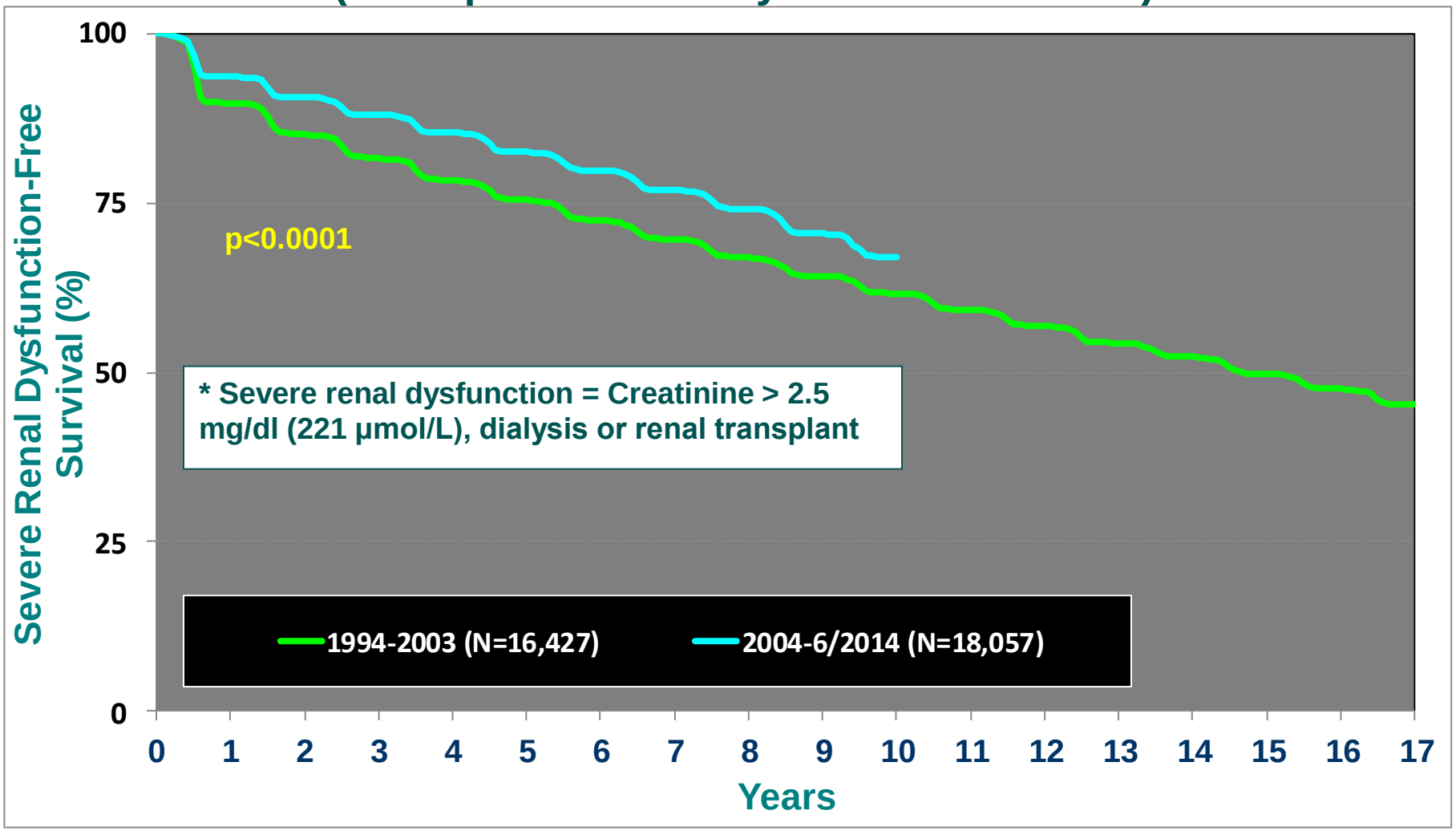
2016

JHLT. 2016 Oct; 35(10): 1149-1205

Adult Heart Transplants

Severe Renal Dysfunction*-Free Survival by Era

(Transplants: January 1994 – June 2014)



ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2016
JHLT. 2016 Oct; 35(10): 1149-1205

Adult Heart Transplants

Post Transplant Malignancy (Transplants: January 1994 – June 2014)

Cumulative Morbidity Rates in Survivors

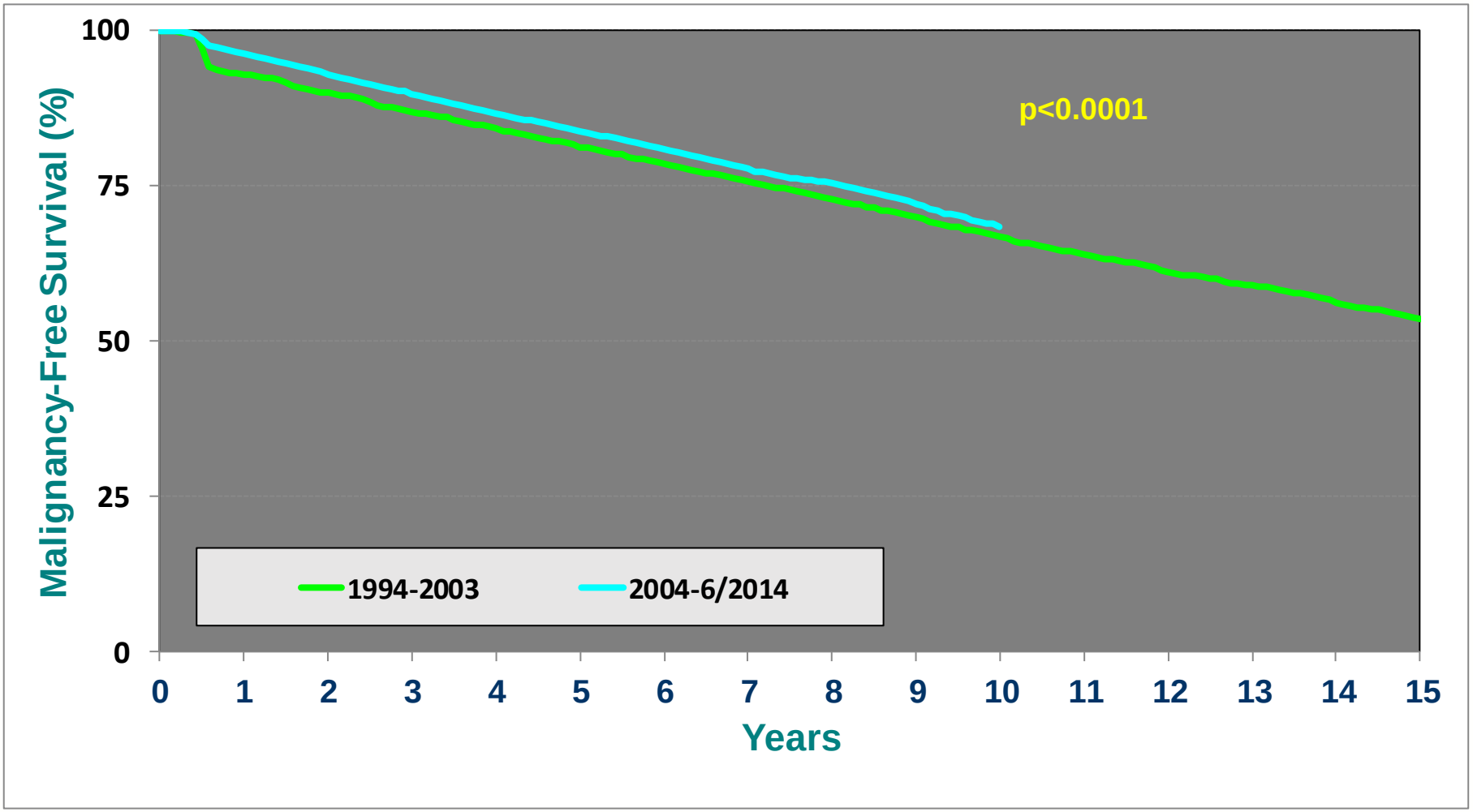
Malignancy/Type		1-Year Survivors	5-Year Survivors	10-Year Survivors
No Malignancy		33,561 (94.9%)	18,347 (84.3%)	7,099 (72.6%)
Malignancy (all types combined)		1,815 (5.1%)	3,428 (15.7%)	2,676 (27.4%)
*Malignancy Type**	*Skin*	*597 (1.7%)*	*2,035 (9.3%)*	*1,772 (18.1%)*
	Lymphoma	*190 (0.5%)*	*243 (1.1%)*	*181 (1.9%)*
	Other	*989 (2.8%)*	*1,339 (6.1%)*	*977 (10%)*
	Type Not Reported	*39 (0.1%)*	*37 (0.2%)*	*16 (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.

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2016
JHLT. 2016 Oct; 35(10): 1149-1205

Adult Heart Transplants
Malignancy-Free Survival by Era
(Transplants: January 1994 – June 2014)

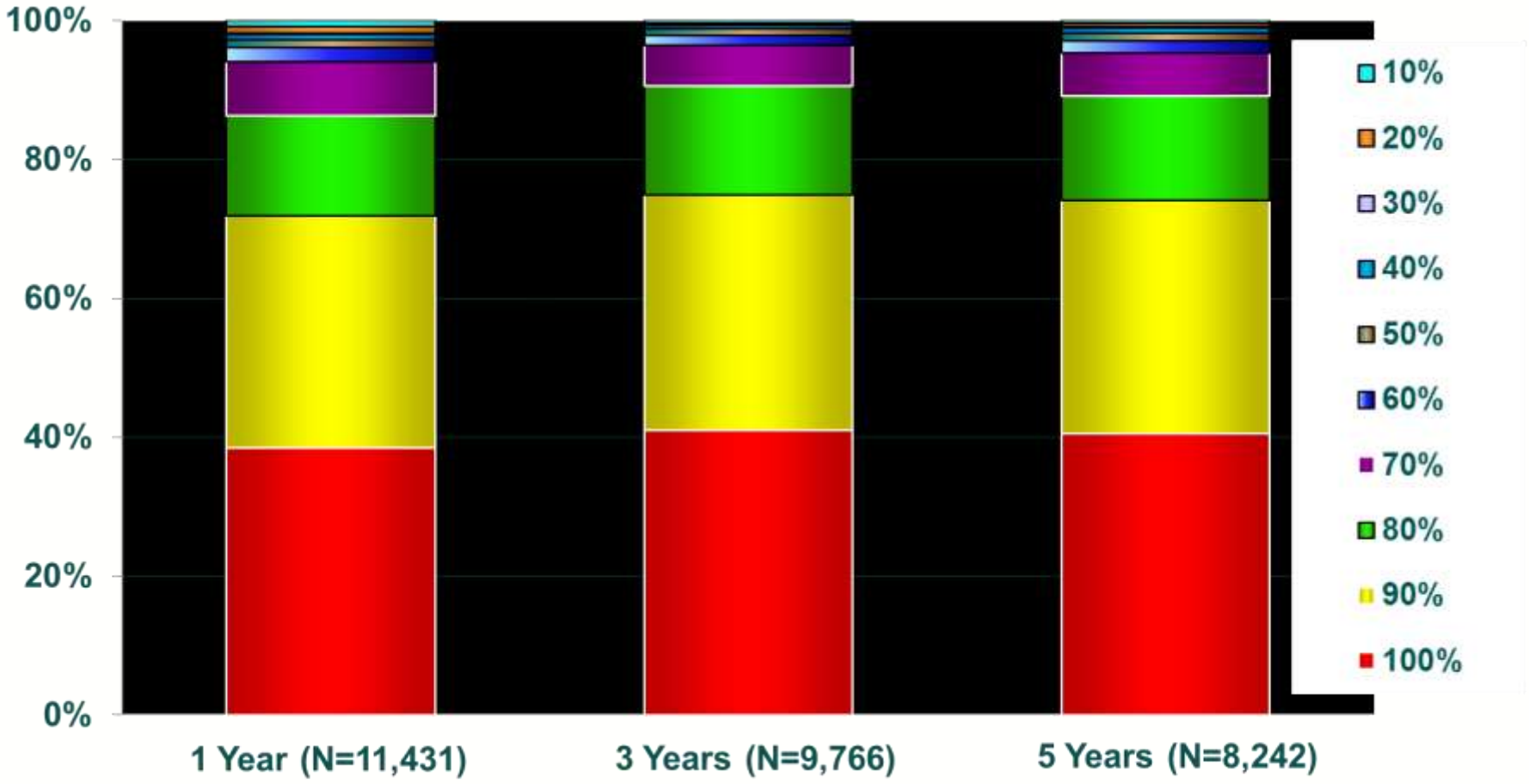


ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2016
JHLT. 2016 Oct; 35(10): 1149-1205

FUNCTIONAL STATUS

Adult Heart Transplants

Functional Status of Surviving Recipients by Karnofsky Score (Follow-ups: January 2009 – June 2015)

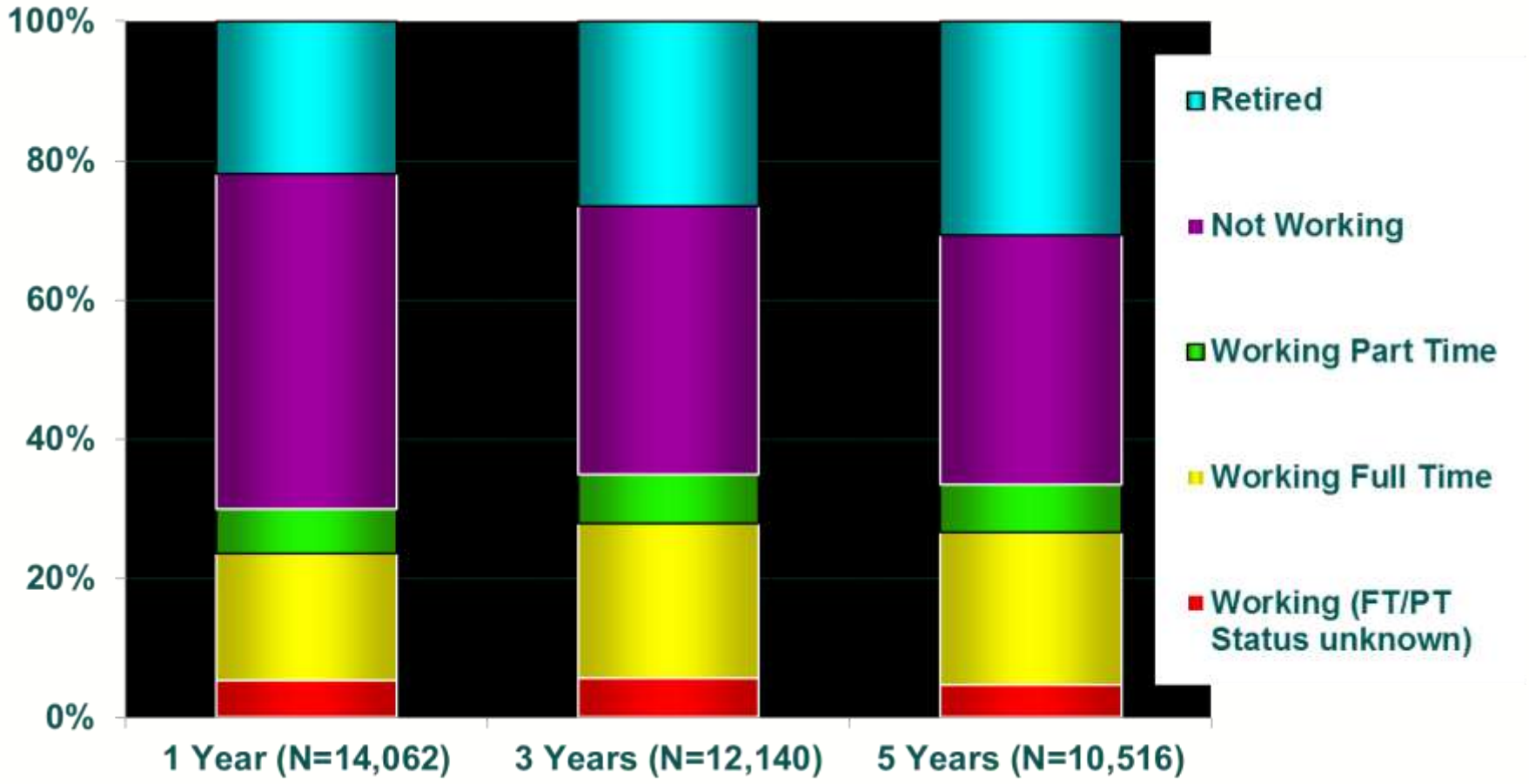


2016

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

JHLT. 2016 Oct; 35(10): 1149-1205

Adult Heart Transplants
Employment Status of Surviving Recipients
(Follow-ups: January 2004 – June 2015)



ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2016
JHLT. 2016 Oct; 35(10): 1149-1205

Adult Heart Transplants
Kaplan-Meier Survival by Employment Status at 1 Year Conditional on Survival to 1 Year
(1 Year Follow-ups: January 2004 – June 2014)

2016

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

JHLT. 2016 Oct; 35(10): 1149-1205

CONCLUSION

- Treatment of choice for selected patients with an advanced heart failure.
- Continuous to evolve including:
  - Refinement of patient selection
  - Donor optimization and selection
  - Optimization of immunosuppression strategies
- Advanced mechanical assists devices, stem cell transplant and improved medical therapy are growing research areas.

THANK YOU