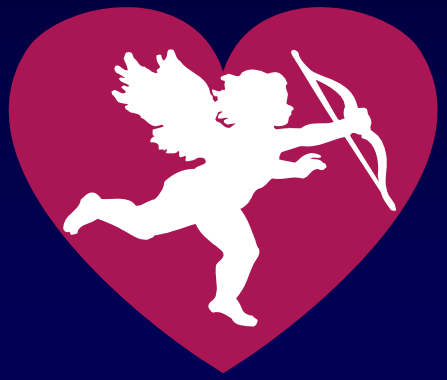
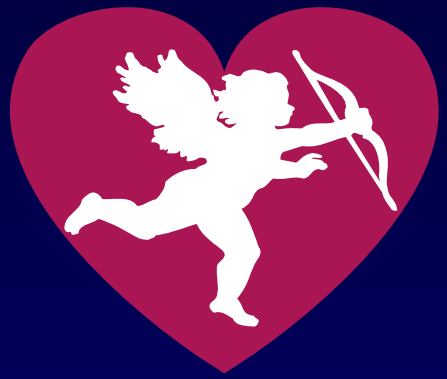
השתלות לב





ד"ר טוביה בן גל (בלצ'ינסקי)
מנהל היחידה לאי ספיקת לב
המרפאה להשתלות לב
מרכז רפואי רבין

The ISHLT:
Guidelines for the care of heart transplant recipients

J Heart Lung Transplant 2010;29:914–956.

COMPETENCE AND TRAINING STATEMENT ACCF/AHA/ACP/HFSA/ISHLT 2010

Clinical Competence Statement on Management of Patients With Advanced Heart Failure and Cardiac Transplant

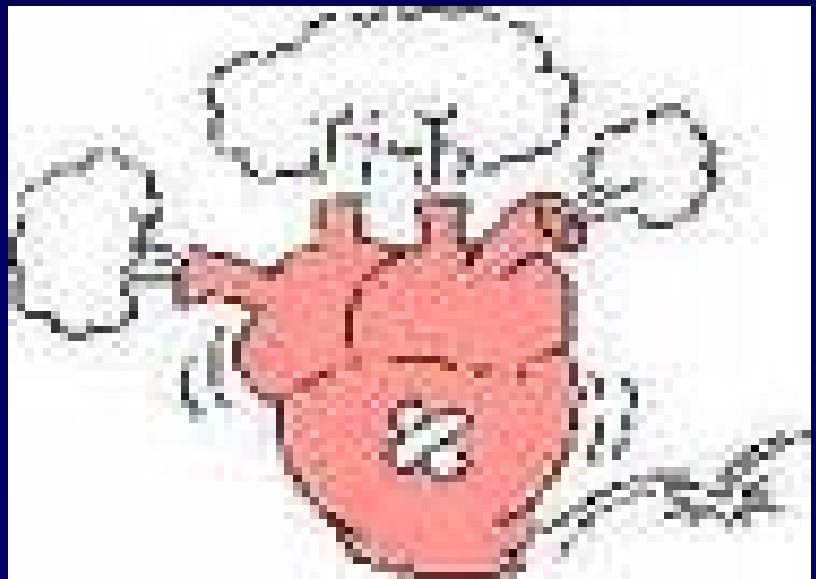
J Am Coll Cardiol, 2010; 56:424-453.

בניתוח להשתלת לב

אז מימין יש לי את הלב החולה

ומשמאל הבריא

או להיפך??



הטיפול באי ספיקת לב מתקדמת

- טיפול תרופתי מיטבי: חוסמי ביטא, אלדקטון, מעכבי ACE, ARB’S
- תכשירים תוך ורידיים מתקדמים כגון לבוסימנדן.
- קוצבים מתוחכמים (AICD, CRT).
- התערבויות כירורגיות כגון CABG, ניתוחי מסתמים, SVR.
- שיקום לב פעיל.
- Assist devices.
- Xenografts.
- Totally artificial heart.

- עדיין למרות הכל, לקבוצת חולים מוגדרת,

השתלת לב היא הפתרון היחידי.

שכיחות אי ספיקת לב

- באוכלוסייה הכללית: בין 0.5% ל- 2%.
- שכיחות עולה עם הגיל ועם השיפור בהישרדות ממצבים קרדיאליים חריפים.
- מהווה גורם תמותה עיקרי בעולם המערבי.
- בארה"ב בין 500,000 למיליון חולים עם CHF מתקדמת.
- בארץ בהתאמה בין 15,000-20,000 חולי CHF מתקדמת.
- סה"כ תרומות לב בעולם בין 2500 ל- 3500.
- תמותה בהמתנה להשתלה ברשימת הממתינים בין 10% ל- 20%.
- תמותה בהמתנה להשתלה ברשימה הדחופה כ- 50%.
- אמורים היו להיות בארץ עד כ- 300 ממתינים השתלת לב.

HEART TRANSPLANTATION

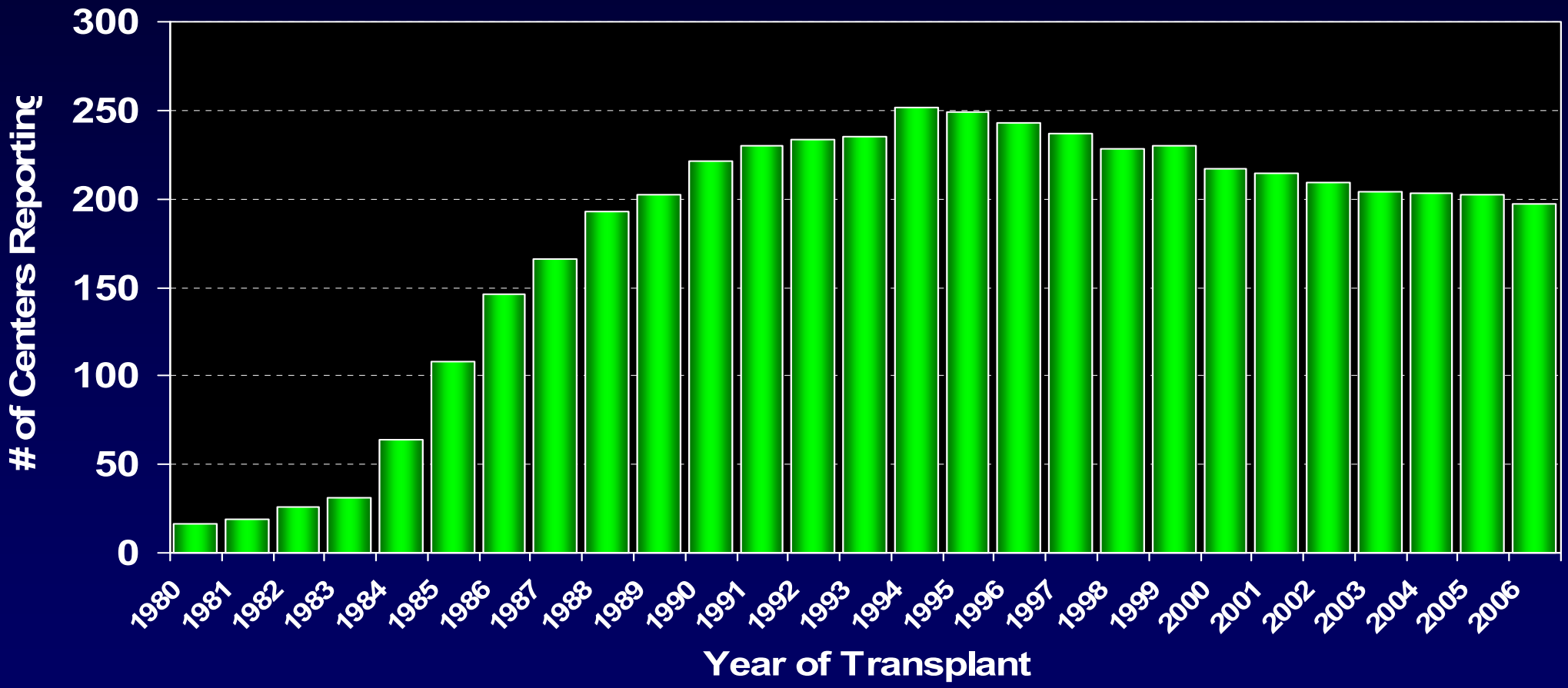
Overall

ISHLT

2009

REGISTRY DATABASE:

Number of Centers Reporting Heart Transplants

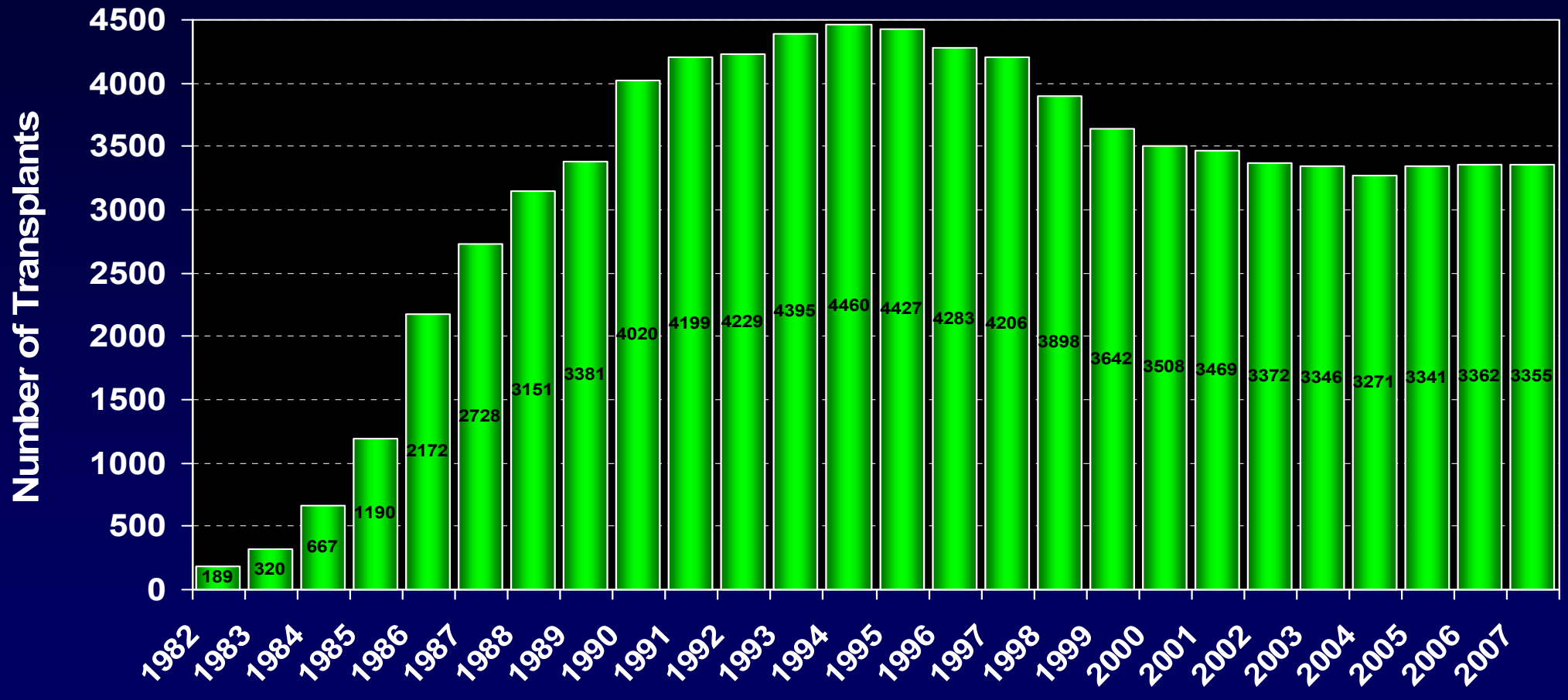


ISHLT

2008

J Heart Lung Transplant 2008;27: 937-983

NUMBER OF HEART TRANSPLANTS REPORTED BY YEAR

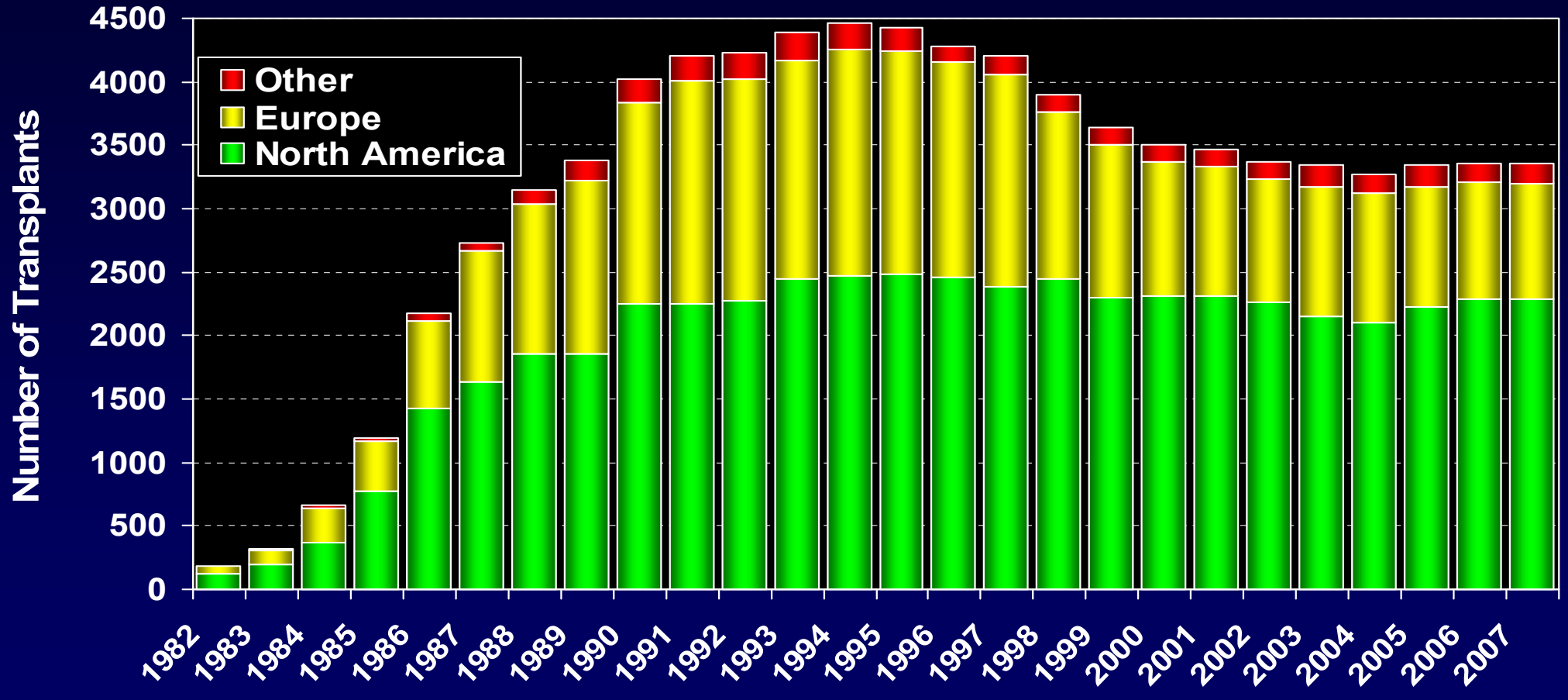


ISHLT

2009

NOTE: This figure includes only the heart transplants that are reported to the ISHLT Transplant Registry. As such, the presented data may not mirror the changes in the number of heart transplants performed worldwide

NUMBER OF HEART TRANSPLANTS REPORTED BY YEAR



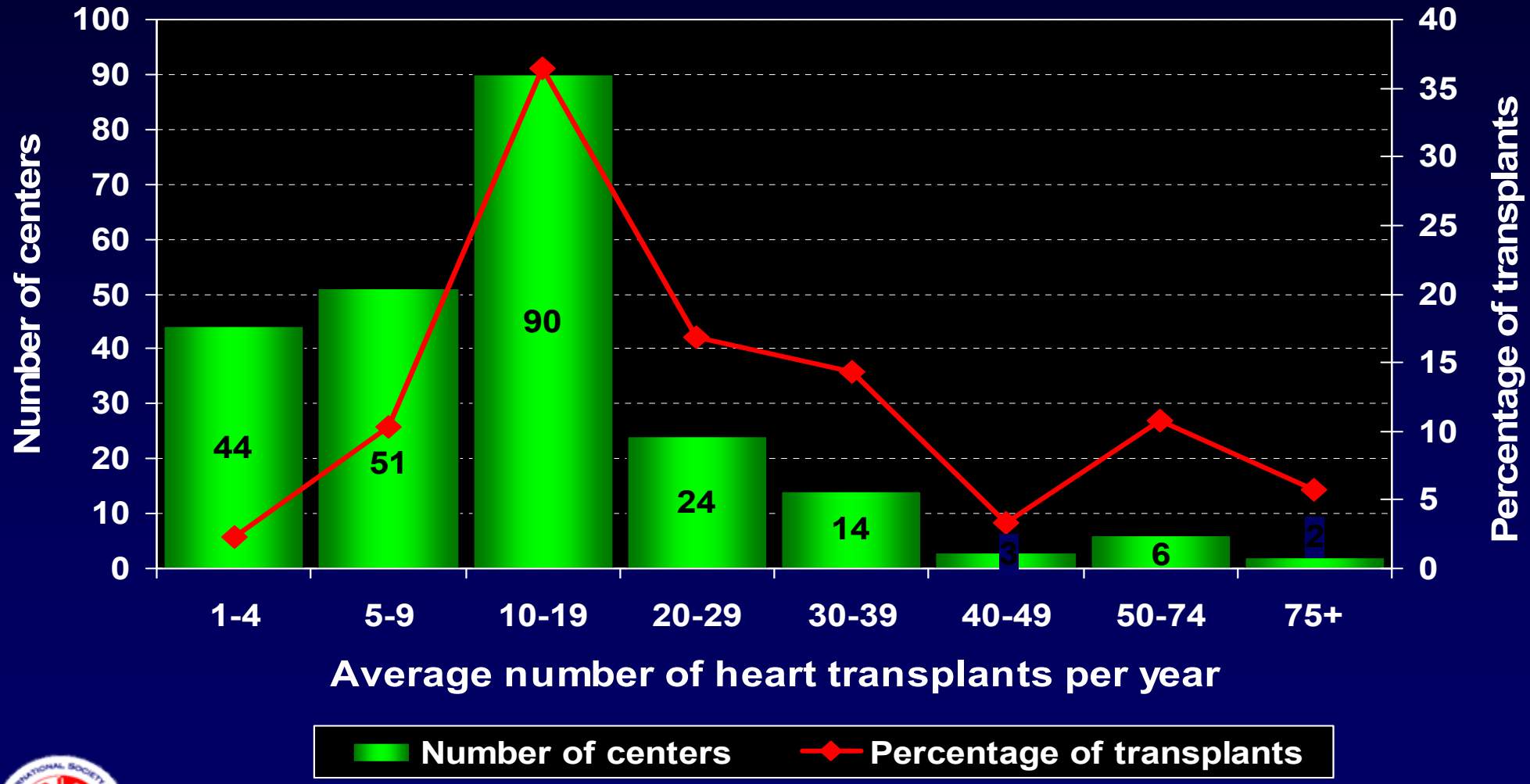
ISHLT

2009

NOTE: This figure includes only the heart transplants that are reported to the ISHLT Transplant Registry. As such, the presented data may not mirror the changes in the number of heart transplants performed worldwide

AVERAGE CENTER VOLUME

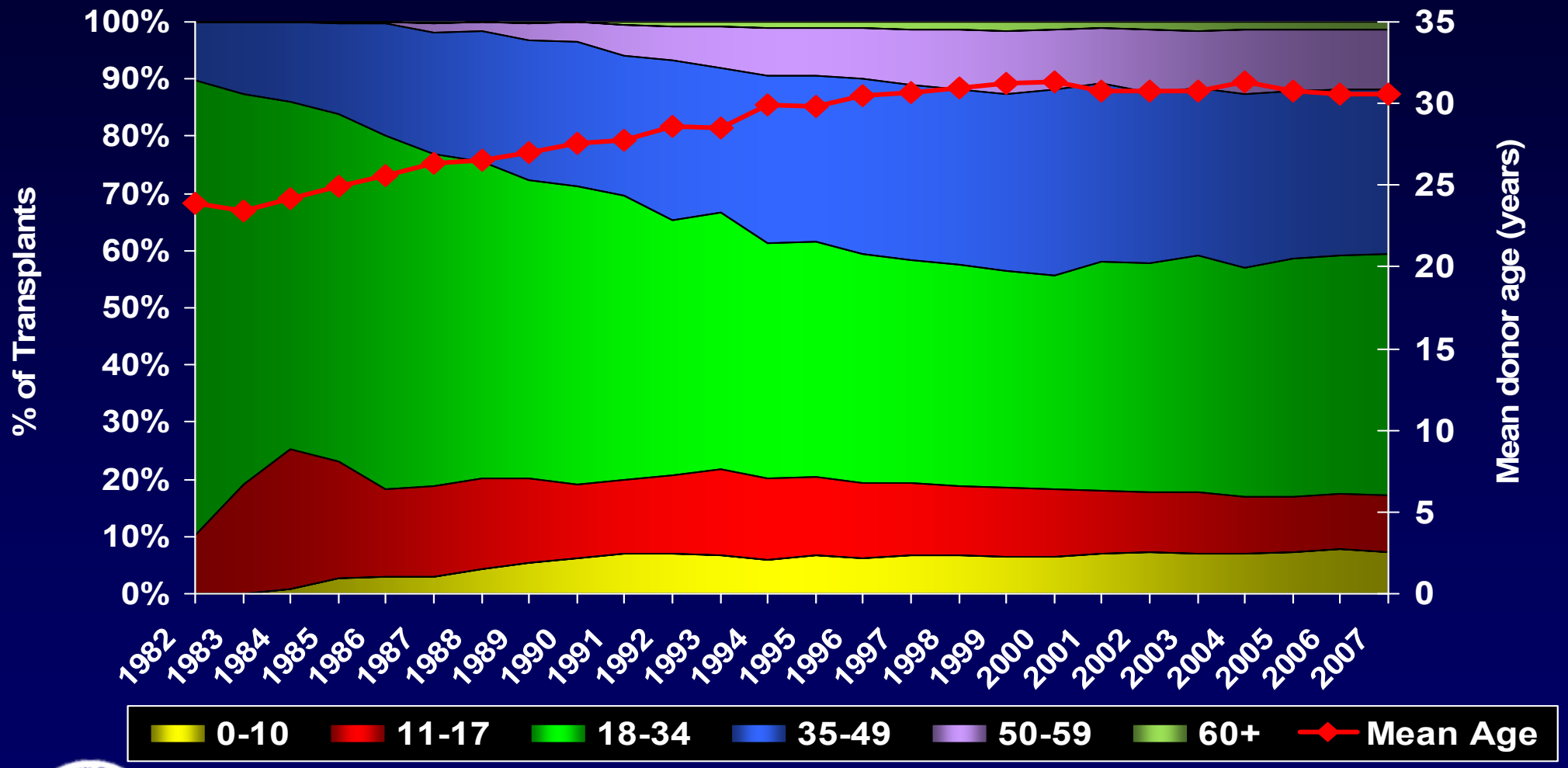
Heart Transplants: January 1, 2003 – June 30, 2008



ISHLT

2009

HEART TRANSPLANTS:
Donor Age by Year of Transplant



ISHLT

2009

Centers Reporting to the ISHLT Transplant Registry

COUNTRY/Center	TXs Performed 1/2006-6/2007 and Reported to ISHLT
ARGENTINA	
Fundacion Favaloro	x
Hospital Italiano	x
AUSTRALIA[1]	
St. Vincent	x
Royal Children	x
The Prince Charles Hospital	x
The Alfred Hospital	x
Royal Perth Hospital	x
AUSTRIA[2]	
Allgemeines Krankenhaus Wien	x
Universitätsklinik Innsbruck	x
Landeskrankenhaus Graz	x

ISHLT

2008

J Heart Lung Transplant 2008;27: 937-983

Centers Reporting to the ISHLT Transplant Registry

COUNTRY/Center	TXs Performed 1/2006-6/2007 and Reported to ISHLT
GERMANY[2] (cont'd)	
Deutsches Herzzentrum München	x
Universitätsklinikum Hamburg	x
Klinikum der Albert-Ludwigs-Universität Freiburg im Breisgau	x
GREECE	
Onassis Cardiac Surgery Center	x
IRELAND[4]	
Mater Hospital	x
ISRAEL	
Rabin Medical Center (Belinson Campus)	x

Centers Reporting to the ISHLT Transplant Registry

COUNTRY/Center	TXs Performed 1/2006-6/2007 and Reported to ISHLT
UNITED STATES[5] (cont'd)	
Univ. of Kentucky Med Ctr, Lexington, KY	x
Ochsner Foundation Hospital, New Orleans, LA	x
Tulane Univ. Medical Center, New Orleans, LA	x
Children's Hospital Boston, Boston, MA	x
Massachusetts General Hospital, Boston, MA	x
Tufts Medical Center, Boston, MA	x
Brigham and Womens Hosp, Boston, MA	x
Johns Hopkins Hospital, Baltimore, MD	x
Univ. of Maryland Med System, Baltimore, MD	x
Children's Hosp of Michigan, Detroit, MI	x
Henry Ford Hospital, Detroit, MI	x
Univ. of Michigan Med Ctr, Ann Arbor, MI	x

אינדיקציות להשתלת לב

- אי ספיקת לב סופנית.
- הפרעות קצב הקשות לשליטה ומסכנות חיים.
- מחלת לב כלילית סימפטומטית, שאינה ניתנת לטיפול.

Indications for Cardiac Transplantation

Absolute Indications in Appropriate Patients For hemodynamic compromise due to HF:

- Refractory cardiogenic shock.
- Documented dependence on IV inotropic support to maintain adequate organ perfusion
- Peak VO_2 less than 10 mL per kg per min with achievement of anaerobic metabolism

Indications for Cardiac Transplantation (Cont.)

Absolute Indications in Appropriate Patients For hemodynamic compromise due to HF:

- Severe symptoms of ischemia that consistently limit routine activity and are not amenable to coronary artery bypass surgery or percutaneous coronary intervention
- Recurrent symptomatic ventricular arrhythmias refractory to all therapeutic modalities

Indications for Cardiac Transplantation (Cont.)

Relative Indications:

- Peak VO_2 11 to 14 mL per kg per min (or 55% predicted) and major limitation of the patient's daily activities
- Recurrent unstable ischemia not amenable to other intervention
- Recurrent instability of fluid balance/renal function not due to patient noncompliance with medical regimen

Indications for Cardiac Transplantation (Cont.)

Insufficient Indications:

- Low left ventricular ejection fraction
- History of functional class III or IV symptoms of HF
- Peak VO_2 greater than 15 mL per kg per min (and greater than 55% predicted) without other indications

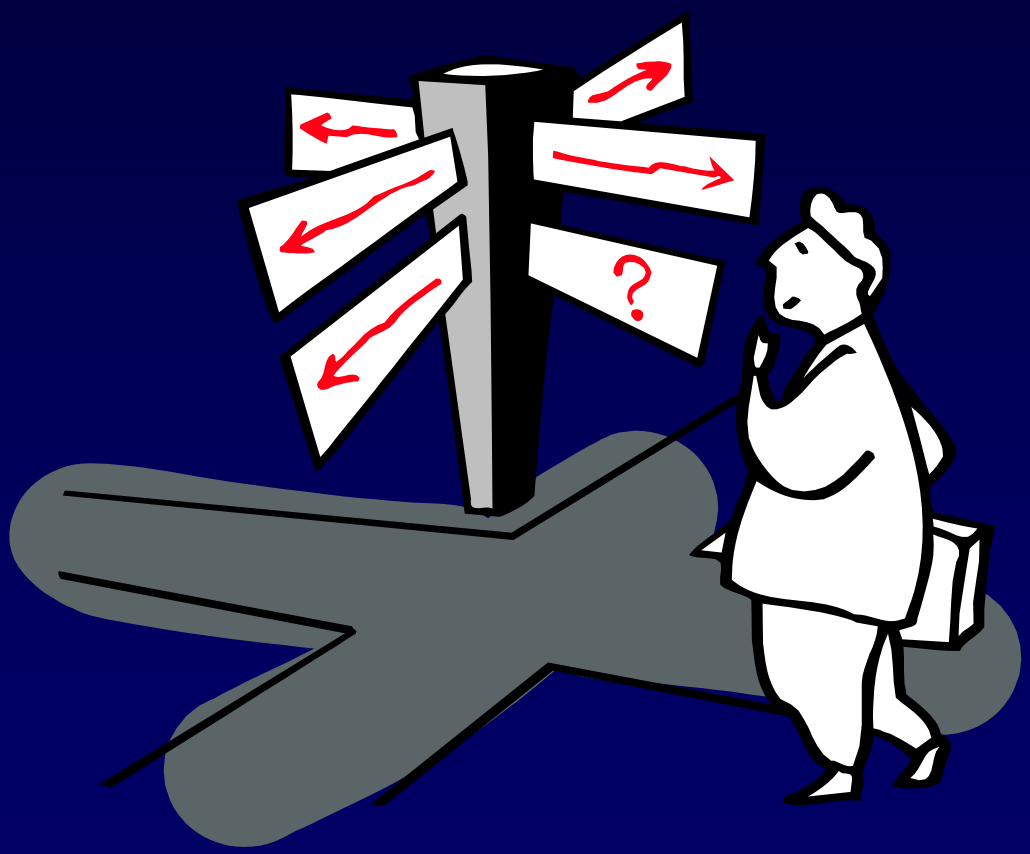
הערכת המועמד להשתלת לב

- שיפור הטיפול התרופתי למיטבי.
- הערכת ההכרח בהשתלת הלב.
- הערכת המצאות התוויות נגד להשתלת לב.

התוויות נגד להשתלת לב:

- הפרעה בלתי הפיכה בתפקודי כבד, כליה, ריאות.
- מחלת כלי דם פריפרית מתקדמת.
- לאחר אירוע מוחי.
- סוכרת עם פגיעה באיברי מטרה.
- זיהום פעיל.
- מחלה סרטנית שמצבה אינו ברור.
- מצבים אחרים עם פרוגנוזה מוגבלת.
- גיל??

ייעוצים



- Gastroenterology
- Urology
- Gynecology
- Ophthalmology
- Dentist
- Vascular Surg.
- Pulmonology

Schedule of Examinations in Candidates for Cardiac Transplantation

Test	Baseline	3 Months	6	9	12
Complete H & P	X				
Follow-up assessment	X	X	X	X	X
Weight/BMI	X	X	X	X	X
Immunocompatibility					
ABO	X				
HLA tissue typing:	Only at transplant				
PRA and flow cytometry	X				
• >10%:	Every 1–2 months				
• VAD:	Every 1–2 months				
• Transfusion:	2 weeks after transfusion and then 9 months x 6 months				

Schedule of Examinations in Candidates for Cardiac Transplantation

Test	Baseline	3 Months	6	9	12
Assessment of heart failure severity:					
CPX with RER	X				X
Echocardiogram	X				X
Rt heart catheter :					
Vasodilator s as indicated	X		X		X
ECG	X				X

Schedule of Examinations in Candidates for Cardiac Transplantation

Test	Baseline	3 Months	6	9	12
Evaluation of multiorgan function:					
Routine lab work	X	X	X	X	X
GFR (MDRD)	X	X	X	X	X
PT/INR More frequent per protocol if on VAD or warfarin					
	X	X	X	X	X
Urinalysis	X	X	X	X	X
GFR (MDRD)	X	X	X	X	X
urine for protein excretion	X	X	X	X	X

Schedule of Examinations in Candidates for Cardiac Transplantation

Test	Baseline	3 Months	6	9	12
Pulm. Func. + arterial gasses	X				
CXR (PA and lateral)	X				X
Abdominal ultrasound	X				
If indicated or >50 y					
Carotid Doppler	X				
Ankle brachial index	X				
Dual energy x-ray abs.	X				
Dental examination	X				X
Ophthalmology in diabetic	X				X

Schedule of Examinations in Candidates for Cardiac Transplantation

Test	Baseline	3 Months	6	9	12
Infectious serology					
Hep B surface Ag	X				
Hep B surface Ab	X				
Hep B core Ab	X				
Hep C Ab	X				
HIV	X				
RPR : rapid plasma reagin	X				
HSV IgG	X				
CMV IgG	X				
Toxoplasmosis IgG	X				
EBV IgG	X				
Varicella IgG	X				

Schedule of Examinations in Candidates for Cardiac Transplantation

Test	Baseline	3 Months	6	9	12
Vaccination					
PPD	X				
Flu shot (q 1 y)	X				
Pneumovax (q 5 y)	X				
Hep B immunizations:					
1_2_3	X				
Hep B surface Ab (immunity):					
	6 weeks after third immunization				

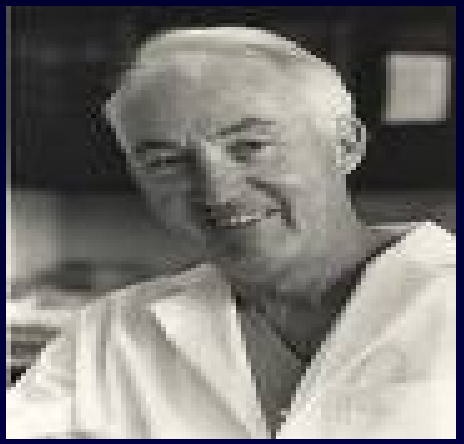
Schedule of Examinations in Candidates for Cardiac Transplantation

Test	Baseline	3 Months	6	9	12
Preventive and malignancy					
Stool for occult blood x 3	X				X
Colonoscopy					
if indicated or >50 y	X				
Mammography					
if indicated or >40 y	X				X
Gyn/Pap					
(if indicated 18 y: active	X				X
PSA and digital rectal					
exam (men >50 y)	X				X

Schedule of Examinations in Candidates for Cardiac Transplantation

Test	Baseline	3 Months	6	9	12
General consultations					
Social work	X				
Psychiatry	X				
Financial	X				
Neuro/psych (if appli)	X				

השתלות לב
ההתחלה



- ב-3 לדצמבר 1967: Christian Barnard בדרום אפריקה.
- עד סוף 1971: 170 השתלות, 65 מרכזים, 15% הישרדות לשנה!!!.
- בשנות ה- 70, השתלות בודדות בעיקר בסטנפורד ע"י *Norman Shumway*
- תחילת שנות ה- 80 נכנס לשימוש: Cyclosporine A

הישרדות לאחר השתלות לב

- לאחרונה בעולם:
  80% עד 85% הישרדות לשנה.
  60% עד 70% לחמש שנים.
  50% שורדים למעלה מ- 11 שנים.
- בארץ:
  75% עד 80% הישרדות לשנה.
  60% עד 70% לחמש שנים.
  50% שורדים למעלה מ- 11 שנים.

- מושתל הכי ותיק חי כ- 30 שנים.
- שיפור בנוגדי הדחייה, שיפור בהישרדות של סוכרתיים ומבוגרים.

Christian Barnard
מחלוצי השתלות הלב בעולם

נולד בדרא"פ שנת 1922.

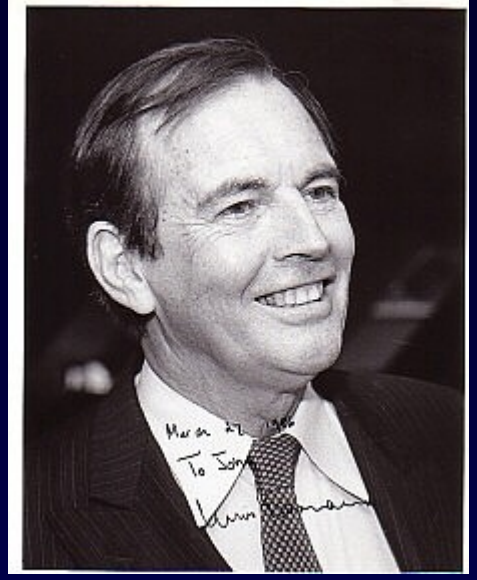
ביצע את השתלת הלב הראשונה בהיותו בן 45.

ב 1969, נפרד מאשתו הראשונה ונישא לשנייה כעבור שנה.

ב 1982, נפרד מאשתו השנייה ונישא לשלישית.

היו לו 5 ילדים משלושת נשותיו.

מת בקפריסין בשנת 2001 מהתקף לב.



Christian Barnard

זמן קצר לפני מותו בראיון לעיתון ה *Time*
אמר פרופ' ברנרד:

"The heart transplant wasn't such a big thing surgically, the point is I was prepared to take the risk.”

“The biggest risk in life is not to take the risk."

ההשתלה הראשונה:

בתחילת דצמבר נפגעה דניס דרוול (Denise Darvall), אישה צעירה בשנות ה 20 לחייה, בתאונת דרכים. היא נפטרה (מוות מוחי) זמן קצר לאחר הגיעה לבית החולים אך הלב שלה עדיין פעם. הוריה הסכימו לתרומת איבריה.

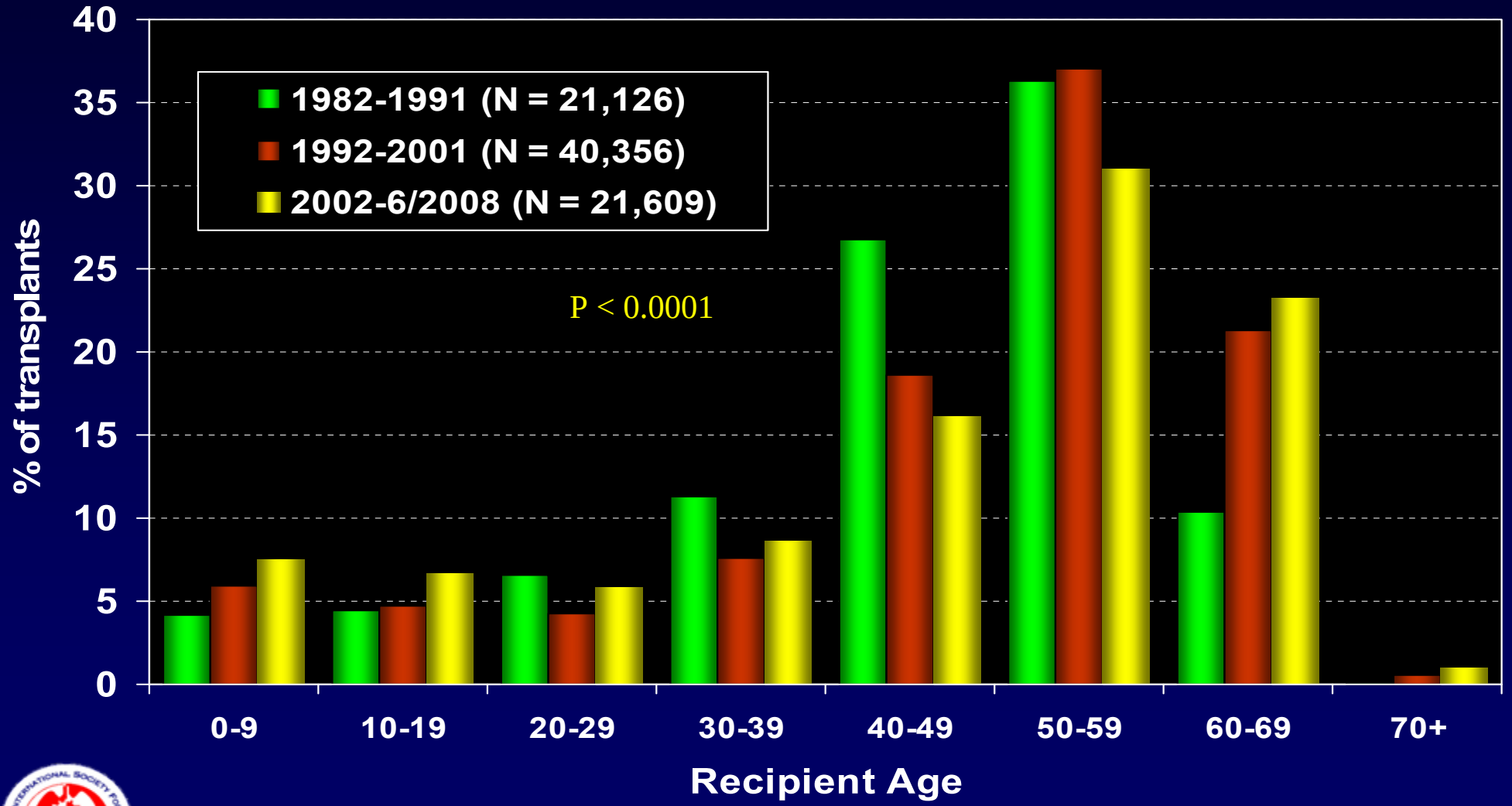
לואיס ושקנסקי (Louis Washkansky) גבר בן 54 שכב בבית החולים לאחר התקפת לב והסכים לעבור את השתלת הלב.

בניתוח שארך 5 שעות ב 3/12/2007 הוחלף ליבו החולה של ושקנסקי בליבה הבריא של דניס.

ושקנסקי שרד 18 יום ומת כתוצאה מדלקת ריאות דו צדדית.

"A heart transplant isn't worth much if he doesn't look good- let's give him a hair transplant, too."

AGE DISTRIBUTION OF HEART TRANSPLANT RECIPIENTS BY ERA

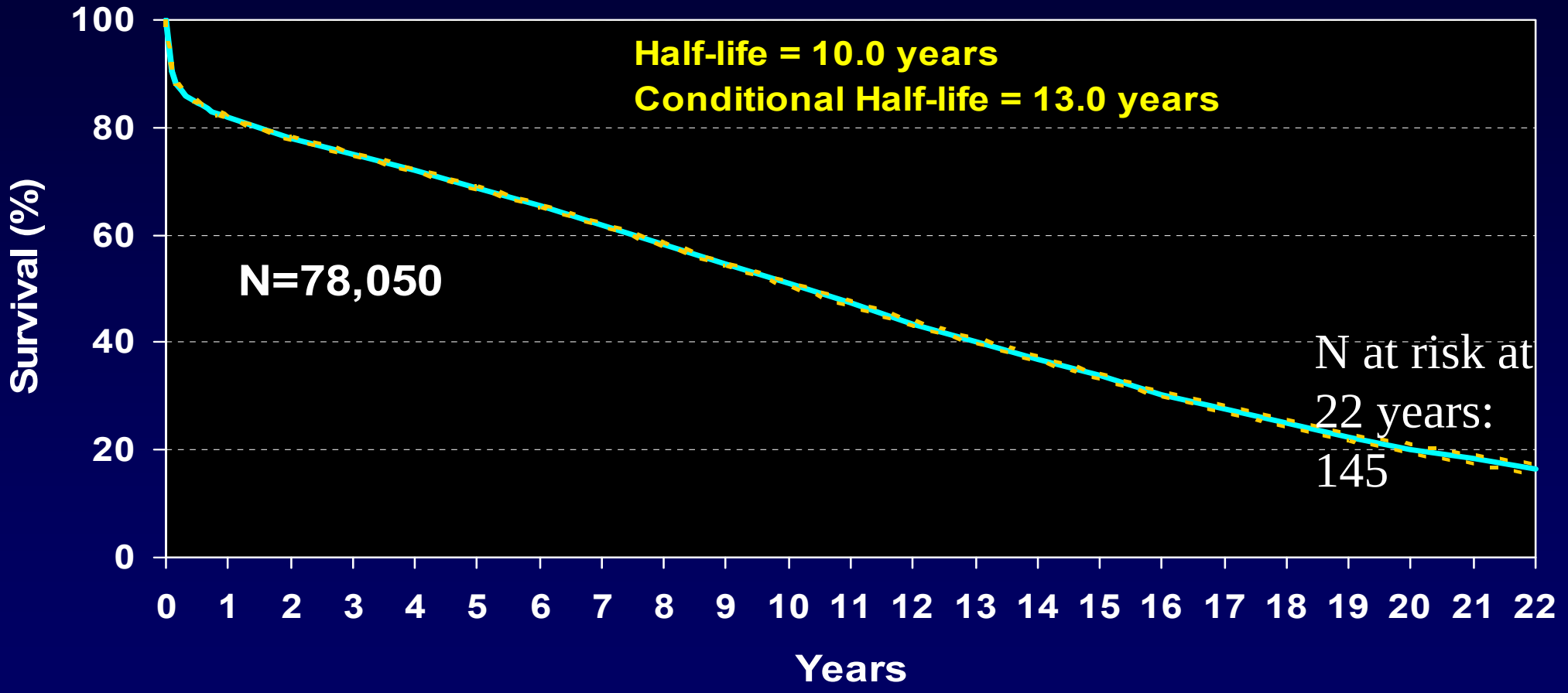


ISHLT

2009

HEART TRANSPLANTATION

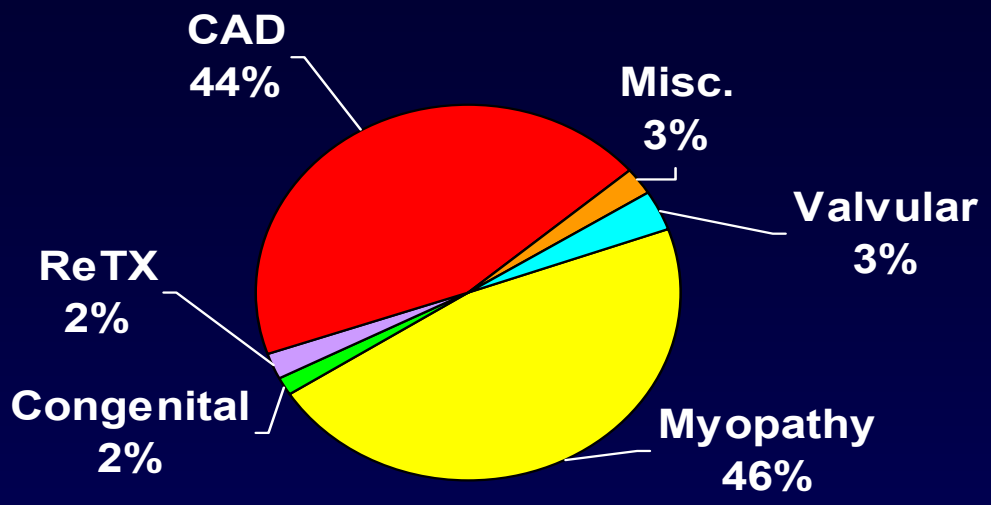
Kaplan-Meier Survival (1/1982-6/2007)



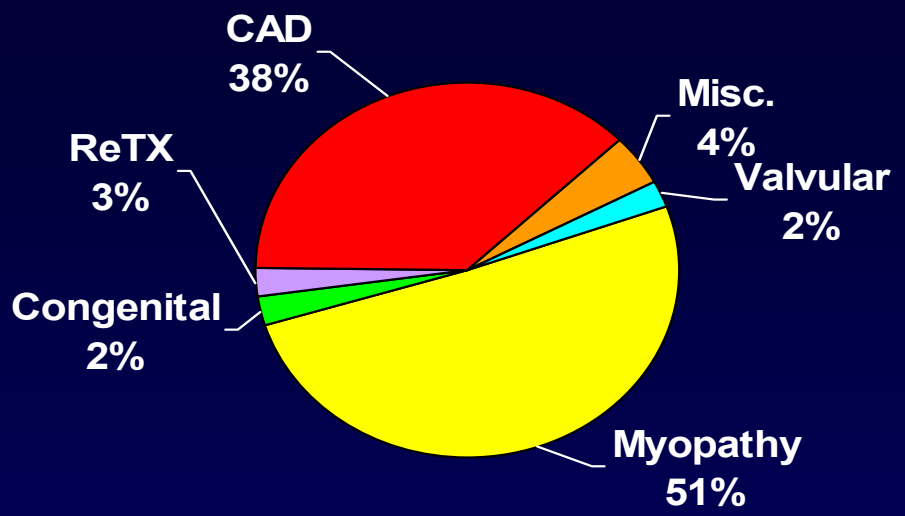
ISHLT

2009

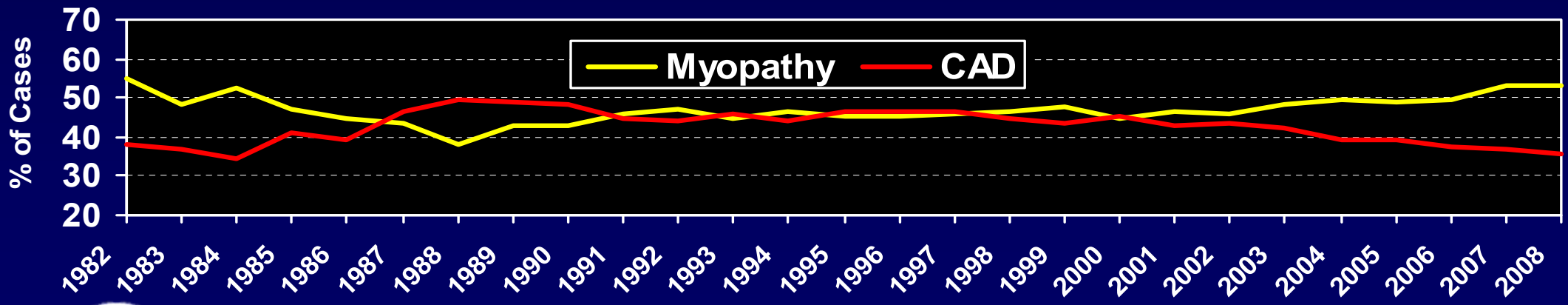
DIAGNOSIS IN ADULT HEART TRANSPLANTS



1/1982-6/2008



1/2005-6/2008



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2009

ADULT HEART TRANSPLANTATION

Characteristics of Donors, Recipients and Transplants

	1992-2001 (N=36,458)	2002-6/2008 (N=18,798)	p-value
Recipient age (years)	51.4 ± 11.0 (18.0 - 79.0)	51.1 ± 12.4 (18.0 - 78.0)	0.0776
Donor age (years)	32.3 ± 12.8 (8.0 - 67.0)	33.6 ± 13.0 (8.0 - 67.0)	<0.0001
Recipient/donor gender (% male)	80.0%/ 67.8%	77.3%/ 69.5%	<0.0001/ <0.0001
Recipient weight (kg)	76.0 ± 14.4 (35.0 - 120.0)	78.3 ± 15.5 (35.0 - 120.0)	<0.0001
Recipient height (cm)	172.7 ± 8.7 (140.0 - 190.0)	172.9 ± 8.9 (140.0 - 190.0)	0.0020
Recipient BMI	25.3 ± 4.1 (11.5 - 50.9)	26.0 ± 4.3 (12.9 - 49.2)	<0.0001
Recipient/donor diabetes mellitus	13.1%/ 1.6%	22.0%/ 2.2%	<0.0001/ <0.0001
Recipient amiodarone use (US only)	22.6%	29.0%	<0.0001
Recipient/donor cigarette history	18.5%/ 37.5%	44.9%/ 25.2%	<0.0001/ <0.0001
Ischemic time (hours)	2.5 ± 1.4 (0.0 - 8.0)	2.8 ± 1.5 (0.0 - 8.0)	<0.0001
Most recent PRA > 10%*			
Overall	7.8%	9.0%	0.0050
Class I		12.3%	
Class II		8.5%	

ISHLT

Continuous factors are expressed as mean ± standard deviation (range)

2009

* Until mid-2004 PRA was collected as a single percentage. After this date, PRA was collected separately for Class I and Class II.

ADULT HEART TRANSPLANTATION
Characteristics of Donors, Recipients and Transplants

	1992-2001 (N=36,458)	2002-6/2008 (N=18,798)	p-value
Creatinine at time of transplant	1.3 ± 0.5 (0.1 - 4.0)	1.3 ± 0.5 (0.1 - 4.0)	0.8009
Pulmonary vascular resistance (Wood units)	2.8 ± 1.5 (1.0 - 11.7)	2.6 ± 1.4 (1.0 - 12.0)	<0.0001
HLA Mismatches			0.0065
0-2	4.8%	4.3%	
3-4	41.5%	40.5%	
5-6	53.7%	55.2%	
Diagnosis			<0.0001
Coronary artery disease	45.2%	39.5%	
Cardiomyopathy	45.9%	49.5%	
Valvular	3.2%	2.4%	
Retransplant	1.9%	2.3%	
Congenital	1.8%	2.4%	
Other causes	1.9%	3.8%	

Data are expressed as mean ± standard deviation (range)

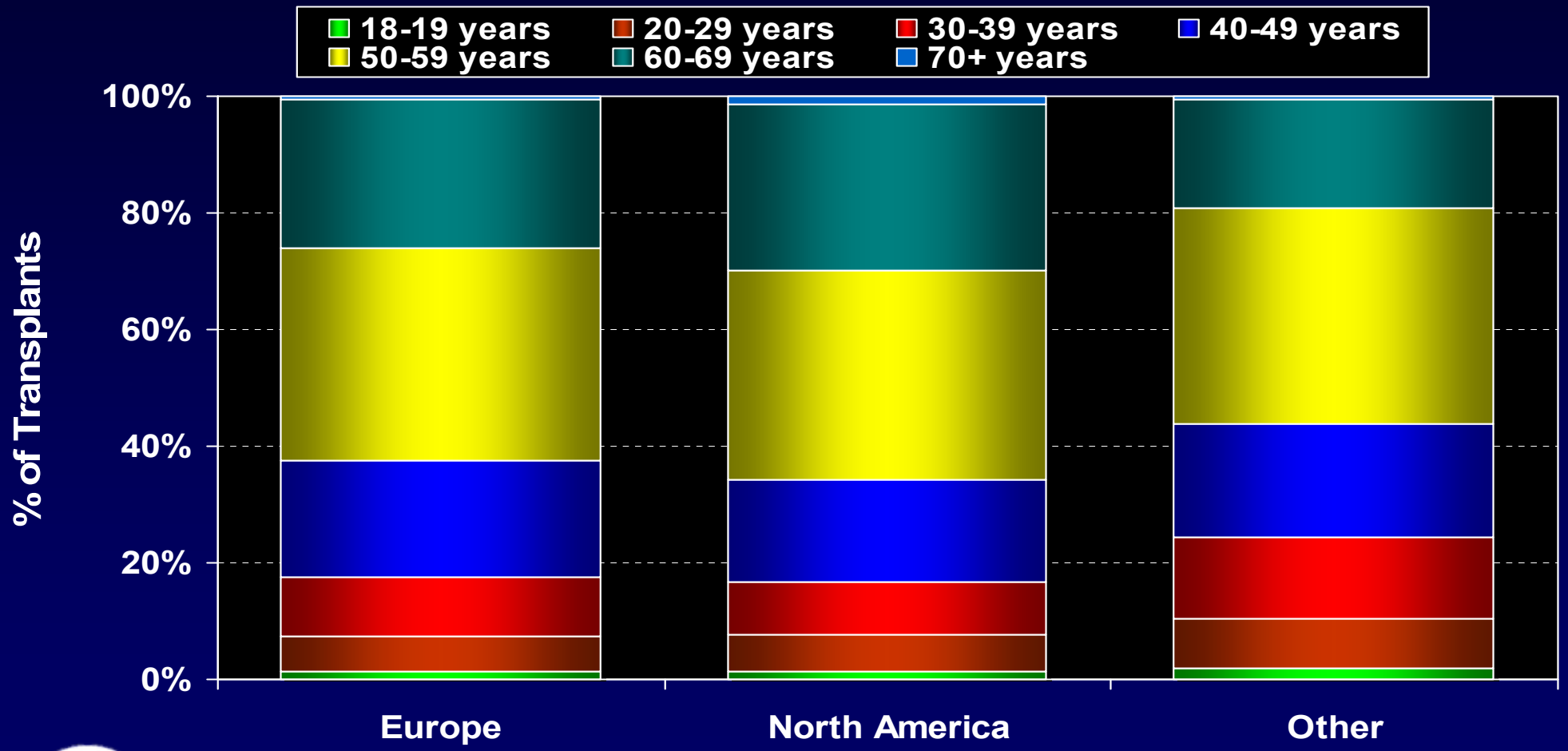
ADULT HEART TRANSPLANTATION

Characteristics of Donors, Recipients and Transplants

	1992-2001 (N=36,458)	2002-6/2008 (N=18,798)	p-value
Donor cause of death			<0.0001
Head trauma	45.2%	52.1%	
Stroke	28.4%	29.6%	
Other	26.5%	18.3%	
Pre-operative support (multiple items may be reported)			
Hospitalized at time of transplant	58.6%	46.4%	<0.0001
On IV inotropes	48.9%	44.8%	<0.0001
LVAD	4.1%	19.0%	<0.0001
IABP	6.8%	6.9%	0.6740
RVAD	0.1%	2.9%	<0.0001
Ventilator	3.1%	2.9%	0.1738
TAH	0.4%	0.4%	0.6900
ECMO	0.3%	0.7%	<0.0001

ADULT HEART TRANSPLANTS:
RECIPIENT AGE DISTRIBUTION BY LOCATION

Transplants between January 2000 and June 2008

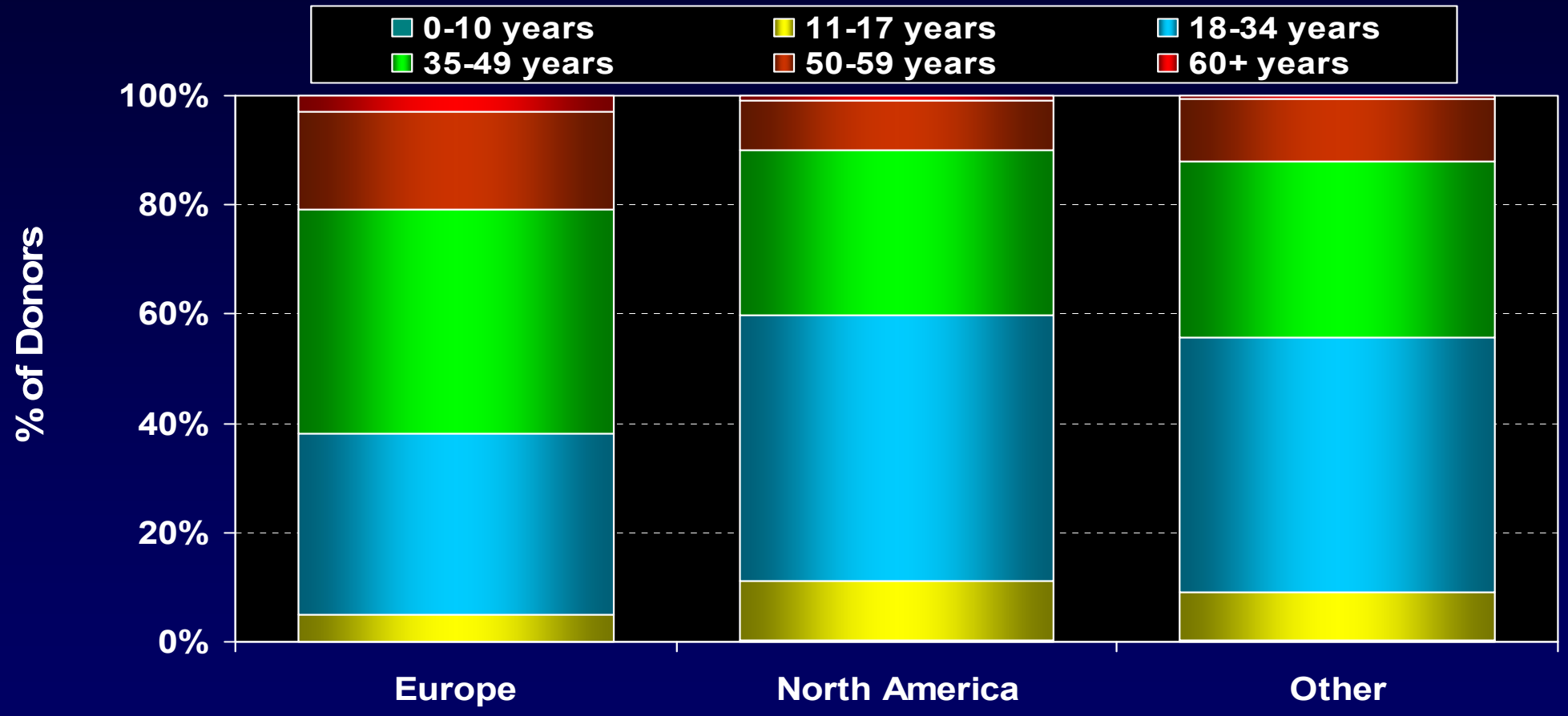


ISHLT

2009

Mean/median recipient age:
Europe = 50.8/53.0
North America = 51.7/54.0
Other = 48.4/51.0

ADULT HEART TRANSPLANTS:
DONOR AGE DISTRIBUTION BY LOCATION
Transplants between January 2000 and June 2008



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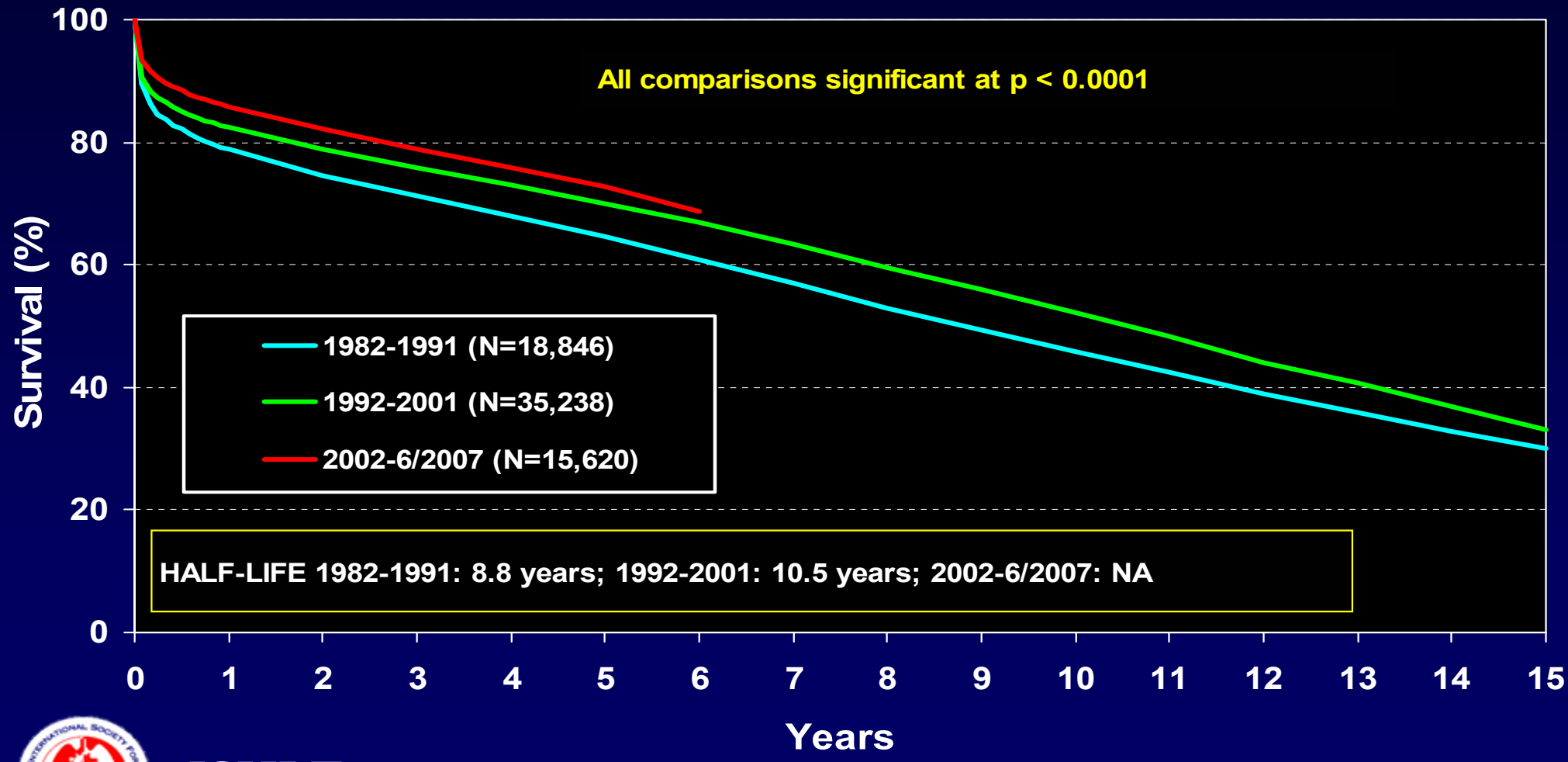
Mean/median donor age:
Europe = 38.0/39.0
North America = 31.6/29.0
Other = 33.0/32.0

ADULT HEART TRANSPLANTATION

Kaplan-Meier Survival by Era (Transplants: 1/1982 – 6/2007)



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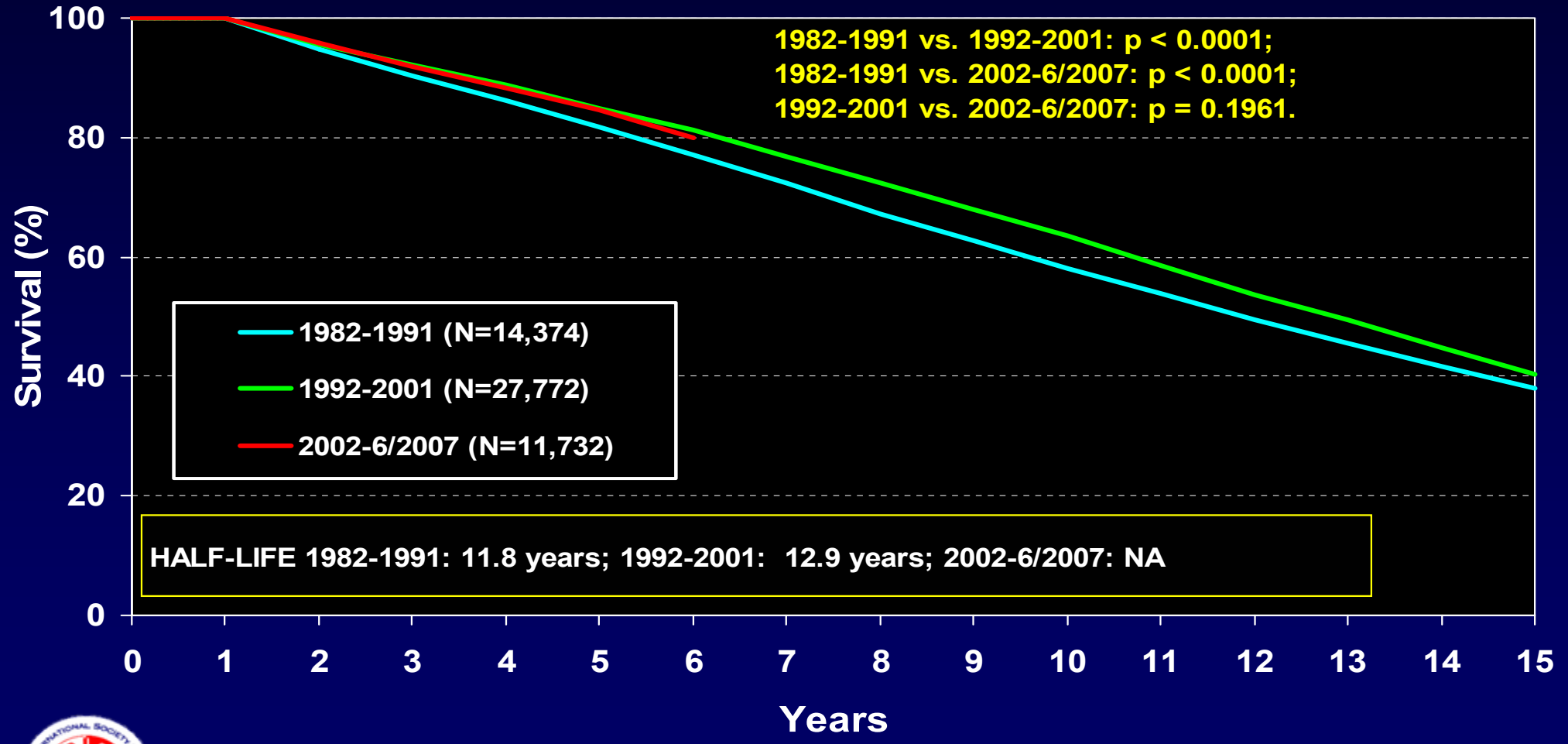
ADULT HEART TRANSPLANTATION

Conditional Kaplan-Meier Survival by Era

(Transplants: 1/1982 – 6/2007)



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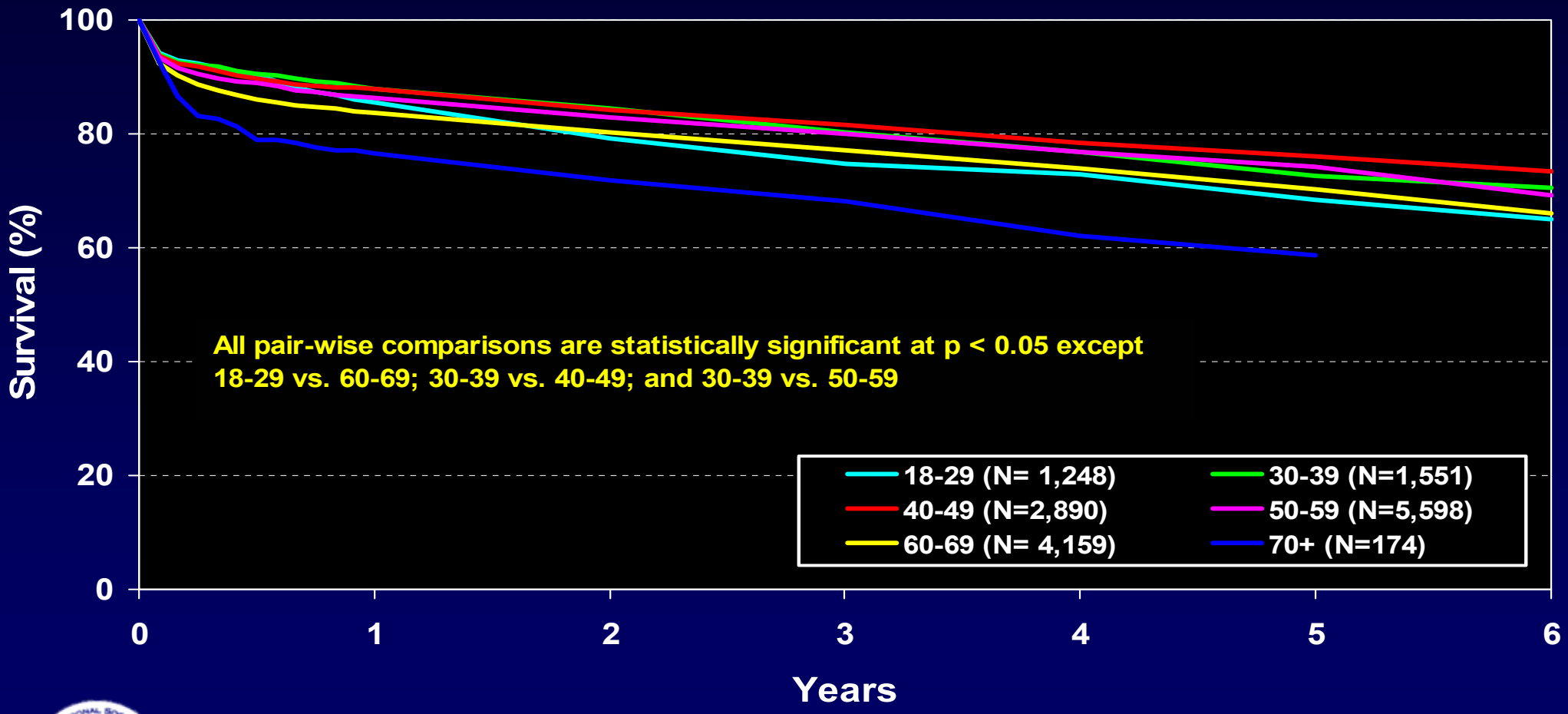
ADULT HEART TRANSPLANTATION

Kaplan-Meier Survival by Age Group (Transplants: 1/2002-6/2007)



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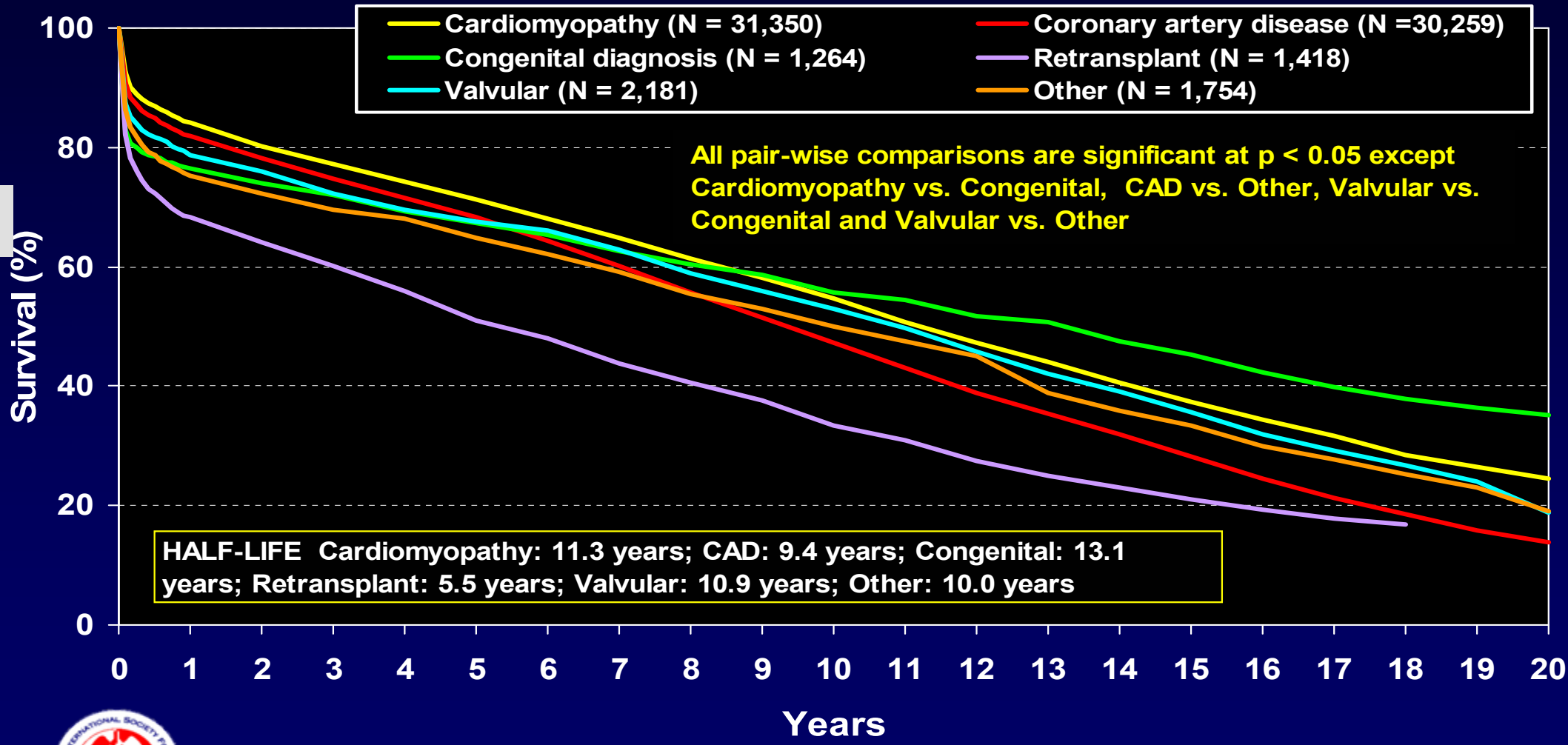
ADULT HEART TRANSPLANTATION

Kaplan-Meier Survival by Diagnosis (Transplants: 1/1982-6/2007)



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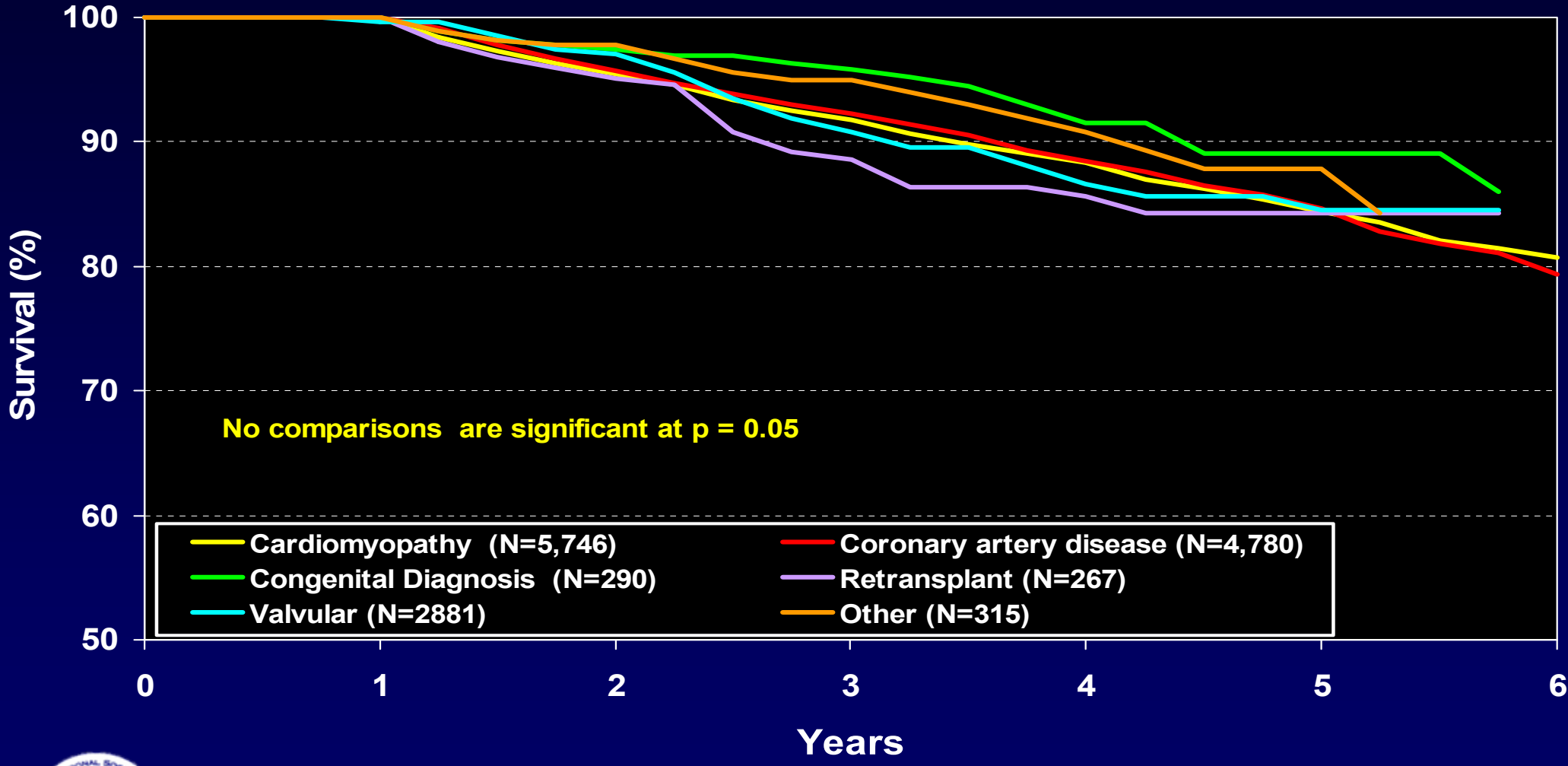
ADULT HEART TRANSPLANTATION

Kaplan-Meier Survival by Diagnosis Conditional on Survival to 1 Year (Transplants: 1/2002-6/2007)



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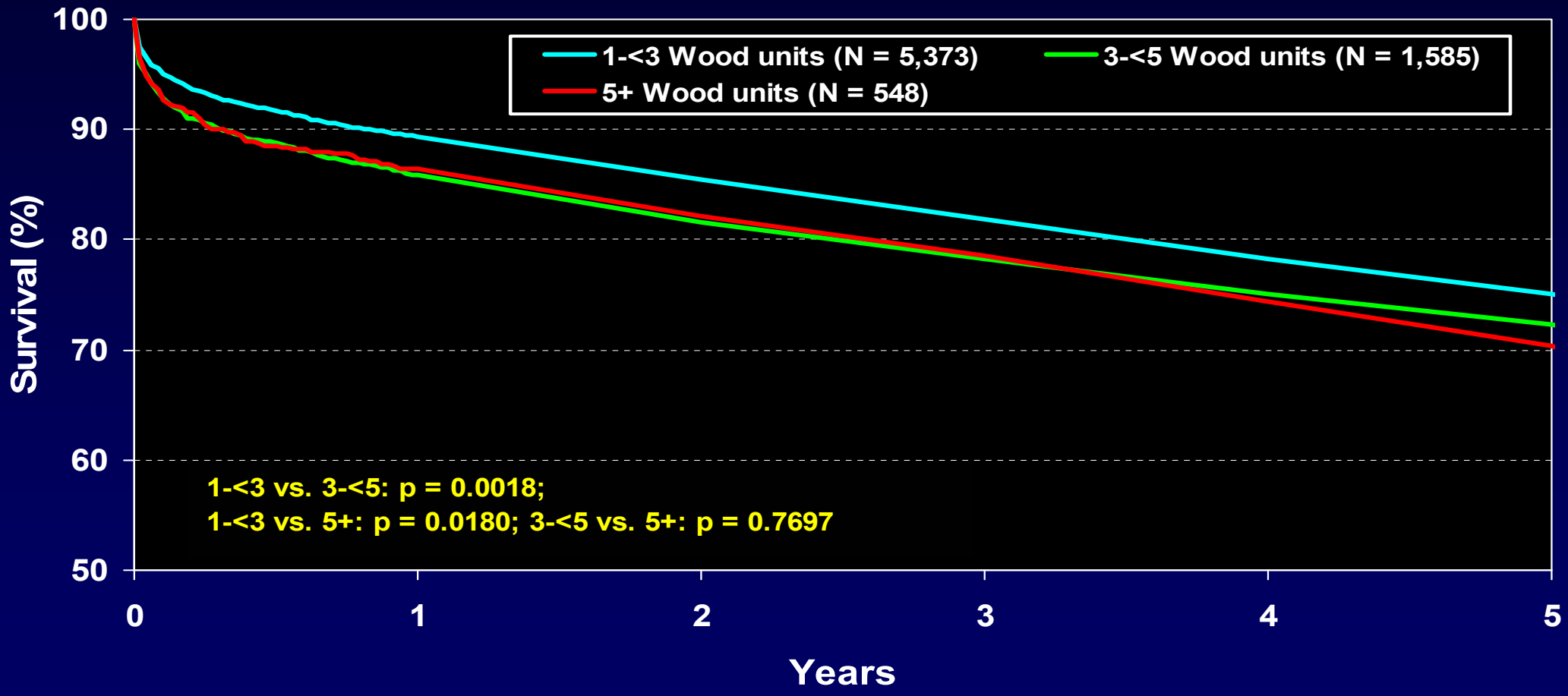
ADULT HEART TRANSPLANTATION

Kaplan-Meier Survival by PVR (Transplants: 1/2002-6/2007)



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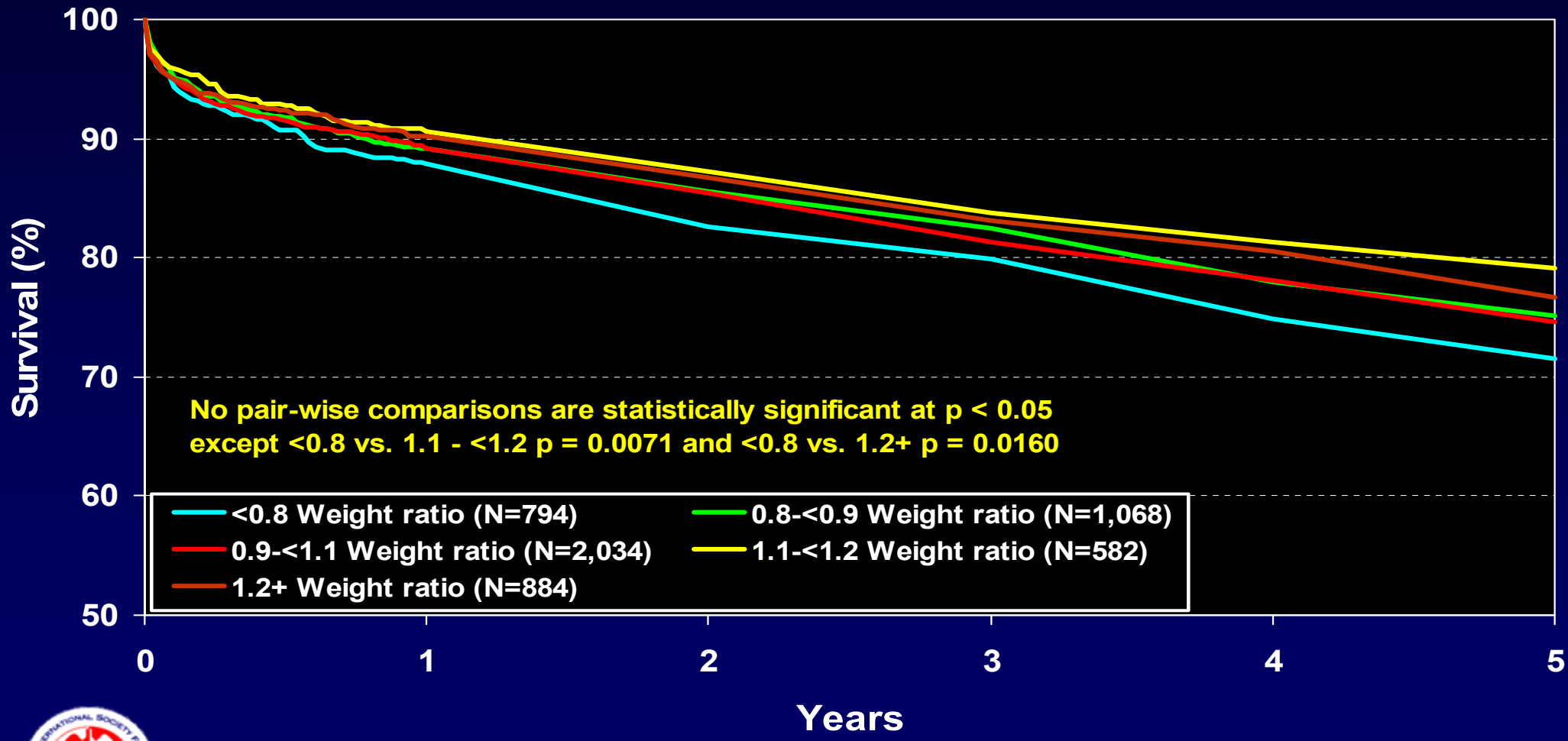
ADULT HEART TRANSPLANTATION

Kaplan-Meier Survival by PVR (Transplants: 1/2002-6/2007)

PVR: 1- < 3 Wood units



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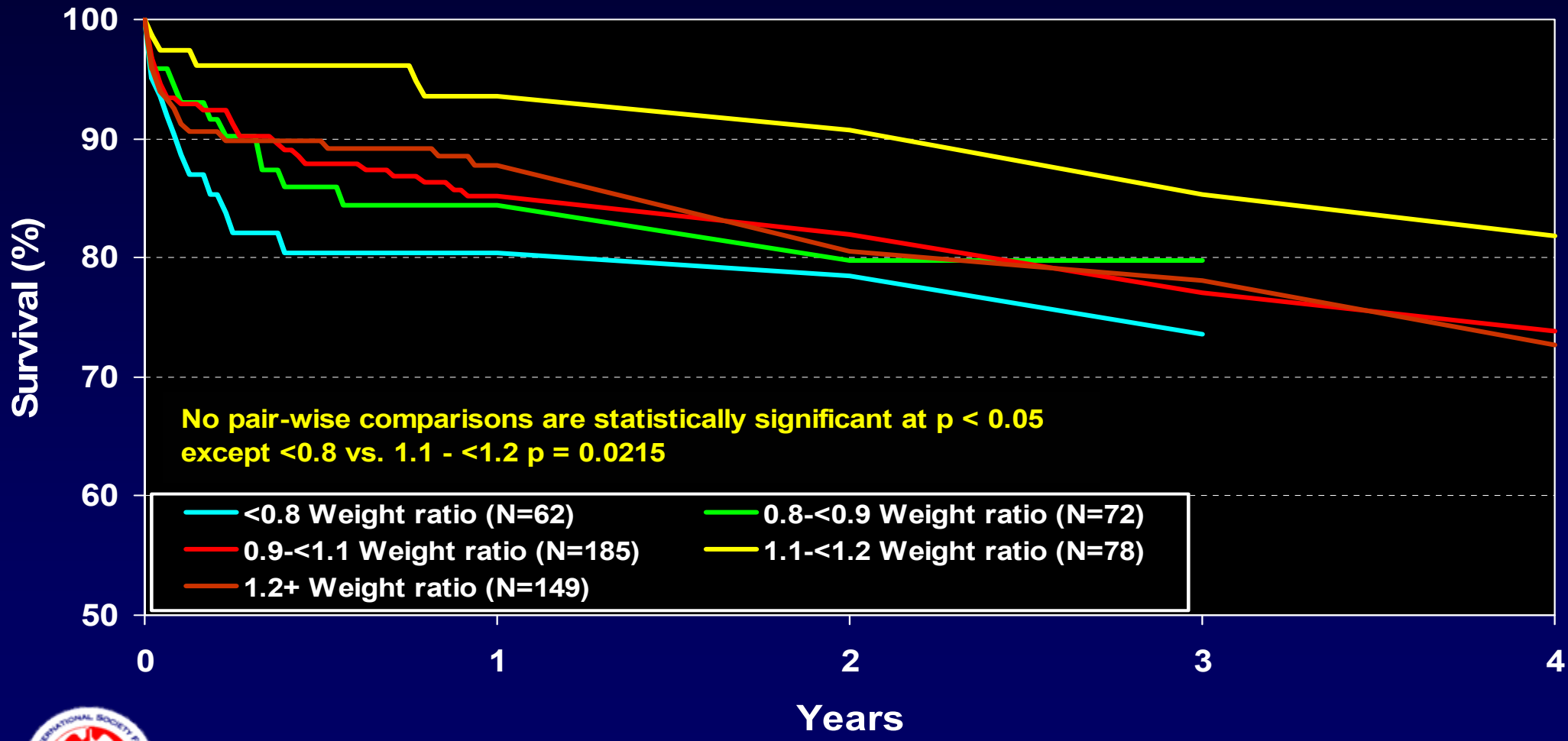
ADULT HEART TRANSPLANTATION

Kaplan-Meier Survival by PVR (Transplants: 1/2002-6/2007)

PVR: 5+ Wood units



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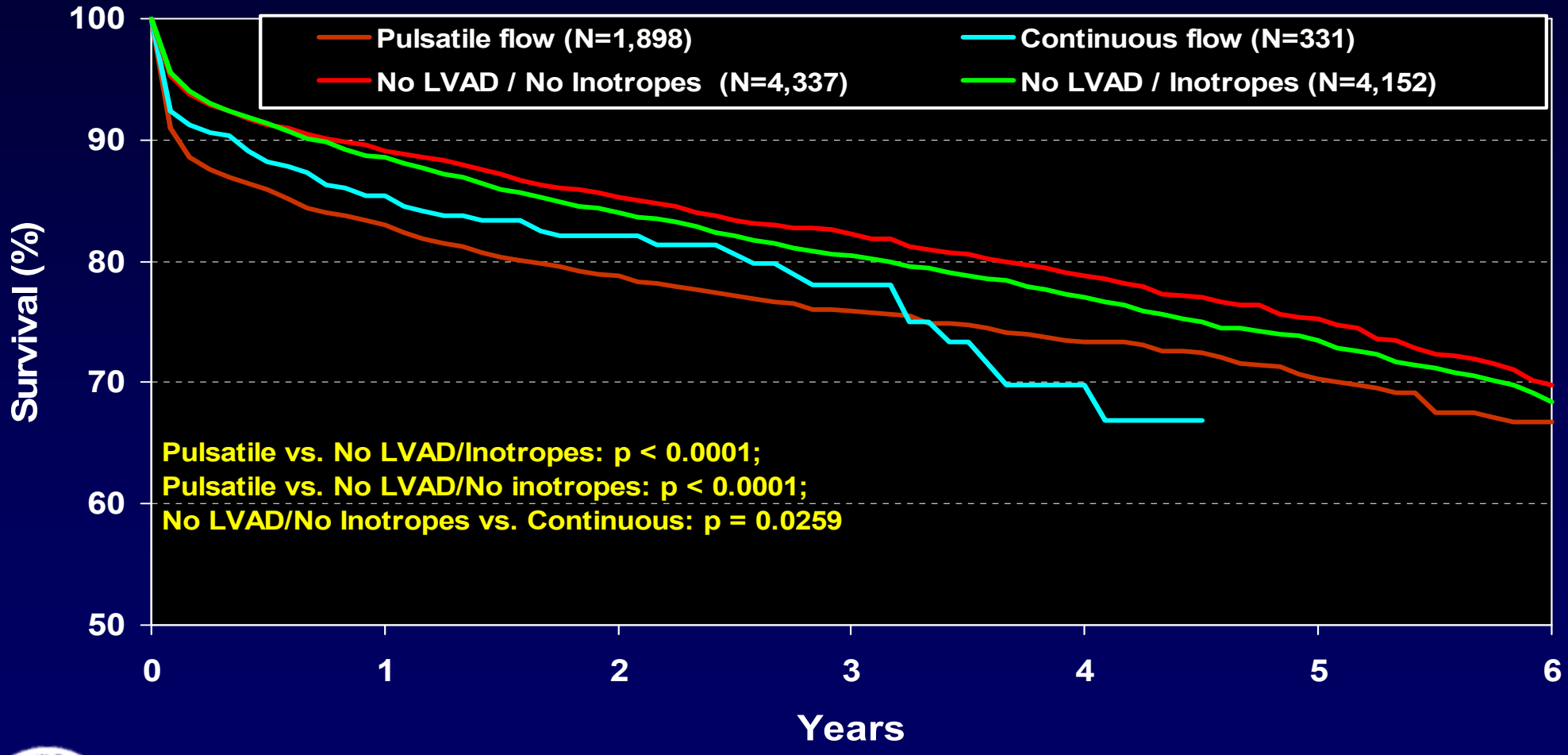
ADULT HEART TRANSPLANTATION

Kaplan-Meier Survival by VAD usage (Transplants: 1/2002-6/2007)



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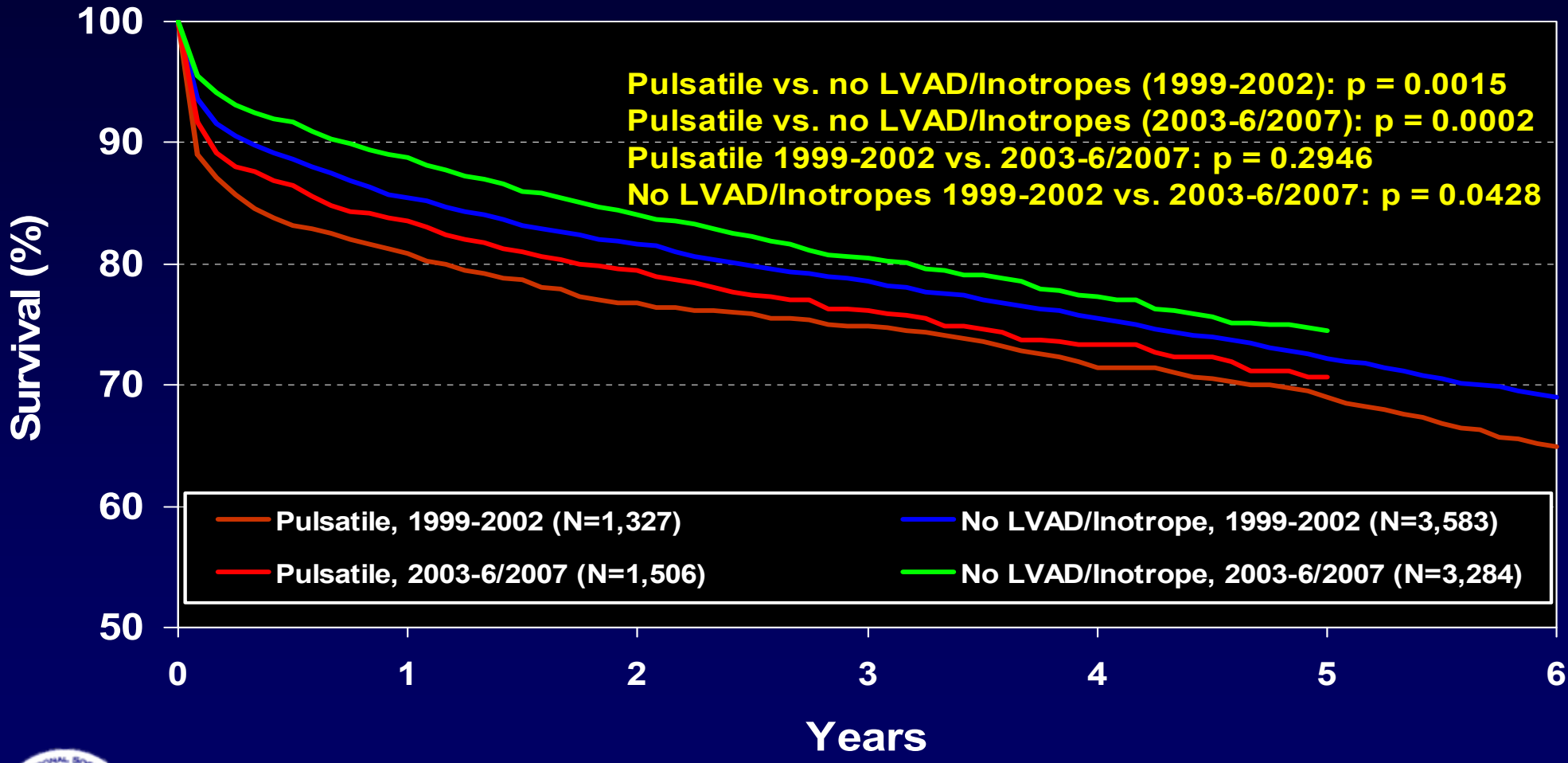
ADULT HEART TRANSPLANTATION

Kaplan-Meier Survival by VAD usage and Era (Transplants: 1/1999-6/2007)



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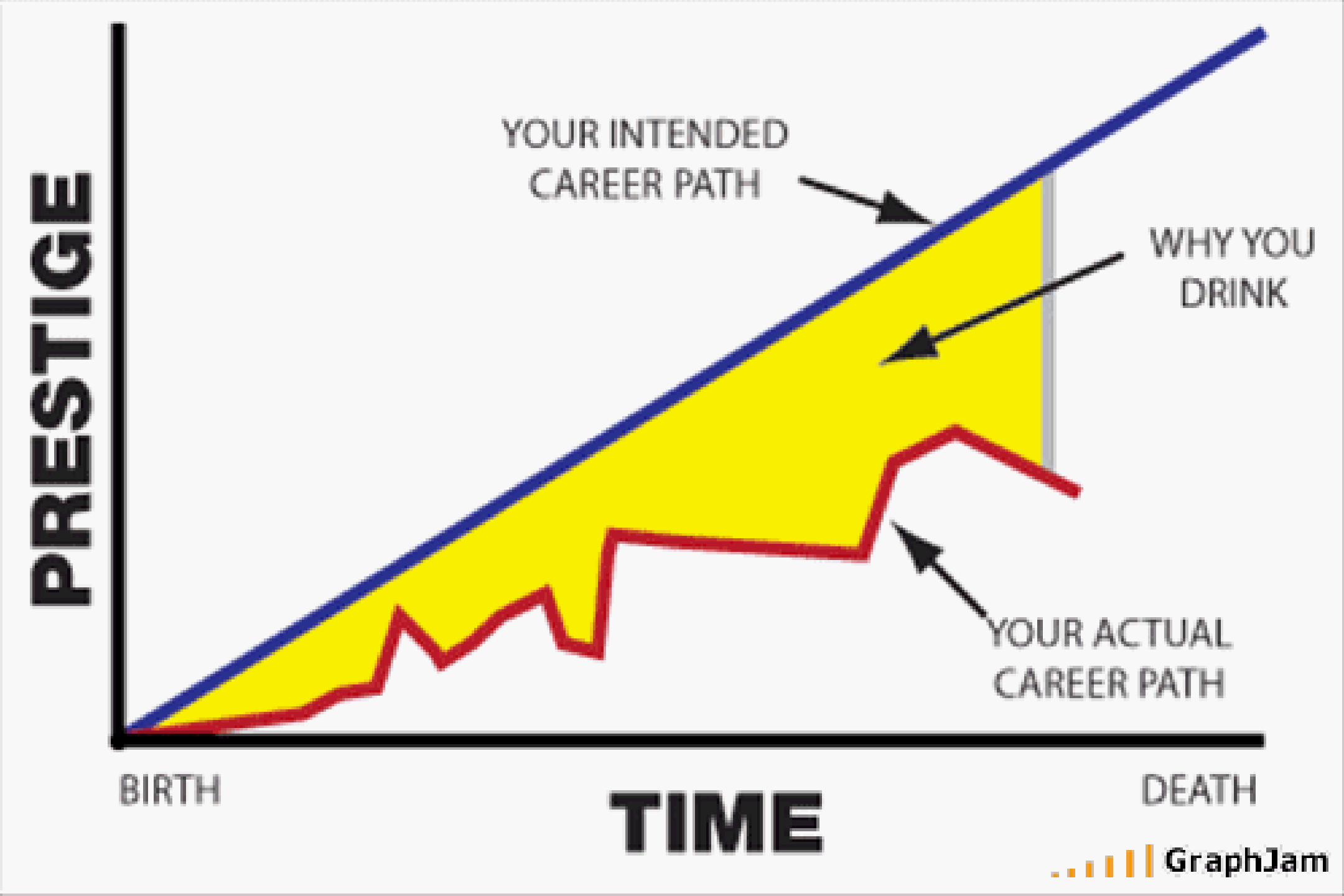
ADULT HEART TRANSPLANT RECIPIENTS:
Cause of Death (Deaths: January 1992 - June 2008)

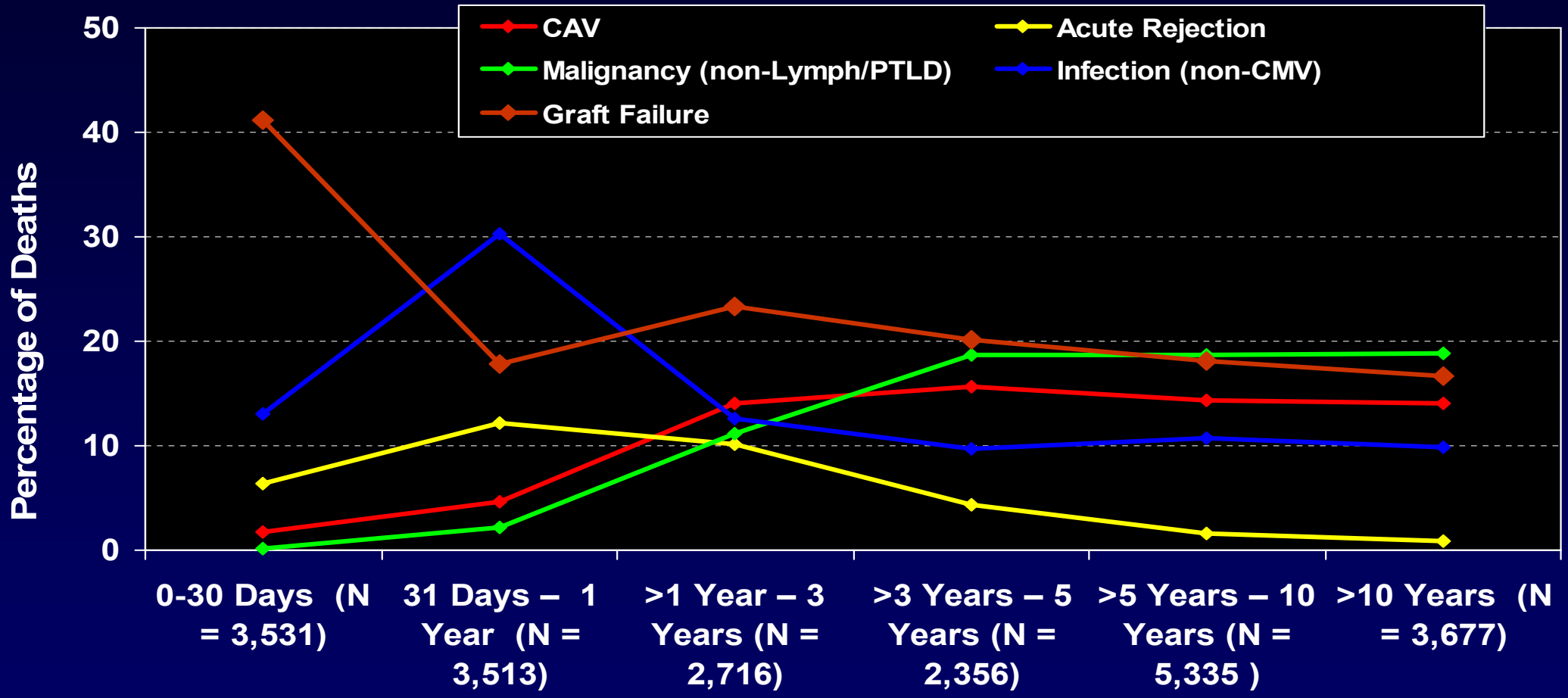
CAUSE OF DEATH	0-30 Days (N = 3,531)	31 Days – 1 Year (N = 3,513)	>1 Year – 3 Years (N = 2,716)	>3 Years – 5 Years (N = 2,356)	>5 Years – 10 Years (N = 5,335)	>10 Years (N = 3,677)
CARDIAC ALLOGRAFT VASCULOPATHY	62 (1.8%)	163 (4.6%)	383 (14.1%)	369 (15.7%)	767 (14.4%)	520 (14.1%)
ACUTE REJECTION	227 (6.4%)	427 (12.2%)	274 (10.1%)	104 (4.4%)	88 (1.6%)	33 (0.9%)
LYMPHOMA	1 (0.0%)	66 (1.9%)	93 (3.4%)	103 (4.4%)	246 (4.6%)	145 (3.9%)
MALIGNANCY, OTHER	4 (0.1%)	78 (2.2%)	301 (11.1%)	440 (18.7%)	999 (18.7%)	690 (18.8%)
CMV	4 (0.1%)	43 (1.2%)	17 (0.6%)	4 (0.2%)	6 (0.1%)	1 (0.0%)
INFECTION, NON-CMV	458 (13.0%)	1,066 (30.3%)	343 (12.6%)	229 (9.7%)	570 (10.7%)	361 (9.8%)
GRAFT FAILURE	1,452 (41.1%)	626 (17.8%)	636 (23.4%)	473 (20.1%)	965 (18.1%)	609 (16.6%)
TECHNICAL	253 (7.2%)	38 (1.1%)	19 (0.7%)	17 (0.7%)	41 (0.8%)	33 (0.9%)
OTHER	209 (5.9%)	303 (8.6%)	272 (10.0%)	220 (9.3%)	531 (10.0%)	364 (9.9%)
MULTIPLE ORGAN FAILURE	451 (12.8%)	386 (11.0%)	135 (5.0%)	122 (5.2%)	369 (6.9%)	293 (8.0%)
RENAL FAILURE	23 (0.7%)	34 (1.0%)	43 (1.6%)	86 (3.7%)	309 (5.8%)	308 (8.4%)
PULMONARY	150 (4.2%)	137 (3.9%)	105 (3.9%)	112 (4.8%)	218 (4.1%)	165 (4.5%)
CEREBROVASCULAR	237 (6.7%)	146 (4.2%)	95 (3.5%)	77 (3.3%)	226 (4.2%)	155 (4.2%)

ADULT HEART TRANSPLANT RECIPIENTS:
Cause of Death from Leading Causes by Era
(Deaths: January 1992 - June 2008)

CAUSE OF DEATH	DATE OF DEATH	0-30 Days (N = 3,531)	31 Days – 1 Year (N = 3,513)	>1 Year – 3 Years (N = 2,716)	>3 Years – 5 Years (N = 2,356)	>5 Years – 10 Years (N = 5,335)	>10 Years (N = 3,677)
ACUTE REJECTION	1992-1997	135 (7.4%)	267 (14.6%)	123 (8.9%)	42 (4.0%)	21 (1.3%)	3 (1.5%)
	1998-6/2008	92 (5.4%)	160 (9.5%)	151 (11.3%)	62 (4.7%)	67 (1.8%)	30 (0.9%)
CARDIAC ALLOGRAFT VASCULOPATHY	1992-1997	39 (2.1%)	100 (5.5%)	224 (16.3%)	222 (21.3%)	314 (19.2%)	47 (24.2%)
	1998-6/2008	23 (1.3%)	63 (3.7%)	159 (11.9%)	147 (11.2%)	453 (12.2%)	473 (13.6%)
GRAFT FAILURE	1992-1997	798 (44.0%)	383 (21.0%)	326 (23.7%)	186 (17.8%)	299 (18.3%)	33 (17.0%)
	1998-6/2008	654 (38.1%)	243 (14.4%)	310 (23.2%)	287 (21.9%)	666 (18.0%)	576 (16.5%)
MALIGNANCY, OTHER	1992-1997	4 (0.2%)	49 (2.7%)	158 (11.5%)	202 (19.3%)	303 (18.5%)	26 (13.4%)
	1998-6/2008	0 (0.0%)	29 (1.7%)	143 (10.7%)	238 (18.1%)	696 (18.8%)	664 (19.1%)


PRESTIGE
YOUR INTENDED CAREER PATH
WHY YOU DRINK
YOUR ACTUAL CAREER PATH
BIRTH
TIME
DEATH
GraphJam

ADULT HEART TRANSPLANT RECIPIENTS:
Relative Incidence of Leading Causes of Death
(Deaths: January 1992 - June 2008)



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ADULT HEART TRANSPLANTS (1/2002-6/2007)

Risk Factors for 1 Year Mortality

VARIABLE	N	Relative Risk	P-value	95% Confidence Interval
Temporary circulatory support*	164	3.05	<0.0001	2.27 -4.09
Diagnosis: Congenital vs. cardiomyopathy	267	2.30	<0.0001	1.72 -3.10
VAD (type not collected)	49	2.25	0.0057	1.27 -4.01
Recipient on ventilator at time of transplant	293	1.59	0.0005	1.23 -2.07
Recipient history of dialysis	324	1.58	0.0001	1.26 -1.99
Female recipient	2460	1.31	0.0002	1.14 -1.50
Chronic pulsatile device	1701	1.25	0.0087	1.06 -1.49
Recipient with infection requiring IV drug therapy within 2 weeks prior to transplant	1116	1.25	0.0075	1.06 -1.47
Not ABO identical	1570	1.21	0.0088	1.05 -1.40
Prior transfusion	2093	1.20	0.0177	1.03 -1.40
Diagnosis: coronary artery disease vs. cardiomyopathy	4701	1.17	0.0221	1.02 -1.33

* Temporary circulatory support includes ECMO and Abiomed.

NOTE: There were too few continuous flow devices to analyze.

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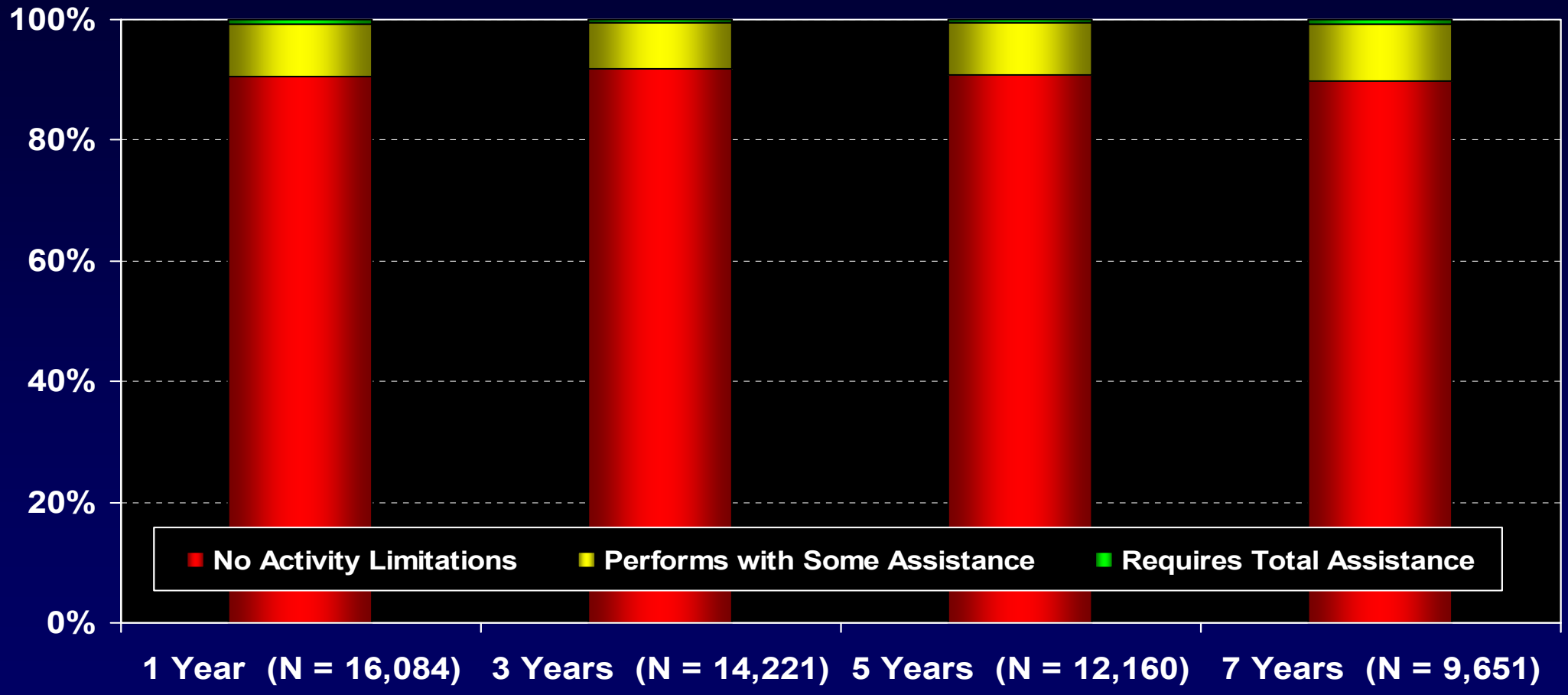
(N=10,705)

ADULT HEART RECIPIENTS

Functional Status of Surviving Recipients

(Follow-ups: 1995 - June 2008)



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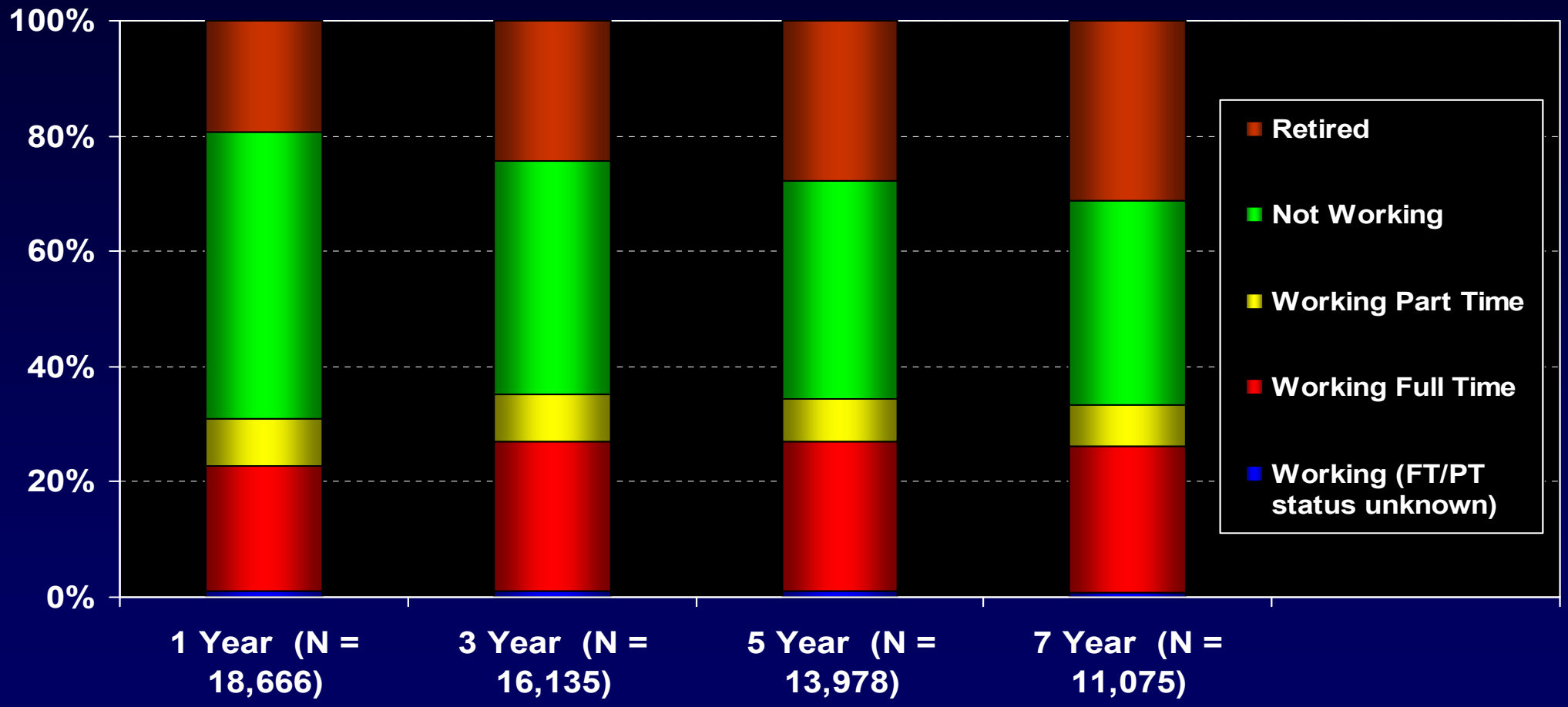
ADULT HEART RECIPIENTS

Employment Status of Surviving Recipients

(Follow-ups: 1995 - June 2008)



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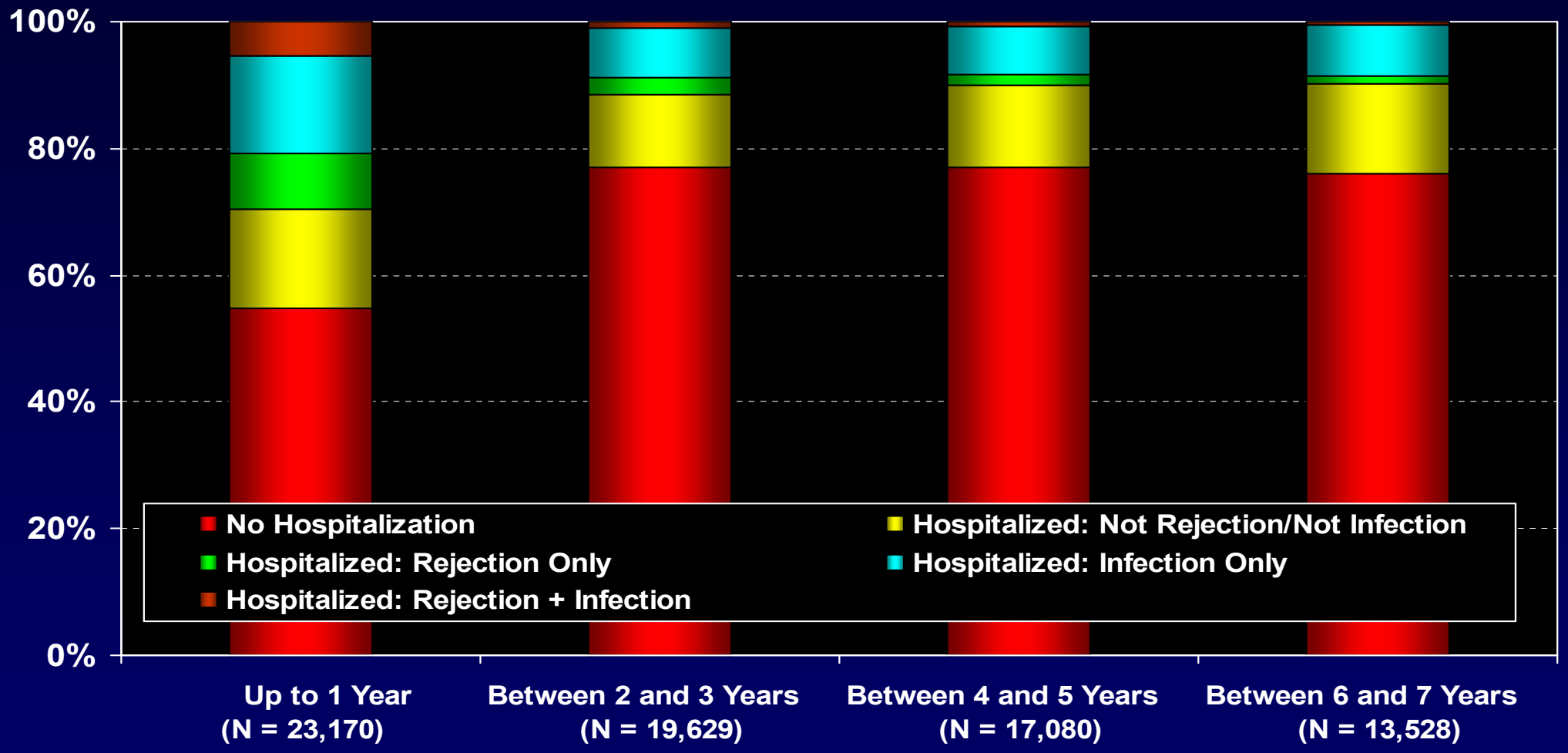
ADULT HEART RECIPIENTS

Rehospitalization Post-transplant of Surviving Recipients (Follow-ups: 1995 - June 2008)



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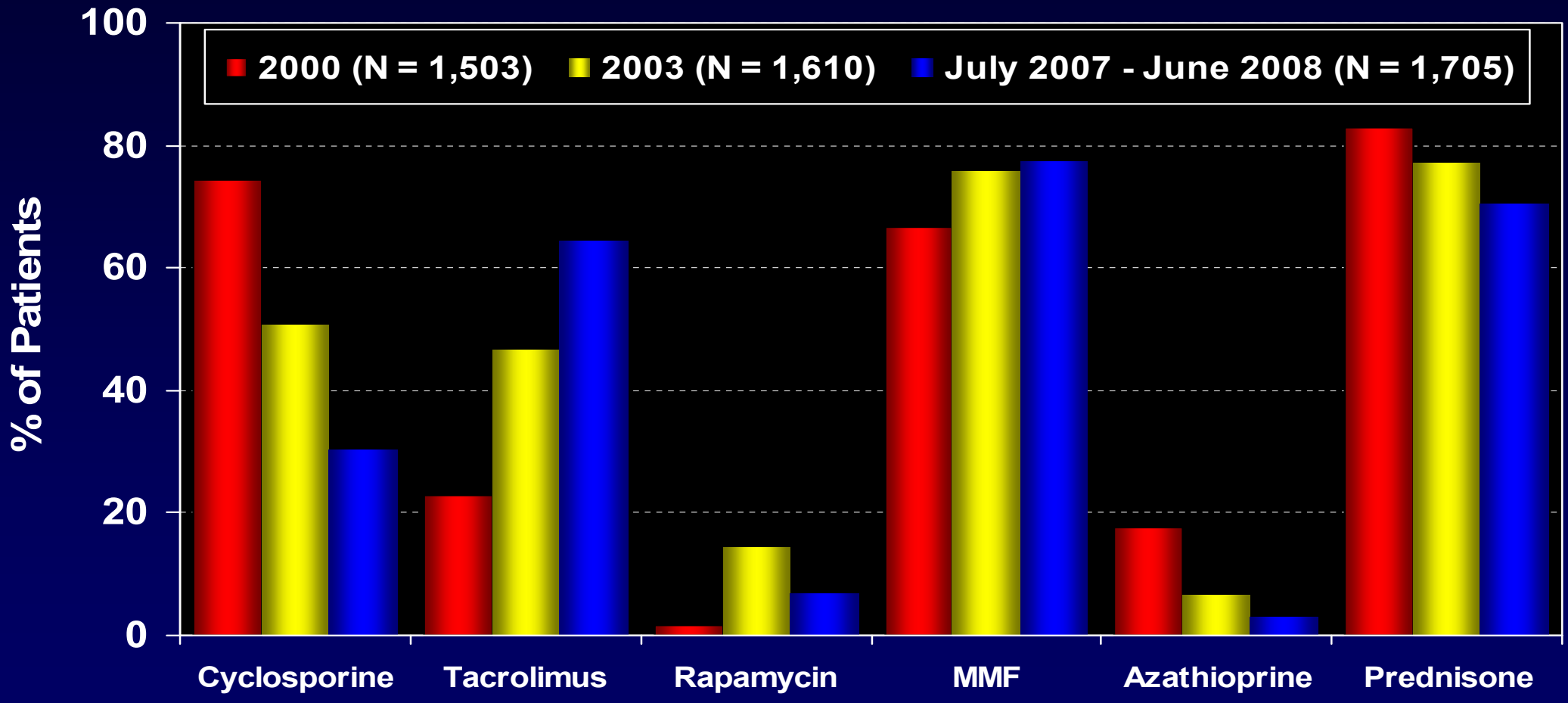
ADULT HEART RECIPIENTS

Maintenance Immunosuppression at Time of 1 Year Follow-up



NOTE: Different patients are analyzed in each time frame.

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

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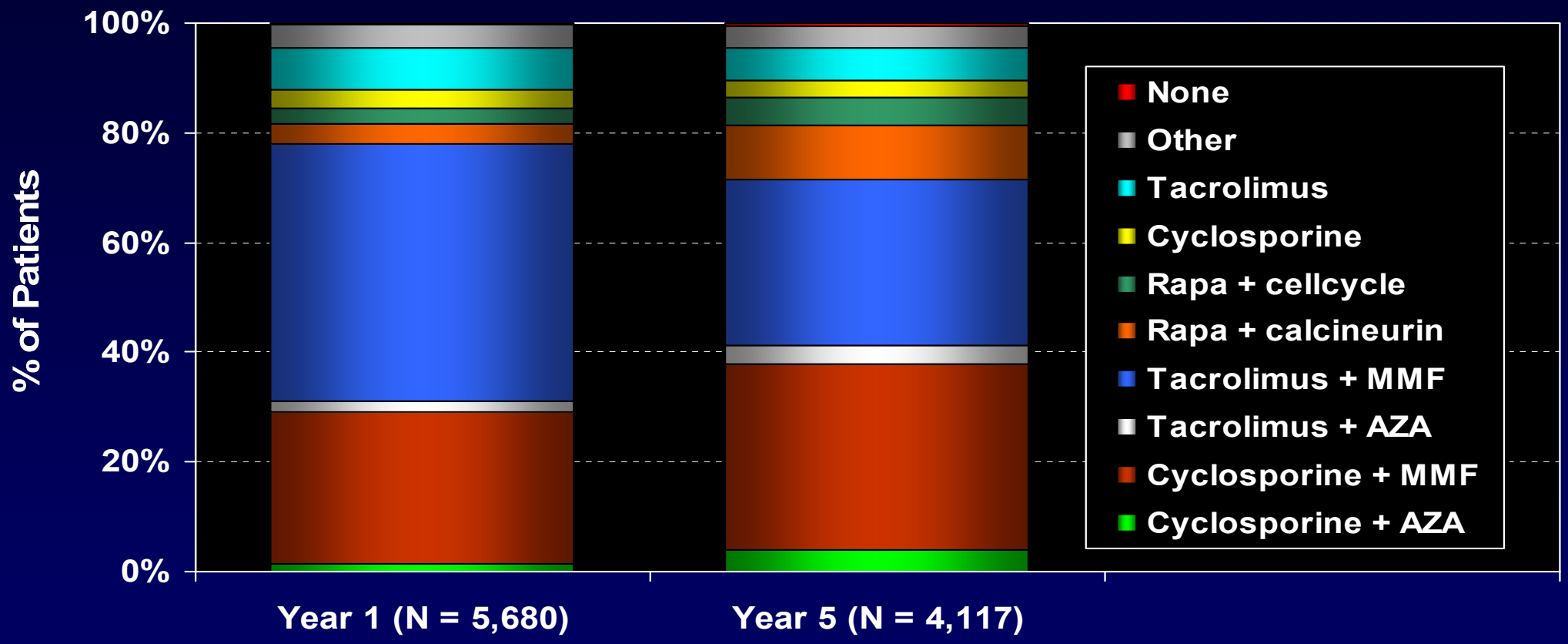
ADULT HEART RECIPIENTS

Maintenance Immunosuppression Drug Combinations at Time of Follow-up (Follow-ups: January 2005 - June 2008)



NOTES: Different patients are analyzed in Year 1 and Year 5. In the Year 1 cohort 72.55% of patients were on prednisone; in the Year 5 cohort 52.13% of patients were on prednisone.

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

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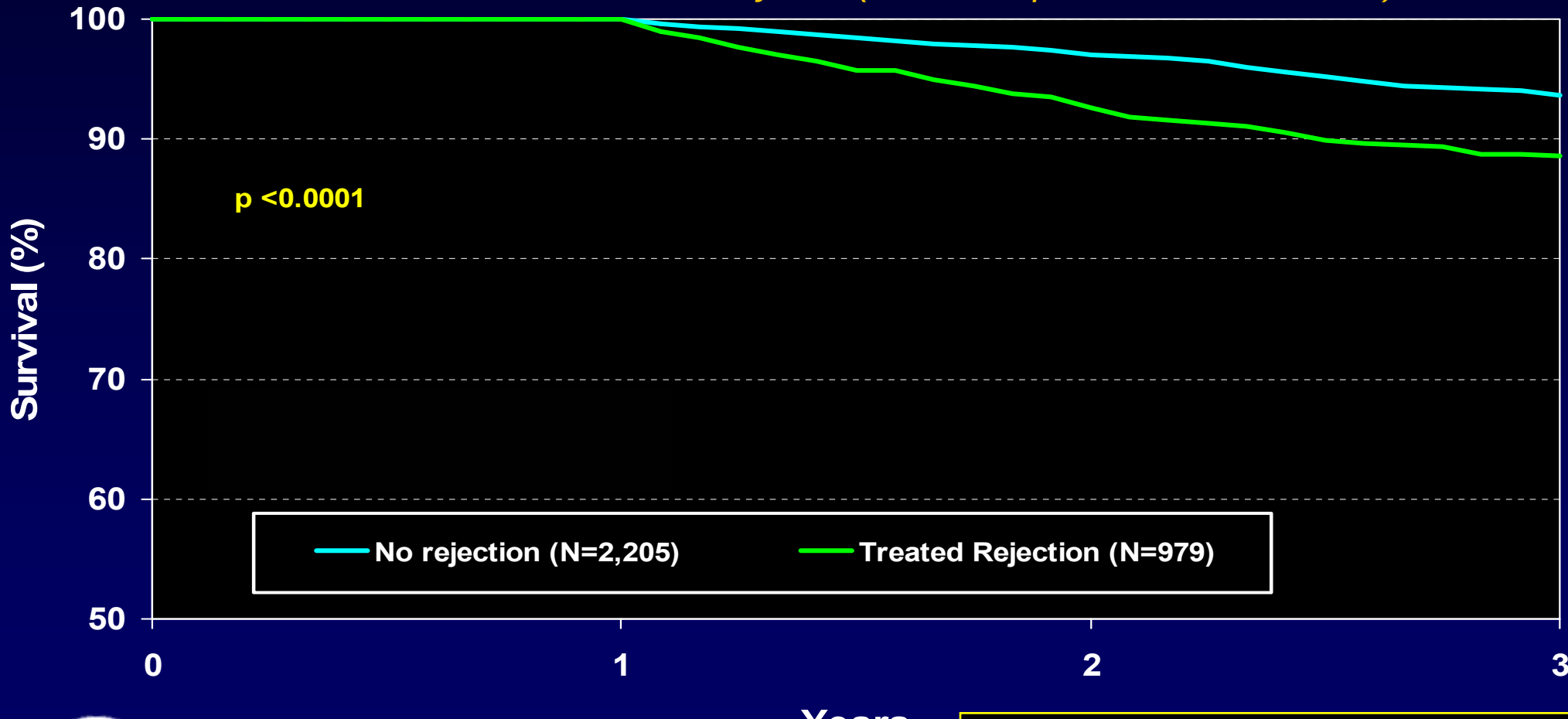
ADULT HEART TRANSPLANTATION

Kaplan-Meier Survival Stratified by Treatment for Rejection Within 1st Year

Conditional on survival to 1 year (follow-ups: 7/2004-6/2007)



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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.
No rejection = Recipient had (i) no acute rejection episodes and (ii) was reported either as not hospitalized for rejection or did not receive anti-rejection agents.

POST-HEART TRANSPLANT MORBIDITY FOR ADULTS

Cumulative Prevalence in Survivors at 1, 5 and 10 Years Post-Transplant (Follow-ups: April 1994 - June 2008)

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	73.3%	(N = 22,977)	93.3%	(N = 9,853)	97.4%	(N = 2,229)
Renal Dysfunction	27.2%	(N = 23,581)	31.9%	(N = 11,110)	38.3%	(N = 3,077)
Abnormal Creatinine < 2.5 mg/dl	*18.5%*		*21.6%*		*24.8%*	
Creatinine > 2.5 mg/dl	*7.0%*		*7.5%*		*7.4%*	
Chronic Dialysis	*1.4%*		*2.4%*		*4.7%*	
Renal Transplant	*0.3%*		*0.4%*		*1.5%*	
Hyperlipidemia	57.6%	(N = 24,319)	87.7%	(N = 11,093)	93.3%	(N = 2,650)
Diabetes	27.8%	(N = 23,623)	36.1%	(N = 10,235)	38.6%	(N = 2,392)
Cardiac Allograft Vasculopathy	7.8%	(N = 21,357)	30.8%	(N = 7,495)	51.9%	(N = 1,542)

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ADULT HEART TRANSPLANTS (1/2002-6/2007)

Risk Factors for 1 Year Mortality

Continuous Factors (see figures)

- Recipient age
- Recipient BMI
- Donor age
- Donor BMI
- Transplant center volume
- Ischemia time
- PCW (borderline)
- Bilirubin
- Serum creatinine
- PVR

ADULT HEART TRANSPLANTS (1/2000-6/2003)
Risk Factors for 5 Year Mortality

VARIABLE	N	Relative Risk	P-value	95% Confidence Interval
Temporary circulatory support*	114	2.00	<0.0001	1.50 -2.67
Ventilator	203	1.78	<0.0001	1.41 -2.24
Diagnosis: Congenital vs. cardiomyopathy	164	1.68	0.0006	1.25 -2.25
Recipient on dialysis at transplant	221	1.62	<0.0001	1.31 -2.01
Previous pregnancy	1022	1.27	0.0193	1.04 -1.55
Recipient history of diabetes	1379	1.25	0.0001	1.11 -1.40
Chronic pulsatile device	1192	1.23	0.0019	1.08 -1.39
Previously cerebrovascular event	416	1.21	0.0414	1.01 -1.45
Diagnosis: Coronary artery disease vs. cardiomyopathy	3405	1.19	0.0025	1.06 -1.33
Hospitalized (including ICU)	3640	1.16	0.005	1.04 -1.28
Male recipient/female donor vs. male recipient/male donor	1286	1.15	0.0345	1.01 -1.31
Transplant year: 2000 vs. 2002/2003	2031	1.14	0.0266	1.01 -1.27
Total number of HLA mismatches	0-3 MM (N= 872) 4-6 MM (N= 6299)	1.06	0.0176	1.01 -1.11

* Temporary circulatory support includes ECMO and Abiomed

NOTE: There were too few continuous flow devices to analyze.

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(N=7,171)

ADULT HEART TRANSPLANTS (1/2000-6/2003)

Risk Factors for 5 Year Mortality

Continuous Factors (see figures)

Recipient age	**Ischemia time**
Donor age	**Serum creatinine**
Recipient height	**Transplant center volume**
Bilirubin	**PA mean pressure**

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2009

(N=7,171)

ADULT HEART TRANSPLANTS (7/1994-6/1998)

Risk Factors for 10 Year Mortality

VARIABLE	N	Relative Risk	P-value	95% Conf. Interval
Repeat transplant	206	1.67	<0.0001	1.38 -2.02
Recipient on dialysis	131	1.57	0.0001	1.25 -1.96
Diagnosis: congenital vs. cardiomyopathy	146	1.5	0.0012	1.17 -1.91
Ventilator at time of transplant	230	1.36	0.0007	1.14 -1.62
Female recipient/male donor	936	1.27	0.0001	1.13 -1.43
Diagnosis: coronary artery disease vs. cardiomyopathy	4468	1.26	<0.0001	1.17 -1.36
Female recipient/female donor	936	1.24	0.0001	1.11 -1.39
Recipient history of diabetes	1230	1.22	<0.0001	1.12 -1.33
Recipient with infection requiring IV drug therapy within 2 weeks prior to transplant	659	1.22	0.0009	1.08 -1.37
Recipient history of malignancy	262	1.21	0.0279	1.02 -1.44
On VAD at time of transplant	837	1.2	0.0008	1.08 -1.34
PRA $\geq$ 10%	567	1.17	0.0128	1.03 -1.32
Year of transplant: 1994/1995 vs. 1997/1998	3310	1.11	0.0067	1.03 -1.19
Male recipient/female donor	1817	1.1	0.029	1.01 -1.21
Number of total HLA mismatches		1.05	0.0026	1.02 -1.08
Year of transplant: 1996 vs. 1997/1998	131	1.08	0.0544	1.00 -1.18

ISHLT 2009 (N=8,818)

ADULT HEART TRANSPLANTS (7/1994-6/1998)
Risk Factors for 10 Year Mortality

Continuous Factors (see figures)

Recipient age	**Creatinine**
Recipient BMI (borderline)	**Bilirubin**
Donor age	**Ischemia time**
Donor BMI	**Volume**

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2009

(N=8,818)

ADULT HEART TRANSPLANTS (7/1994-6/1998)

Risk Factors for 10 Year Mortality
Conditional on Survival to 3 Years

VARIABLE	N	Relative Risk	P-value	95% Confidence Interval
Recipient history of malignancy	186	1.30	0.0339	1.02 -1.65
CAV within 1st year	376	1.28	0.0062	1.07 -1.52
Recipient history of diabetes	810	1.25	0.0005	1.10 -1.42
Drug-treated infection prior to discharge	1101	1.22	0.0008	1.09 -1.37
Diagnosis: coronary artery disease vs. cardiomyopathy	3086	1.21	0.0004	1.09 -1.34
Recipient with infection requiring IV drug therapy within 2 weeks prior to transplant	434	1.20	0.0357	1.01 -1.42
Rejection between discharge and 1st year	1713	1.19	0.0006	1.08 -1.31
Transplant year: 1994/1995 vs. 1997/1998	2313	1.13	0.0247	1.02 -1.25
Donor CMV+/ Recipient CMV-	1018	0.87	0.0316	0.76 -0.99

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(N=6,175)

ADULT HEART TRANSPLANTS

Risk Factors for 10 Year Mortality Conditional on Survival to 3 Years

Continuous Factors (see figures)

Recipient age	**Creatinine**
Donor BMI	**PA mean pressure**

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(N=6,175)

ADULT HEART TRANSPLANTS

Risk Factors for 15 Year Mortality
Conditional on Survival to 5 Years

Continuous Factors (see figures)

Recipient age

Donor age

PRA prior to transplant

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2009

(N=4,816)

ADULT HEART TRANSPLANTS (1982-6/1987)

Risk Factors for 20 Year Mortality

VARIABLE	N	Relative Risk	P-value	95% Confidence Interval
Transplant year: 1982 vs. 1986/1987	132	1.99	<0.0001	1.64 -2.42
Transplant year: 1983 vs. 1986/1987	225	1.43	<0.0001	1.22 -1.68
Transplant year: 1984 vs. 1986/1987	447	1.37	<0.0001	1.22 -1.55
Transplant year: 1985 vs. 1986/1987	965	1.17	0.0004	1.07 -1.28
Diagnosis: Coronary artery disease vs. cardiomyopathy	1789	1.16	0.0002	1.07 -1.26

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(N=4,487)

ADULT HEART TRANSPLANTS
Risk Factors for 20 Year Mortality

Continuous Factors (see figures)

Recipient age

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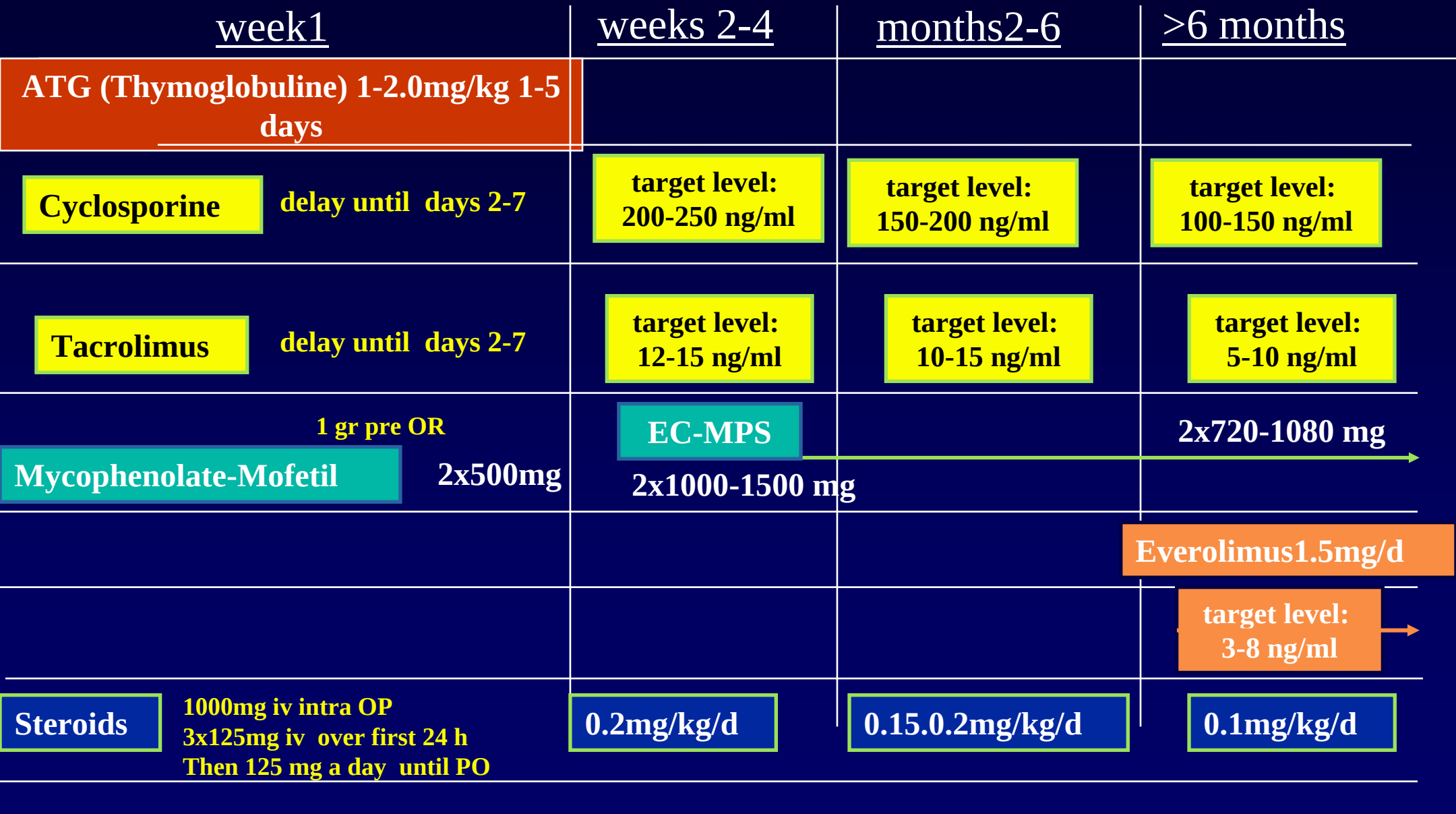
(N=4,487)

Immunosuppressive Management RMC



Cardiac biopsy grading

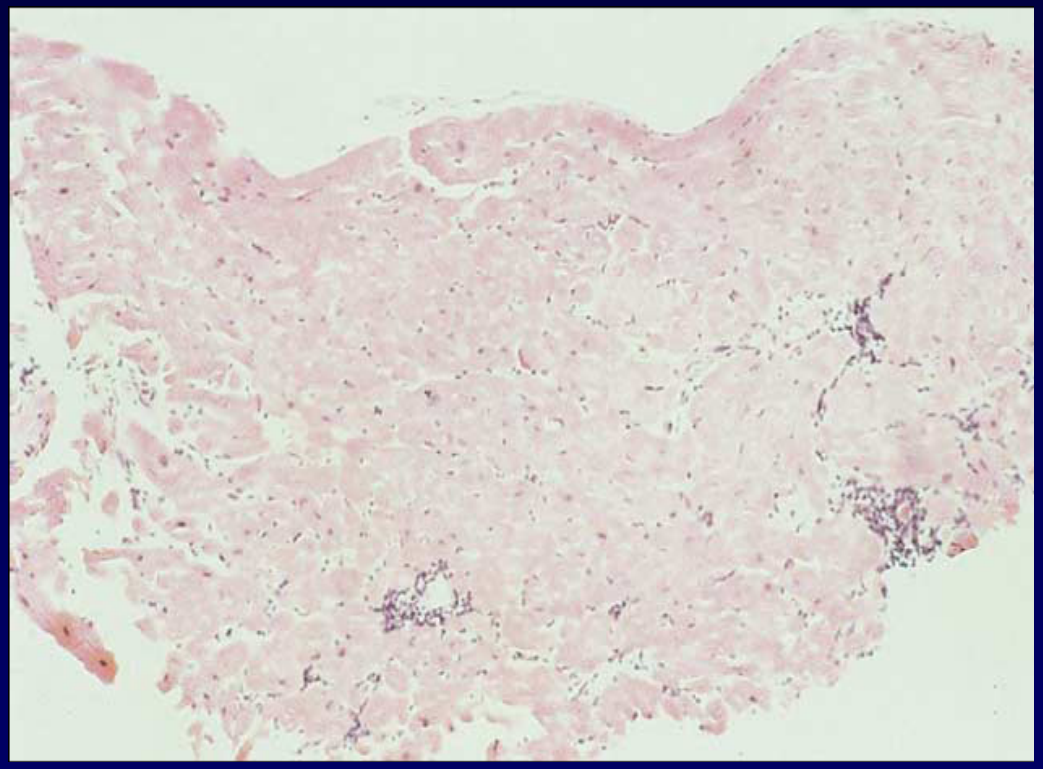
Table 1. ISHLT Standardized Cardiac Biopsy Grading: Acute Cellular Rejection[b]

2004		1990	
Grade 0 R[a]	No rejection	Grade 0	No rejection
Grade 1 R, mild	Interstitial and/or perivascular infiltrate with up to 1 focus of myocyte damage	Grade 1, mild A—Focal	Focal perivascular and/or interstitial infiltrate without myocyte damage
		B—Diffuse	Diffuse infiltrate without myocyte damage
		Grade 2 moderate (focal)	One focus of infiltrate with associated myocyte damage
Grade 2 R, moderate	Two or more foci of infiltrate with associated myocyte damage	Grade 3, moderate A—Focal	Multifocal infiltrate with myocyte damage
Grade 3 R, severe	Diffuse infiltrate with multifocal myocyte damage ± edema, ± hemorrhage ± vasculitis	B—Diffuse	Diffuse infiltrate with myocyte damage
		Grade 4, severe	Diffuse, polymorphous infiltrate with extensive myocyte damage ± edema, ± hemorrhage + vasculitis

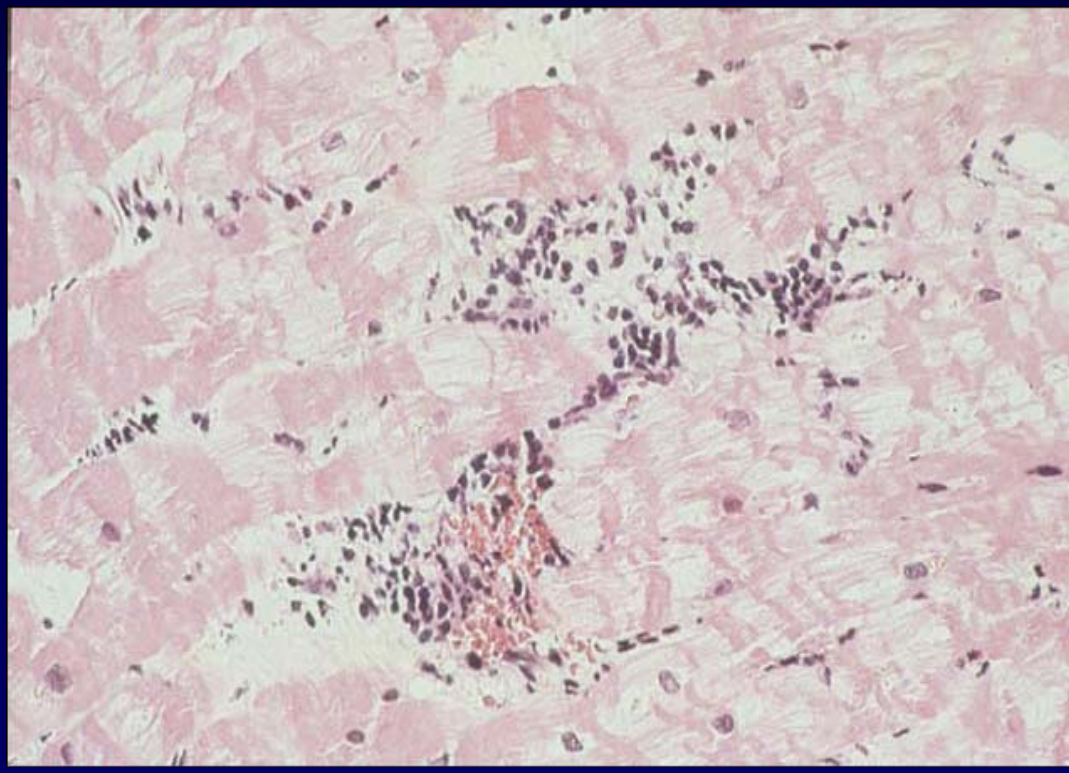
[a]Where "R" denotes revised grade to avoid confusion with 1990 scheme.

Acute rejection grade 1R:

No myocyte damage, previously 1A



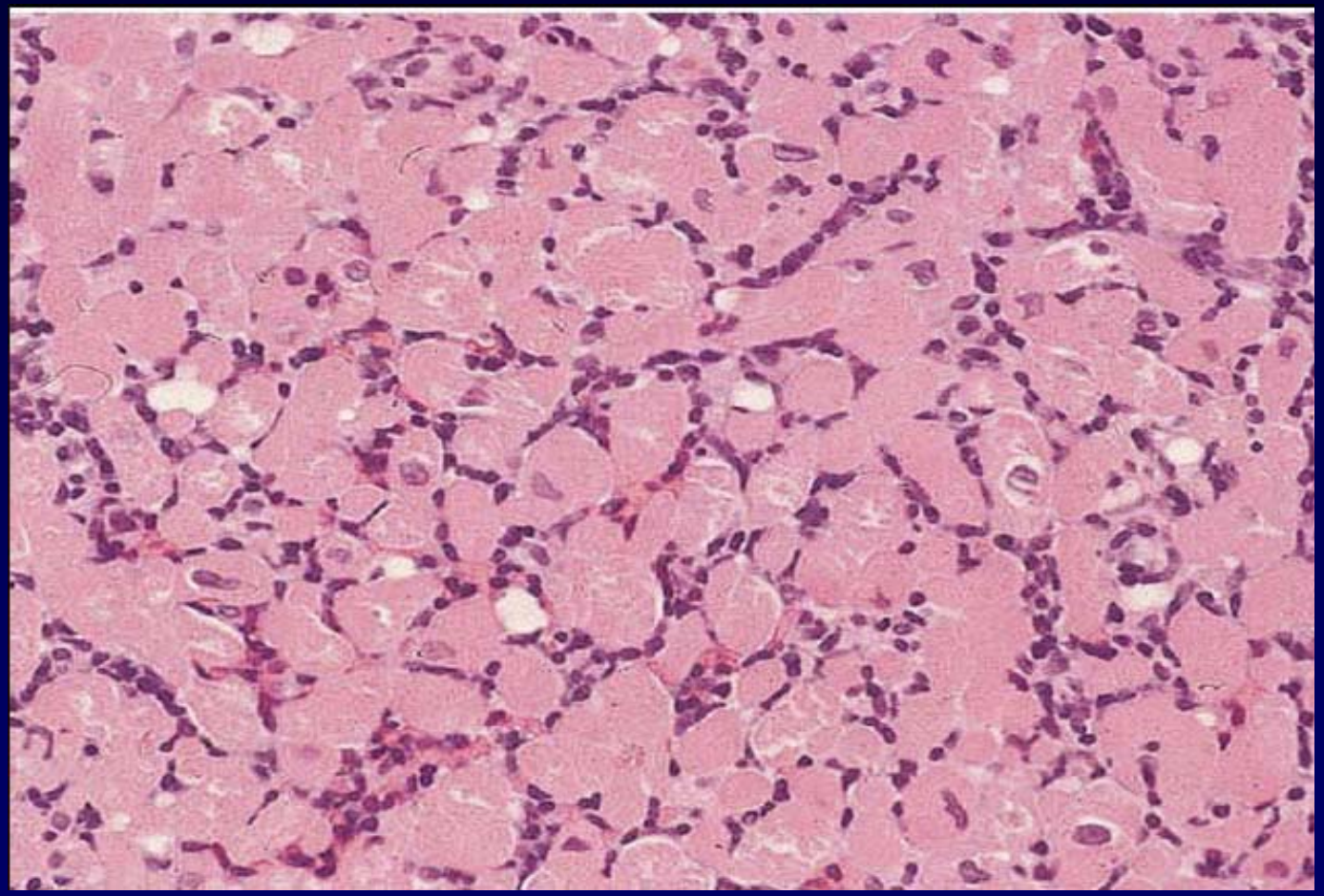
Three focal, perivascular infiltrates



perivascular and interstitial infiltrates

Acute rejection grade 1R:

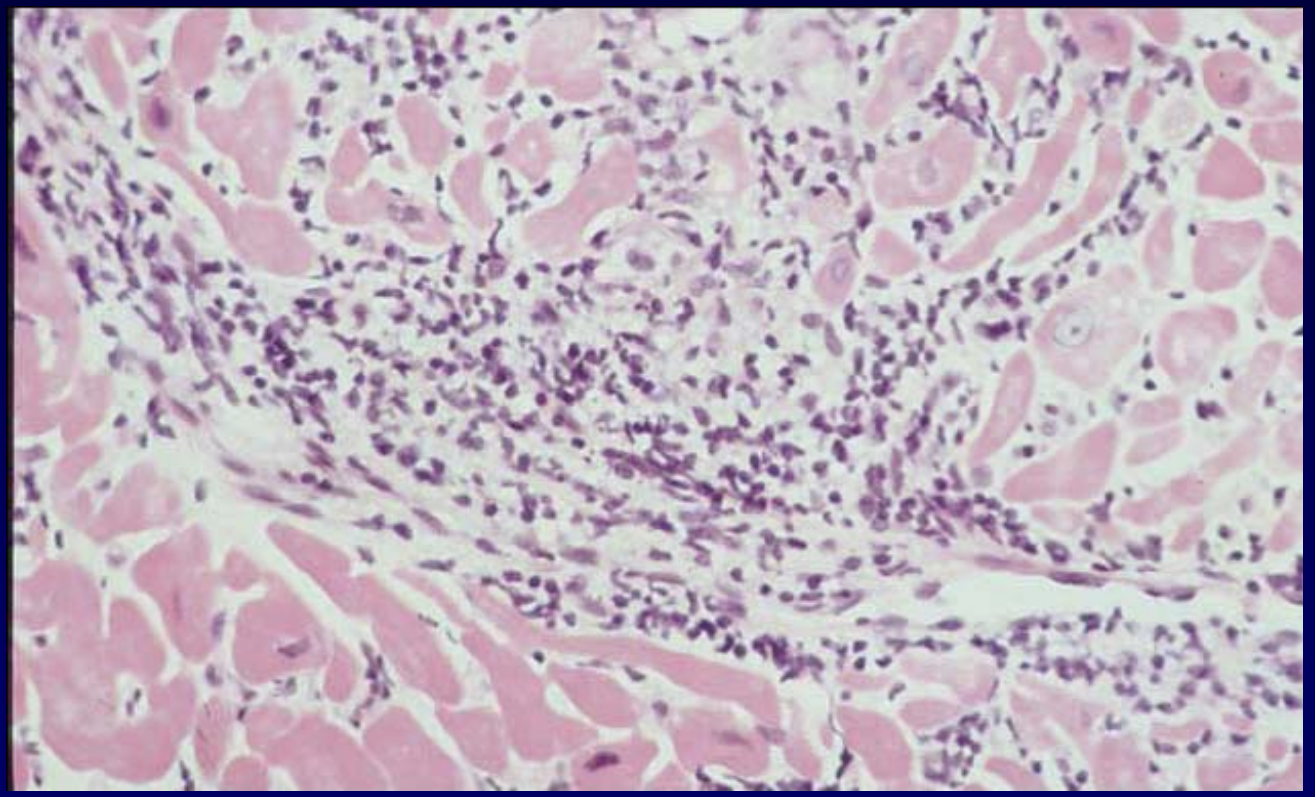
without associated myocyte damage. Previously Grade 1B.



Diffuse mononuclear cell infiltrate with an interstitial pattern of lymphocytes between and around myocytes

Acute rejection grade 1R:

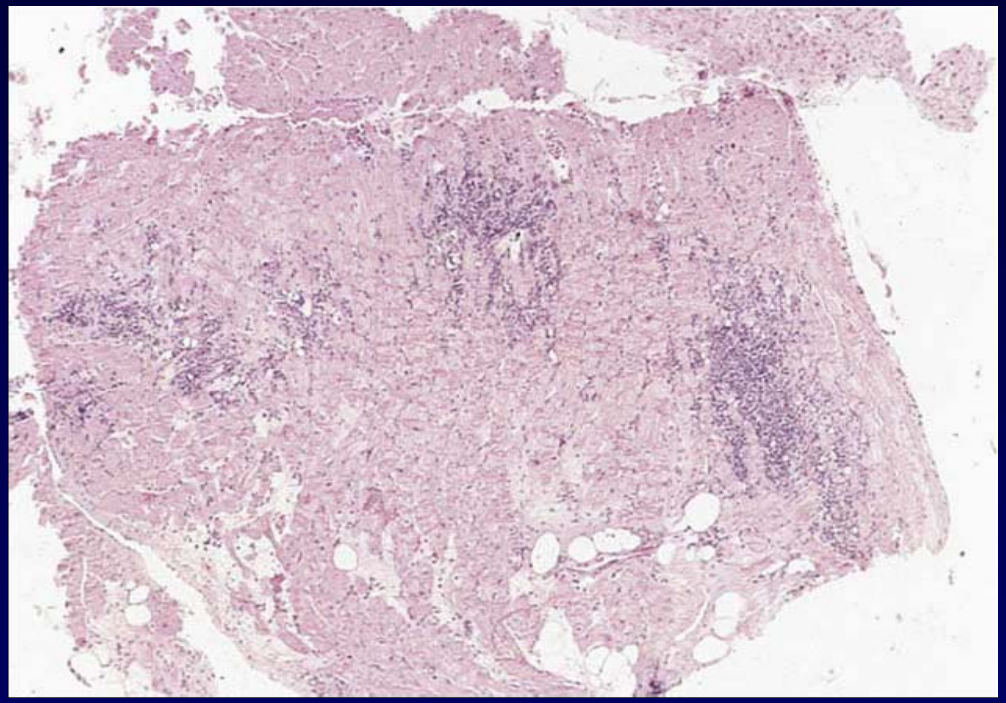
With damage to myocytes and distortion of architecture. Previously Grade 2.



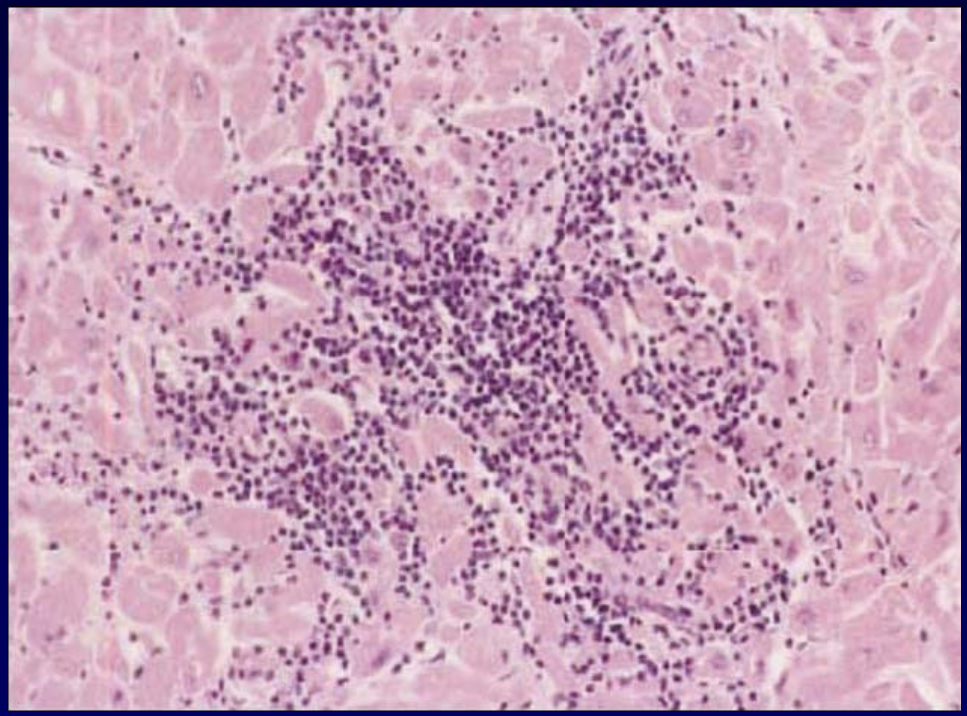
Mononuclear infiltrate extending from a perivascular position into adjacent myocardium. This is a single focus in the biopsy series and therefore is included in the revised mild grade of acute rejection, grade 2.

Grade 2 R:

Previously Grade 3A



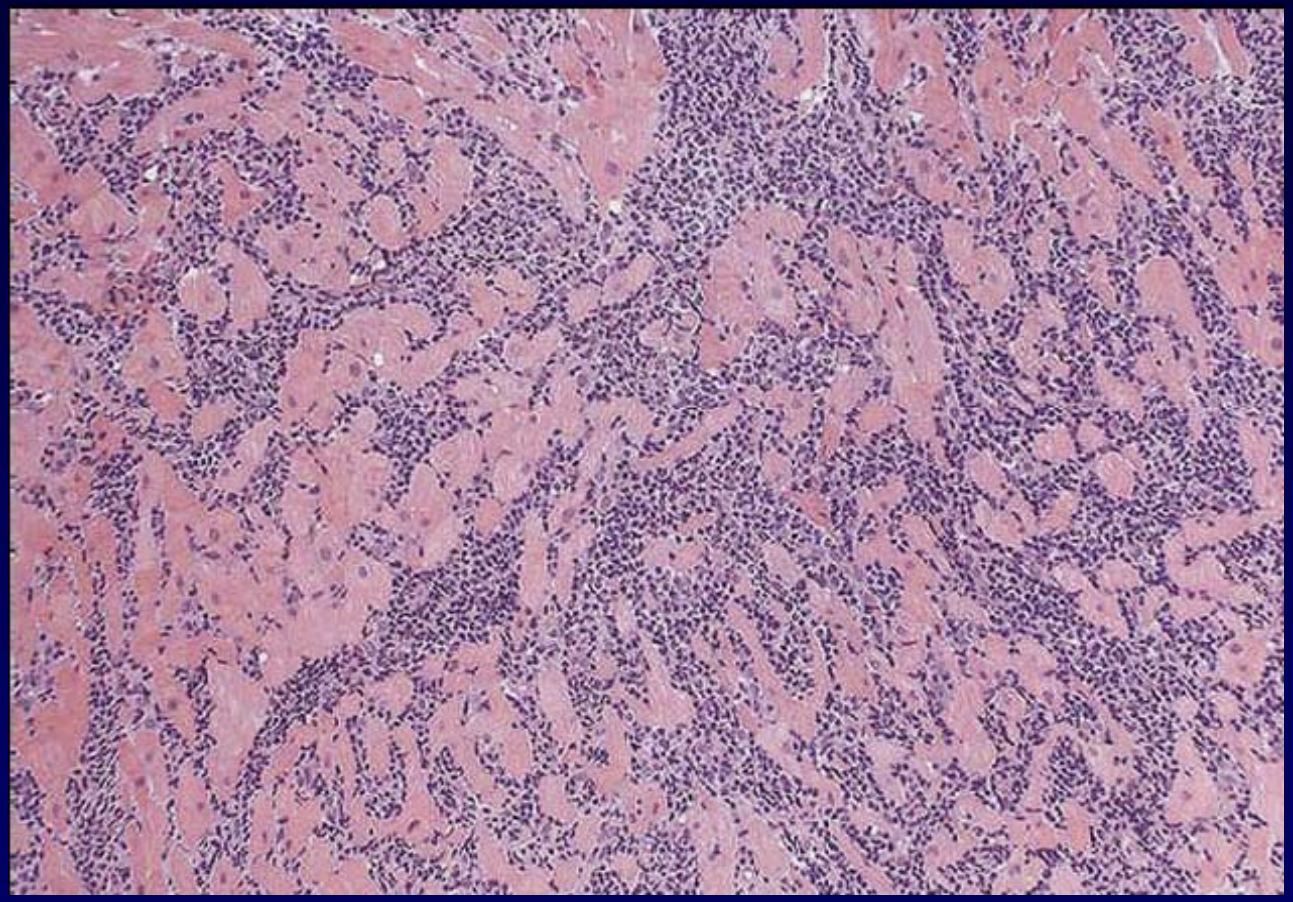
Three foci of damaging mononuclear cell infiltrate with normal myocardium intervening



One focus of damaging infiltrate with myocyte damage and architectural distortion

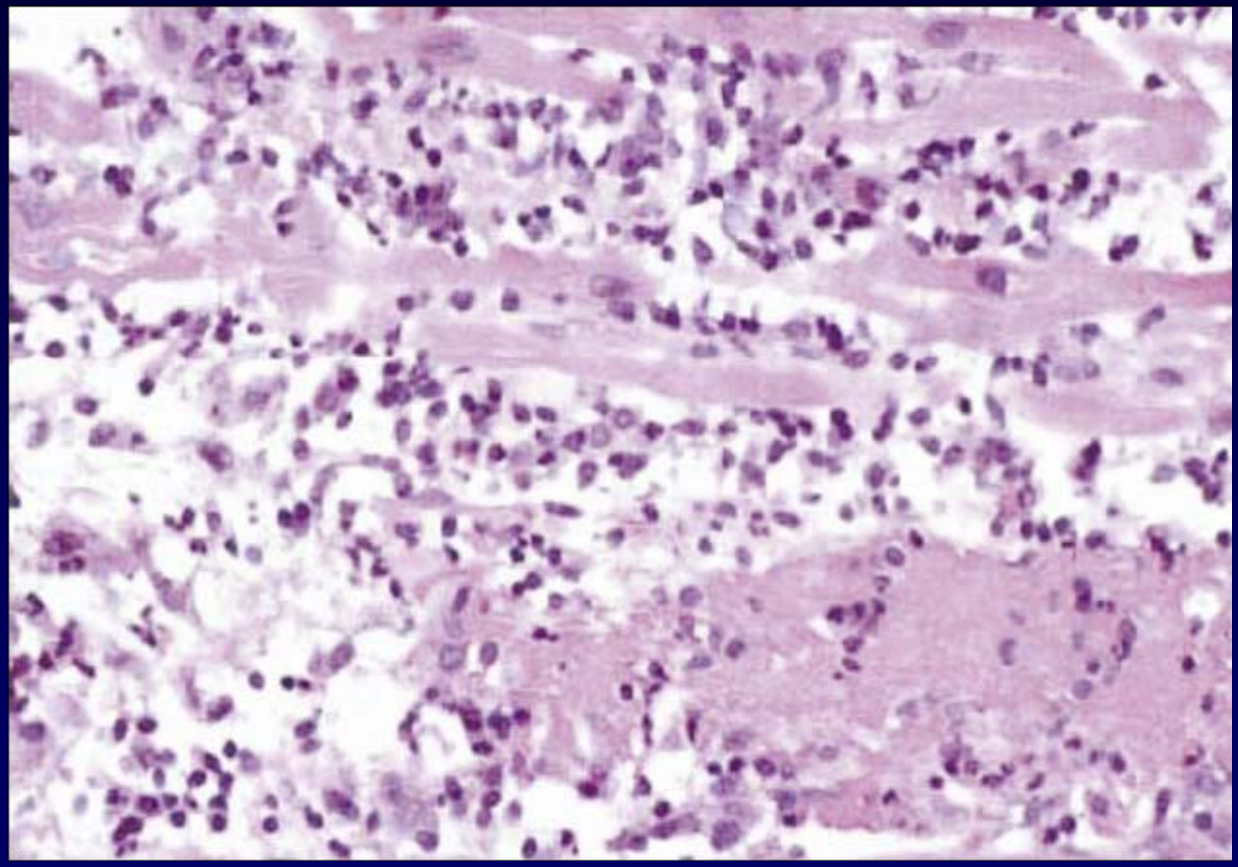
Grade 3 R:

Previously Grade 3B.



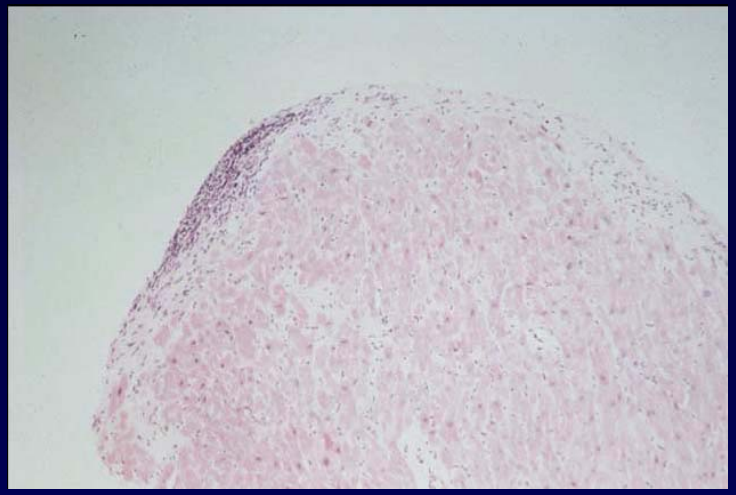
Diffuse damaging infiltrates with encroachment of myocytes and disruption of normal architecture.

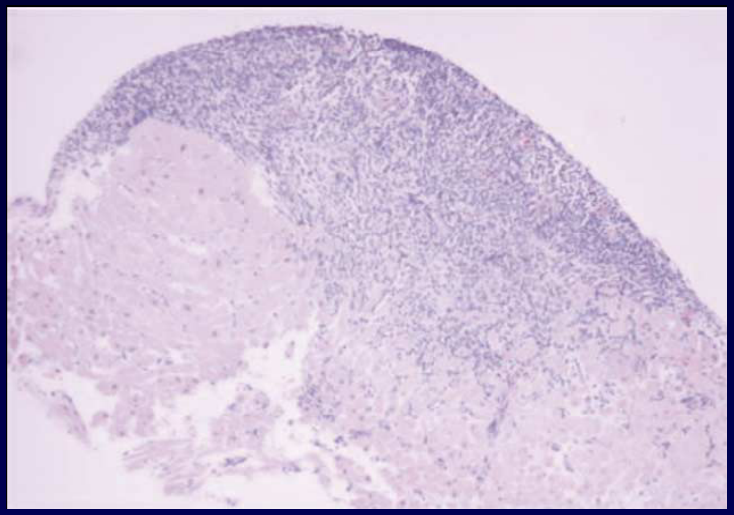
Grade 3 R:
Previously Grade 4

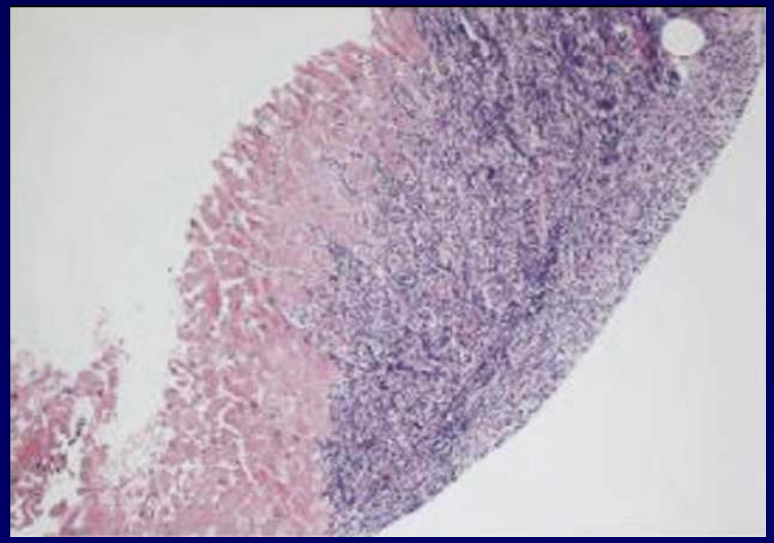


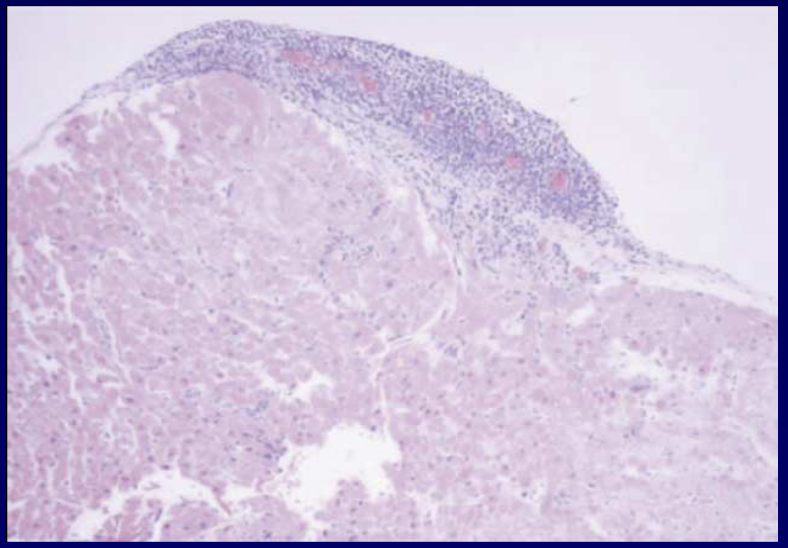
Severe acute rejection with widespread myocyte damage and some necrosis. The diffuse infiltrate includes polymorphs as well as lymphocytes, macrophages and plasma cells.

Quilty Effect









There are no apparent benefits from surveillance biopsy beyond 5 years post-transplant.

Surveillance biopsy between 2 and 5 years post-transplant was found to reduce mortality in African-American recipients.

Non-African-American recipients at high risk for late rejection will likely benefit from surveillance up to 5 years post-transplant.

Severe TR > 31 EMB

Monitoring immunosuppressive Tx:

Therapeutic drug monitoring of CysA & FK levels.

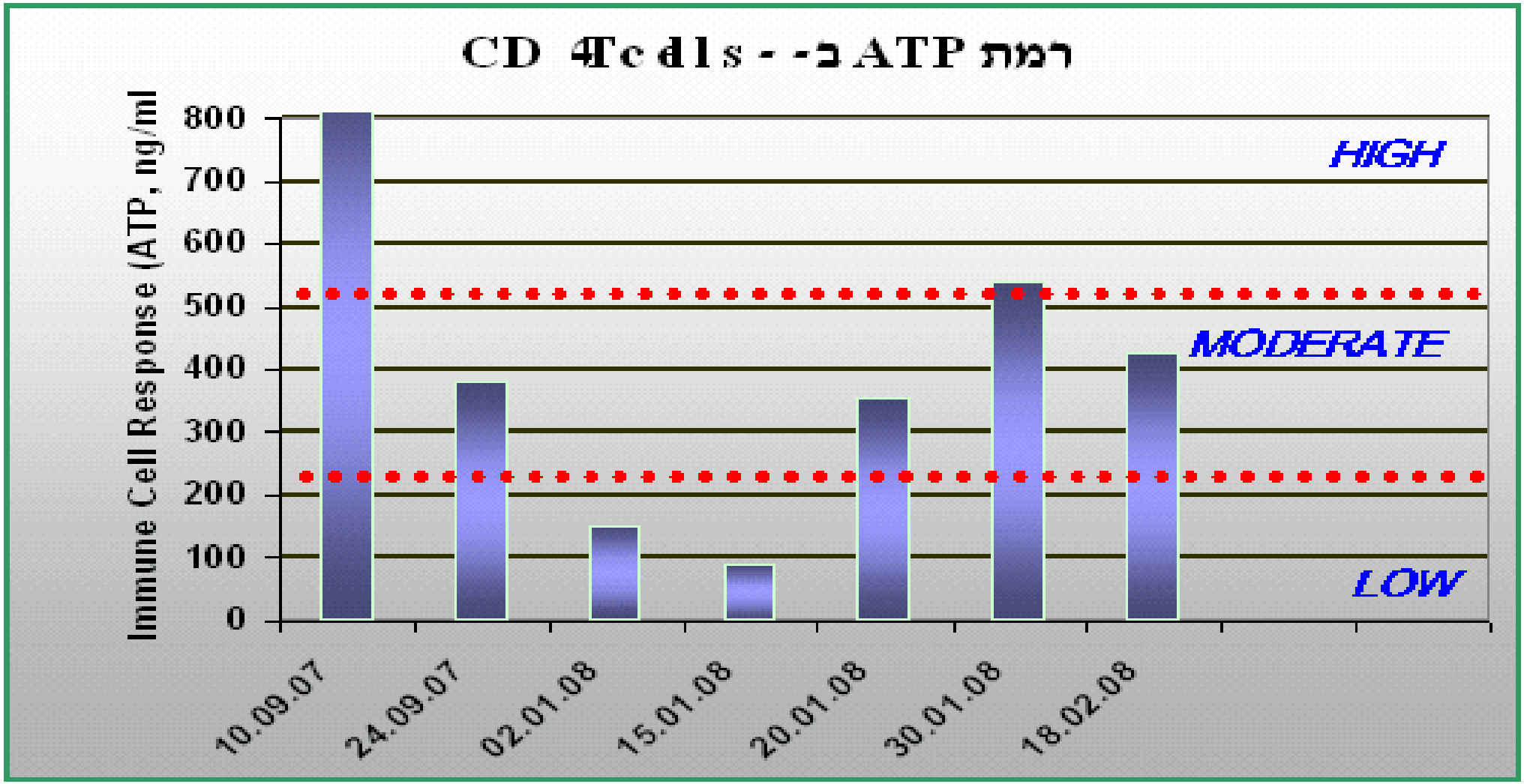
However:

1. The blood drug levels do not directly correlate with the dose of drug administered because of individual pharmacokinetic differences and the monoclonal antibody methodology used for their detection.

2. The blood drug levels determined by immunoassay do not correlated with immunosuppressive drug efficacy.

Immune Response	מקרא
Low	מתחת ל- 225
Moderate	226-525
High	מעל ל- 526

תאריך לידה:	17/06/1905
מין:	נקבה
תאריך השתלה:	
סוג השתלה:	לב



CylexTM (Immuknow assay) In HTx

Levels below 225 indicate over

and above 525 indicate under immune suppression.

The immunosuppressive tx of some of the HTx transplanted at our center needed re-assessment due to:

1. Severe complicated infections.

2. Biopsy proven rejection despite optimal drug levels

3.Toxic drug effects.

אמצעי להגדלת מספר החתומים על כרטיס התורם

- כל מועמד להשתלת איבר יקבל נקודות זכות במיקומו ברשימת הממתינים להשתלה במידה וימצא חתום על כרטיס התורם בתאריך הקודם בשנה אחת לפחות לתאריך רישומו כמועמד להשתלה.
- נקודות זכות זהות יקבלו גם קרובי משפחת נפטר שנתנו הסכמתם לתרומת איבר יקירם וכן תורם חי שתרם כליה.

תודה על תשומת הלב