

**ADVANCES IN CARDIAC
ARRHYTHMIAS
and
GREAT INNOVATIONS
IN CARDIOLOGY**

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Università degli Studi di Torino



Azienda Ospedaliera
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della Scienza di Torino

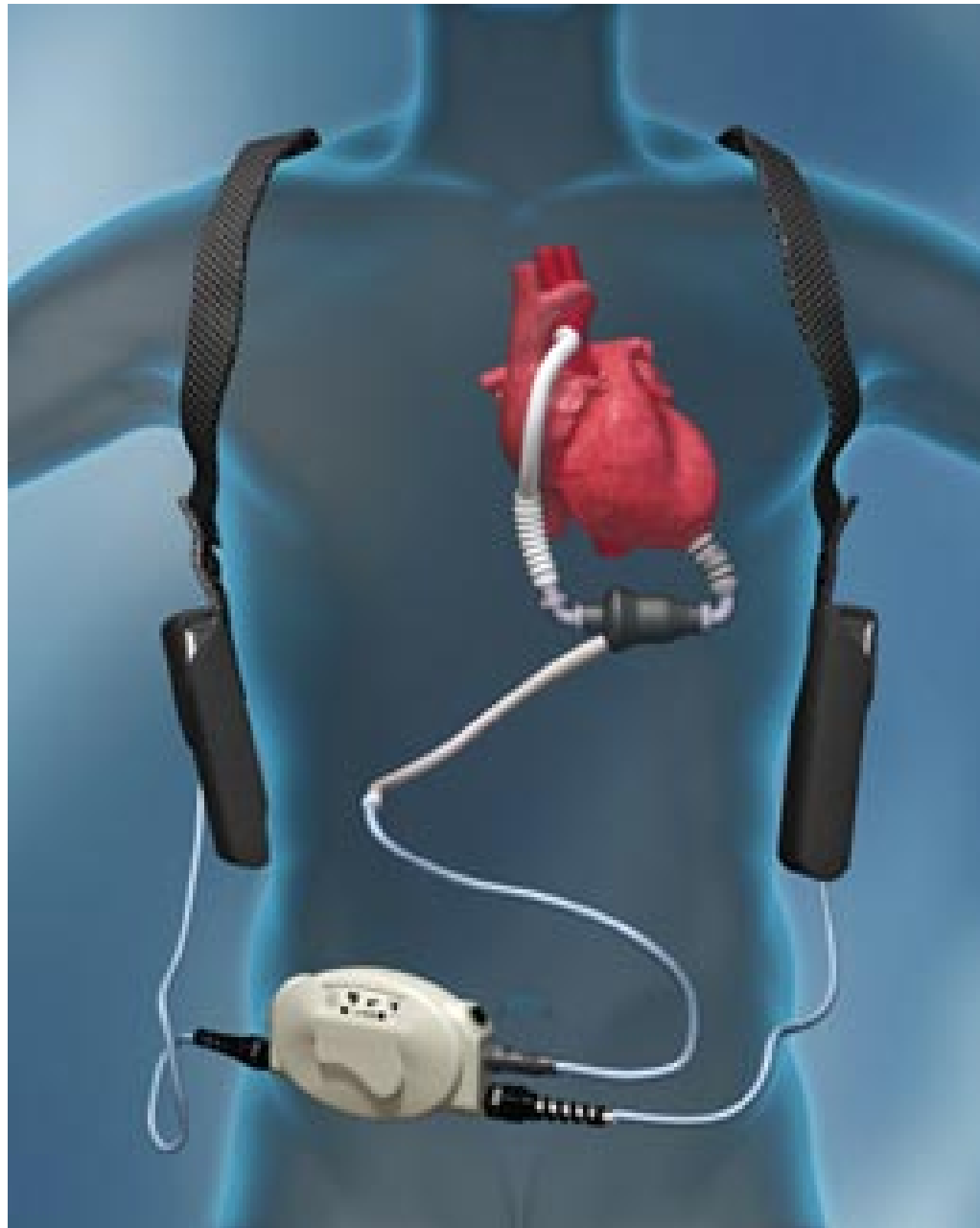


When to implant VAD in patients with heart transplantation indication

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LVAD strategies

	In waiting list?	Goal
Bridge to transplant	Yes	To keep pts alive up to HTx
Bridge to candidacy	Not yet	To treat high PVR
Bridge to decision	Unknown	To keep pts alive for evaluation
Destination therapy	No	Definitive therapy
Bridge to recovery	Not yet	To allow myocardial recovery

LVAD strategies

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LVAD: evolution of technology & indications

1990

Refractory cardiogenic shock

End-organ injury recovery

**Short term
paracorporeal VAD
(days-weeks)**

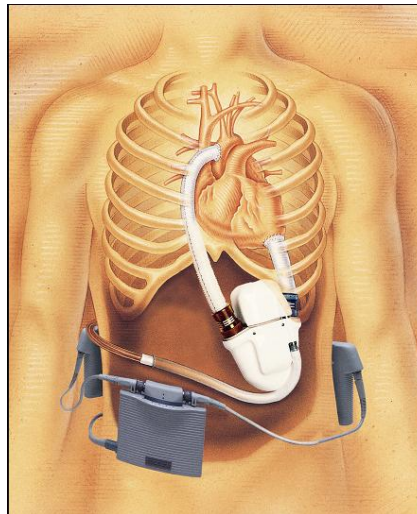


2000

Impending cardiogenic shock

Prevention of end-organ injury

**Medium term intracorporeal
VAD(months)**



Elective implant

Treatment of high PVR

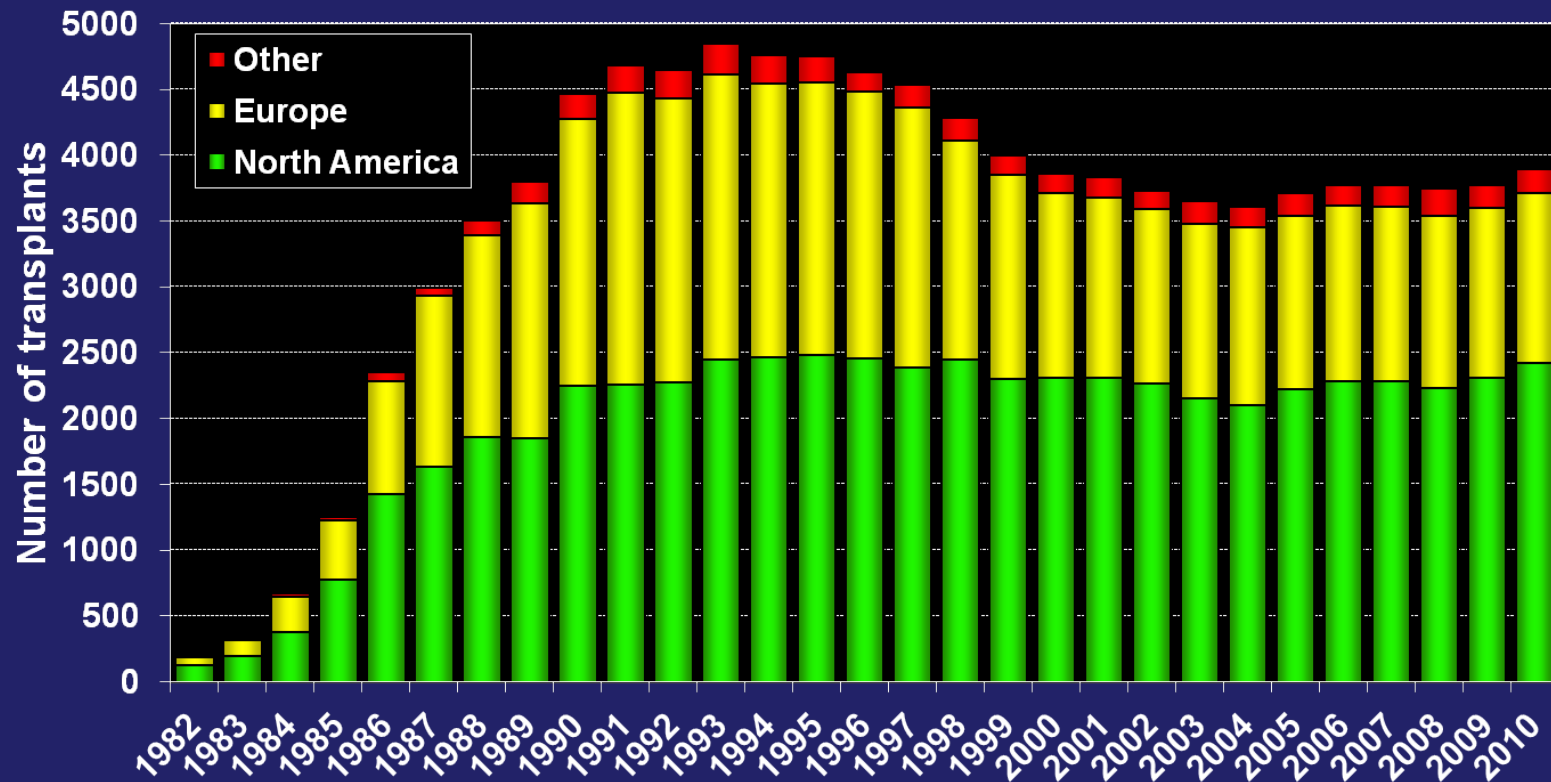
**Long term intracorporeal
VAD (years)**



**Why
BTT?**

Heart transplant: a scarce resource

NUMBER OF HEART TRANSPLANTS BY YEAR AND LOCATION



ISHLT

2012

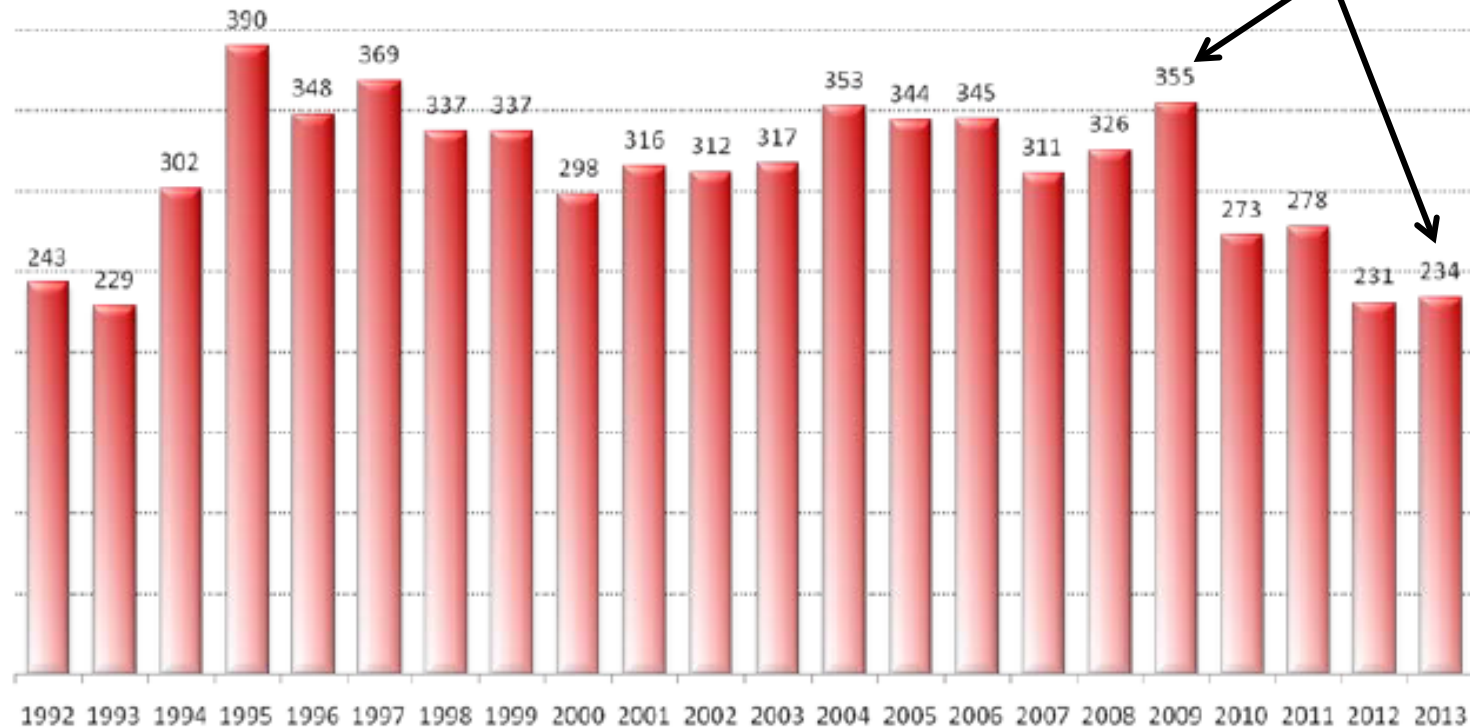
J Heart Lung Transplant. 2012 Oct; 31(10): 1045-1095



HTx in Italy: an even scarcer resource



Mortality in
waiting list: $\cong 10\%$



Uncertainty & competing risks

**Risk of
deterioration**

**Risks during
support**

**Chance
to find a donor**



**Risks of
implantation**

**Quality
of donor**

**Risks
of HTx**



Who?

Contraindications to LVAD

Ineligible for LVAD

- Right ventricular failure (CVP/PCWP ratio > 0.63)
- Hypertrophic/restrictive cardiomyopathy
- Very small BSA ($< 1,5 \text{ m}^2$)
- Moderate or severe aortic regurgitation
- Mechanical valve prosthesis
- Contraindications to chronic multiple antithrombotic therapy
- Patient refusal of device



Minimal preimplant goals

Parameter	Desired value
Renal	
Blood urea nitrogen	<40 mg/dl
Serum creatinine	<2.5 mg/dl
Estimated GFR	>50 ml/kg/min
Hematology	
INR	<1.2
Hemoglobin	>10 g/dl
Platelets	>150,000/mm
Nutritional	
Pre-albumin	>15 mg/dl
Albumin	>3 g/dl
Transferrin	>250 mg/dl
Hepatic	
Total bilirubin	<2.5 mg/dL
ALT, AST	<2 times normal
Hemodynamic	
Right atrial pressure	<15 mm Hg
PCWP	<24 mm Hg

Longer waiting time in list

Risk factors

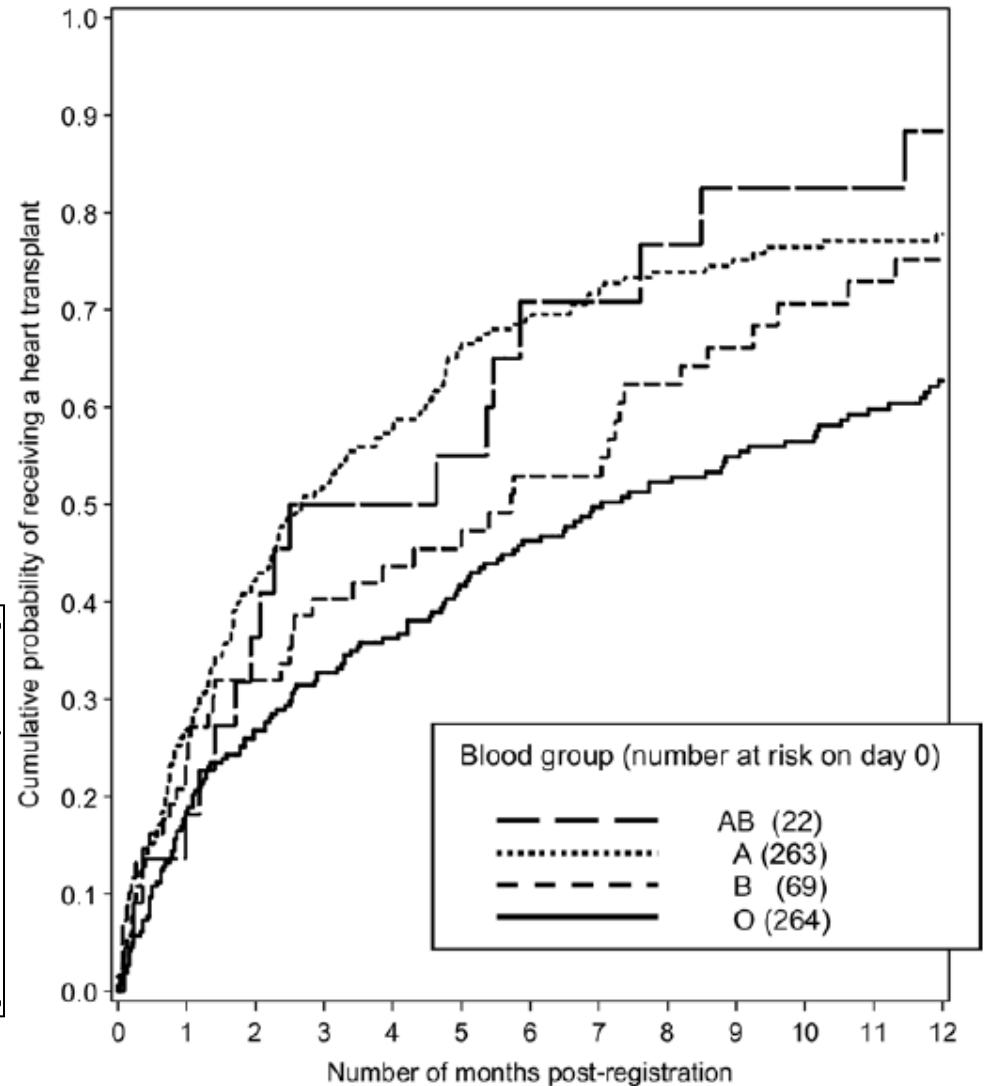
- Group O
- Large body size
- Hyperimmunization
- Pulmonary hypertension (undersized donor undesirable)

Influence of Blood Group on Mortality and Waiting Time Before Heart Transplantation in the United Kingdom: Implications for Equity of Access

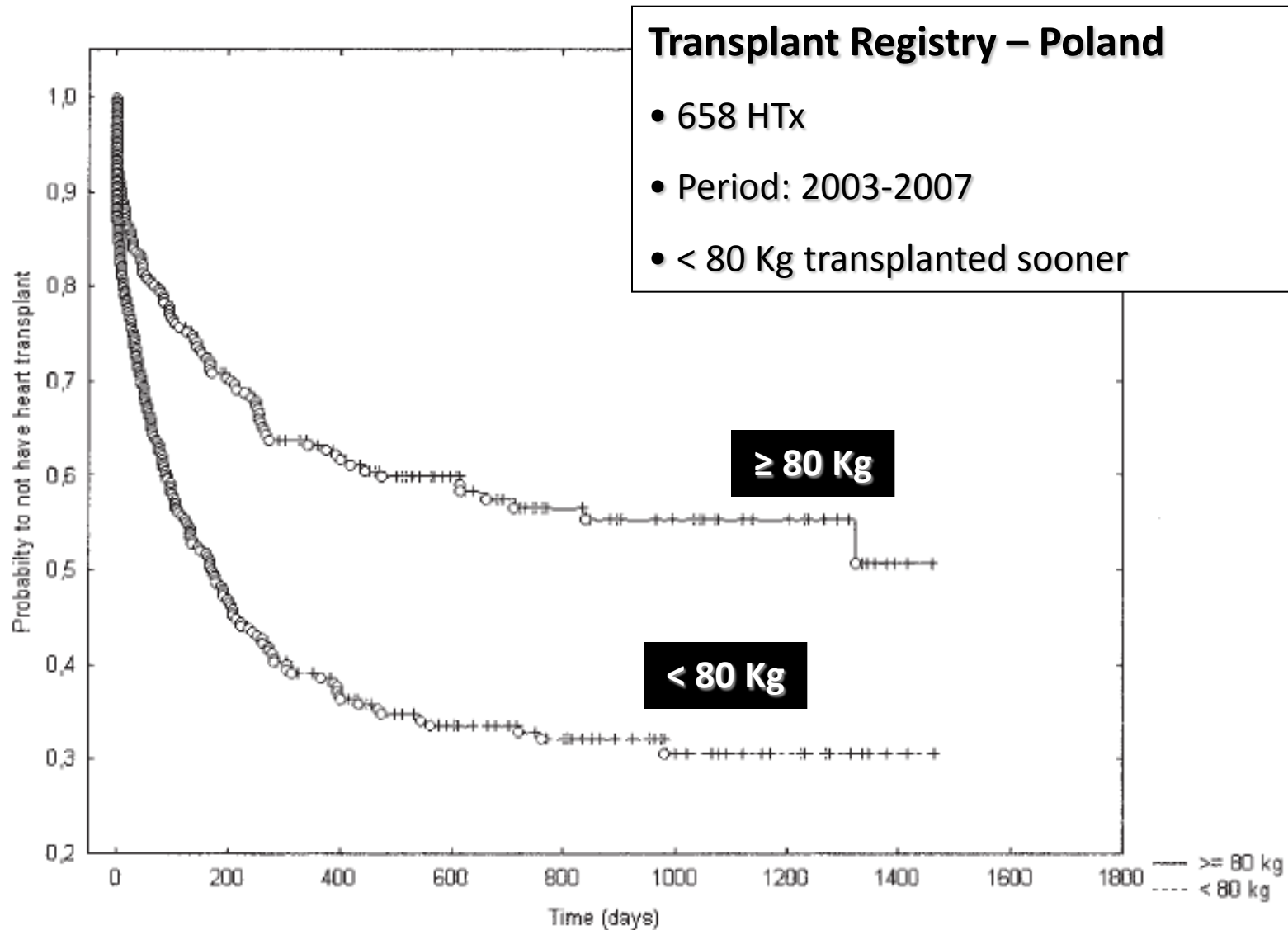
National Transplant Database – UK

- 622 HTx
- Period: 1999-2003
- A and AB transplanted sooner
- No difference in mortality in waiting list between groups

Recipient blood group		Number of registrations	Median waiting time to transplant (days)
O	43%	264	214
A	42%	263	81
B	11%	69	174
AB	4%	22	76
Total		618	143



Recipient weight and chance of HTx



J.A. Yang,¹ Y. Naka,¹ T. Ota,¹ R.C. Neely,¹ N. Uriel,² P.C. Colombo,² U.P. Jorde,² D.M. Mancini,² H. Takayama.¹ ¹*Division of Cardiac Surgery, Dept of Surgery, Columbia University Medical Center, New York, NY;* ²*Division of Cardiology, Dept of Medicine, Columbia University Medical Center, New York, NY.*

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				<u>UNOS Region</u>	
				1 →	11
				2 →	5
				3 →	0
				4 →	5
				5 →	3
				6 →	6
				7 →	6
				8 →	4
				9 →	15
				10 →	4
				11 →	5

<u>Blood Type</u>		<u>Height (cm)</u>	
A →	5	≤180 →	0
B →	5	>180 →	2
AB →	0		
O →	14		

<u>PRA</u>		<u>Weight (kg)</u>	
≤10% →	0	<90 →	0
>10% →	7	≥90 →	5

Impending deterioration and death on waiting list

Prognostic determinants

Clinical data

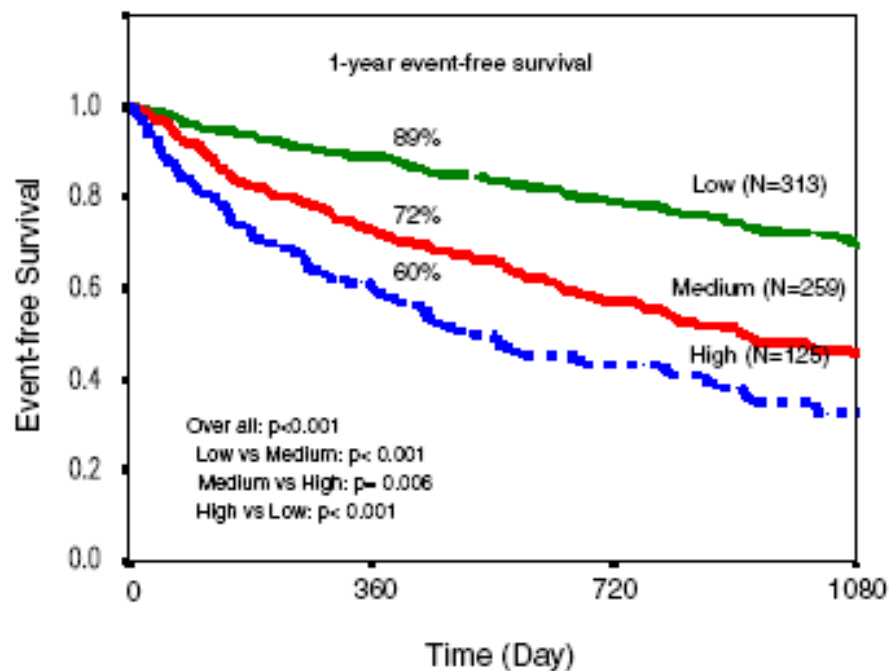
- Male sex
- Advanced age
- > 1 rehospitalization in past 6 mo
- III or IV NYHA class
- Weight loss
- Intolerance to neurohormonal antagonists
- Increased diuretic requirement
- Hypotension
- Failed CRT
- Inotrope dependence

Laboratory data

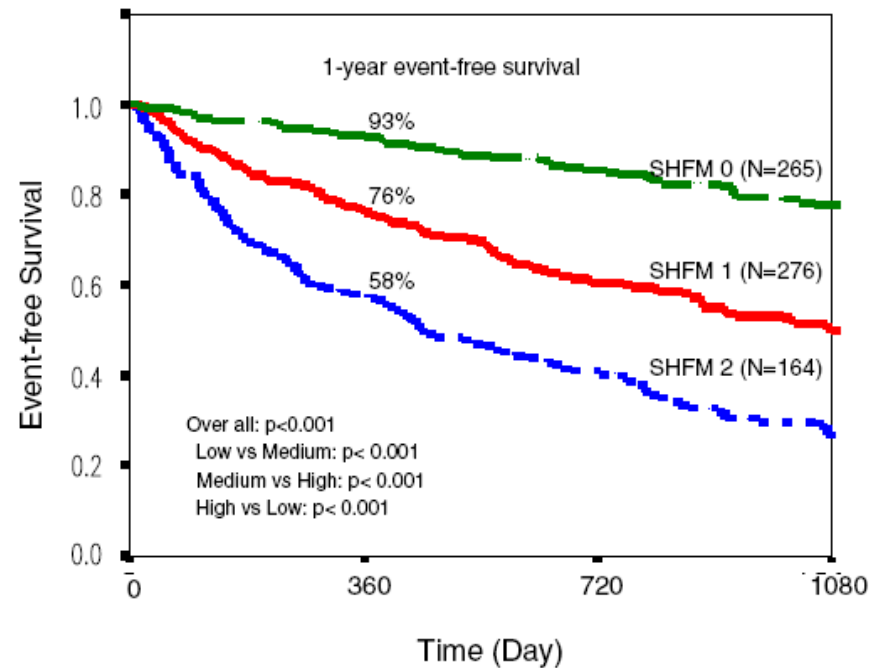
- Hyponatremia
- Renal insufficiency (BUN/serum creatinin)
- Hepatic insufficiency
- Increased filling pressures
- Increased pulmonary vascular resistance
- Low peak VO_2 (12–14 mL kg⁻¹ min⁻¹)
- Low 6-min walk test distance (<300 m)

Predictive models: HFSS & SHFM

HFSS



SHFM



Predictive Models in Heart Failure Who Cares?

***Among 5 externally validated prediction models,
HFSS and SHFM models demonstrated
modest discriminative capacity
and questionable calibration.***

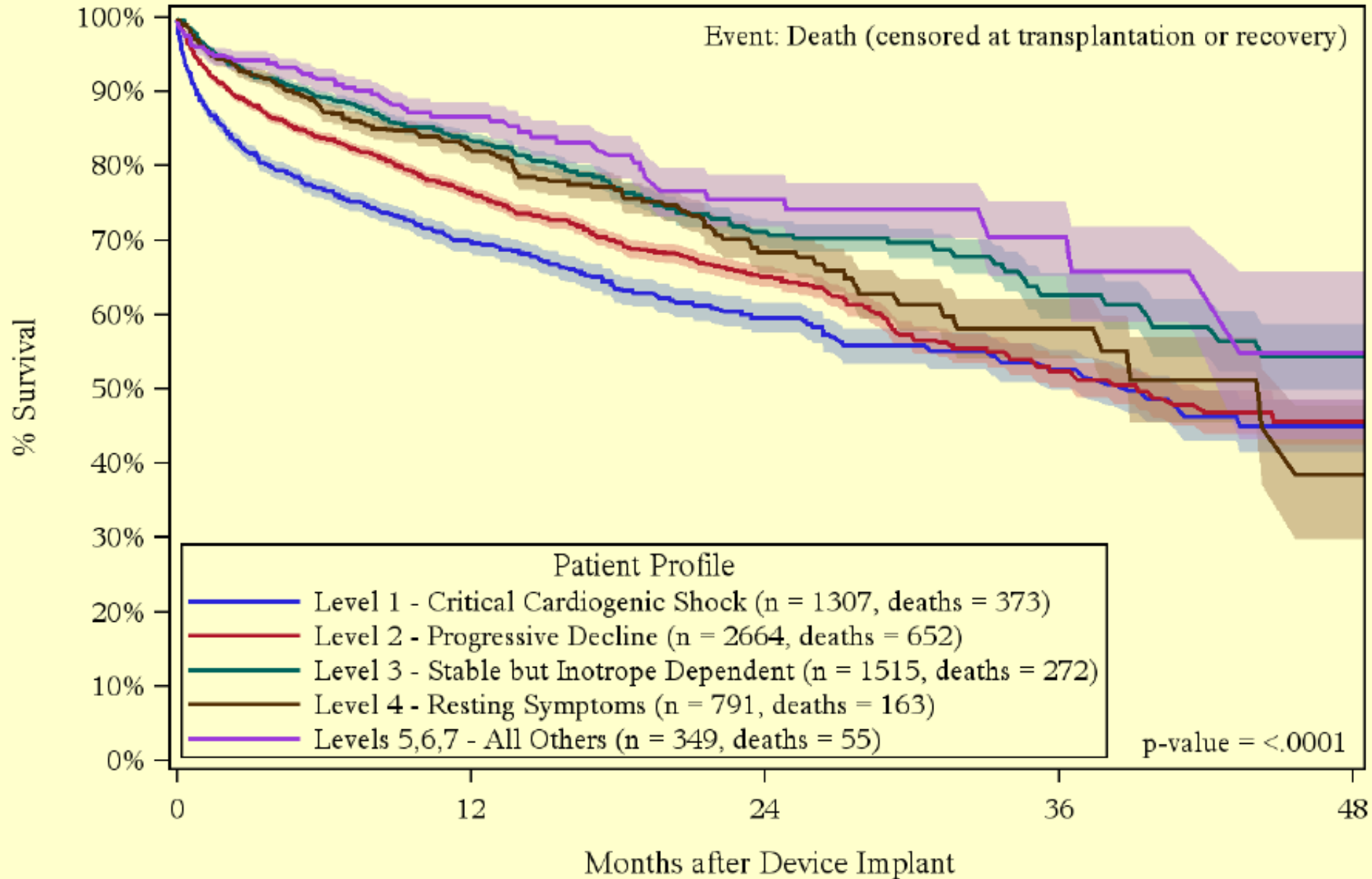
When?

INTERMACS levels

ADULT PROFILES	<i>Current CMS - DT Functional Indication</i>	IV INO*	Official Shorthand	NYHA CLASS Assumed
INTERMACS LEVEL 1	Met	X	"Crash and burn"	IV
INTERMACS LEVEL 2	Met	X	"Sliding fast" on inotropes	IV
INTERMACS LEVEL 3	Met	X	"Stable" continuous inotrope dependent * Can be in hospital or at home	IV
INTERMACS LEVEL 4	+ Peak VO₂ ≤ 12		<u>Resting symptoms</u> on oral therapy at home	A/MB IV
INTERMACS LEVEL 5	+ Peak VO₂ ≤ 12		"Housebound", Comfortable at rest, symptoms with minimum activity ADL	A/MB IV
INTERMACS LEVEL 6			"Walking wounded"-ADL possible but meaningful activity limited	IIIB 
INTERMACS LEVEL 7			Advanced Class III	III

INTERMACS - Kaplan-Meier Survival by Patient Profile at Implant

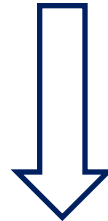
Primary Prospective Implants: June 23, 2006 to June 30, 2012



CONTEMPORARY INDICATION CRITERIA

Too late
Excess of
mortality

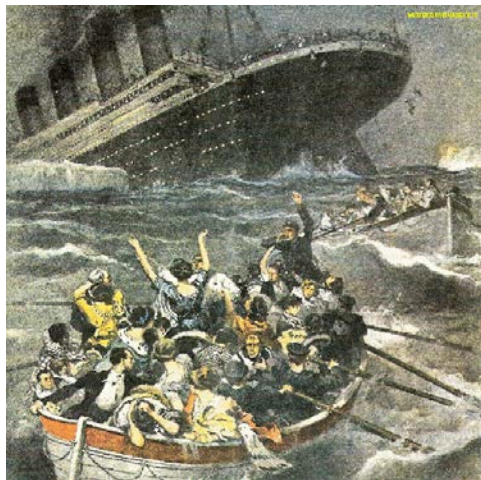
Too early



INTERMACS
1

INTERMACS
3-4

INTERMACS
5-7

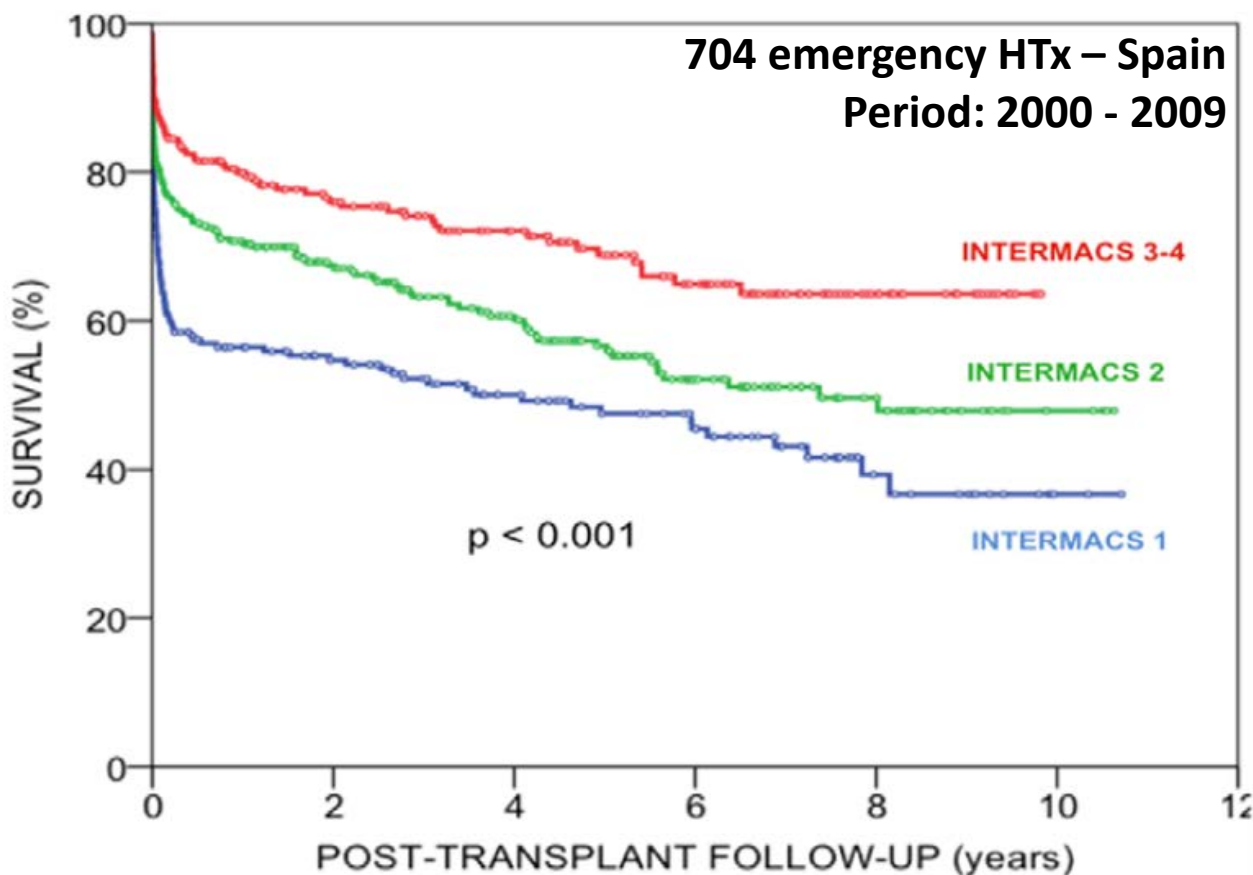


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Preoperative INTERMACS Profiles Determine Postoperative Outcomes in Critically Ill Patients Undergoing Emergency Heart Transplantation

Analysis of the Spanish National Heart Transplant Registry



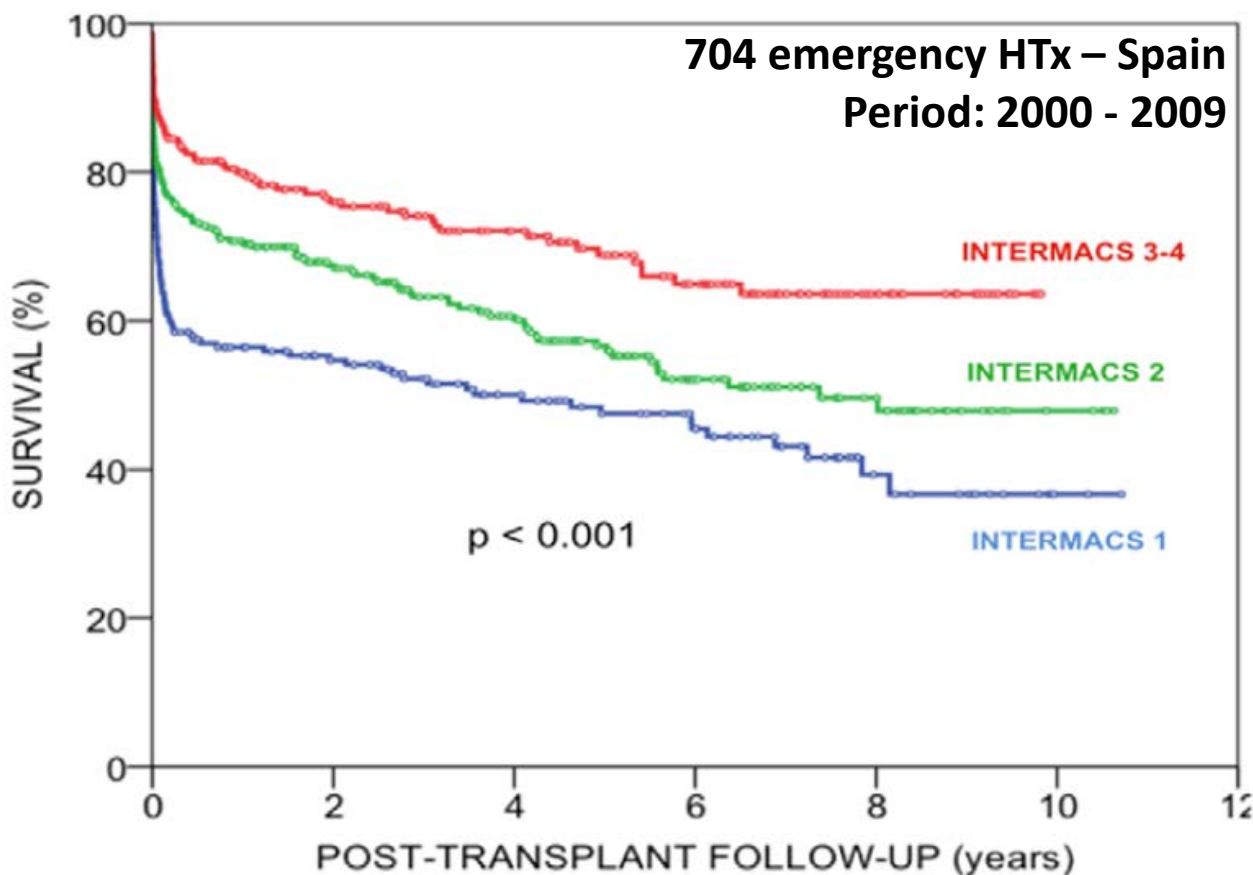
HTx in-hosp mortality

Level 1	43%
Level 2	27%
Level 3-4	18%

... post-HTx outcomes in patients with INTERMACS profiles 1 and 2 were not satisfactory

Preoperative INTERMACS Profiles Determine Postoperative Outcomes in Critically Ill Patients Undergoing Emergency Heart Transplantation

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VAD in-hosp mortality

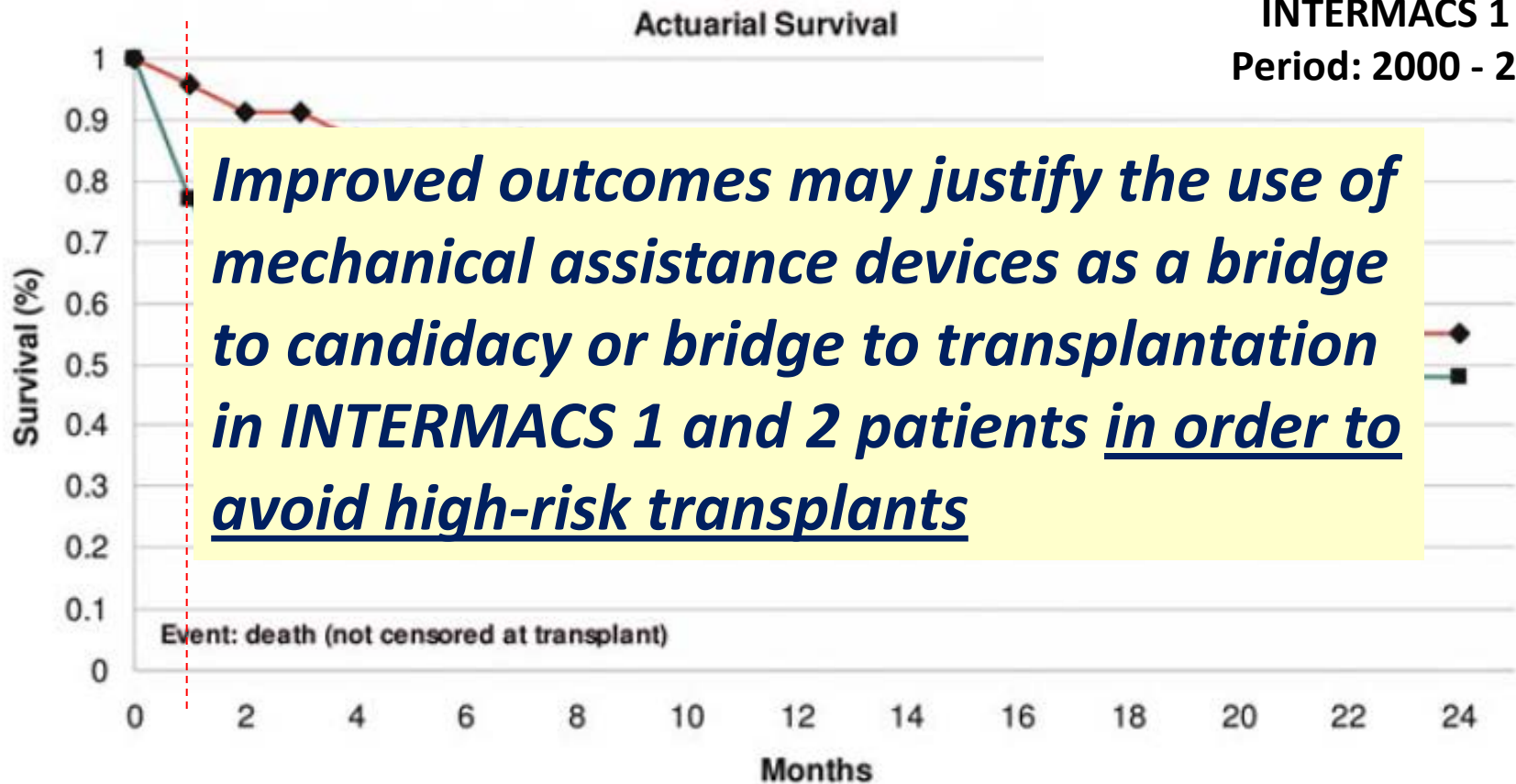
INTERMACS data 2013

Level 1	15%
Level 2	10%
Level 3-4	7%

Advanced heart failure in critical patients (INTERMACS 1 and 2 levels): ventricular assist devices or emergency transplantation?[†]

Matteo Attisani^{a,*}, Paolo Centofanti^a, Michele La Torre^a, Massimo Boffini^a, Davide Ricci^{a,b}, Marco Ribezzo^a,
Andrea Baronetto^a and Mauro Rinaldi^a

49 emergency HTx – Torino
INTERMACS 1 & 2
Period: 2000 - 2009



Emergency HTx vs LVAD

Italy, 2010-2012

From CNT data	N	%
Requests	317	100%
WL: Dead/worsened	79	25%
WL: Improved ^(a)	38	12%
Transplanted	200	63%
Alive post-HTx ^(b)	148	74% TxC
Alive after emergency request ^(a+b)	186	59%
MCS, BTT: 1-y survival	78/106	74%
MCS, profiles 1-3, 1-y survival	106/165	64%

BTT vs emergency HTx

- **Better to BTT early, in INTERMACS levels 3-4**
- **However, in INTERMACS levels 1-2 BTT seems to be at least non inferior to emergency HTx**
 - prompt availability of LVAD
 - pump performance is predictable
 - waiting time for a donor is uncertain
 - quality of the donor heart is uncertain (*not much choice...*)
 - *primary graft failure is the 1th cause of death following HTx*

Summary

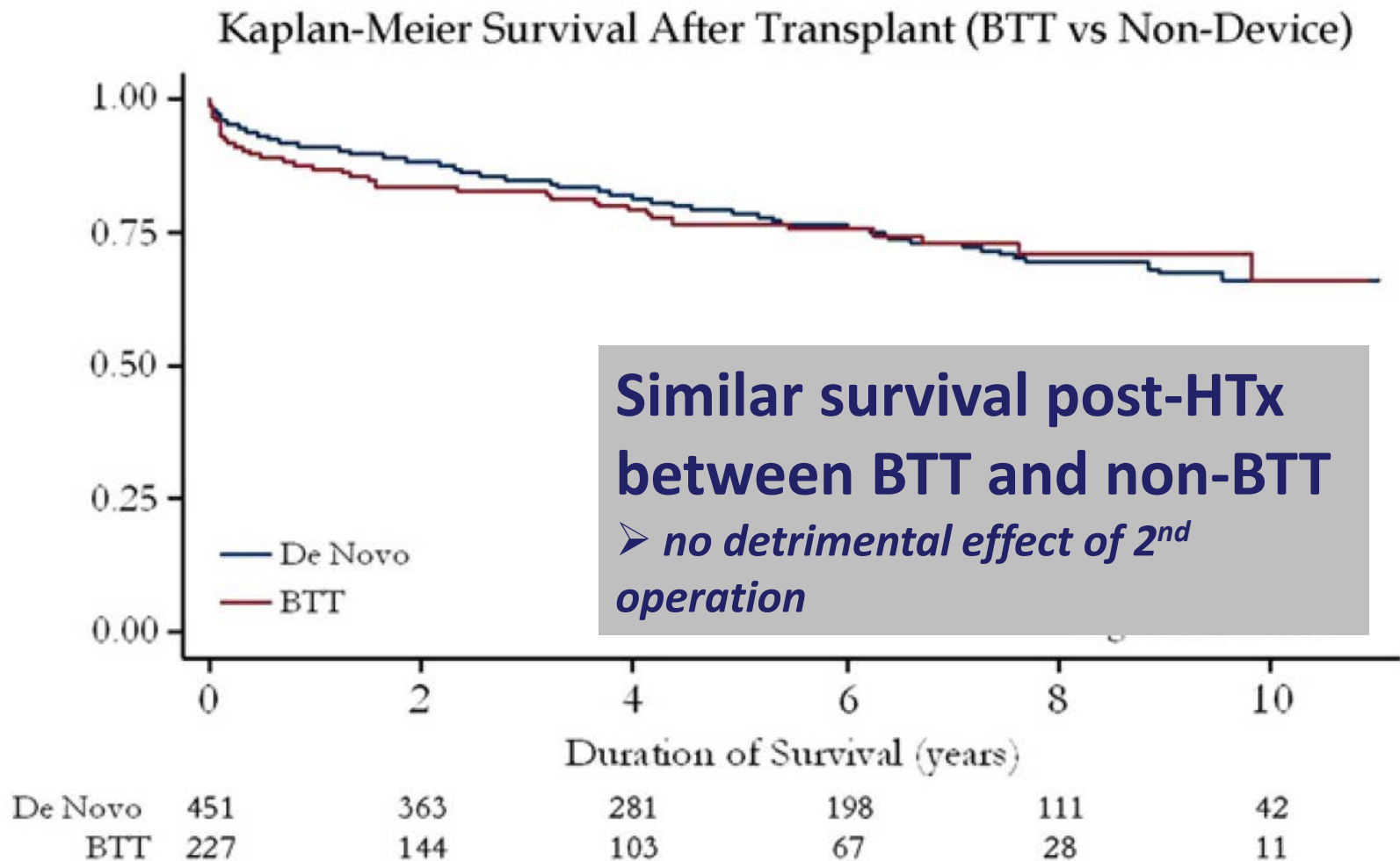
LVAD as bridge to transplant should be considered

- **in all the LVAD-eligible patients** in the waiting list
- **early** in stable patients (INTERMACS 3-4) with risk factors for longer waiting time for HTx
- **frequently re-evaluated** in stable patients showing signs of clinical deterioration
- **promptly** in unstable patients (INTERMACS 1-2)

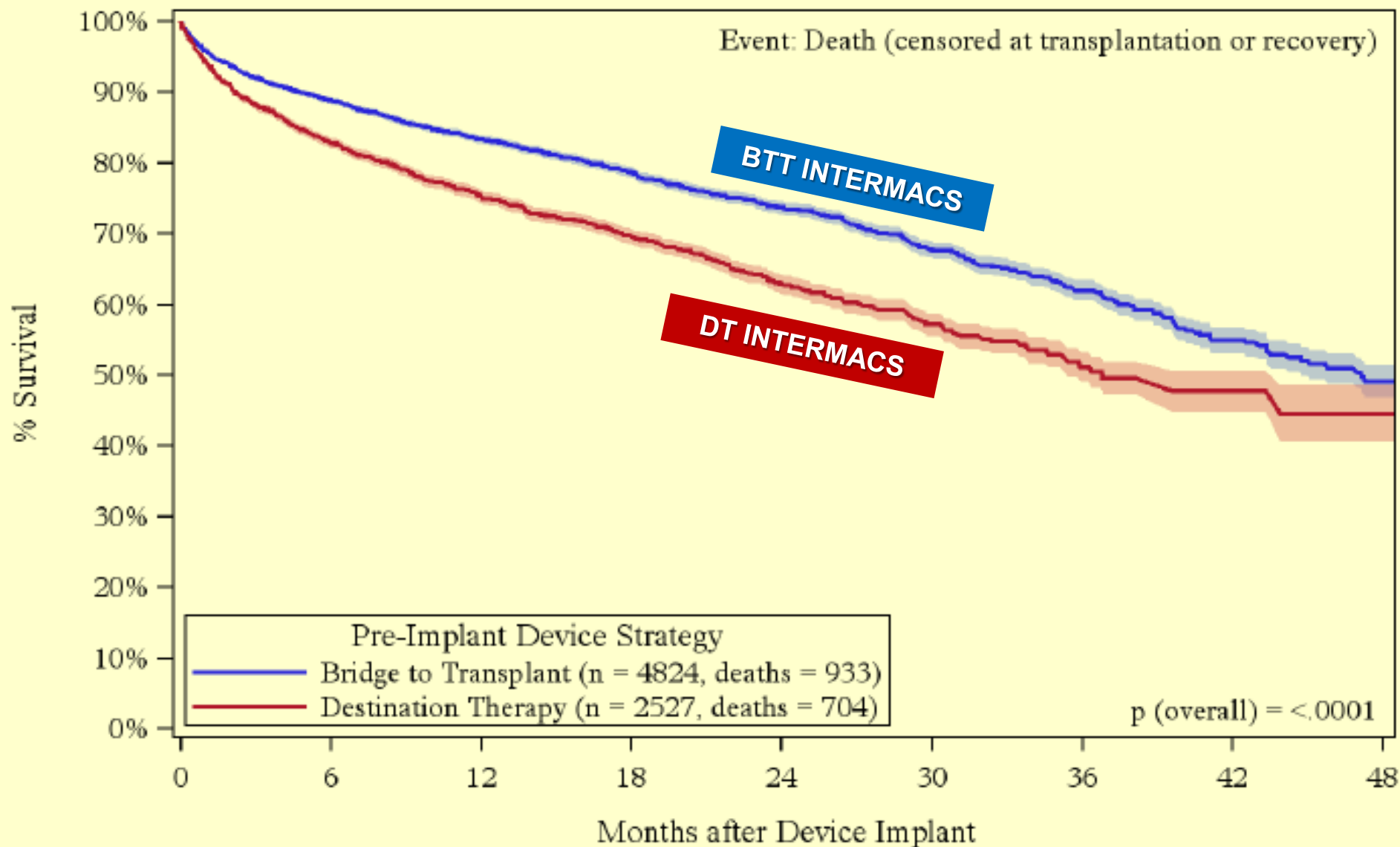
Bridged to...
what?

Impact of long term left ventricular assist device therapy on donor allocation in cardiac transplantation

Experience at Columbia Univ, NY



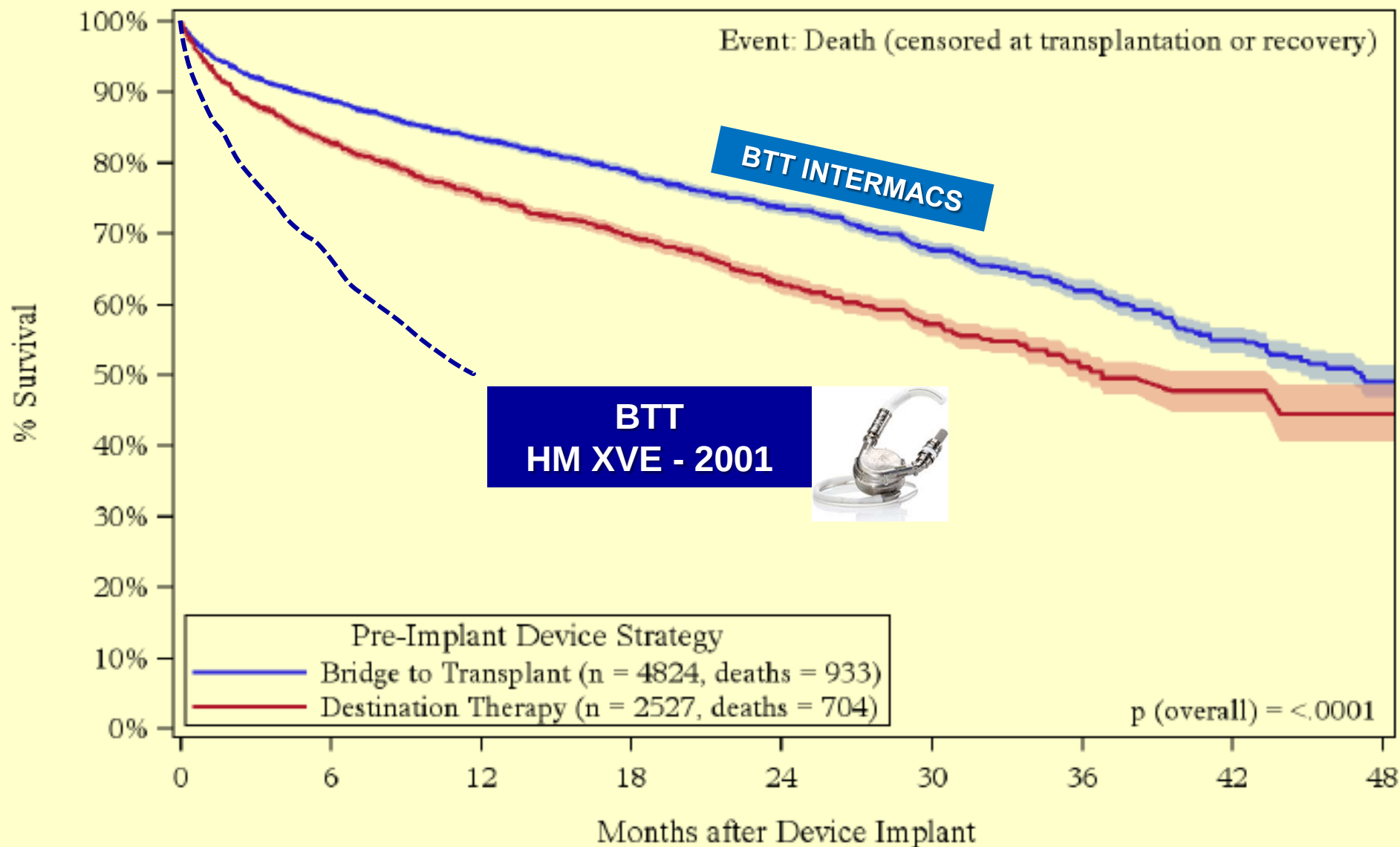
INTERMACS - Kaplan-Meier Survival for Continuous Flow LVADs (with or without RVAD implant at time of LVAD operation) by Pre-Implant Device Strategy
Primary Prospective Implants: June 23, 2006 to March 31, 2013



Shaded areas indicate 70% confidence limits



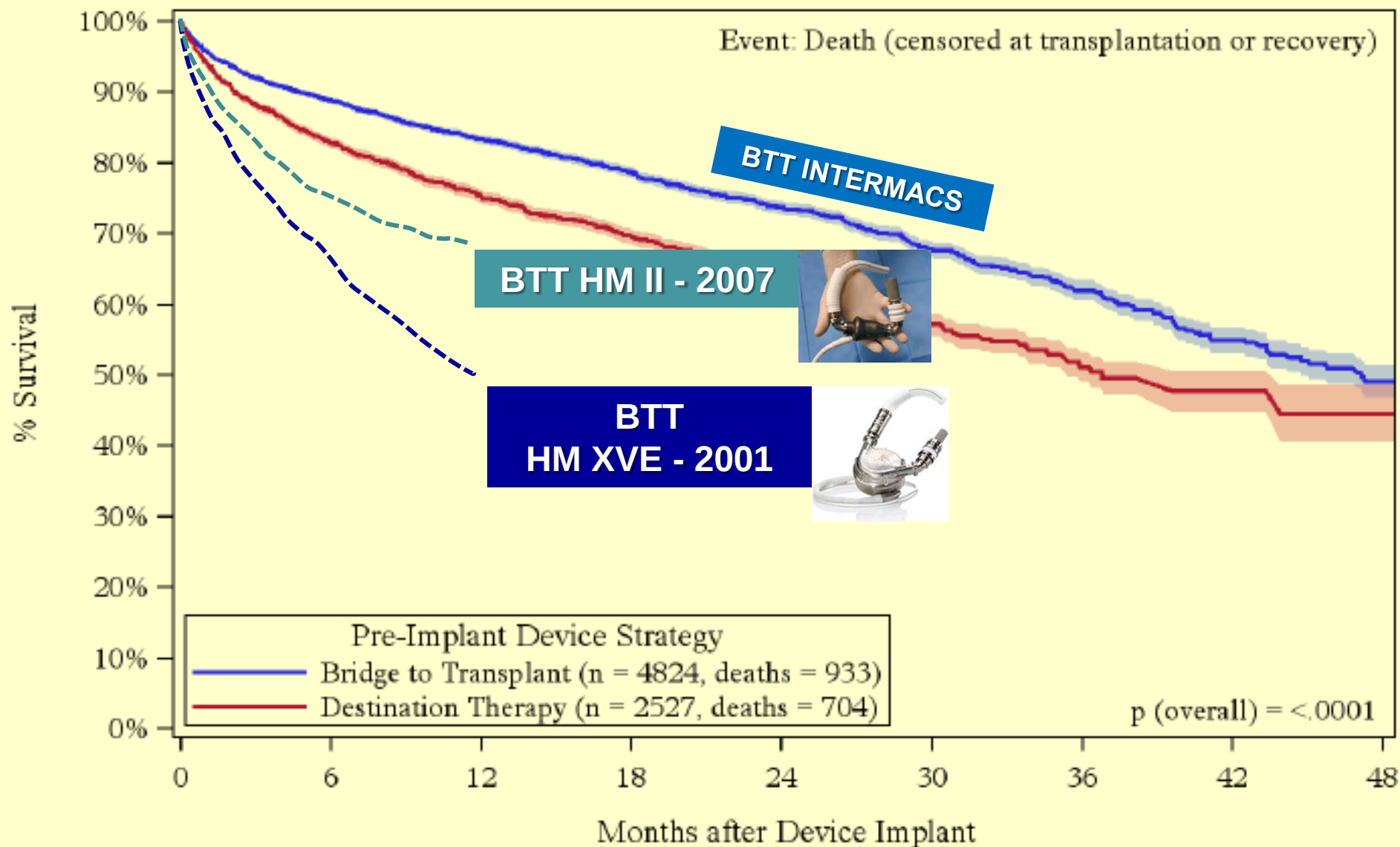
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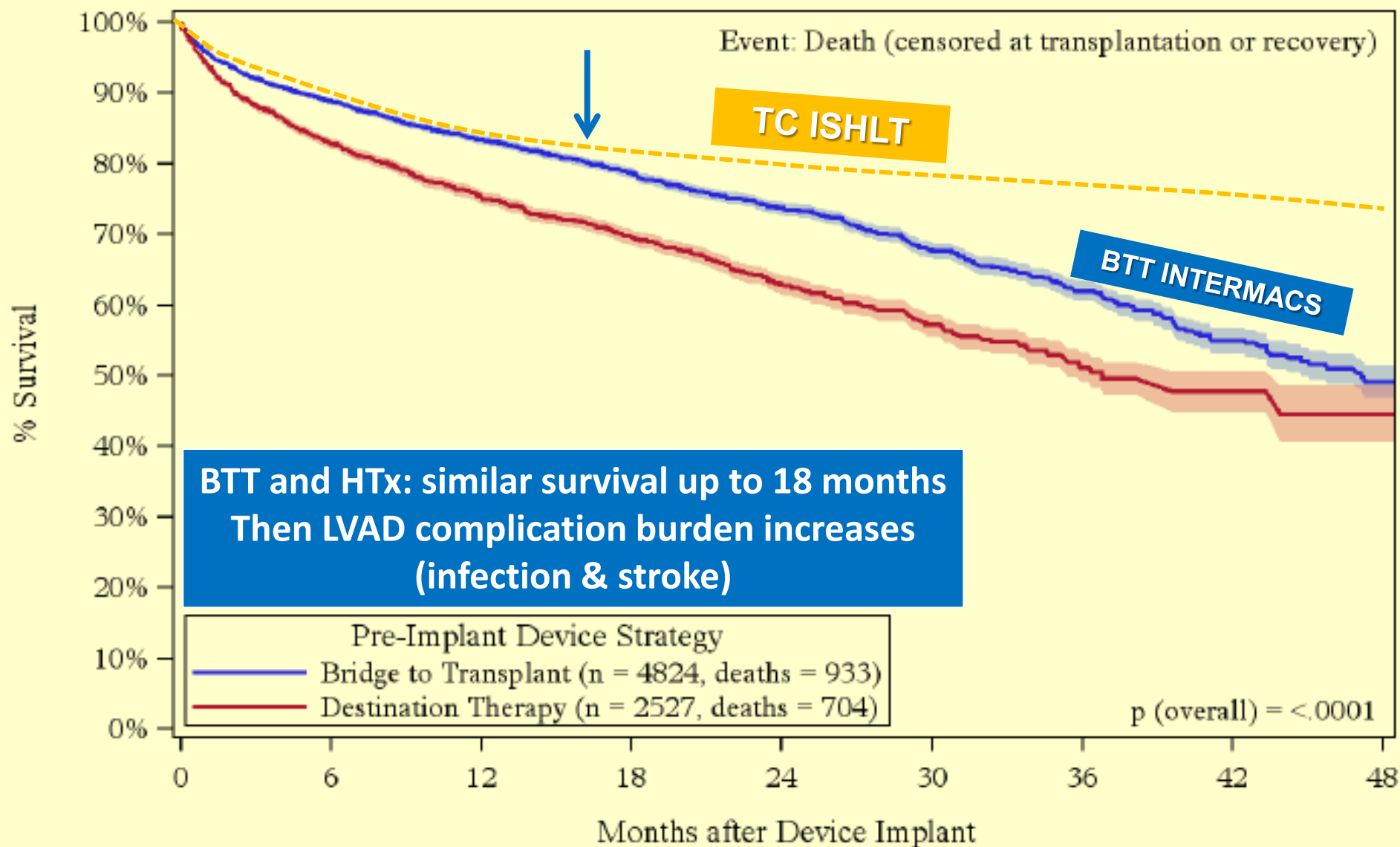
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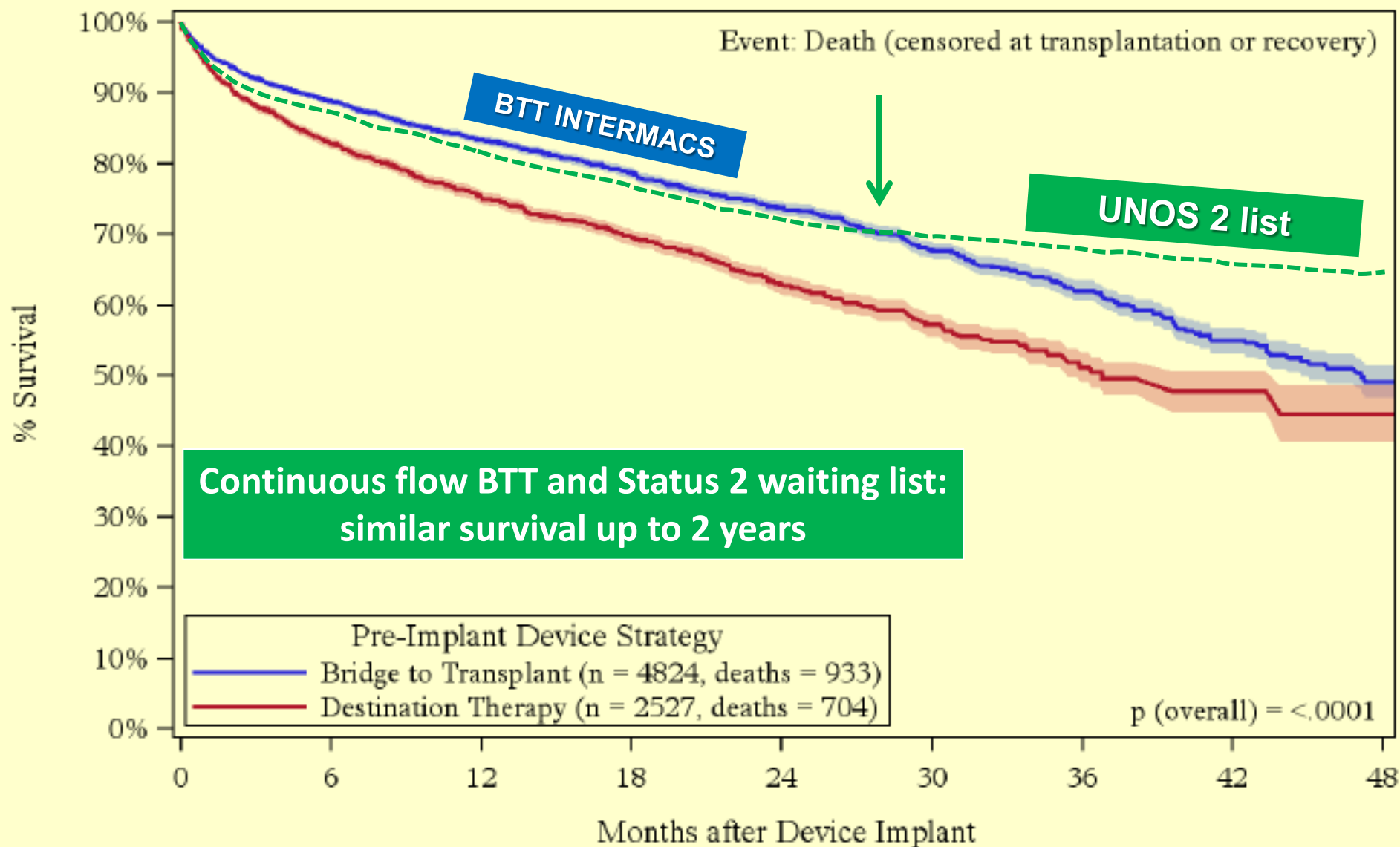
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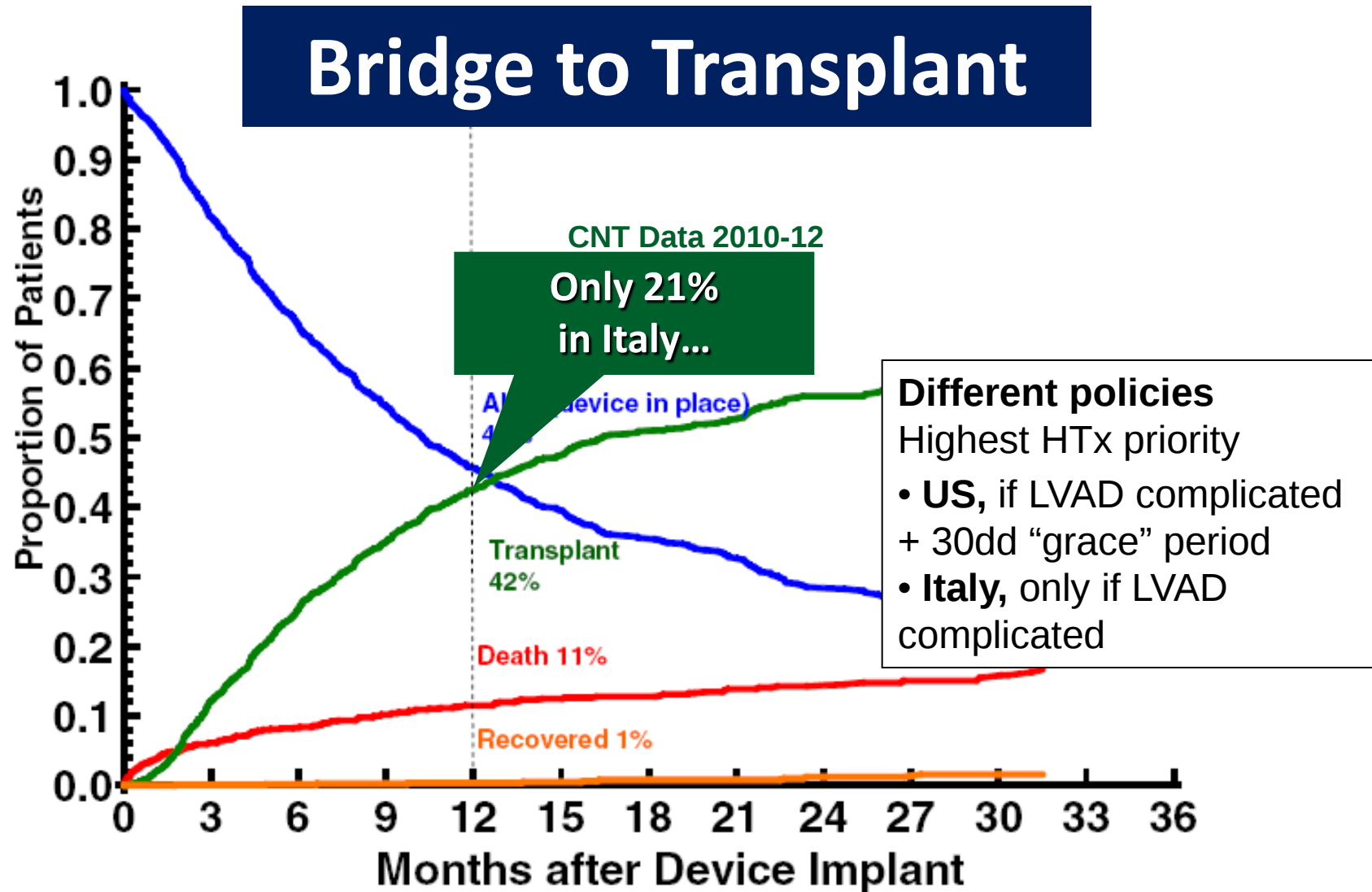


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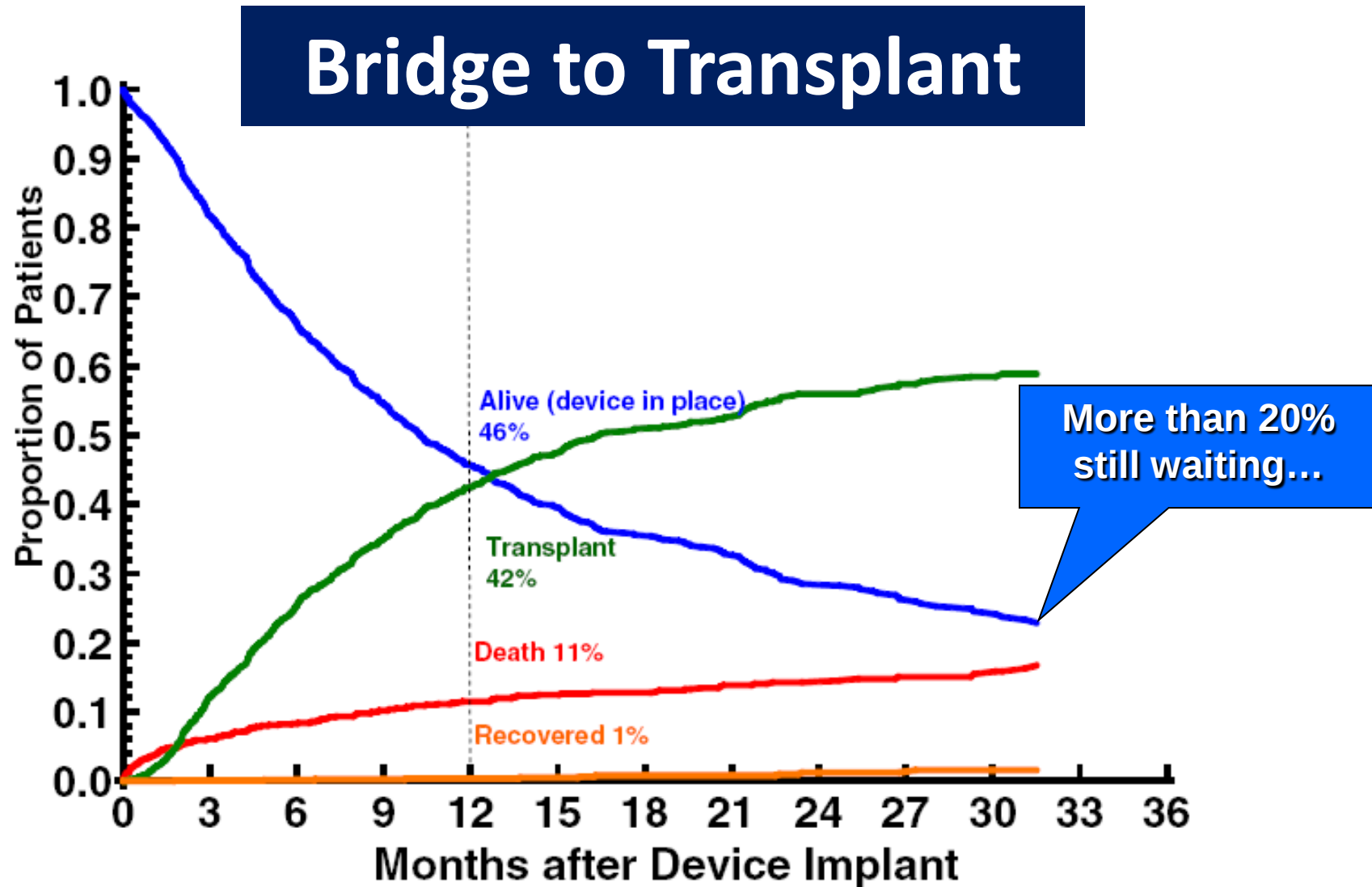


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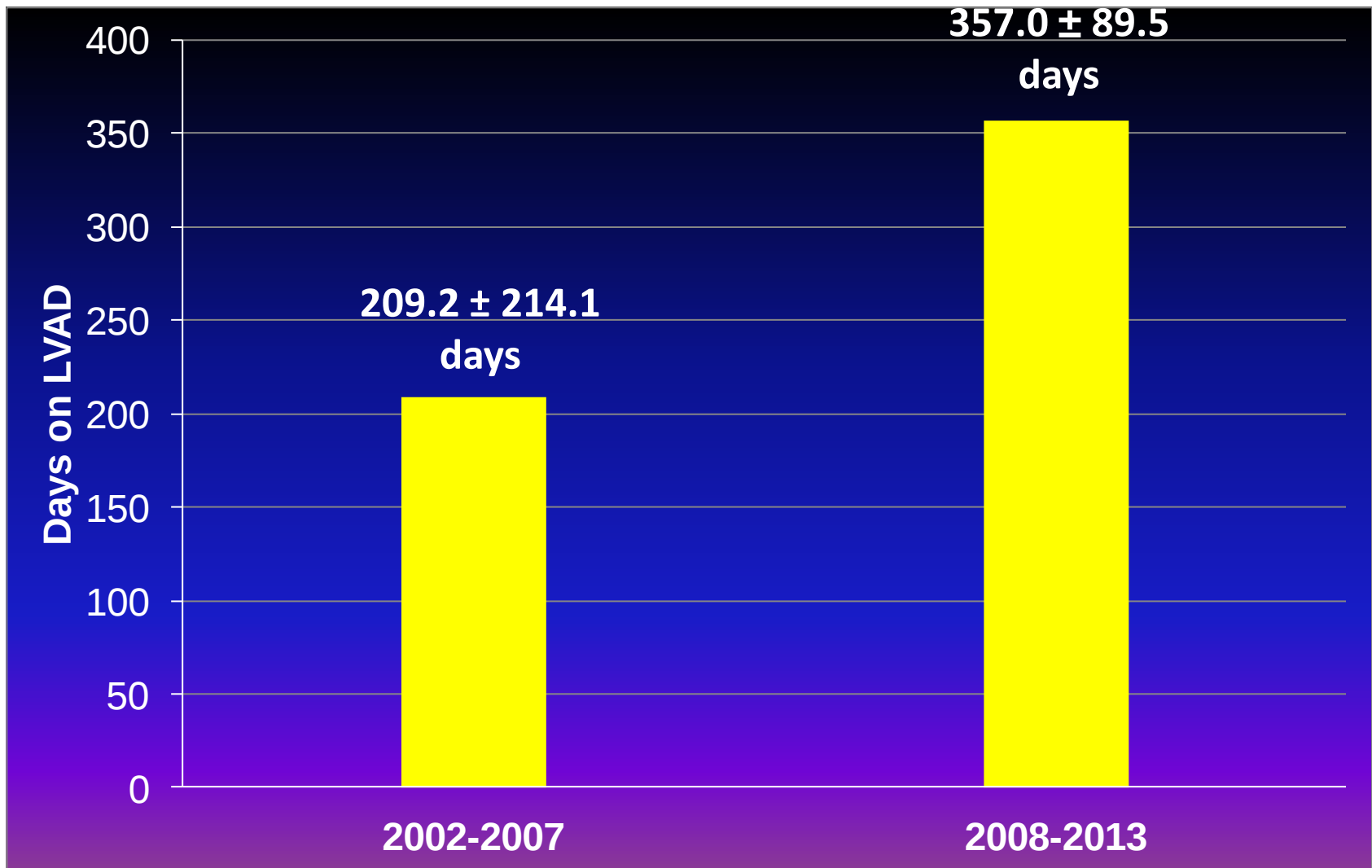
The Fourth INTERMACS Annual Report: 4,000 implants and counting



The Fourth INTERMACS Annual Report: 4,000 implants and counting



Waiting time for HTx on LVAD



Intracorporeal LVAD

Experience at Niguarda Hospital (2008-2013)

Follow-up results (52 patients)

Mean LVAD support

440.5 ± 380.4 days (5 - 1286 days)

Bridged to HTx

8

Still on LVAD

32

Thromboembolism

0

Major GI bleeding

2

Intracranial hemorrhage

3

Driveline infection

20

Broken driveline

2

LVAD malfunction

4

(2 LVAD failures in end-stage cancer)

LVAD replacement

3

Broken driveline	2
Inflow cannula misalignment	1
LVAD infection	4
Recurrent GI bleeding	1

Abstract 18438: Long Term Left Ventricular Assist Device as Bridge to Heart Transplantation — is it Really a Bridge?

Nir Uriel; Sang-Woo Pak; Mauer Biscotti; Bartlomiej Kachniarz;
Daniel Sims; Hiroo Takayama; Yoshifumi Naka; Donna Mancini;
Ulrich P Jorde

Columbia Univ, New York, NY



Conclusion: After utilizing the initial 30 day 1A grace period, many LVAD BTT patients (particularly those with blood type 0) are **unlikely to be transplanted** in our procurement region **unless they experience a device complication** justifying upgrade of UNOS status to 1°

As device technology improves and complication rates fall, many of these patients will have **de facto destination therapy**

De facto
permanent LVAD

Conclusions

- BTT is still a compelling need because of chronic scarcity of donors
- Technology improved dramatically BTT results, and they are now comparable to HTx up to 18 mo
- BTT seems to be non-inferior, or even superior, to HTx in INTERMACS levels 1-2
- In a significant number of patients BTT becomes *de facto* permanent support

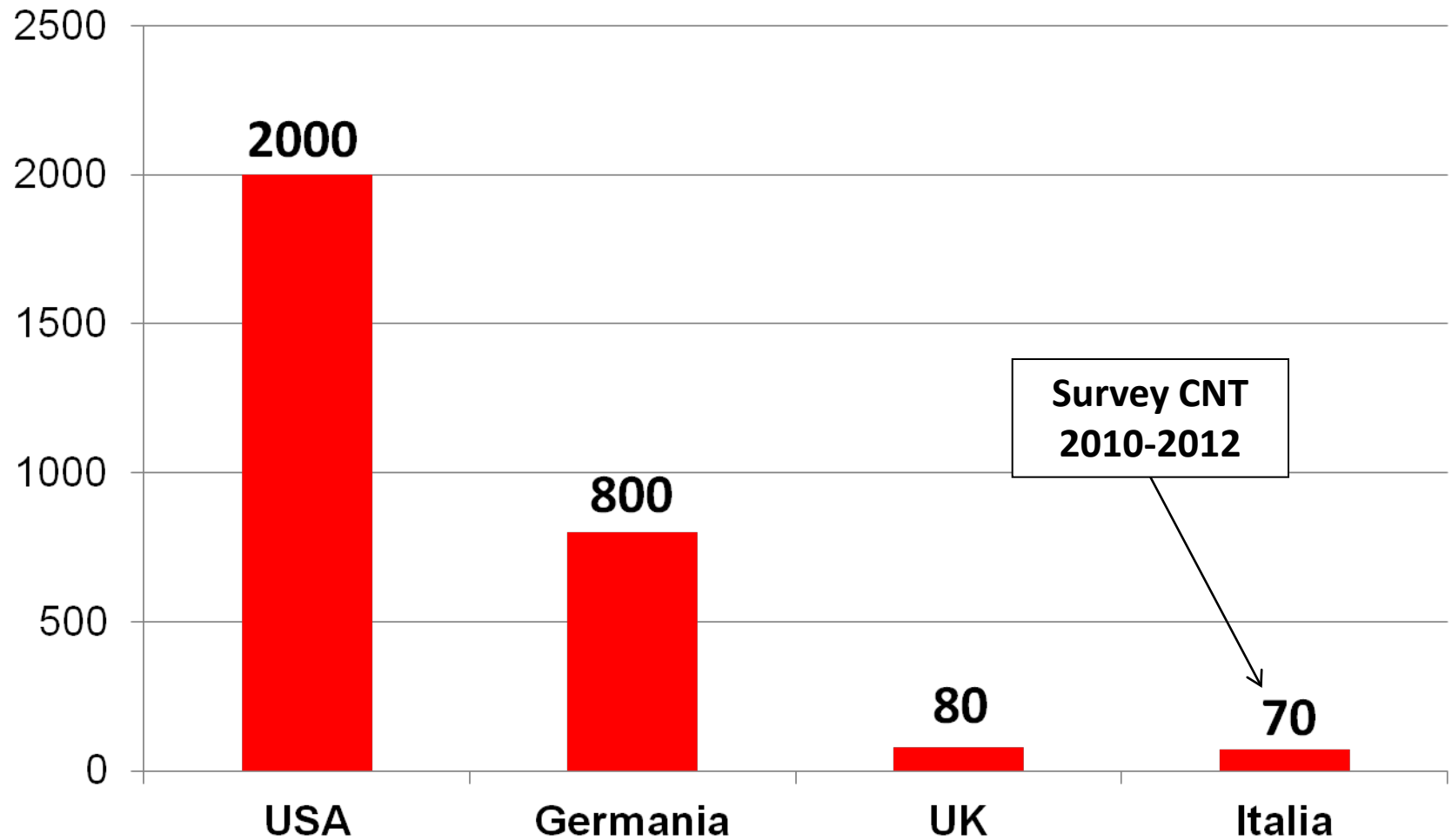
Conclusions

The key-points for successful bridge to transplant are

- to identify actively all the LVAD-eligible patients in the waiting list**
- to consider LVAD early in stable patients if long waiting time is likely**
- to re-evaluate frequently patients sliding on inotropes**
- to implant without further delay critical patients**

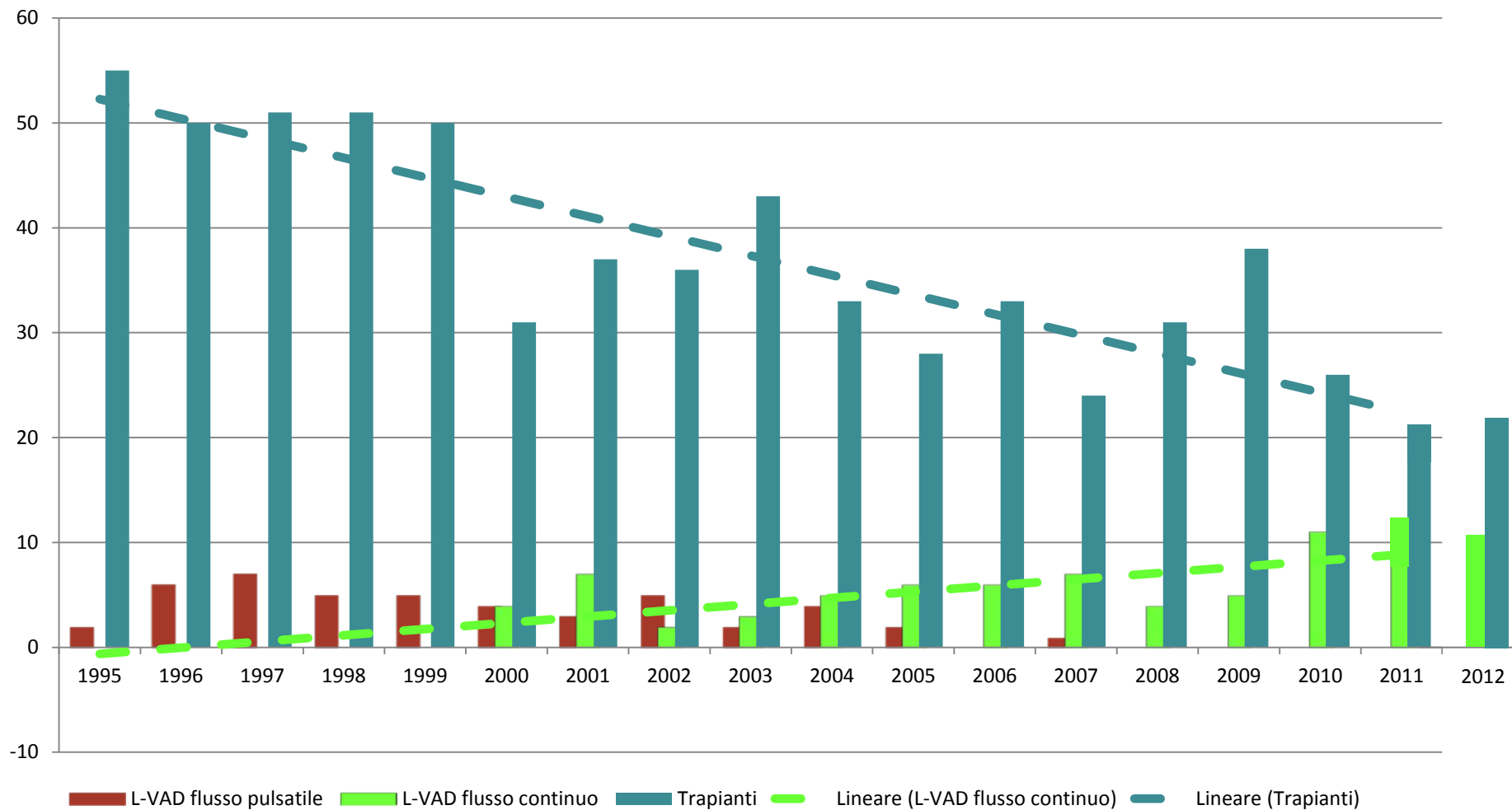
LVAD nel mondo

Impianti LVAD/anno



Long-term LVAD since 1994

(AO Niguarda Milano)



Cost of Ventricular Assist Devices

Can We Afford The Progress?

Costs of Treating Advanced Stage Illness

