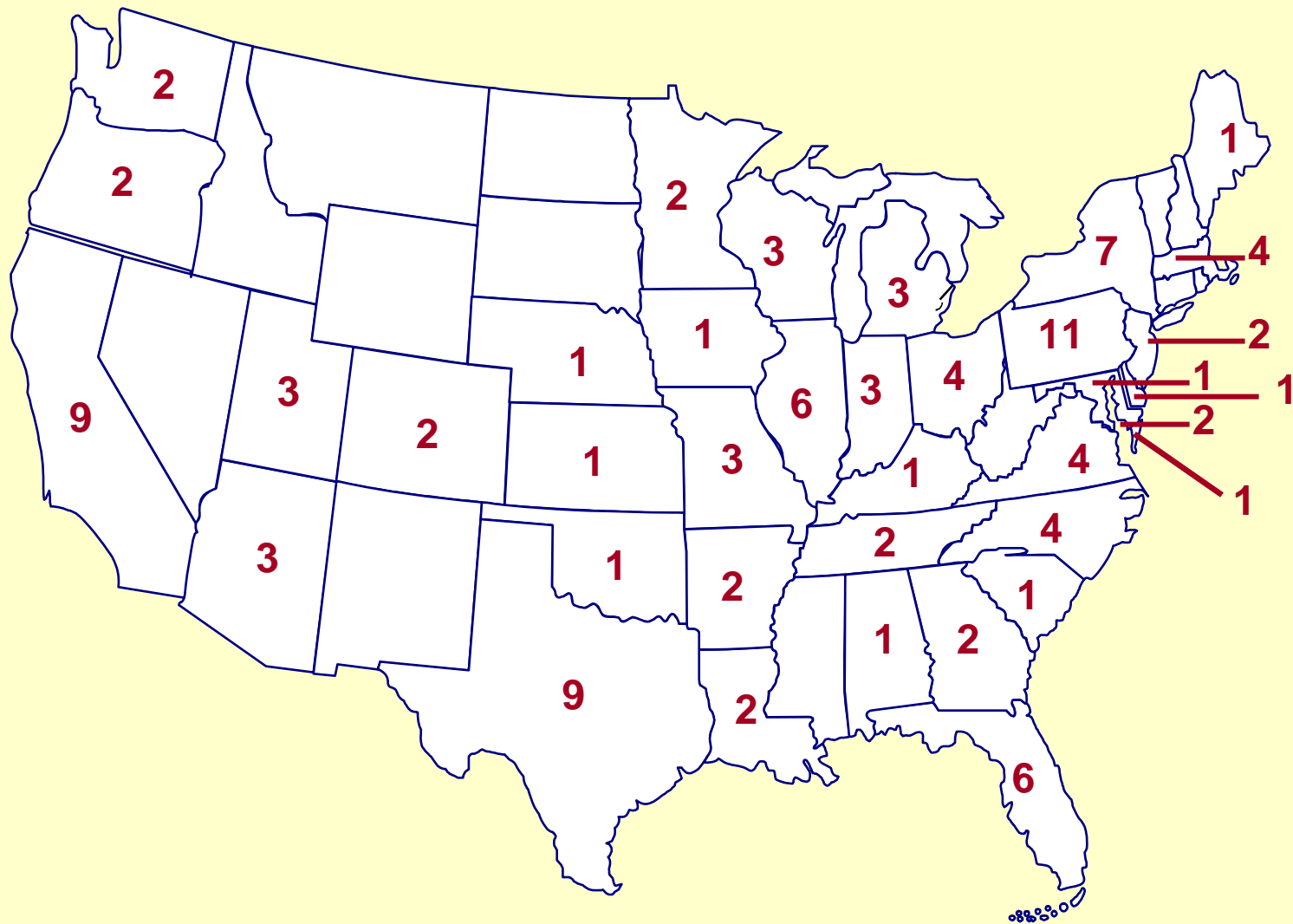


What is INTERMACS ?

INTERMACS is a United States national registry for patients who are receiving durable mechanical circulatory support device therapy to treat advanced heart failure. This registry was devised as a joint effort of the National Heart, Lung and Blood Institute (NHLBI), the Centers for Medicare and Medicaid Services (CMS), the Food and Drug Administration (FDA), clinicians, scientists and industry representatives.

Participating Centers per State – March 25, 2008 (112 Sites)



Goals of the Registry

- Facilitate the **refinement of patient selection** to *maximize outcomes* with current and new device options.
- Identify **predictors of good outcomes as well as risk factors** for adverse events after device implantation.
- Develop consensus “**best practice**” **guidelines** to improve clinical management by reducing short and long term complications of MCS D therapy.
- Utilize Registry **information to guide improvements in technology**, particularly as next generation devices evolve.
- Guide **clinical testing** and approval of **new devices**.

Gender:	Males	328 (78%)
	Females	92 (22%)

Race:	White	302 (72%)
	African American	86 (20%)
	Other	32 (8%)

Age at Implant:

mean:	50.9 yrs
range:	4.5 to 79.0
below 19 yrs:	12 (3%)

Implants:

LVAD:	314 (75%)
RVAD:	5 (1%)
Bi-VAD:	77 (18%)
TAH:	24 (6%)
<hr/>	
Total:	420 (100%)

INTERMACS**June 2006 – December 2007, n = 420**

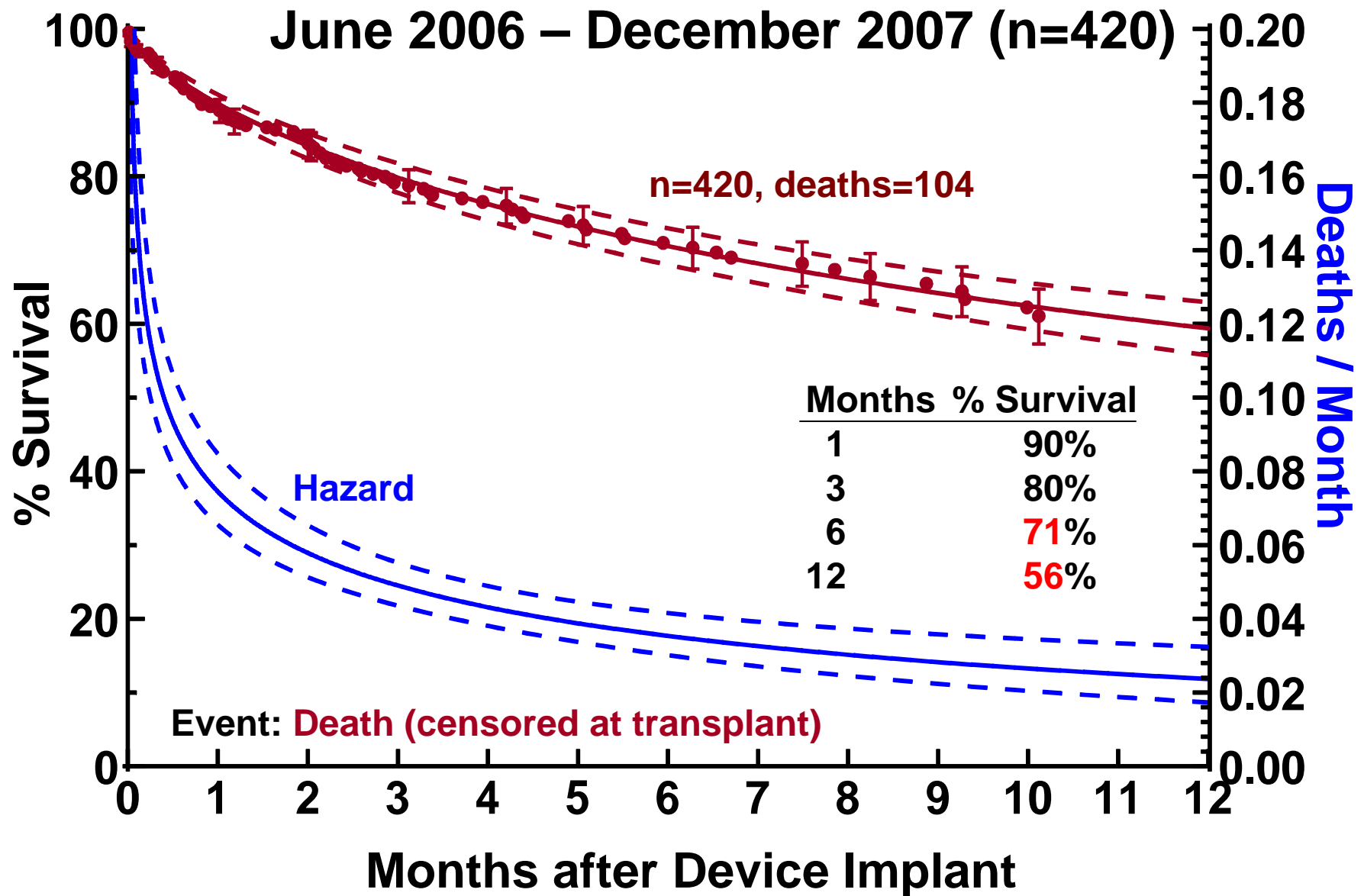
Pre-Implant Device Strategy	n	% of 420
Patient currently listed for transplant (BTT)	179	43%
Bridge to Candidacy (BTC)	157	37%
Patient likely never eligible for transplant (DT)	63	15%
Bridge to Recovery (BTR)	21	5%
Total	420	100%

INTERMACS**June 2006 – December 2007, n = 420**

INTERMACS LEVEL (Pre-Implant)	Ventricular Arrhythmia Modifier			Total	
	No	Yes	%	n	% of 420
1. Critical cardiogenic shock	143	43	23%	186	44%
2. Progressive decline	123	25	17%	148	35%
3. Stable but inotrope dependent	31	4	11%	35	8%
4. Recurrent advanced HF	25	8	24%	33	8%
5. Exertion intolerant	3	2	40%	5	1%
6. Exertion limited	5	1	17%	6	1%
7. Advanced NYHA III	7	0	0%	7	2%
Total	337	83		420	100%

Overall Results:

Deaths (prior to transplant):	104 (24%)
Transplants:	156 (37%)
Recovery:	11 (3%)
Alive (device in place):	149 (36%)
<hr/>	
Total	420 (100%)



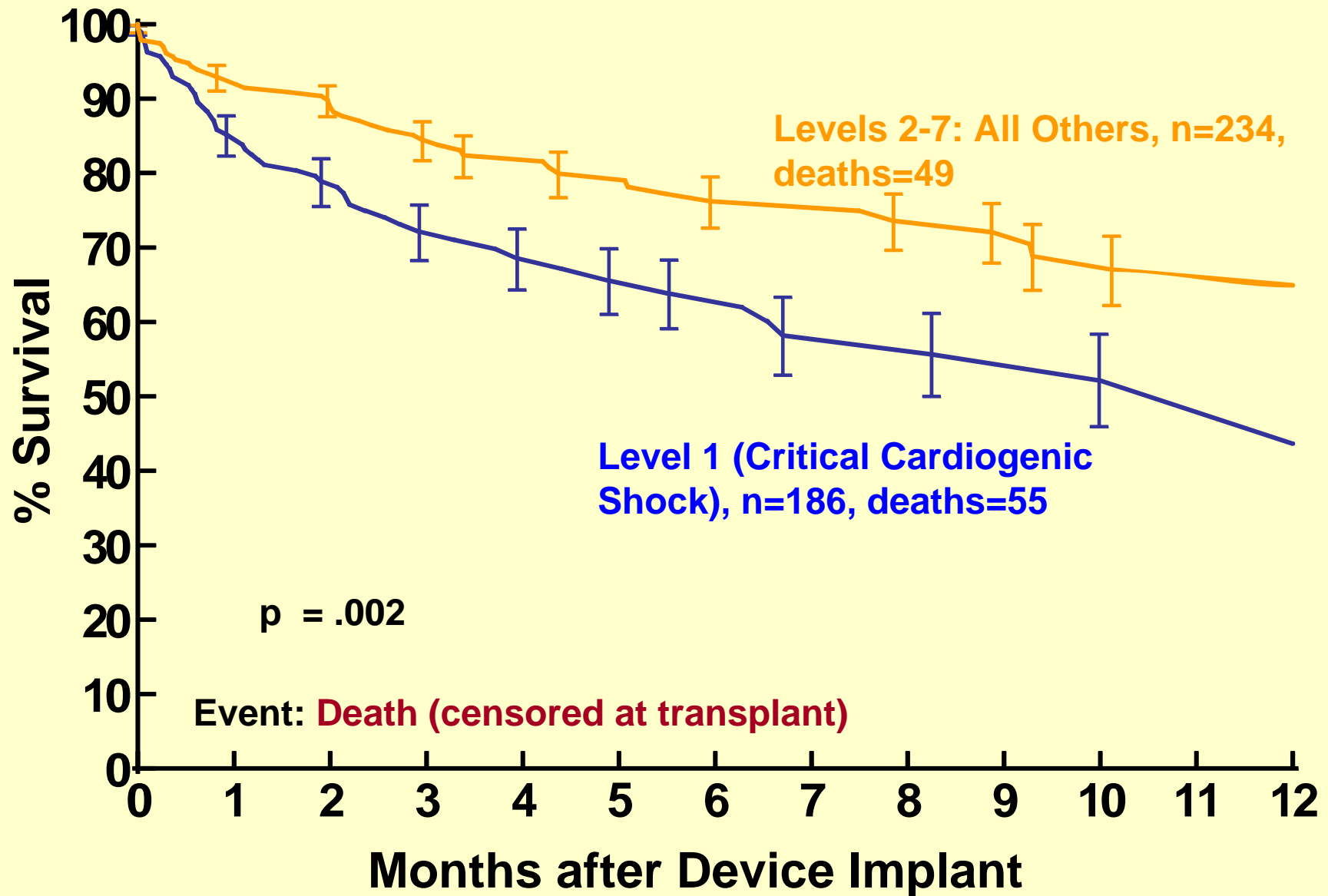
INTERMACS**June 2006 – December 2007, n = 420**

Risk Factors	relative risk	p-value
INTERMACS Level 1	1.59	.02
Age(older)*	1.41	< .001
Ascites	2.04	.003
Bilirubin(higher)**	1.49	.05
Bi-VAD implant	2.12	.002
Total Assist Heart implant	2.41	.03

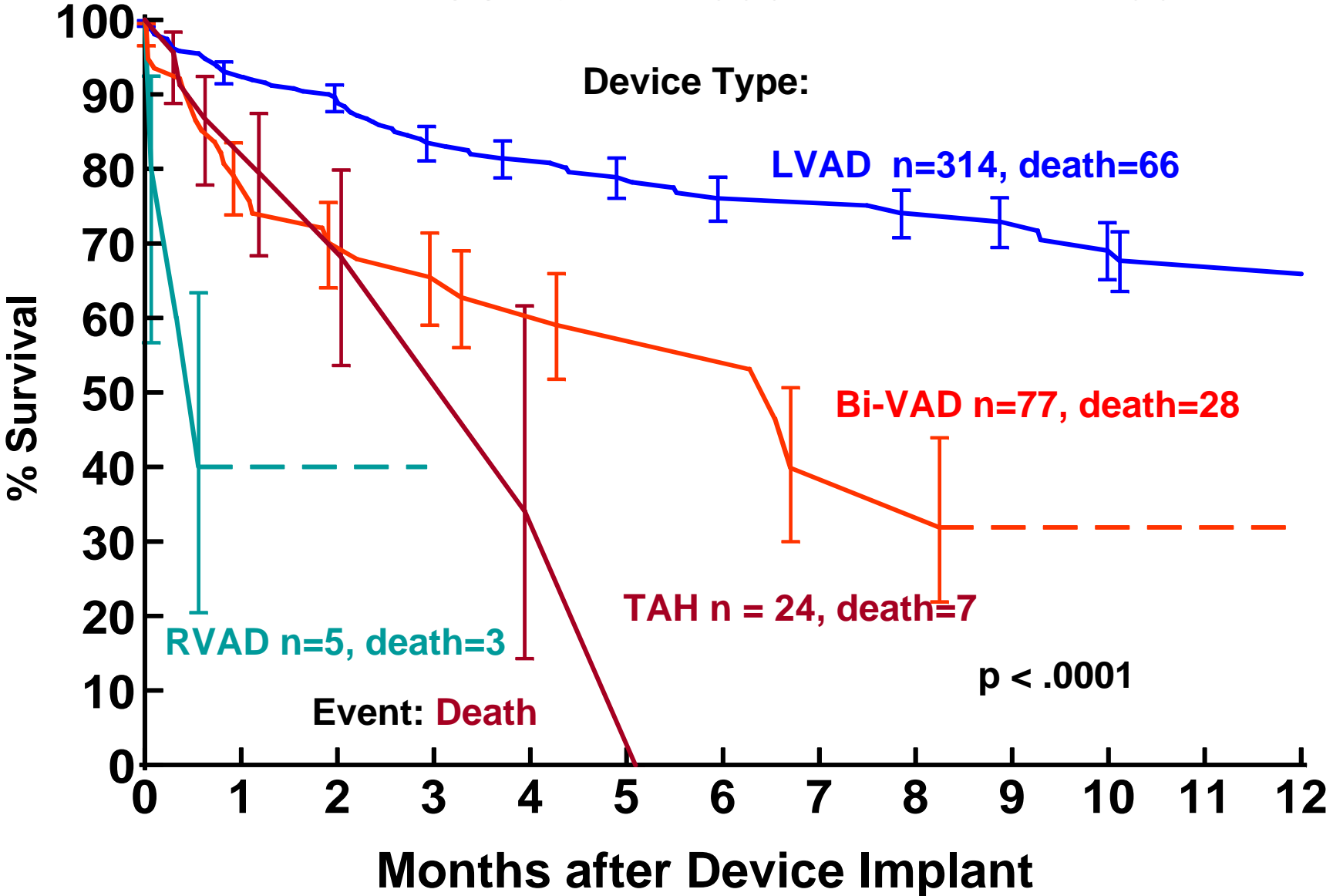
***Compares increased risk from age 50 to 60 years**

****Compares increased risk from bilirubin = 1 to 6(mg/dl)**

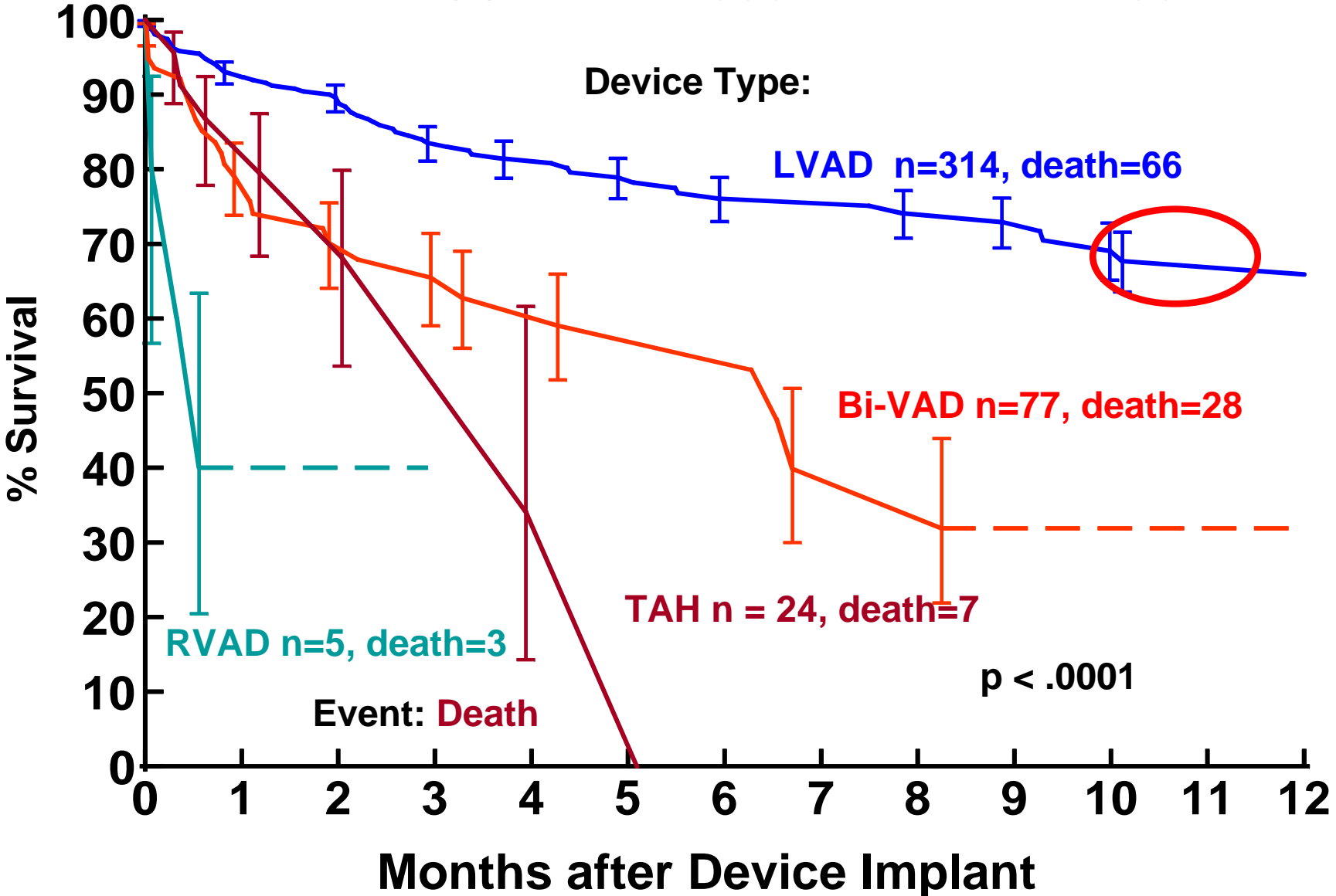
Patient Survival Among Profiles



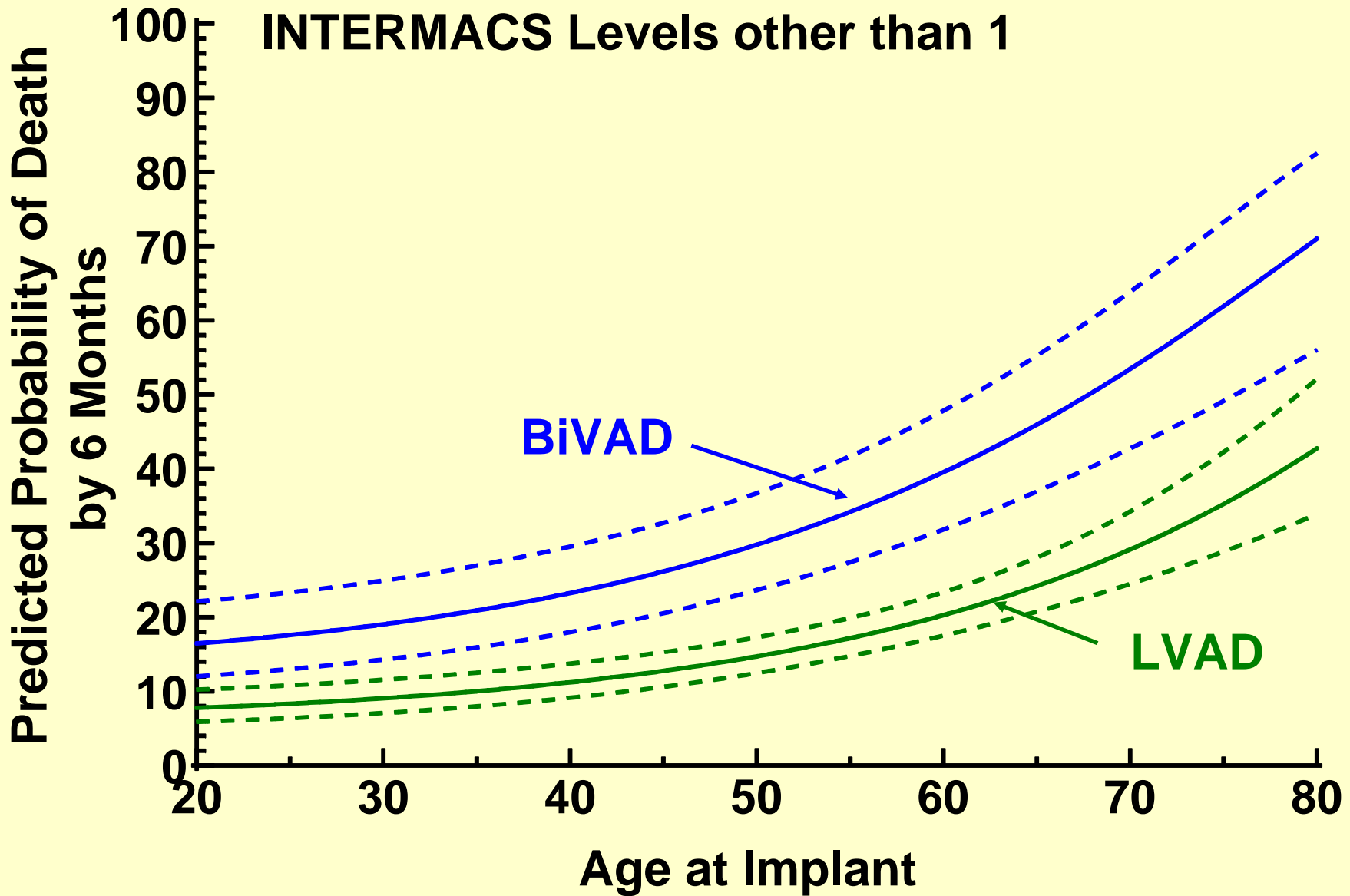
INTERMACS: June 2006 – December 2007



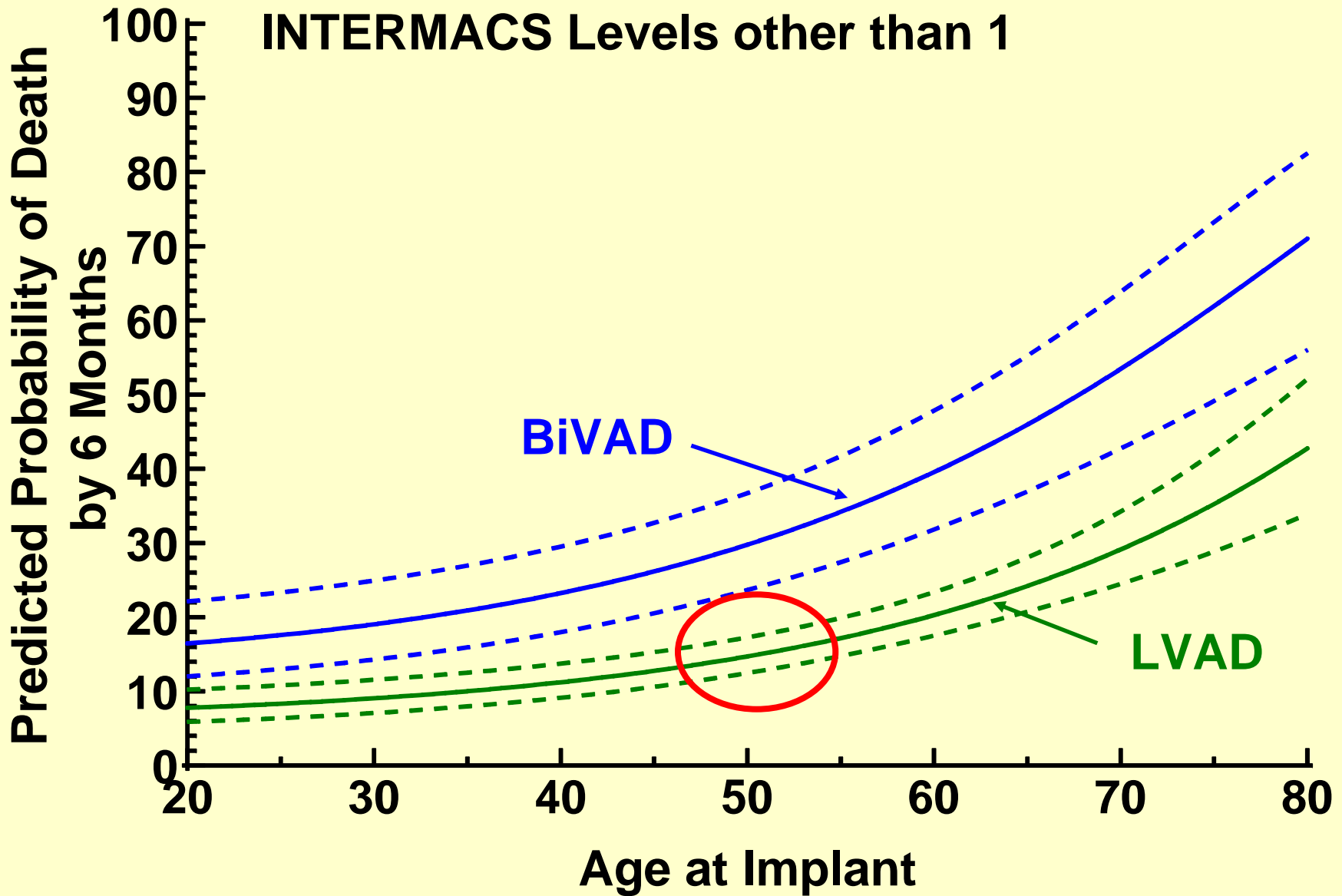
INTERMACS: June 2006 – December 2007



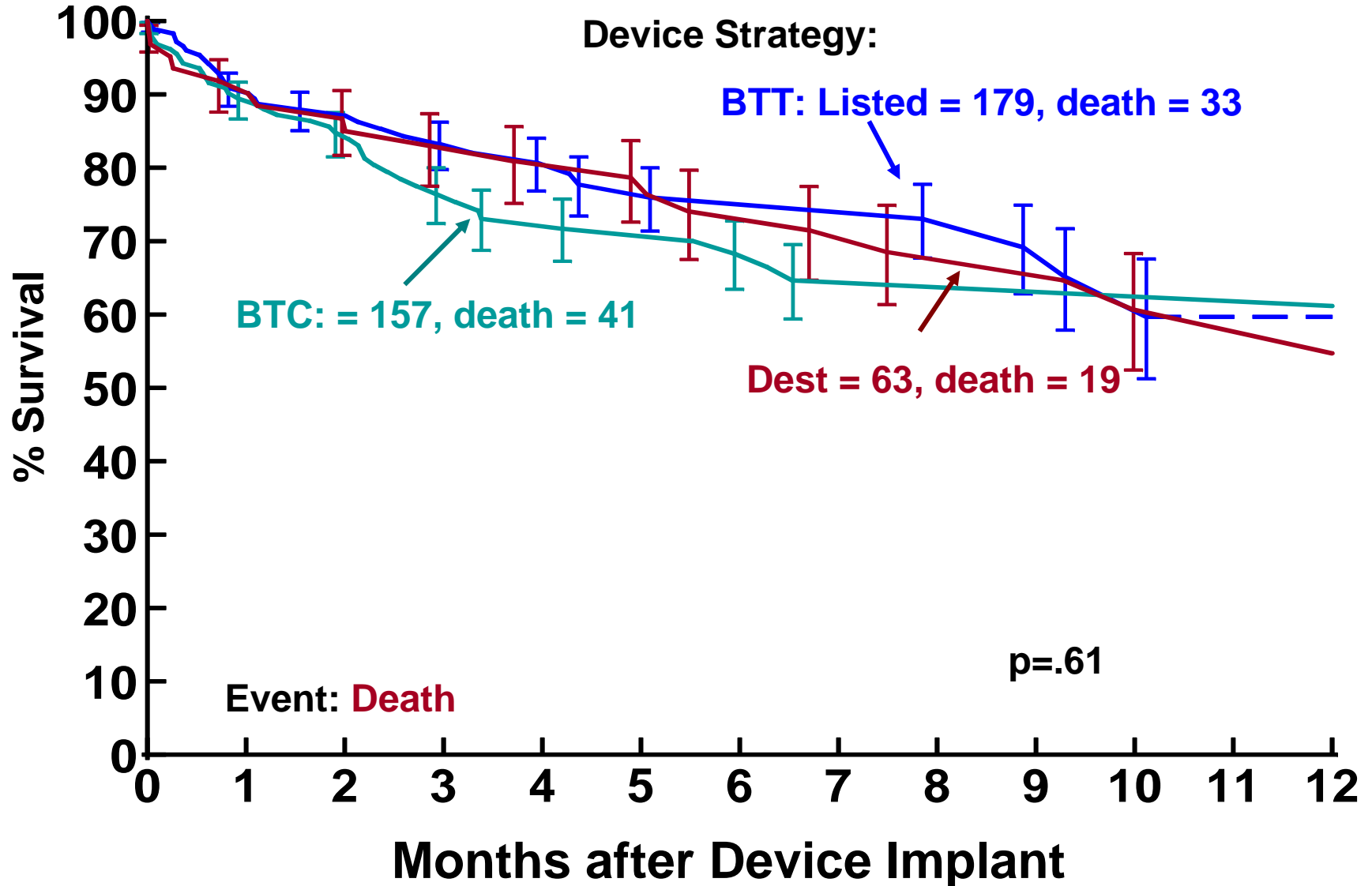
INTERMACS Levels other than 1



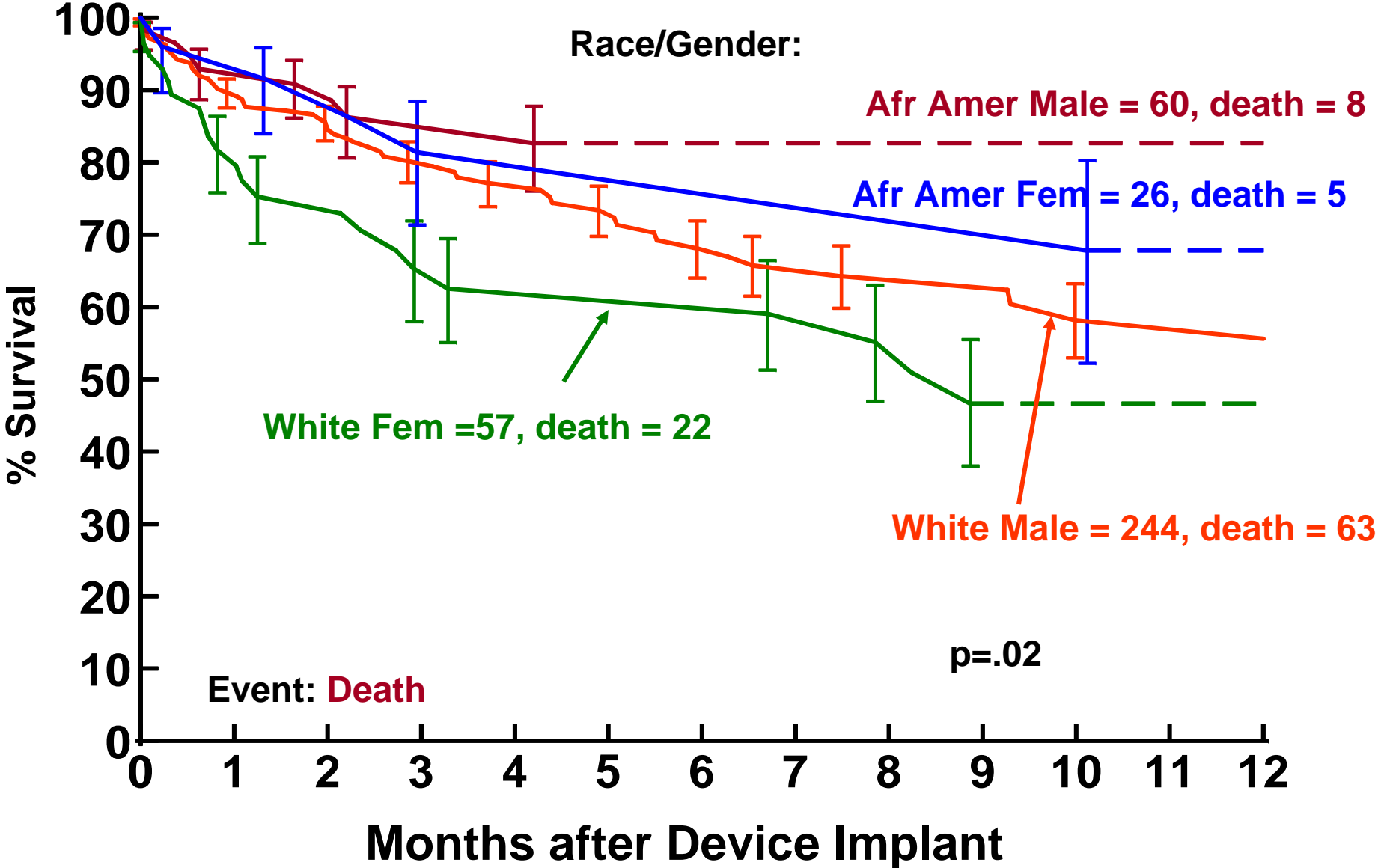
INTERMACS Levels other than 1



INTERMACS: June 2006 – December 2007



INTERMACS: June 2006 – December 2007



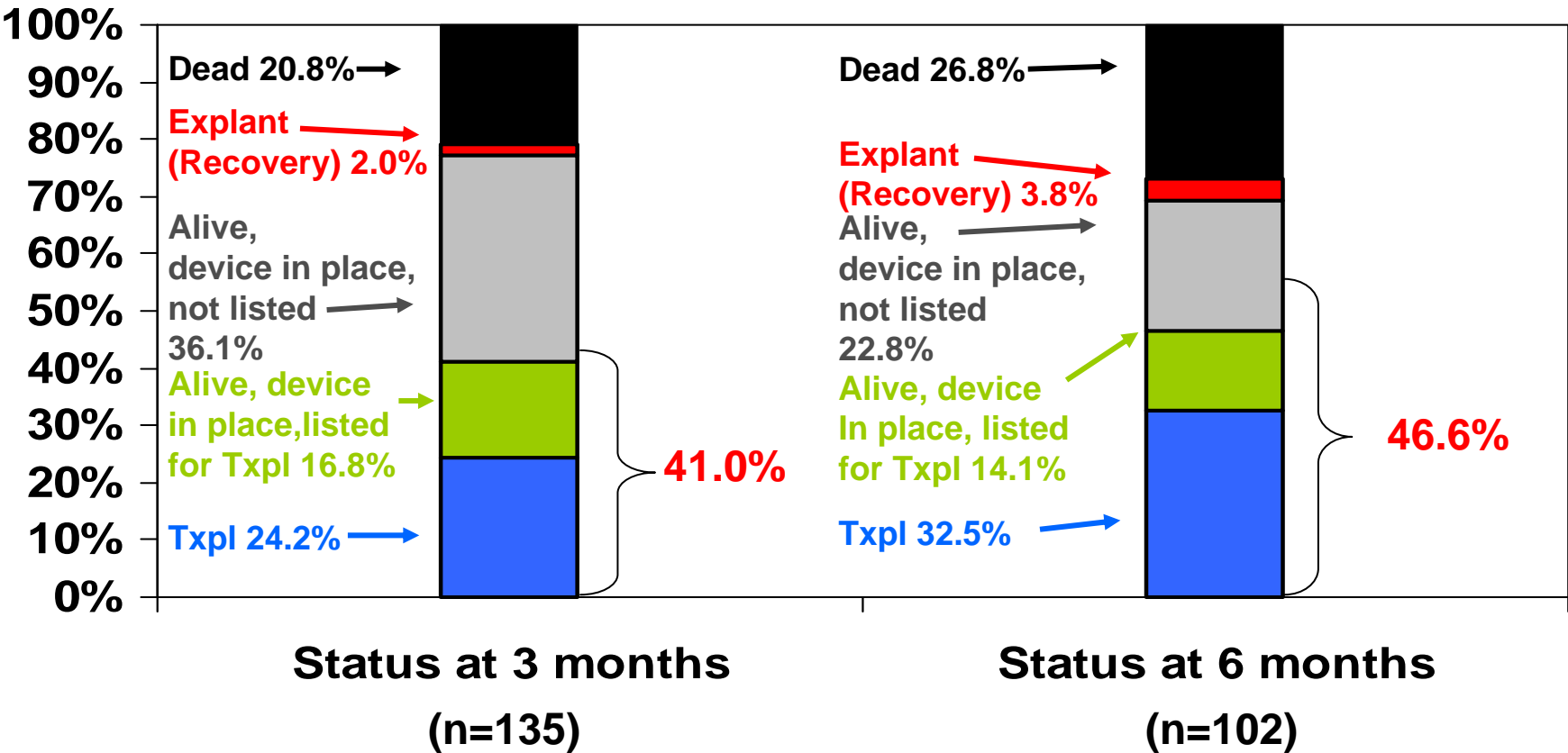
Bridge to Candidacy

INTERMACS**June 2006 – December 2007, n = 420**

Pre-Implant Device Strategy	LVAD	RVAD	BiVAD	TAH	Total
Bridge to Transplant: Listed (BTT)	123	2	35	19	179
Bridge to Candidacy (BTC)	119	0	33	5	157
BTT – Listing Likely	56	0	23	4	83
BTT – Listing Moderately Likely	36	0	8	0	44
BTT – Listing Unlikely	27	0	2	1	30
Destination (DT)	60	0	3	0	63
Bridge to Recovery (BTR)	12	3	6	0	21
Total	314	5	77	24	420

INTERMACS Implant Dates: Jun 23, 2006 – Dec 30, 2007

Bridge to Candidacy (BTC) patients at implant:
Status at 3 and 6 months post implant (n=157)

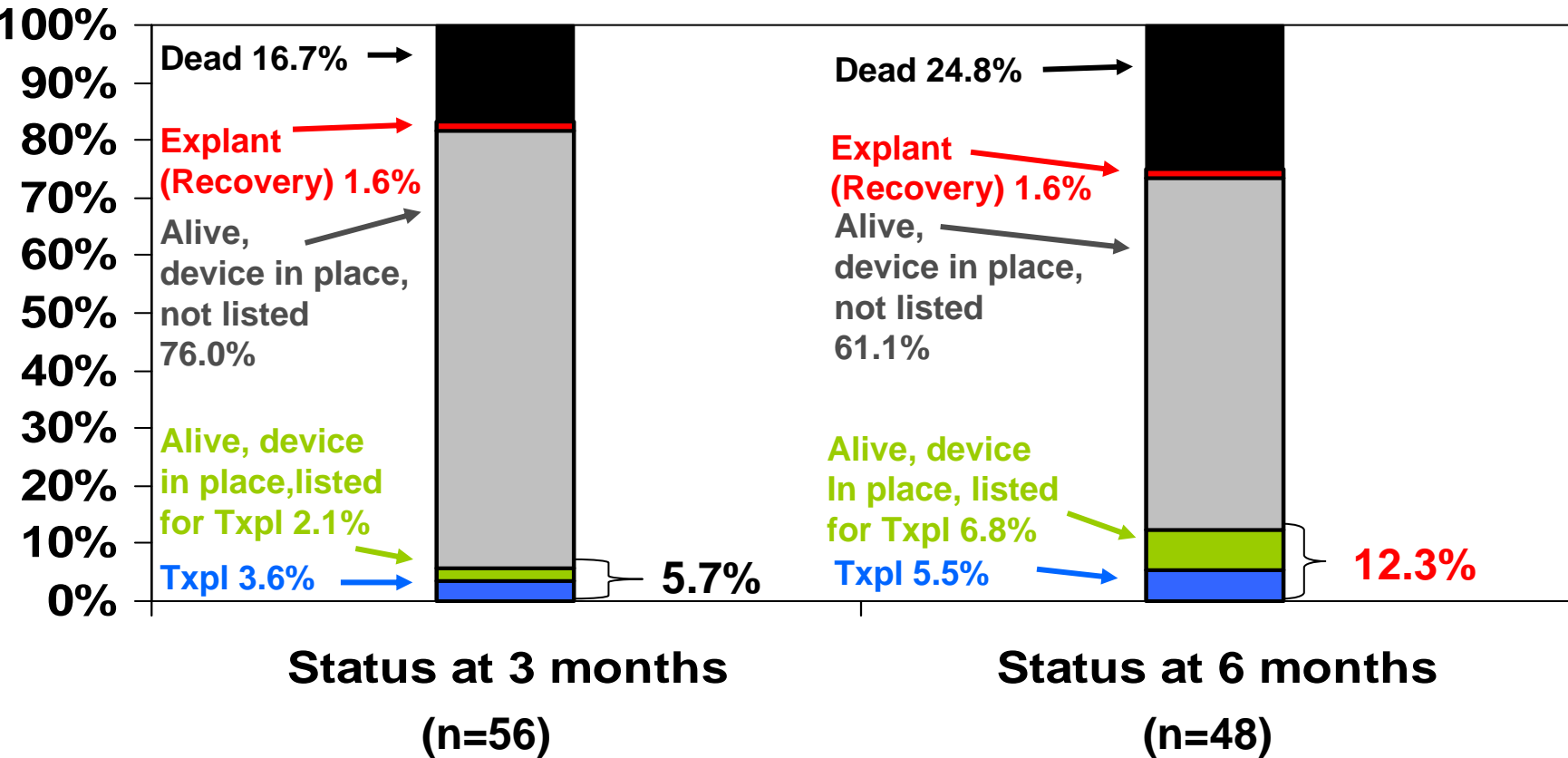


Bridge to Candidacy at Time of Implant

Contraindication	<u>Pre-Implant</u> n=157		<u>3 Months</u> n=61		<u>6 Months</u> n=27	
	n	%	n	%	n	%
None	35	22%	7	11%	0	0%
Large BMI	20	13%	9	15%	6	22%
Renal dysfunction	16	10%	1	0%	1	4%
Still smoking	14	9%	2	3%	1	4%
Frailty	12	8%	9	15%	0	0%
Limited social support	12	8%	4	7%	1	4%
Pulmonary hypertension	11	7%	4	7%	0	0%
Illicit drug use	7	4%	3	5%	0	0%
Alcohol abuse	7	4%	1	2%	0	0%
Pulmonary disease	7	4%	1	2%	0	0%

INTERMACS Implant Dates: Jun 23, 2006 – Dec 30, 2007

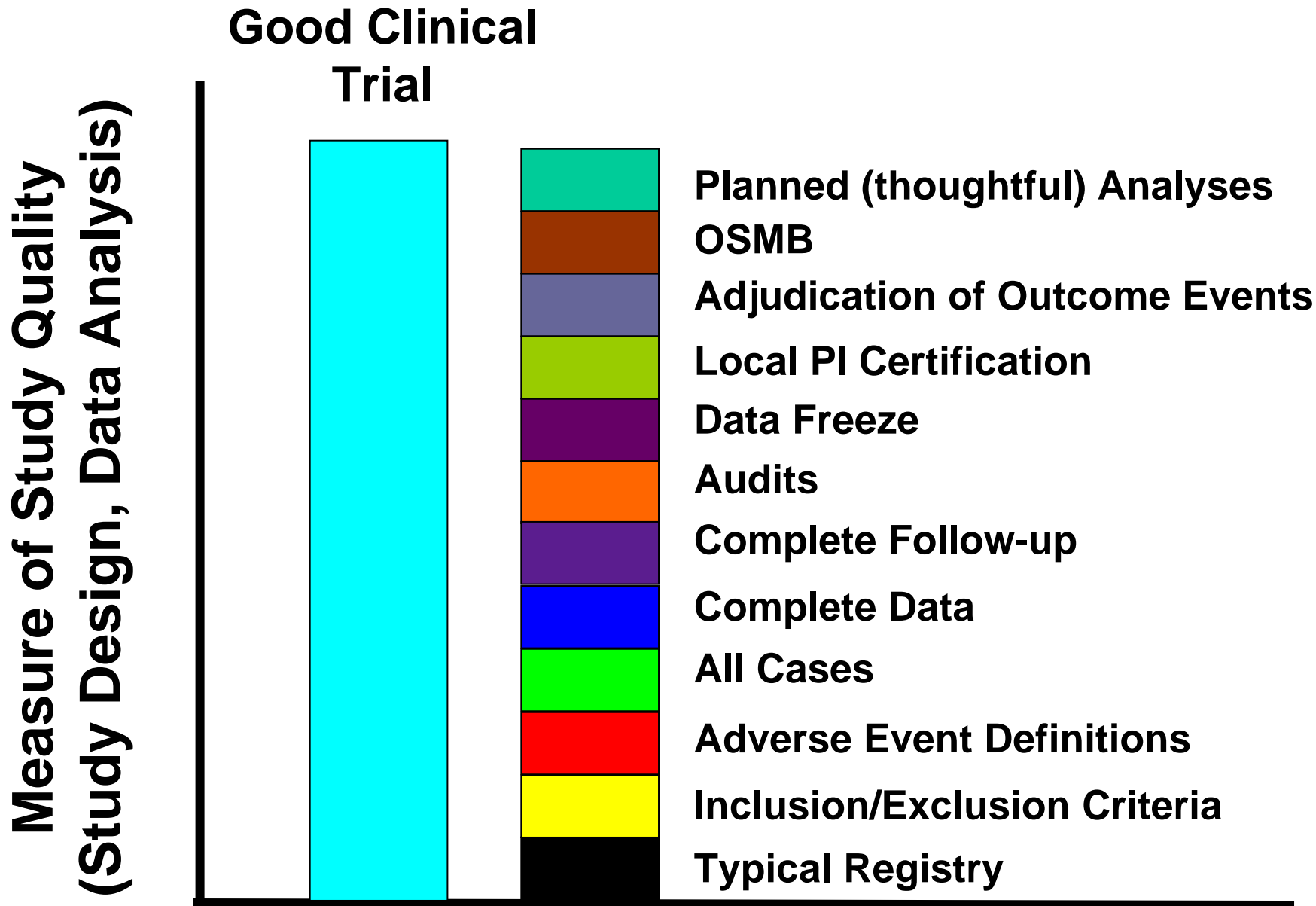
Destination patients at implant:
Status at 3 and 6 months post implant (n=63)



Adverse Events

June 2006 – December 2007, n = 420

Adverse Event	≤ 30 days (pt)	> 30 days (pt)	Episodes (Pts)
Device Malfunction	15 (12)	52 (42)	67 (53)
Bleeding	227 (114)	156 (64)	383 (146)
Cardiac/Vascular			
Right Heart Failure	21 (21)	6 (5)	27 (25)
Myocardial Infarction	1 (1)	0	1 (1)
Cardiac Arrhythmia	92 (62)	35 (22)	127 (77)
Pericardial Drainage	36 (31)	4 (3)	40 (34)
Hypertension	29 (28)	61 (41)	90 (66)
Arterial Non-CNS Thromb	9 (7)	5 (5)	14 (12)
Venous Thromb Event	16 (14)	7 (6)	23 (18)
Hemolysis	8 (7)	14 (11)	22 (17)
Infection	161 (100)	194 (107)	355(160)
Neurological Dysfunction	61 (51)	39 (33)	100(77)
Renal Dysfunction	65 (54)	13 (12)	78 (64)
Hepatic Dysfunction	31 (27)	24 (18)	55 (41)
Respiratory Failure	93 (74)	17 (14)	110 (84)
Other			
Wound Dehiscence	2 (2)	4 (4)	6 (6)
Psychiatric Episode	14 (14)	37 (28)	51 (38)
Other AEs	89 (60)	151 (90)	240 (136)
Total AEs (prospective)	970	819	1789



Concluding Remarks

- Overall survival after isolated left ventricular support currently exceeds 70% at 1 year.
- Risk factors for death relate strongly to very advanced age, shock-like states at implant, and right ventricular dysfunction severe enough to require biventricular support.
- The strategy designations BTT, BTC, and DT have no discernible effect on survival and frequently change within the first 6 months

Future Directions

- **INTERMACS is poised to combine its experience with the emerging ISHLT Mechanical Support Registry and other databases that can advance the application of this vital therapy.**
- **The rigor of this database provides a major opportunity to provide OPC and concurrent controls for new device trials.**

Adverse Events

Psychiatric
Episode

Neurological
Dysfunction

Major Infection

Right Heart
Failure

Device Malfunction

Myocardial Infarction

Respiratory Failure

Renal Dysfunction

Arterial Non-CNS
Thromboembolism

Cardiac Arrhythmia

Venous Thrombosis

Pericardial Drainage

Wound Dehiscence

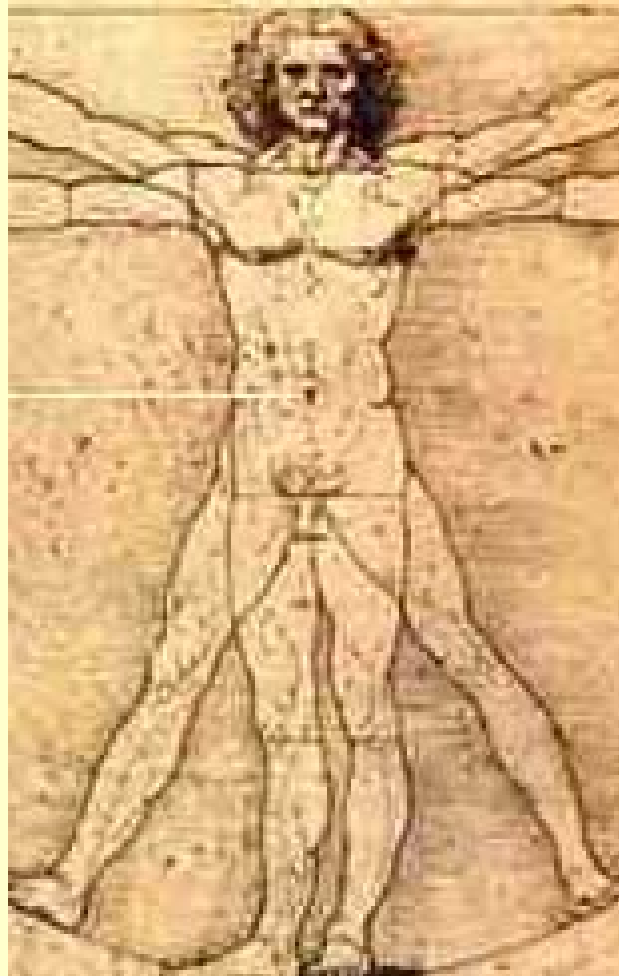
Hypertension

Bleeding

Hemolysis

Hepatic
Dysfunction

Other Major
SAE



Right Heart Failure

Events = 9
Patients=9

Myocardial Infarction

Events = 0
Patients=0

Bleeding

Events =108
Patients= 53

Renal Dysfunction

Events = 31
Patients=27

Cardiac Arrhythmia

Events = 47
Patients=31

Pericardial Drainage

Events = 20
Patients=16

Hypertension

Events = 37
Patients=30

Hemolysis

Events = 7
Patients=3

Hepatic Dysfunction

Events = 21
Patients=15

Psychiatric Episode

Events = 17
Patients=15

Other Major SAE

Events = 67
Patients=46

Major Infection

Events = 127
Patients= 60

Neurological Dysfunction

Events = 54
Patients=35

Device Malfunction

Events = 24
Patients=20

Respiratory Failure

Events = 56
Patients=44

Arterial Non-CNS Thromb

Events = 0
Patients=0

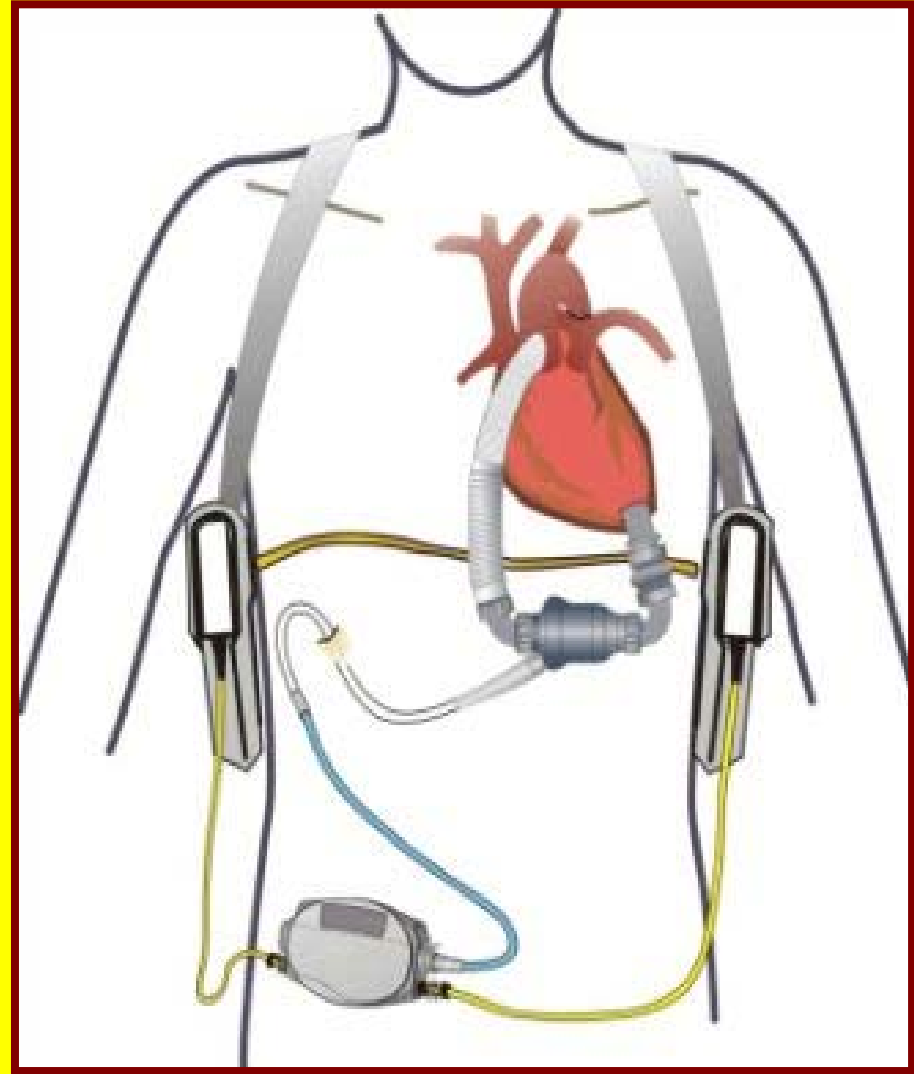
Venous Thrombosis

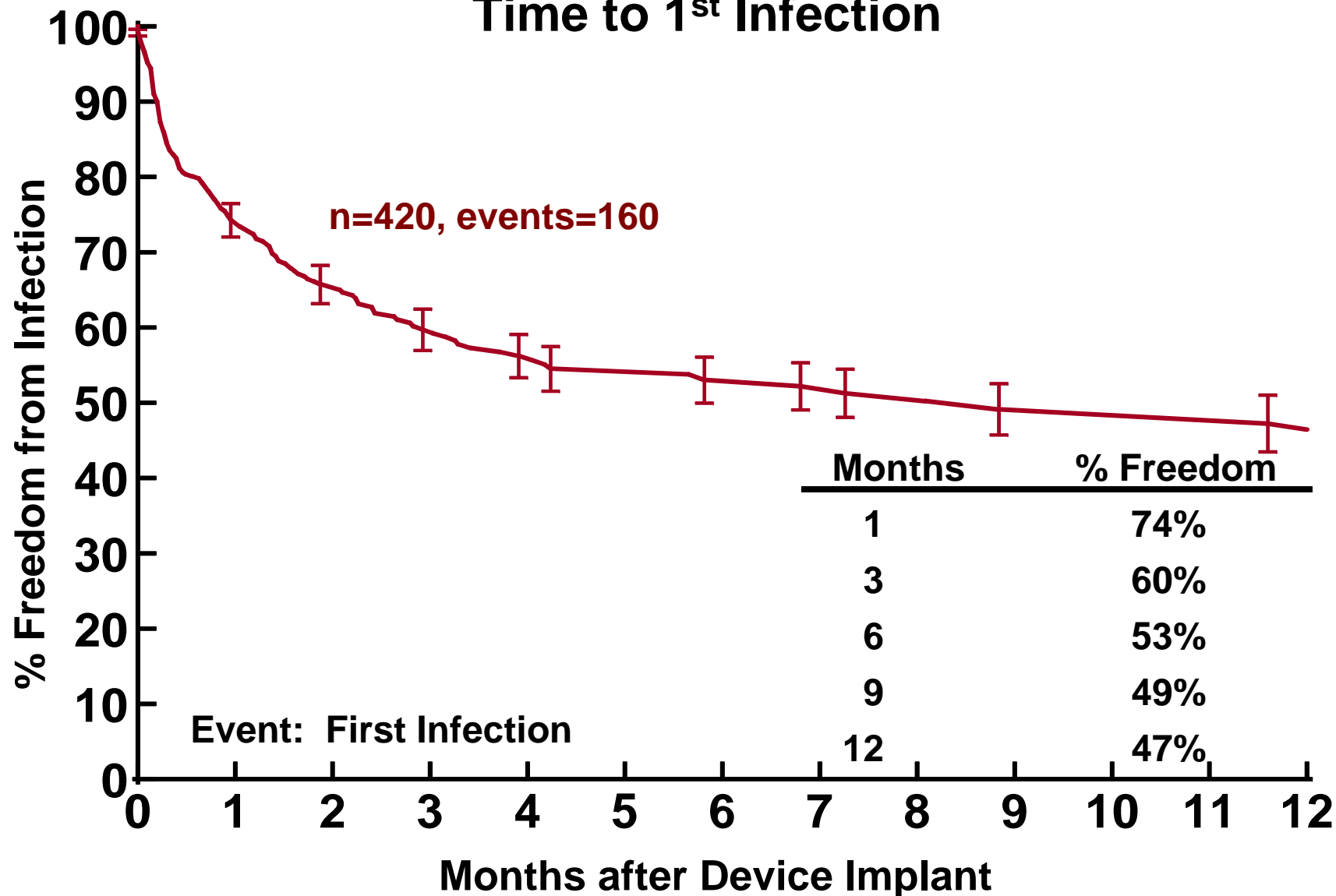
Events = 9
Patients=8

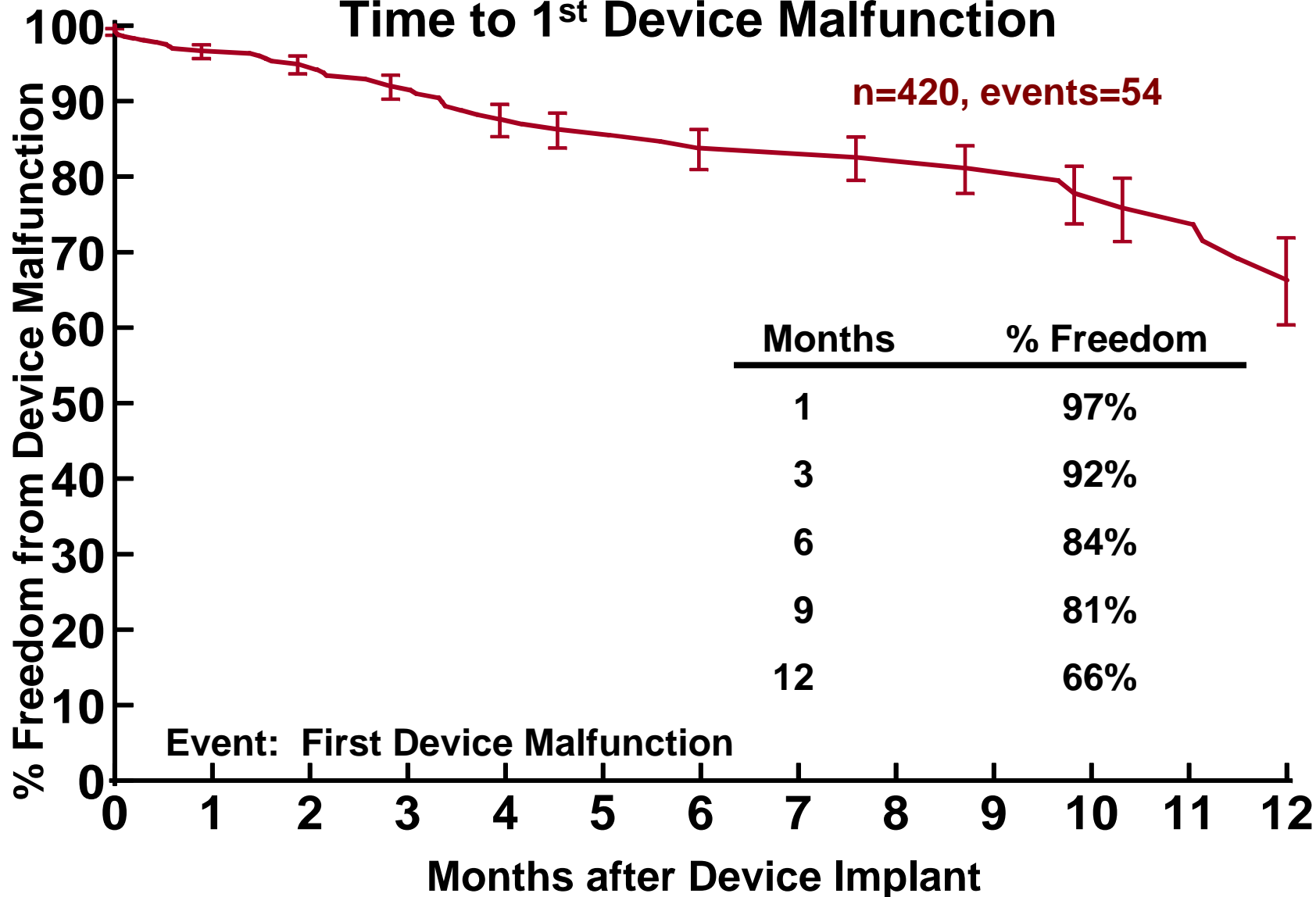
Wound Dehiscence

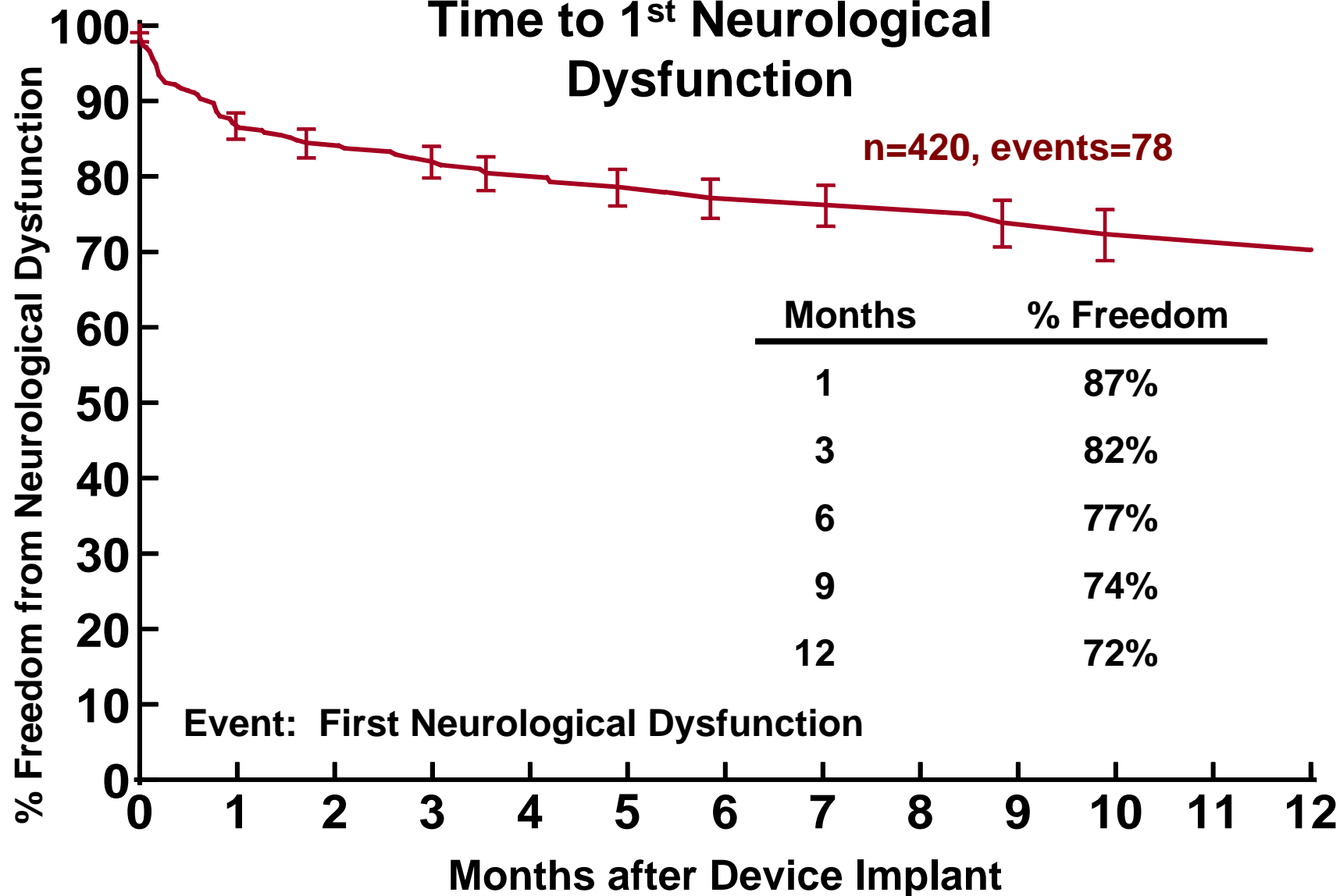
Events = 4
Patients=3

18 Adverse Events



INTERMACS: June 2006 – December 2007**Time to 1st Infection**

INTERMACS: June 2006 – December 2007**Time to 1st Device Malfunction**

INTERMACS: June 2006 – December 2007**Time to 1st Neurological
Dysfunction**

TABLES

Goals of INTERMACS

I believe that Peggy has this table in her manuscript file.

Data Collected	Pre-Implant	Implant	1wk/1mth	Disch	3mth/q 6mth
Demographic	X				
Medical Support Status	X				
Co-morbidities	X				
Hemodynamics	X		X	X	X
Medications	X		X	X	X
Laboratory	X		X	X	X
Medical Condition	X		X		X
Exercise Functions	X				X
Patient Status	X				X
Device Information		X			
Device Details		X			
Device Parameters				X	X
Quality of Life	X				X
Trail Making Test	X				X
Adverse Event Reminders			X	X	X
Chronology of Hospital Time				X	

List of adverse events.

I believe that Peggy has this table in her manuscript file.

INTERMACS**June 2006 – December 2007, n = 420**

Risk Factors	relative risk	p-value
INTERMACS Level 1	1.59	.02
Age(older)*	1.41	< .001
Ascites	2.04	.003
Bilirubin(higher)**	1.49	.05
Bi-VAD implant	2.12	.002
Total Assist Heart implant	2.41	.03

***Compares increased risk from age 50 to 60 years**

****Compares increased risk from bilirubin = 1 to 6(mg/dl)**

Data for ISHLT 2008 Abstracts

Implant Dates: June 23, 2006 – December 31, 2007

Follow-up Date: December 31, 2007

Total Hospitals Enrolled: 89

Hospitals that have contributed data: 75

Total Patients: 511

Retrospective: 91

Prospective: 420

Note: These analyses will only examine the 420 prospective patients

IV. What are the challenges?

- Pre-implant informed consent
- Complete EuroQoL data
- Complete Trail Making data
- Timely entry of data
- Ongoing regulatory compliance
-
-
-

V. What happens next with the data?

- More extensive hospital reports
- Focus on adverse events
- Serve as control data for pre-market studies
- Provide basis for calculation of Objective Performance Criteria (OPCs) for pre-market studies

Risk Factors for death	relative risk	p-value
INTERMACS Level 1	1.59	.02
Age(older)*	1.41	< .001
Ascites	2.04	.003
Bilirubin(higher)**	1.49	.05
Bi-VAD implant	2.12	.002
Total Assist Heart implant	2.41	.03

***Compares increased risk from age 50 to 60 years**

****Compares increased risk from bilirubin = 1 to 6(mg/dl)**

MCS Scientific Issues best answered with a rigorous database

- What are the real patient-specific risk factors for death after implantation of axial flow vs centrifugal flow vs volume displacement pumps ?
- Which patients (with their unique disease and patient risk factors) are better suited for MCS therapy than medical therapy or transplantation?
- When (what are the specific clinical predictors) is right ventricular dysfunction severe enough that isolated LVAD support is ill-advised?

MCS Scientific Issues best answered with a rigorous database

- Using simple but uniformly applied QOL tools, for which patients does chronic MCS therapy offer a better quality of life than heart transplantation for for a specified time interval?
- For which patient subsets does the total artificial heart provide the best quality and duration of survival?
- What are the optimal monitoring and management strategies that minimize thromboembolic complications during MCS therapy?

Critical Outcome Indicators in the Evaluation of MCS Therapy

- **Death**
- **Device failure**
- **Occurrence of other strictly defined adverse events**
- **Impact on quality of life**

**The fundamental question,
then, is “do we want an
international database?”**

**The Pace of Progress in the
Application of Mechanical
Circulatory Support will be
Enhanced and Energized by a
Quality International Database:
Is it worth the Effort?**

Data Access, Analysis & Publications

Chair: F Pagani
 Members: L Edwards & M Parides
 D Naftel & X. Tian
 D. Farrar & J. Rogers
 E Blume
 OC Rep: M Miller
 DCC Rep: C Collum & S Myers

Adverse Events & Adjudication

Chair: R Kormos & W Holman
 Members: D Ascheim & M Acker
 M Jessup & J Teuteberg
 F Pagani & K Aaronson
 M Camacho & C Milano
 V Jeevanandam
 OC Rep: R Kormos
 DCC Rep: C Collum & S Myers

Pediatrics

Chair: E Blume
 Members: R Jaquiss & B Duncan
 J Chen & B Kaufman
 D Rosenthal & S Webber
 D Morales & E Devaney
 OC Rep: J Kirklin
 DCC Rep: ML Clark & C Collum

Industry Relations & Device Development

Chair: J Watson
 Members: O.H. Frazier & R Bostic
 H Zintak & J Antaki & E
 Rose & Industry Reps*
 OC Rep: T Baldwin
 DCC Rep: J Kirklin & C Collum

Focused Research & Mission Activities

Chair: S Koenig & M Jessup
 Members: K Grady & A Moskowitz
 L Miller & R Starling
 D McNamara & J Antaki
 P Nickens
 OC Rep: C Collum & ML Clark
 DCC Rep:

Coordinators Council

Chair: T Cleeton & K Chisholm
 T Martin & S Wissman
 Members: P Blood & DeeDee Epstein
 M Massey & L Stevenson
 OC Rep: K Ulisney
 DCC Rep: C Collum & ML Clark

Hospital Training and Standards

Chair: J Long
 Members: T. Martin
 OC Reps: J Young
 DCC Rep: K Philibin & M Massey
 D Naftel & ML Clark
 C Collum

International

Chair: R. Kormos
 Members: E Chen
 OC Rep: L Stevenson & J Kirklin
 DCC Rep: C Collum

Is this the figure you wanted? Or the one on the next page?

Figures

INTERMACS: What Have We Learned So Far?

- I. What have we learned from the process of creating and maintaining INTERMACS?
- II. What have we learned about hospital and patient enrollment?
- III. What have we learned from the data about MCSD patients and their outcomes?
- IV. What are the challenges?
- V. What happens next with the data?

Goals of the Registry

- **Facilitate the refinement of patient selection to *maximize outcomes* with current and new device options.**
- **Identify predictors of good outcomes as well as risk factors for adverse events after device implantation.**
- **Develop consensus “*best practice*” guidelines to improve clinical management by reducing short and long term complications of MCSD therapy.**
- **Utilize Registry information to guide improvements in technology, particularly as next generation devices evolve.**
- **Guide clinical testing and approval of new devices.**

INTERMACS Goals

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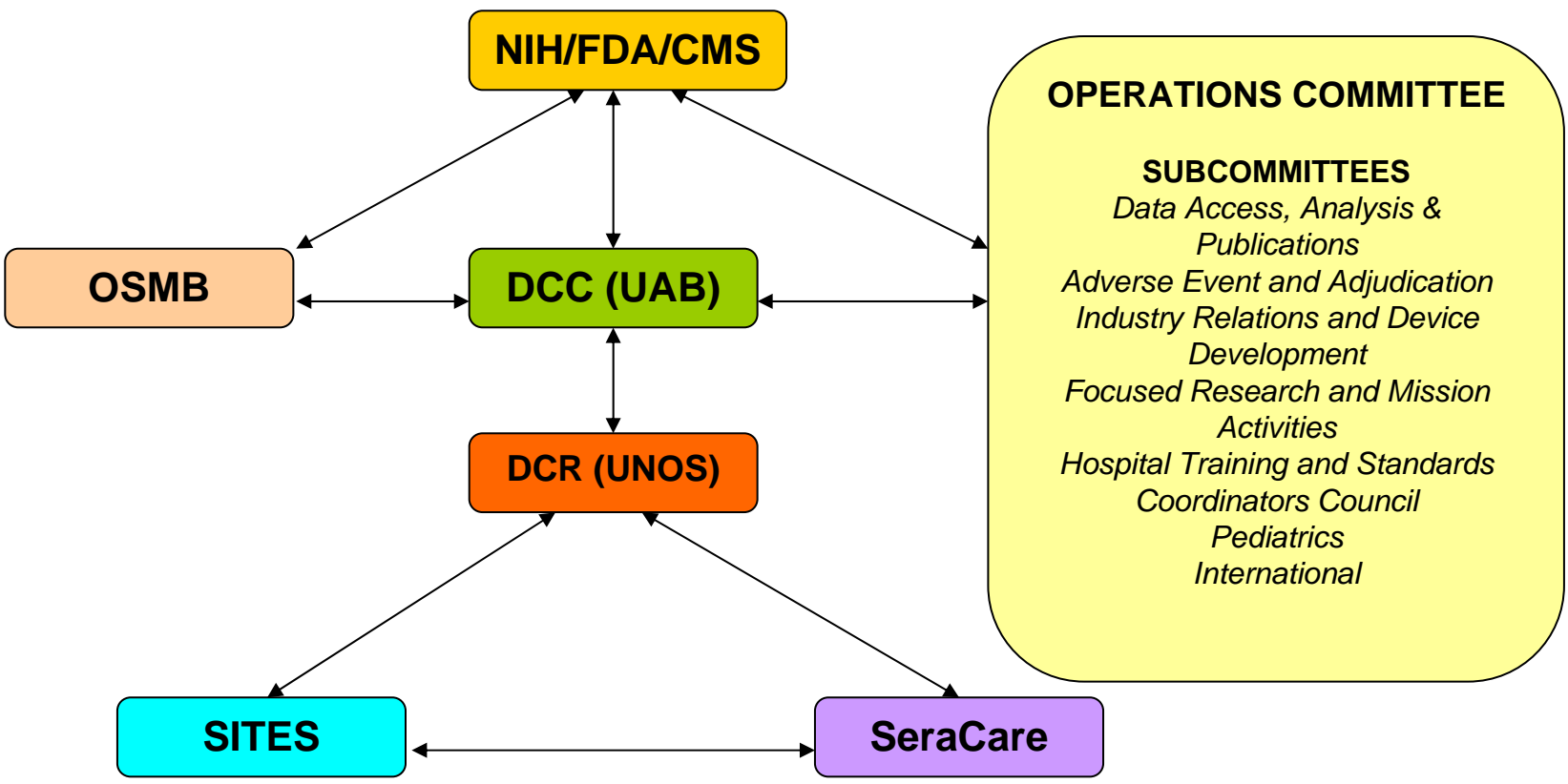
INTERMACS Goals

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INTERMACS Goals

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- Develop consensus “best practice” guidelines to improve clinical management by reducing short and long term complications of MCSD therapy.
- Guide clinical use and evolution of next generation devices.
- **Utilize Registry information to guide improvements in technology, particularly as next generation devices evolve.**

INTERMACS Organizational Chart



NIH - National Institutes of Health
CMS - Center for Medicare and Medicaid Services
DCC - Data and Clinical Coordinating Center
UNOS - United Network for Organ Sharing
SeraCare - Blood and Tissue Repository

FDA - Food and Drug Administration
OSMB - Observational Safety Monitoring Board
UAB - University of Alabama at Birmingham
DCR - Data Collection Repository

INTERMACS**June 2006 – December 2007, n = 420****INTERMACS LEVEL*****(Pre-Implant)***

	BTR	BTT	BTC	DT	Total
1. Critical Cardiogenic Shock	17	68	84	17	186
2. Progressive Decline	1	74	51	22	148
3. Stable but Inotrope Dep.	1	15	10	9	35
4. Recurrent Advanced HF	2	15	8	8	33
5. Exertion Intolerant	0	3	1	1	5
6. Exertion Limited	0	1	2	3	6
7. Advanced NYHA Class III	0	3	1	3	7
Total	21	179	157	63	420

INTERMACS Devices

- FDA approved durable mechanical circulatory support devices (MCSD)
- Devices approved as of March 1, 2008

AbioCor TAH

HeartMate IP

HeartMate VE

HeartMate XVE

MicroMed DeBakey

VAD-Child

Novacor PC

Novacor PCq

SynCardia CardioWest

Thoratec IVAD

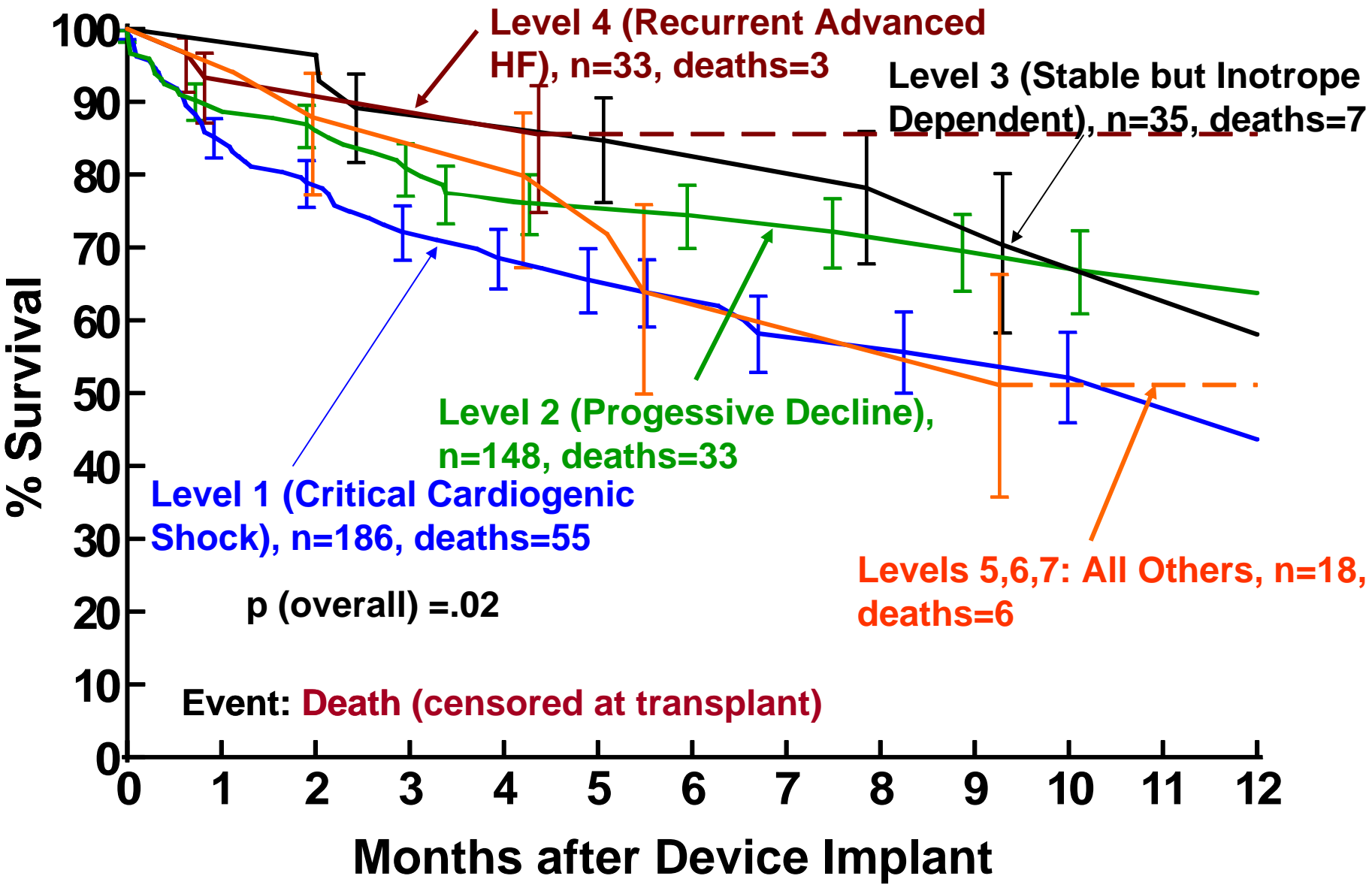
Thoratec PVAD

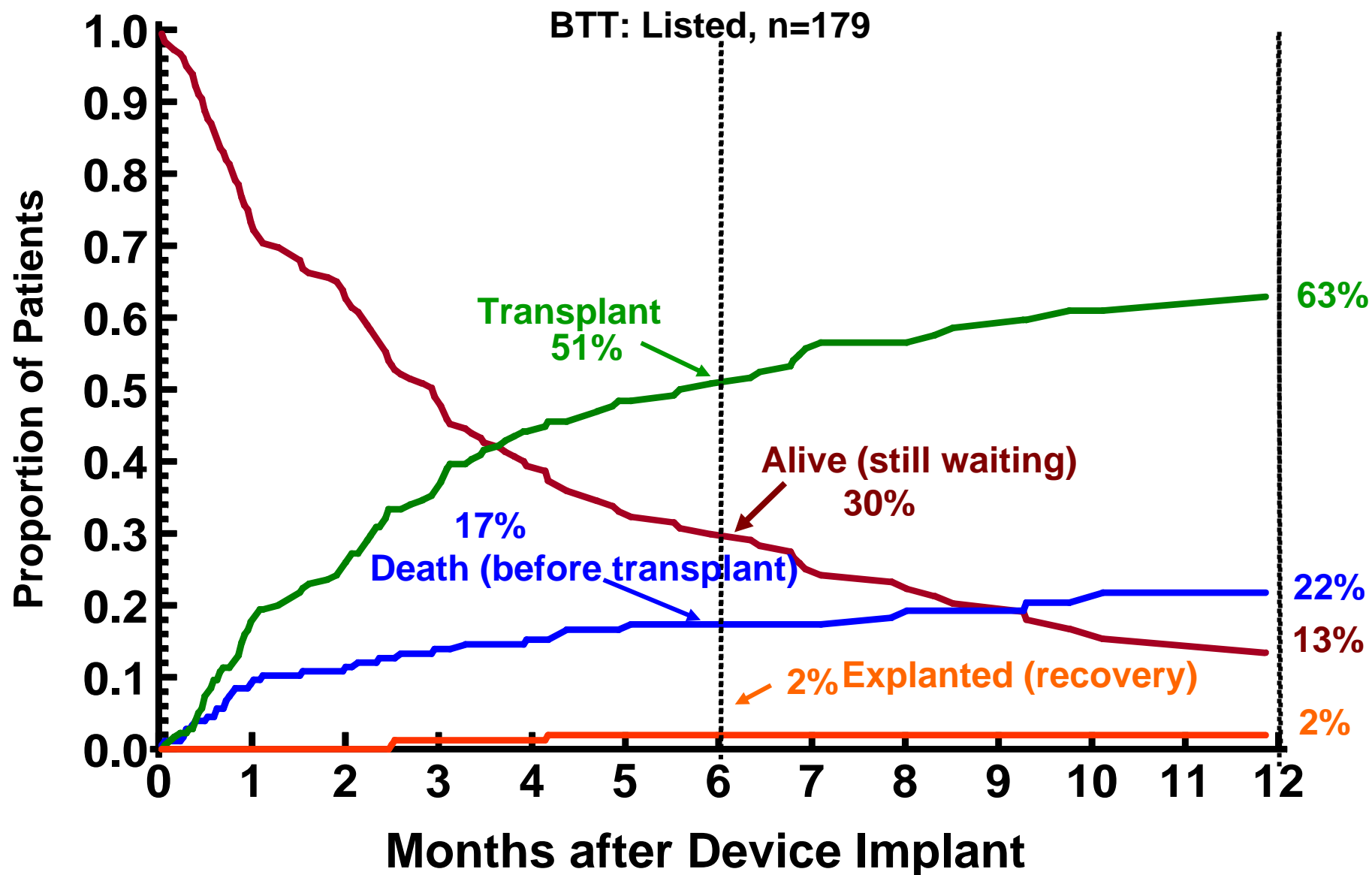
INTERMACS**June 2006 – December 2007, n = 420, deaths=104**

Primary Cause of Death	Early (≤ 1 mo)		Later (> 1 mo)		Total	
	n	% of 42	n	% of 62	n	% of 104
CNS Event	6	14.3%	13	21.0%	19	18.3%
Multi-Organ Failure	8	19.0%	9	14.5%	17	16.4%
Cardiac Failure*	10	23.8%	6	9.7%	16	15.4%
Infection	1	2.4%	7	11.3%	8	7.7%
Respiratory Failure	3	7.1%	5	8.1%	8	7.7%
Device Failure	1	2.4%	4	6.5%	5	4.8%
Hepatic Failure	4	9.5%	0	0%	4	3.8%
Pulmonary Embolism	2	4.8%	1	1.6%	3	2.9%
Surgical Bleeding	1	2.4%	2	3.2%	3	2.9%
GI Bleed	0	0%	2	3.2%	2	1.9%
Renal Failure	1	2.4%	1	1.6%	2	1.9%
Other	5	11.9%	12	19.4%	17	16.4%
Total	42	100.0%	62	100.0%	104	100.0%

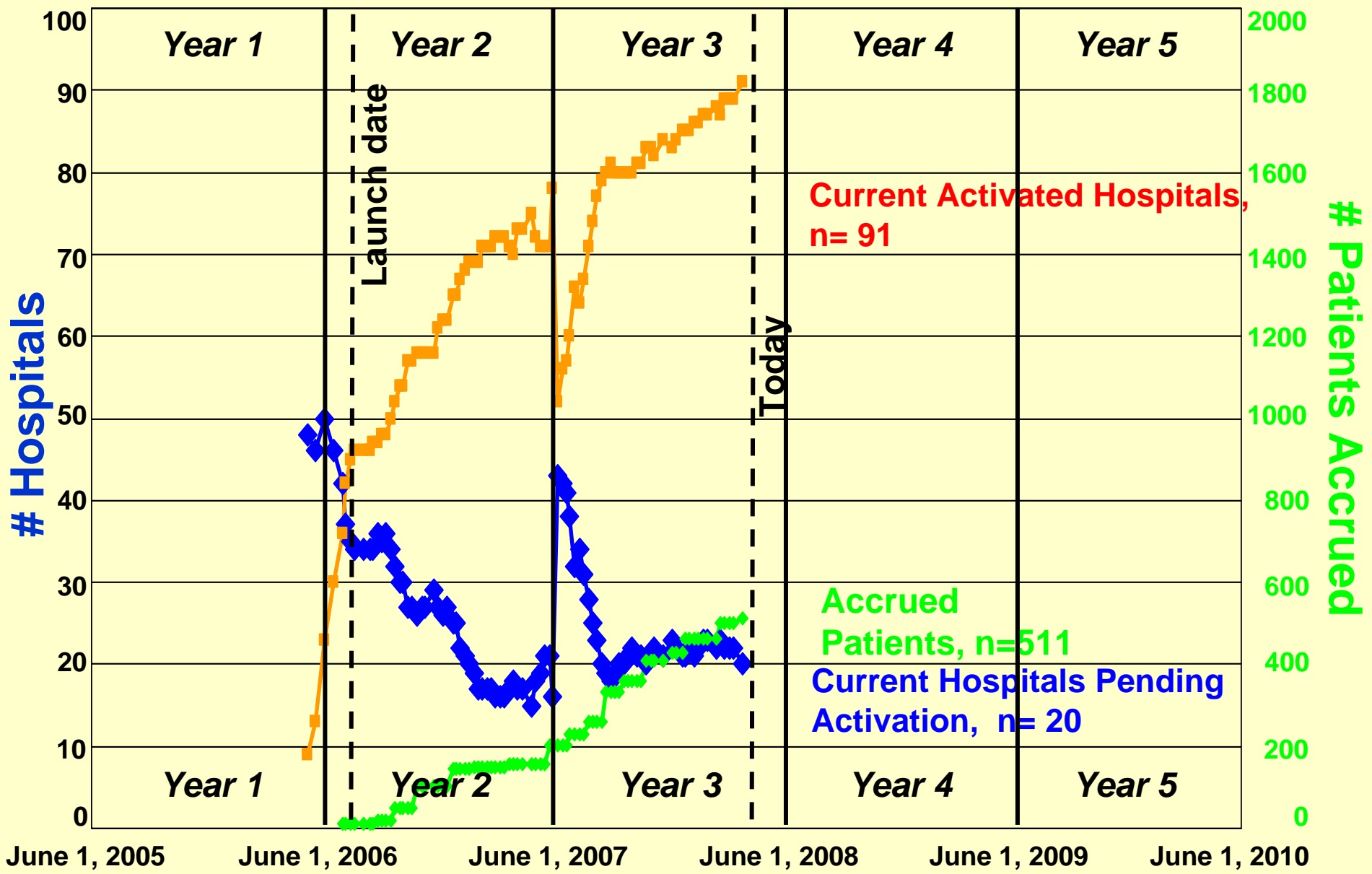
*Cardiac Failure includes RV Failure and VT/VF

INTERMACS: June 2006 – December 2007



INTERMACS: June 2006 – December 2007

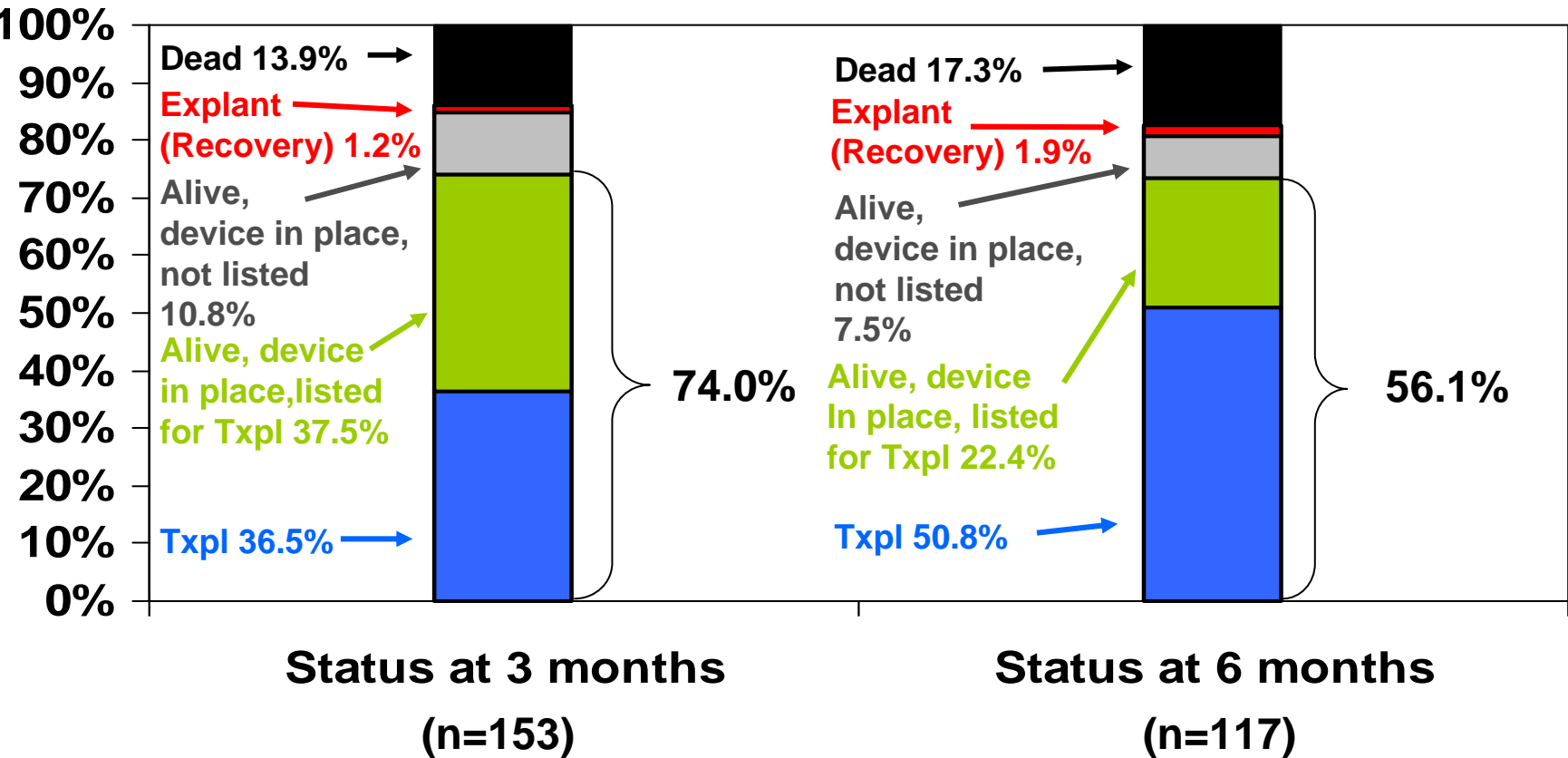
Hospital Enrollment and Patient Summary: Mar 31, 2008



SURVIVAL

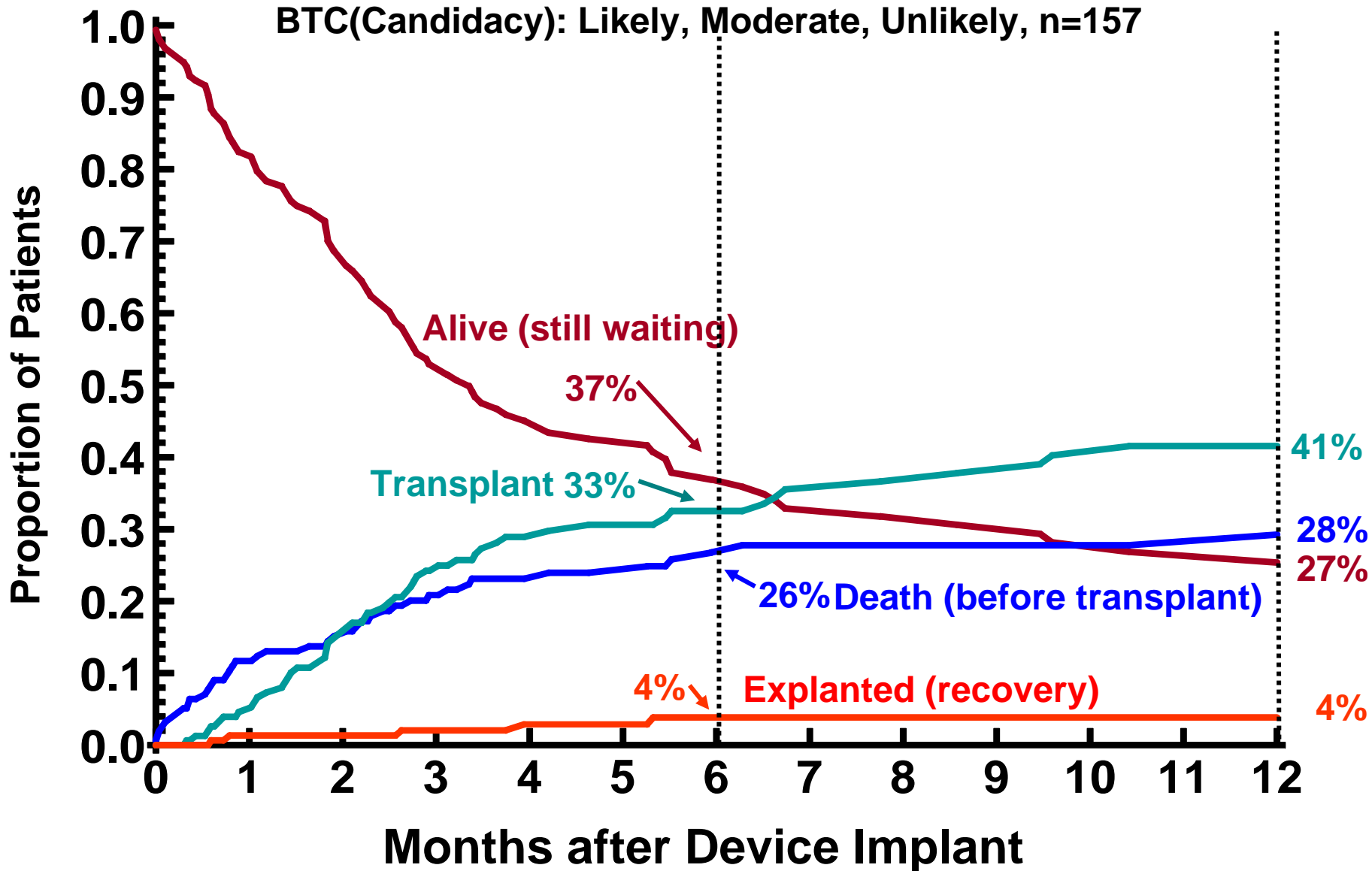
INTERMACS Implant Dates: Jun 23, 2006 – Dec 30, 2007

Bridge to Transplant: Currently Listed (BTT) patients at implant: Status at 3 and 6 months post implant (n=179)



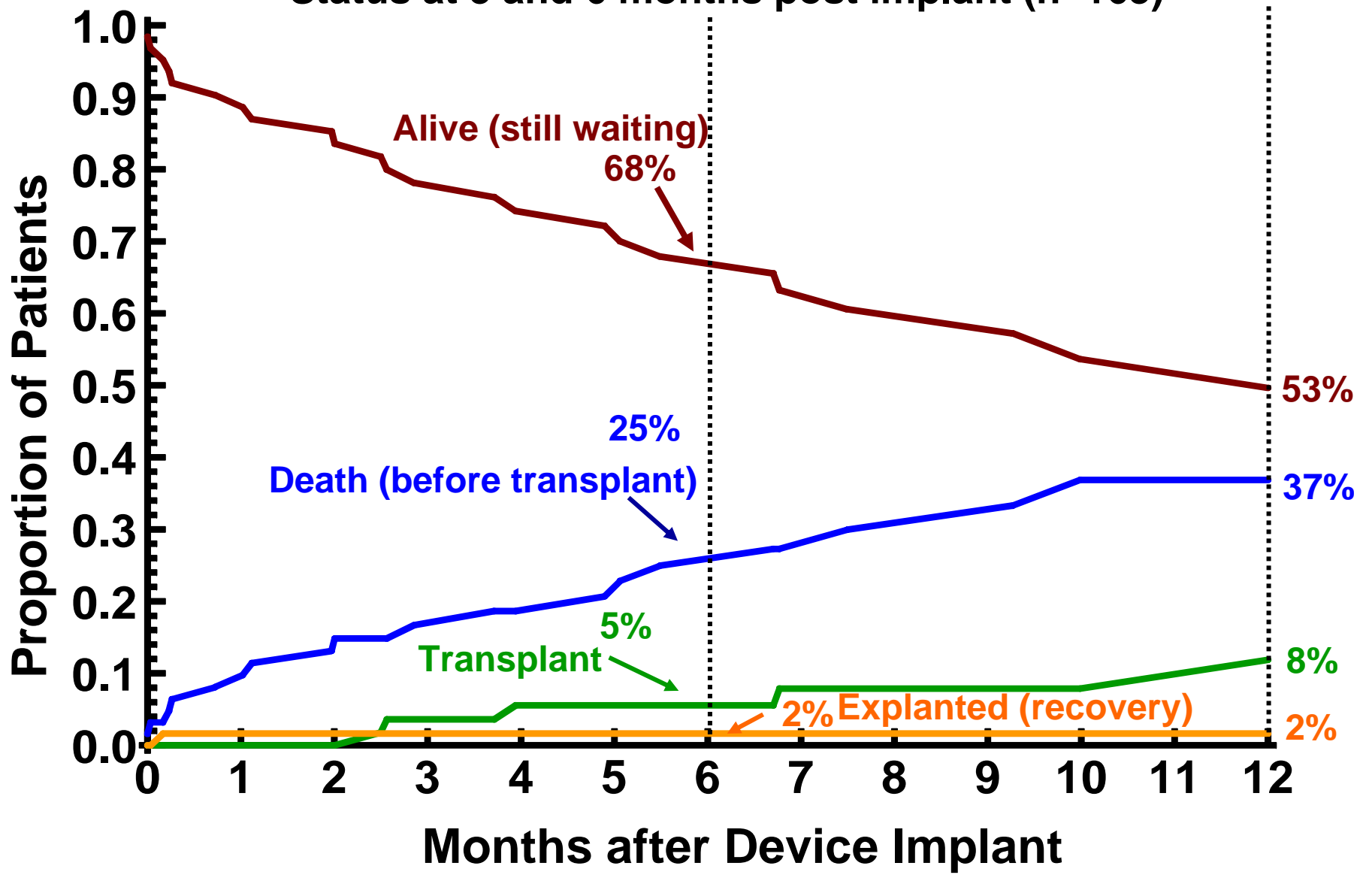
INTERMACS: June 2006 – December 2007

BTC(Candidacy): Likely, Moderate, Unlikely, n=157



INTERMACS Implant Dates: Jun 23, 2006 – Dec 30, 2007

Destination patients at implant:
Status at 3 and 6 months post implant (n=163)



INTERMACS: June 2006 – December 2007**Time to 1st Bleeding**