

Making Decisions: One Patient At A Time

- **Evaluations in parallel**
- **Making a decision *about* the patient**
 - Sick enough to have better outcome with VAD?
 - Well enough to have good outcome with VAD?
 - Knowledge gaps in profile 4 and less sick
 - Decision with intent
 - Experience of Transplant/VAD Heart Team
- **Shared decision-making *with* the patient**
 - Key elements of information for patient and family
 - Knowledge gaps for outcomes beyond survival
 - Experience of Transplant/VAD Heart Team
 - Including Palliative Care team members
- **Summary of present knowledge gaps**

Triage In Advanced Heart Failure



To Distinguish

- 1. Those who will have much to gain from intervention.**
- 2. Those who will fare badly with or without intervention**
- 3. Those who will fare well with or without intervention**

General Conception of HF Survival

Heart Disease 2005
Bristow M "Heart Failure"
Editor: Braunwald EB
Page 606

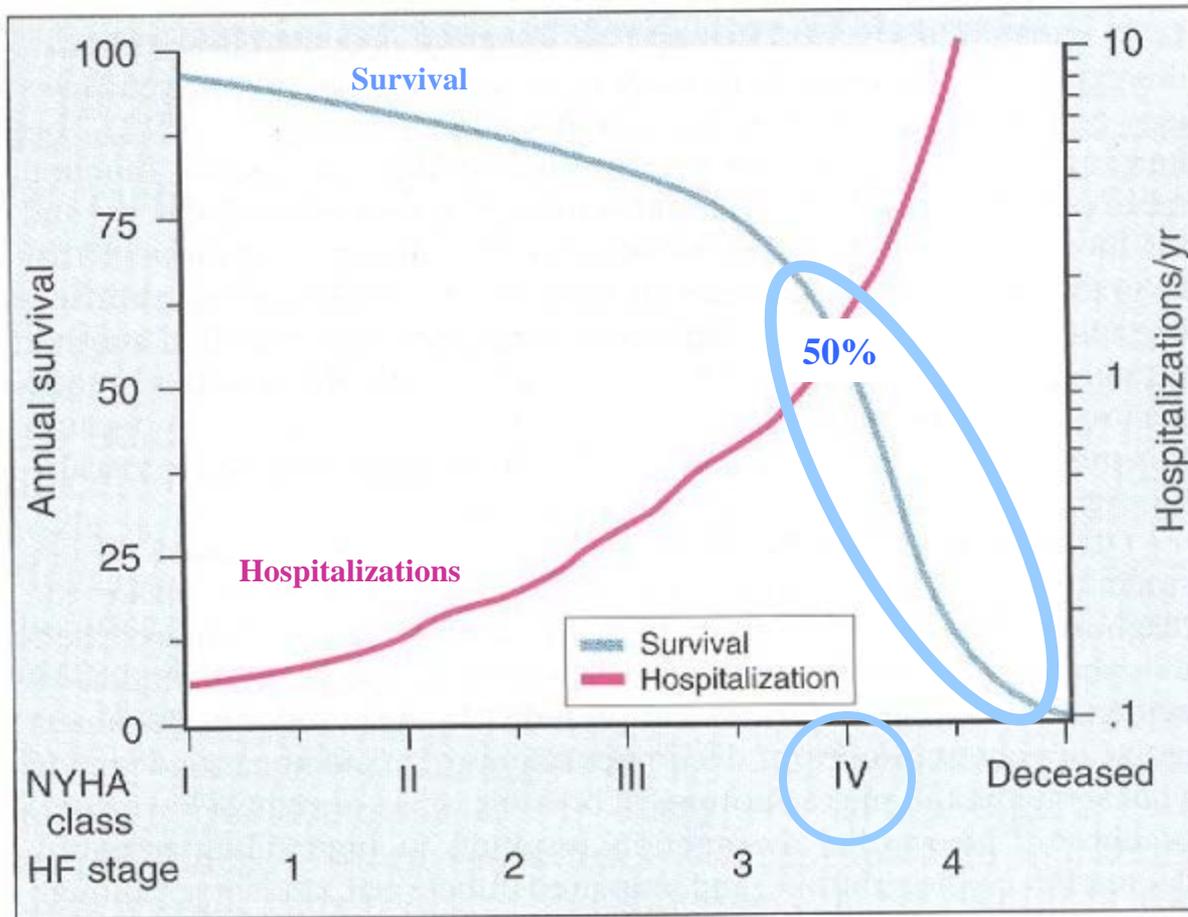


FIGURE 24-4 Plot of the relationship between survival or hospitalization frequency and New York Heart Association (NYHA) class or heart failure (HF) stage in chronic HF.

PROFILE-LEVEL <i>Triage and Designation by Experienced Centers*</i>	PRIMARY LVADs 2011- 12	Official Shorthand	1 Yr Survival With CF LVAD	2 Yr Survival With CF LVAD	Likely survival At 1 year Without LVAD *
INTERMACS LEVEL 1	16%	“Crash and burn”	64%	---	< 5%
INTERMACS LEVEL 2	38%	“Sliding fast” on ino	74%	58%	<11- 22% <i>REMATCH INTREPID</i>
INTERMACS LEVEL 3	27%	Stable but Ino- Dependent Can be hosp or home	When survival without VAD is close to 0%, absolute LVAD survival is what we need to know.		
INTERMACS LEVEL 4	13%	<u>Resting symptoms</u> on oral therapy at home.			
INTERMACS LEVEL 5	3%	“Housebound”, Comfortable at rest, symptoms with minimum activity ADL			
INTERMACS LEVEL 6	1.6%	“Walking wounded”-ADL possible but meaningful activity limited			
INTERMACS LEVEL 7		Advanced Class III			

Multiple Series Snow Poor Survival With Continuous Home IV Inotropic Therapy

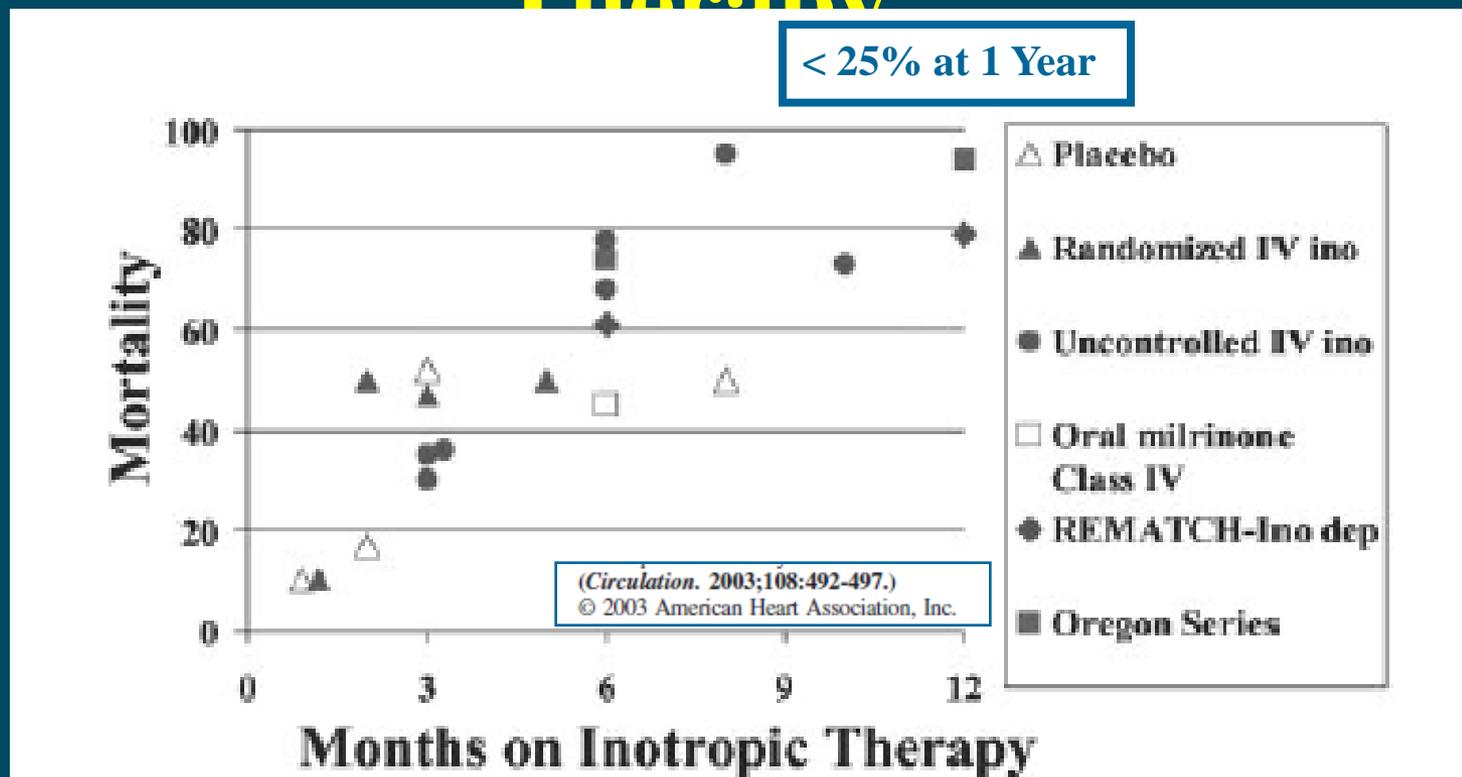
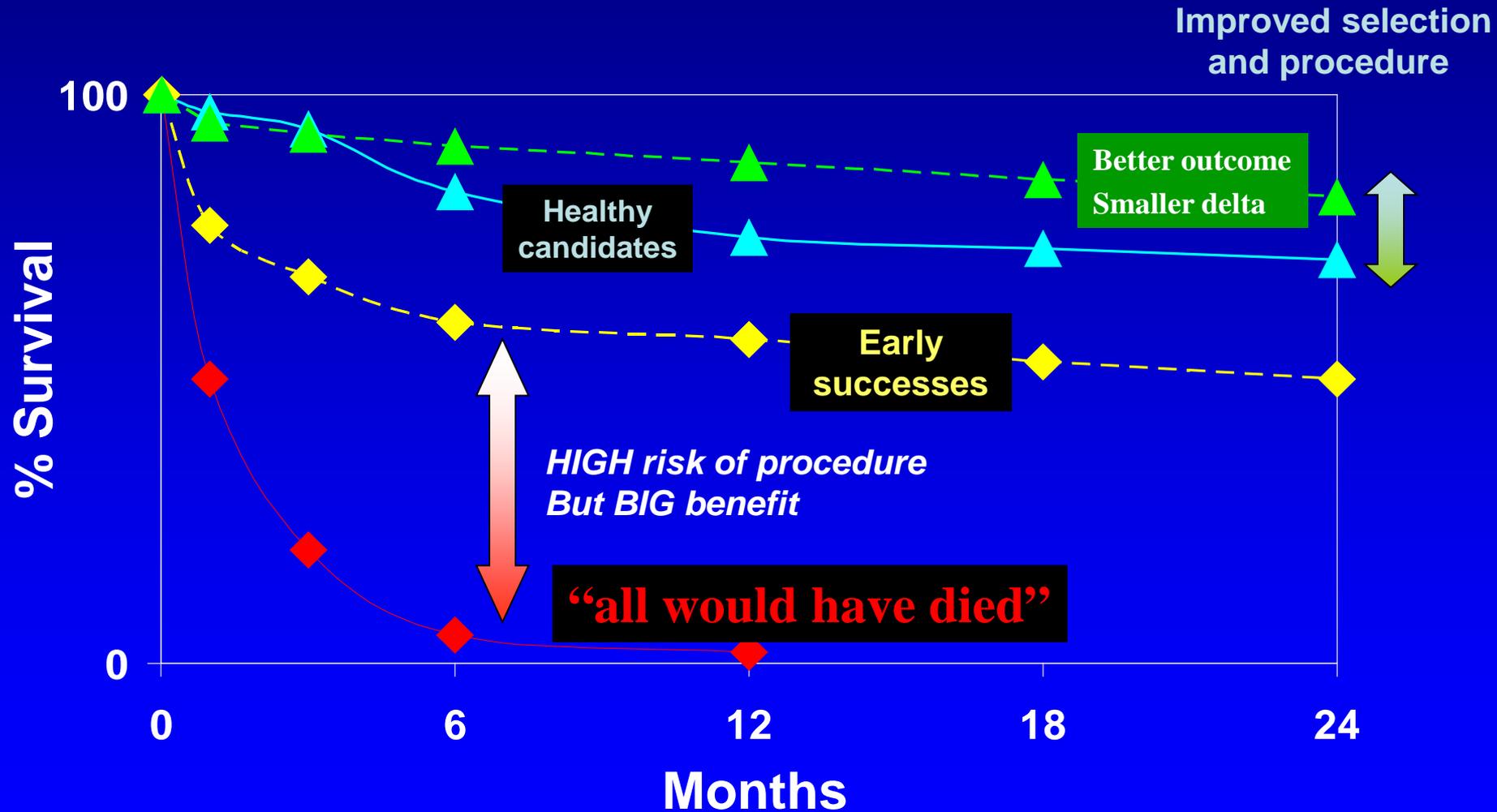


Figure 1. Mortality estimated from selection of experiences with intravenous inotropic (ino) therapy. Mortality in intravenous inotropic trials from controlled experiences is shown in shaded triangles, with placebo mortality in open triangles.¹⁶⁻¹⁹ Circles represent uncontrolled experiences.^{5-7,13,14,35,36} Where available,

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INTERMACS LEVEL 2	38%	“Sliding fast” on ino	75%	60%	<10- 20% REMATCH INTREPID
INTERMACS LEVEL 3	27%	Stable but Ino-Dependent Can be hosp or home	80%	75%	< 25%
INTERMACS LEVEL 4	13%	<u>Resting symptoms</u> on oral therapy at home.			
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With Improved Outcomes Downshift of Risk



Advanced Heart Failure Trials on Oral Therapies

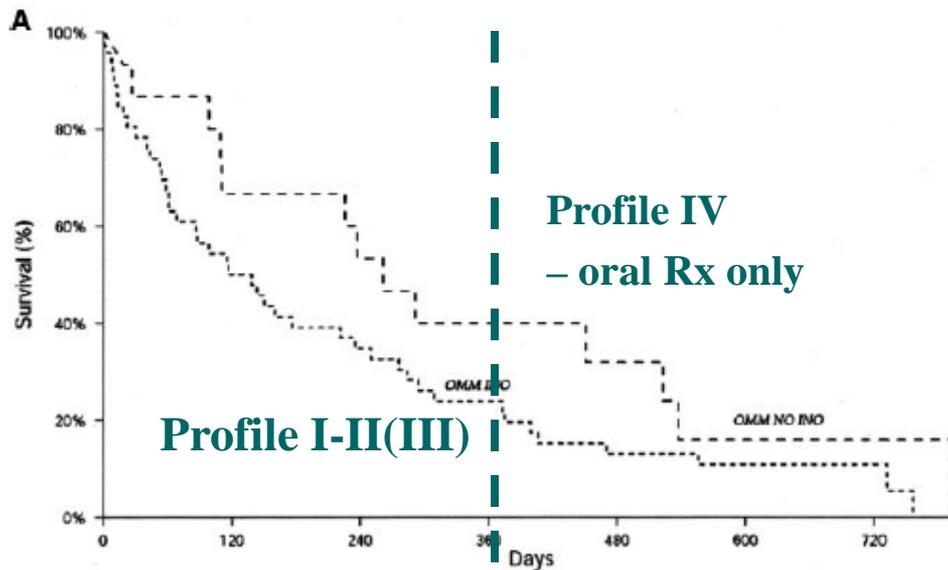
Trial	Year Published	Clin Class	1 Year Survival	
CONSENSUS (on ACEI)	1987	IV	50%	CONSENSUS Study Group
FIRST (placebo)	1997	IIIB-IV	50%	Califf et al
PROMISE (placebo)	1991	IV	60%	Packer et al
COMPANION (CRT ± D)	2007	Ambulatory IV	70%	Lindenfeld et al
RALES (spironolactone)	1999	III-IV	77%	Pitt et al
BEST (bblocker bucindolol)	2003	IV	78%	Bristow et al
COPERNICUS (beta blocker)	2002	Ambulatory IV	85%	Packer et al

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INTERMACS LEVEL 3	27%	Stable but Ino-Dependent Can be hosp or home	80%	75%	< 25%
INTERMACS LEVEL 4	13%	<u>Resting symptoms</u> on oral therapy at home. (REMATCH pk VO2 ≤12)			40% <i>REMATCH</i>
INTERMACS LEVEL 5	3%	“Housebound”, Comfortable at rest, symptoms with minimum activity ADL			
INTERMACS LEVEL 6	1.6%	“Walking wounded”-ADL possible but meaningful activity limited			
INTERMACS LEVEL 7		Advanced Class III			

REMATCH Destination Study

“Optimal Medical Rx” Arm

978 *Circulation* August 24, 2004



Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION



Left Ventricular Assist Device as Destination for Patients Undergoing Intravenous Inotropic Therapy : A Subset Analysis From REMATCH (Randomized Evaluation of Mechanical Assistance in Treatment of Chronic Heart Failure)
Lynne Warner Stevenson, Leslie W. Miller, Patrice Desvigne-Nickens, Deborah D. Ascheim, Michael K. Parides, Dale G. Renlund, Ronald M. Oren, Steven K. Krueger, Maria Rosa Costanzo, L. Samuel Wann, Ronald G. Levitan and Donna Mancini

PROFILE-LEVEL <i>Triage and Designation by Experienced Centers*</i>	PRIMARY LVADs 2011- 12	Official Shorthand	1 Yr Survival With CF LVAD	2 Yr Survival With CF LVAD	Likely survival At 1 year Without LVAD *
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INTERMACS LEVEL 2	38%	“Sliding fast” on ino	74%	58%	< 5%
INTERMACS LEVEL 3	27%	Stable but Ino- Dependent Can be hosp or home	80%	75%	< 25%
INTERMACS LEVEL 4	13%	<u>Resting symptoms on oral therapy at home.</u>	≥ 80%	≥ 75%	40%? (15 pts in REMATCH)
INTERMACS LEVEL 5	3%	“Housebound”, Comfortable at rest, symptoms with minimum activity ADL	} Can meet current indications if peak VO2 < 12-14		
INTERMACS LEVEL 6	1.6%	“Walking wounded”-ADL possible but meaningful activity limited			
INTERMACS LEVEL 7		Advanced Class III			

Peak VO₂

Measured During Exercise

- **Objective and reproducible**
Describes both functional capacity and prognosis
- **Integrates many cardiac and non-cardiac factors**
- **REMATCH: Cut-off of peak VO₂ 12  14 ml/kg/min late in trial**
(Ambulatory pts ON inotropic Rx: 9_±2 ml/kg/min)

Resting = 3-4 ml/kg/min

Walking = 10 ml/kg/min

Ballroom dancing = 10

Golf with cart = 11

Household tasks without heavy lifting = 12

Gardening = 14

Golf without cart = 15

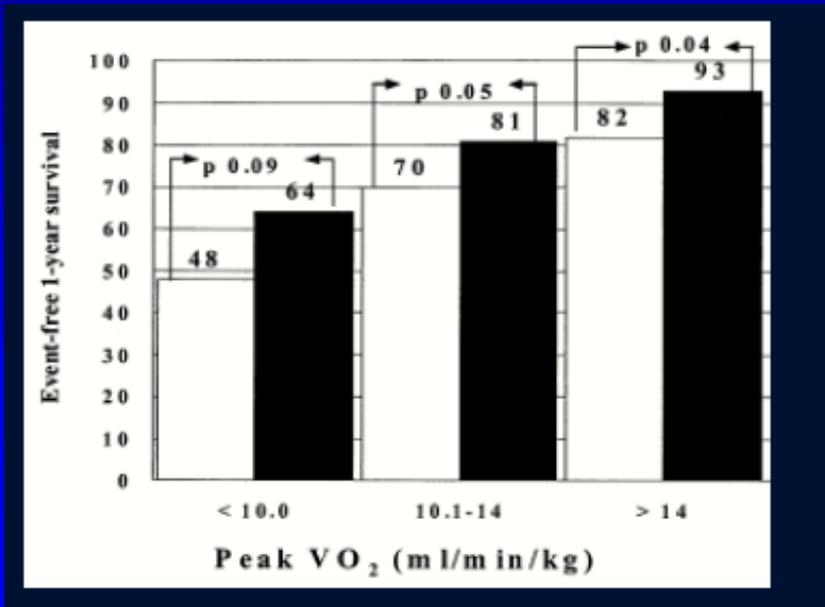
Slow swimming = 16

Pk VO₂ is highly dependent on heart rate
increase during exercise.

Beta blockers can DECREASE pkVO₂
But Beta blockers improve survival

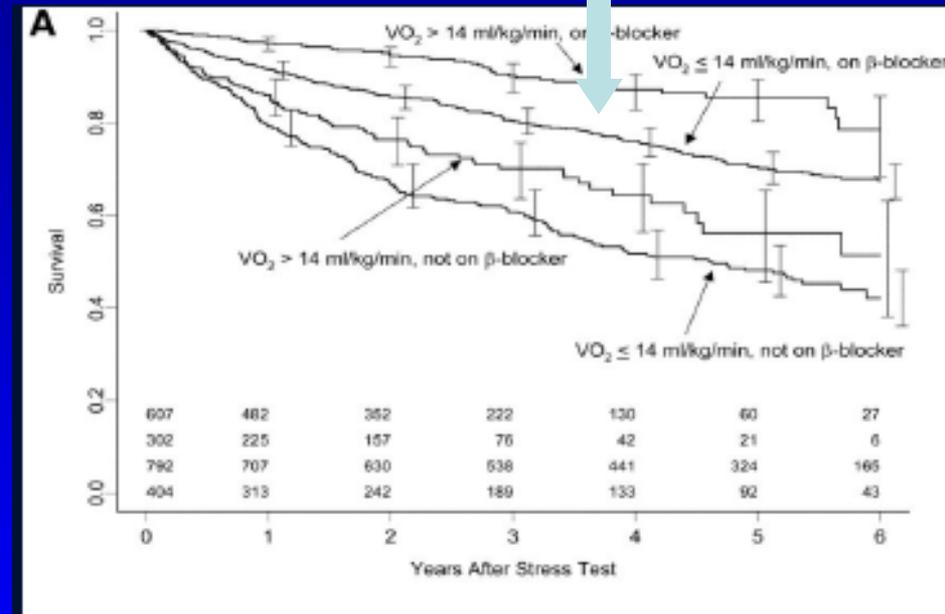
Peak VO₂ As Predictor of Outcome With and Without Beta Blockers- What Threshold?

Peak VO₂ 10-14 ml/kg/min on beta blocker
81% one-year survival



Butler et al, JACC 2004

Peak VO₂ ≤ 14 on beta blocker
> 80% Survival at 3 YEARS!



O'Neill et al Circulation 2005

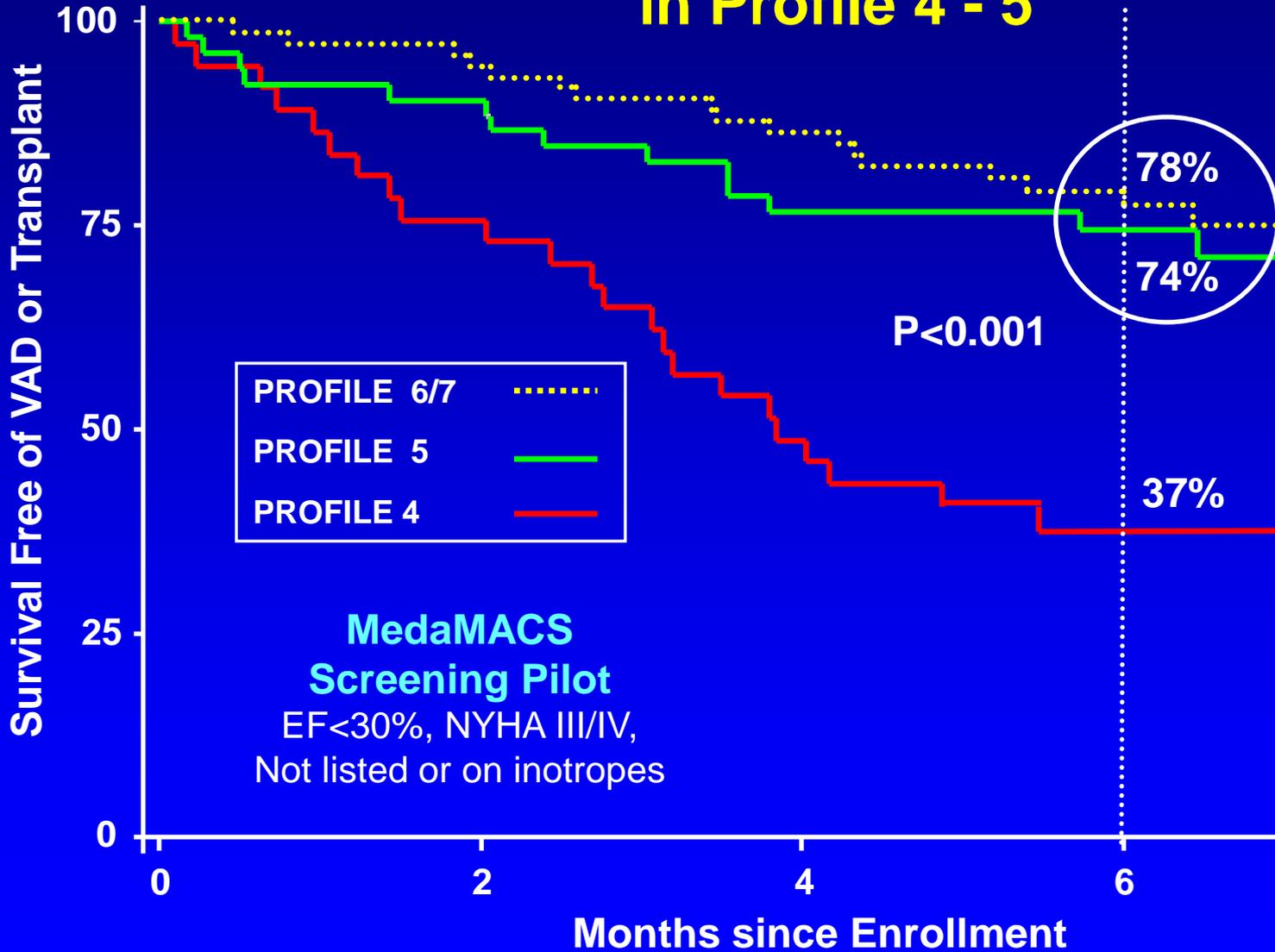
Risk Scores To Estimate Survival Without LVAD –A Skeptic's Position

- Derived from different populations than contemporary LVAD candidates:
 - Younger with fewer co-morbidities than the anticipated destination population populations
 - Patients signing up for randomized trials of heart failure therapies (Seattle HF model) without standard inclusion of renal function and BNP/NT-pro BNP
 - Patients evaluated for cardiac transplantation prior to standard use of ICD and CRT devices (HFSS) although now modified
- Many factors in risk score for death **without** VAD are also risk factors for death **with** VAD
- Risk scores are more useful to characterize populations than to counsel individual patients on the VAD decision
 - Wide confidence intervals around estimates of **survival, all or none** for each individual.
 - Even more difficulty when comparing 2 therapies with different variances and timing of risks
 - The **unknown unknown** is often the most potent factor in outcome.

MedaMACS description

- **Pilot study of patients on medical Rx at U.S. Transplant/VAD centers**
- **2 HF hospitalizations or 1 + high risk factor**
- **Screening pilot = 168 pts**
- **Initiation of NHLBI-Thoratec sponsored study of 300 ambulatory patients**
- **Attention to adverse events and detailed quality of life and patient attitudes to medical and VAD therapy: parallel to INTERMACS fields 2.0**
 - **G. Stewart et al**
UAB, Brigham and Women's, Cleveland Clinic, Univ Michigan, Cedars-Sinai LA, Univ Colorado, Penn, UTSouthwestern, Univ of Iowa, Univ S Florida

MedaMACS: High Event Rates with Medical Therapy in Profile 4 - 5



Stewart et al
For MedaMACS
Investigators
ISHLT April 2012

Knowledge Gap:-
≤ Class IV :Housebound and Walking Wounded
Stand At The Edge
of Current Indications

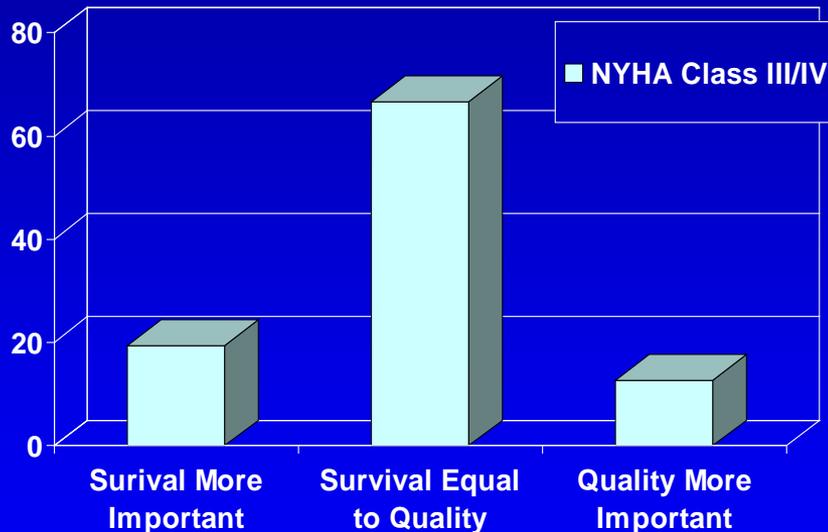
- If a patient is comfortable at rest and meets VAD criteria with peak $VO_2 < 14$, what is the difference in anticipated survival with VAD versus no VAD?
 - When survival on medical therapy is up to 50% at a year, early post-operative risk could potentially shorten survival for some patients.
 - Does this patient lose if we wait until he/she gets sicker, and if so, how much is lost?
- This patient is right at the edge of current indications.

What Does the Patient with Advanced Heart Failure Want?



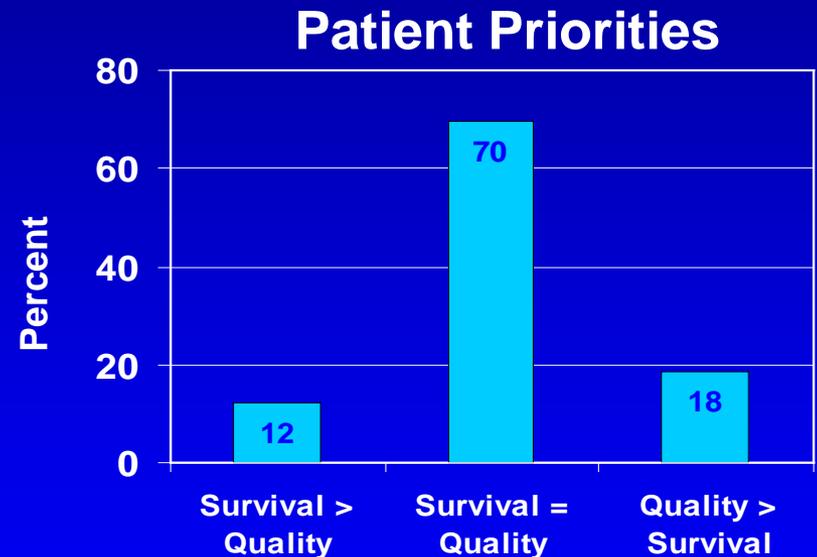
Patient Preferences for Quality/Survival Are Not Changing Across Time

*Harvard Partners Ambulatory HF
2 Centers 2008*



Stewart et al, JHLT 2009

*MedaMACS Screening Pilot
10 Centers - 2011*



Stewart et al. J Card Failure 2011;17:S37-38.

Patients answer the question: What is most important to you when considering a device that would support your heart to keep you alive?

PROFILE-LEVEL <i>Triage and Designation by Experienced Centers*</i>	PRIMARY LVADs 2011- 12	Official Shorthand	1 Yr Overall QOL With LVAD 100= Best	1 Yr % Pts w/ Problems w/ Usual Activities w/LVAD	Likely QOL At 1 year Without LVAD *
INTERMACS LEVEL 1	16%	“Crash and burn”	(85) Small #	(19%) Small #	1 / ∞
INTERMACS LEVEL 2	38%	“Sliding fast” on ino	76	40%	1 / ∞ <i>(37 preVAD)</i>
INTERMACS LEVEL 3	27%	Stable but Ino- Dependent Can be hosp or home	72	40%	---
INTERMACS LEVEL 4	13%	<u>Resting symptoms on oral therapy at home.</u>	70 Small #	55% Small #	≤51 MedaMACS Enrollment
INTERMACS LEVEL 5	3%	“Housebound”, Comfortable at rest, symptoms with minimum activity ADL		<i>Grady et al ISHLT 2012</i>	? ?
INTERMACS LEVEL 6	1.6%	“Walking wounded”-ADL possible but meaningful activity limited			? ?
INTERMACS LEVEL 7		Advanced Class III			

**Knowledge Gap:-
Housebound and Walking Wounded
Stand At The Edge
of Current Indications
For Both Survival and Quality of Life Benefits**

- If a patient is comfortable at rest and meets VAD criteria with peak $VO_2 < 14$, what is the difference in anticipated survival **and QOL** with VAD versus no VAD?
- When survival on medical therapy is up to 50% at a year, early post-operative risk could potentially reduce survival **and/or QOL** for some ambulatory patients.
- Does this patient lose and if so by how much if we wait until he/she gets sicker?
- This patient is right at the edge of current indications.

Making Decisions

One Patient At A Time

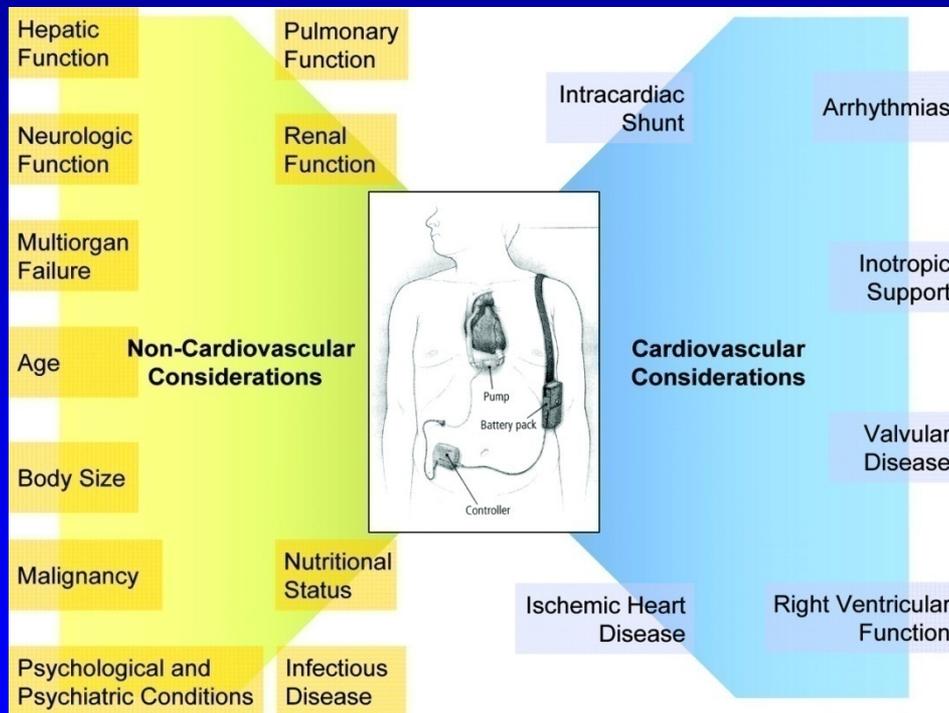
- Is the patient sick enough?

Line up outcomes With VAD minus outcomes without VAD

- Profiles in survival
 - Peak VO₂ for calibration and comparison
 - Profiles in quality of life
 - Limitations of risk scores
- **Is the patient healthy enough?**



Patient Selection for VAD: “Too Sick” or “Too Well”?



Risk with Ongoing Medical Therapy



Risk with VAD Operation

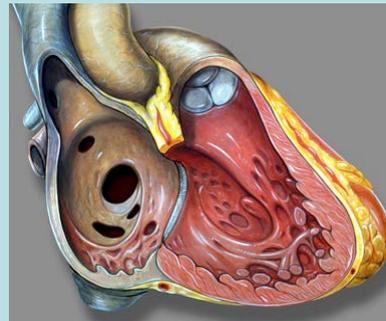
“Too Sick” for VAD Operation: Right Heart Failure – A Main Factor Decreasing QOL and HF Survival Without VAD

No current “destination”
options for right HF

RHF after LVAD carries
~6fold increase in mortality

DT Risk Score²
*AST, INR, albumin,
BUN, Low PAP*
(5 of 9)

**RV Mechanics in
Continuous Flow**



HeartMate II Risk Score³
Albumin, INR, Creatinine
(3 of 6)

**Various RV Failure Risk
Scores Proposed^{4,5,6}**

1. <http://radiopaedia.org/images/25224>
2. Lietz et al. Circ 2007; 116: 497-505.
3. Cowger, et al. ISHLT 2011.

4. Matthews et al. JACC 2008; 51:2163-72.
5. Fitzpatrick et al. JHLT 2008; 27:1286-92
6. Drakos et al. Am J Cardiol 2010;105:1030-5.

Device Options

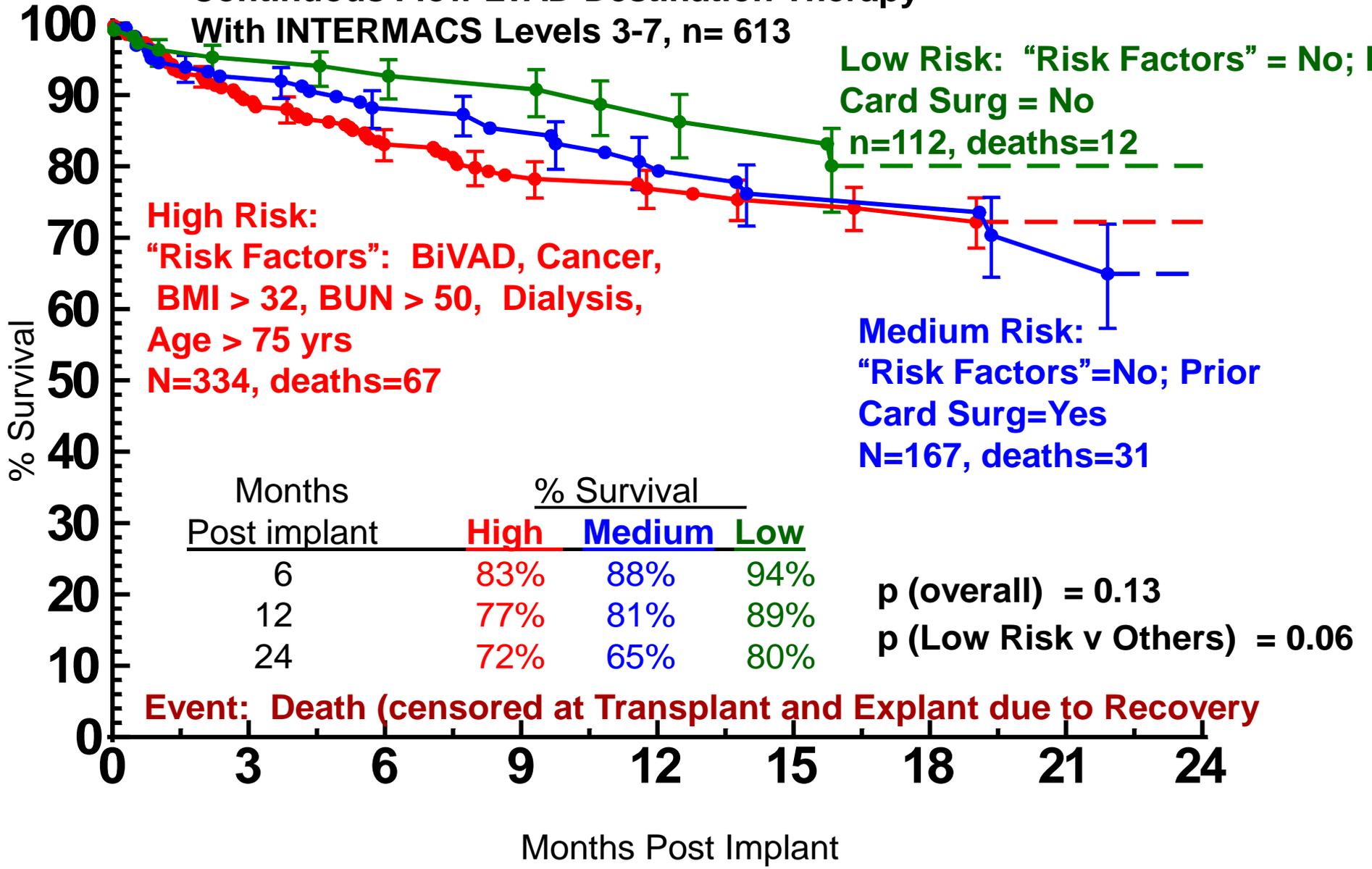
Determined by RV and Intent

	RV function normal	RV dysfunction mild	RV dysfunction moderate or newly severe	RV dysfunction Severe Chronic
Clinical status on med Rx	Usually can be compensated < Class IV	Often compensated < Class IV	Frequent decompensation, Some RV dysfunction may be reversible with intensive unloading	Chronic decompensation with RHF, Liver dysfunction, Malnutrition, Cardio-renal
Device as Bridge to transplant	Med Rx or LVAD	LVAD	LVAD and see if RVAD needed.	LVAD+RVAD Or Total Art Heart
Destination (Lifetime Support)	Med Rx or LVAD	Med Rx or LVAD	<u>Big gamble</u> may need temp RVAD or prolonged inotropes	NO OPTION

Risk Factors for Death in Destination Therapy Patients – Adult Primary Implants: INTERMACS, June 2006 - December 2011

Risk Factors	<u>Early hazard</u>		<u>Constant hazard</u>	
	HR	p-value	HR	p-value
Age (older)			1.24	.01
BMI (higher)			1.04	.03
History of cancer	1.89	.04		
History of cardiac surgery	1.69	.001		
Dialysis	3.14	.004		
BUN			1.08	.009
INTERMACS Level 1	4.58	<.0001		
INTERMACS Level 2	2.35	.02		
Use of pulsatile LVAD			2.63	<.0001
RVAD in same operation			3.22	.002

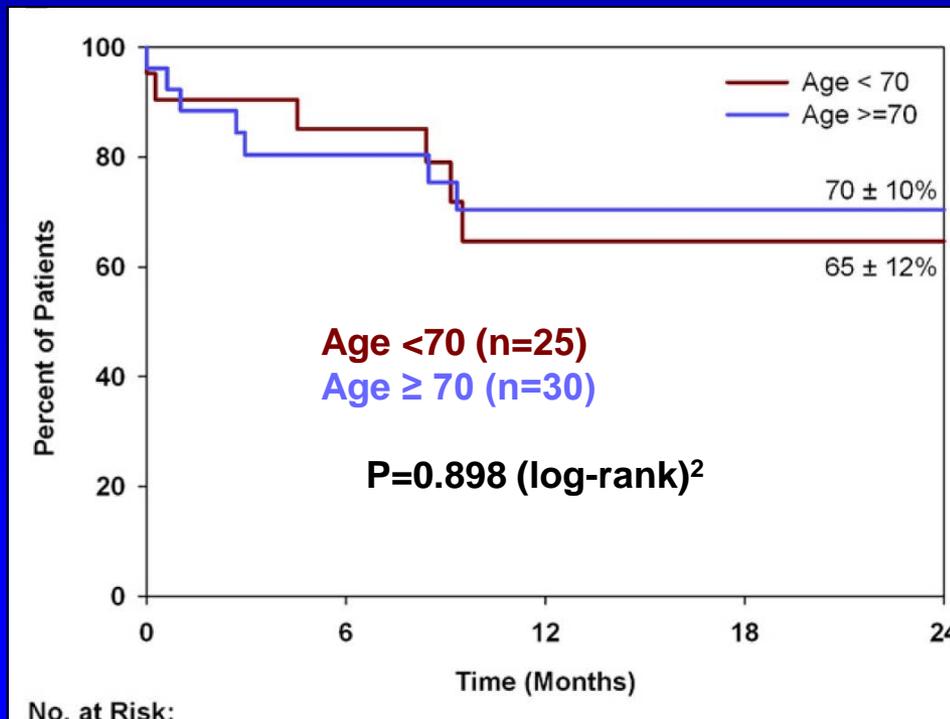
Continuous Flow LVAD Destination Therapy With INTERMACS Levels 3-7, n= 613



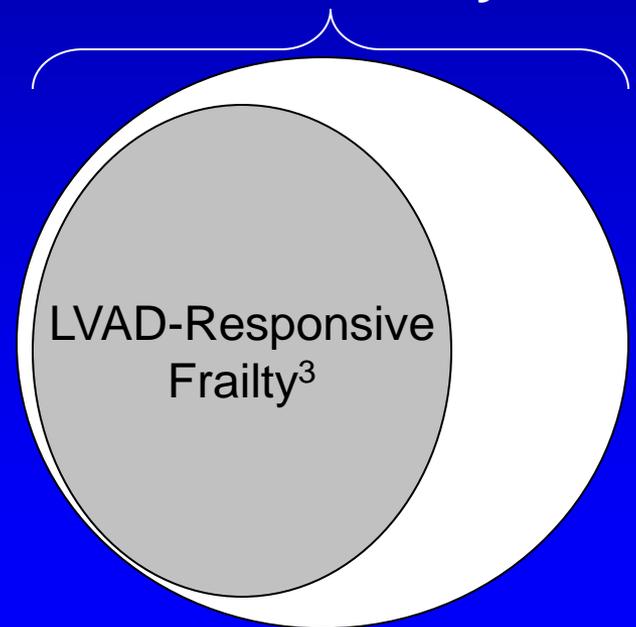
Age and VAD Operation

Increasing Focus on Frailty Assessment

- Average age of hospitalization for low EF heart failure in U.S. is 75 years old¹
- Advanced age is a contraindication to transplant
→ Target for DT LVAD



Overall Frailty



1. Mehra MR, et al. JHLT 2006;25:1024-42.
2. Adamson RM et al. JACC 2011; 57:2487-95.
3. Flint KM, Circ Heart Fail 2012;5:286-93.

Coping for patient and caregivers

Who Should Define Contra-indications for LVAD?

Process is evolving as it did for cardiac transplantation

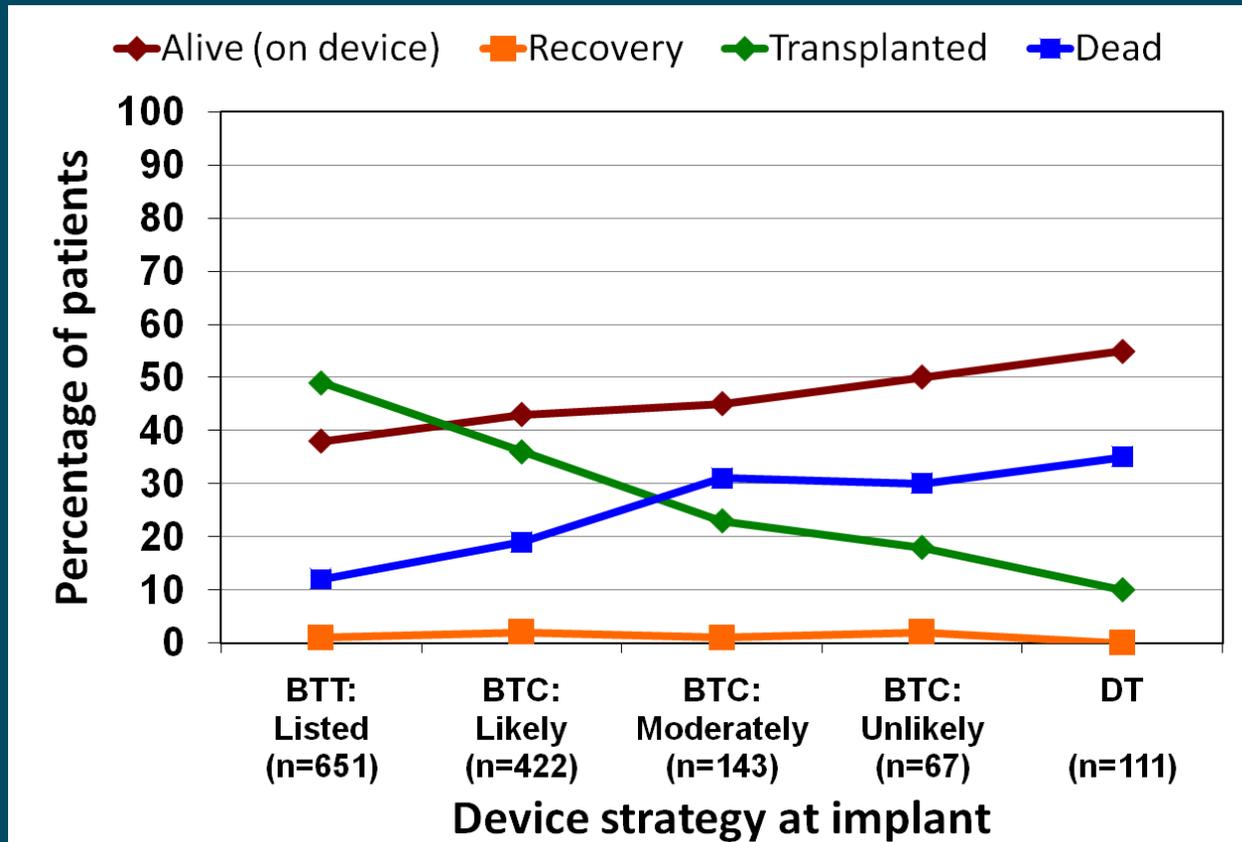
- Only a few absolute contra-indications
- Lots of relative contra-indications
 - Degree of severity of other organ system dysfunction
 - Combined impact, e.g.
 - Previous mild stroke limiting manual dexterity, with uncertain support in the home
 - Borderline RV function and chronic renal impairment causing diuretic resistance
 - Likelihood of reversibility with LVAD support
- For VAD, added uncertainty regarding option of heart transplant as a best or “bail-out” option?

More realistic to establish criteria of center experience

where patients will be evaluated

than to dictate exact precise contra-indications.

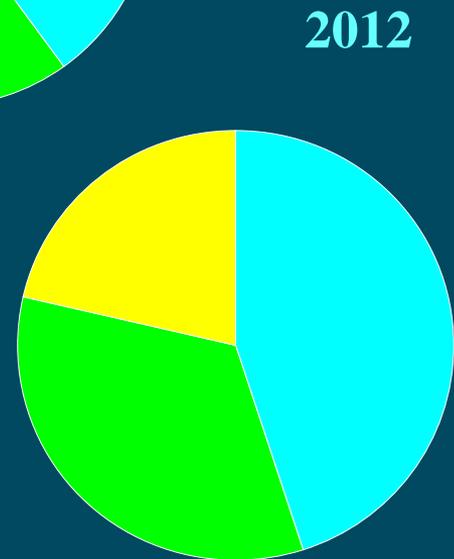
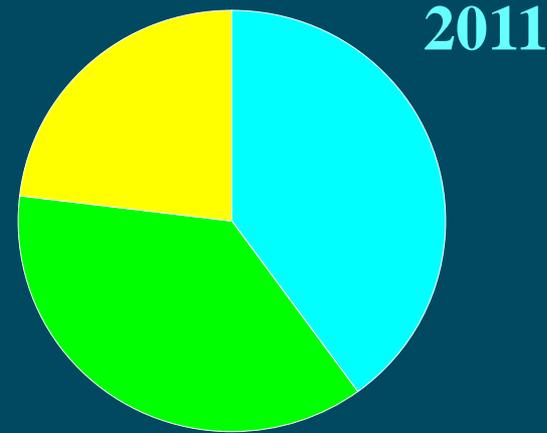
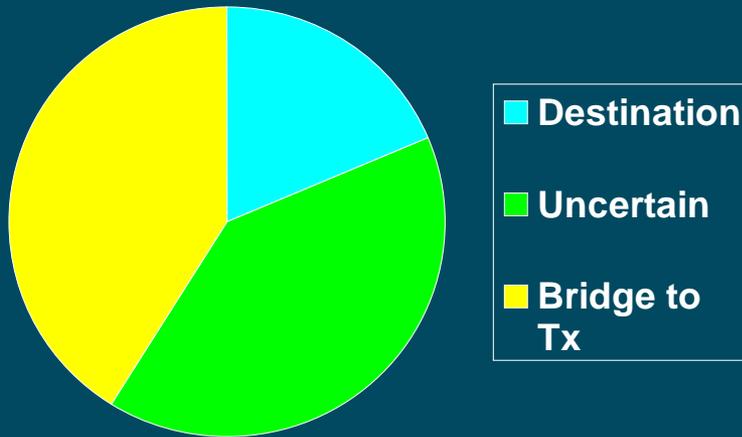
Competing Outcomes By Intent of VAD At Time of VAD Implant



Teuteberg, Stewart et al for INTERMACS
ISHLT 2012

Evolution From Bridge Through Uncertainty To Destination

BEFORE 2011



INTERMACS Data

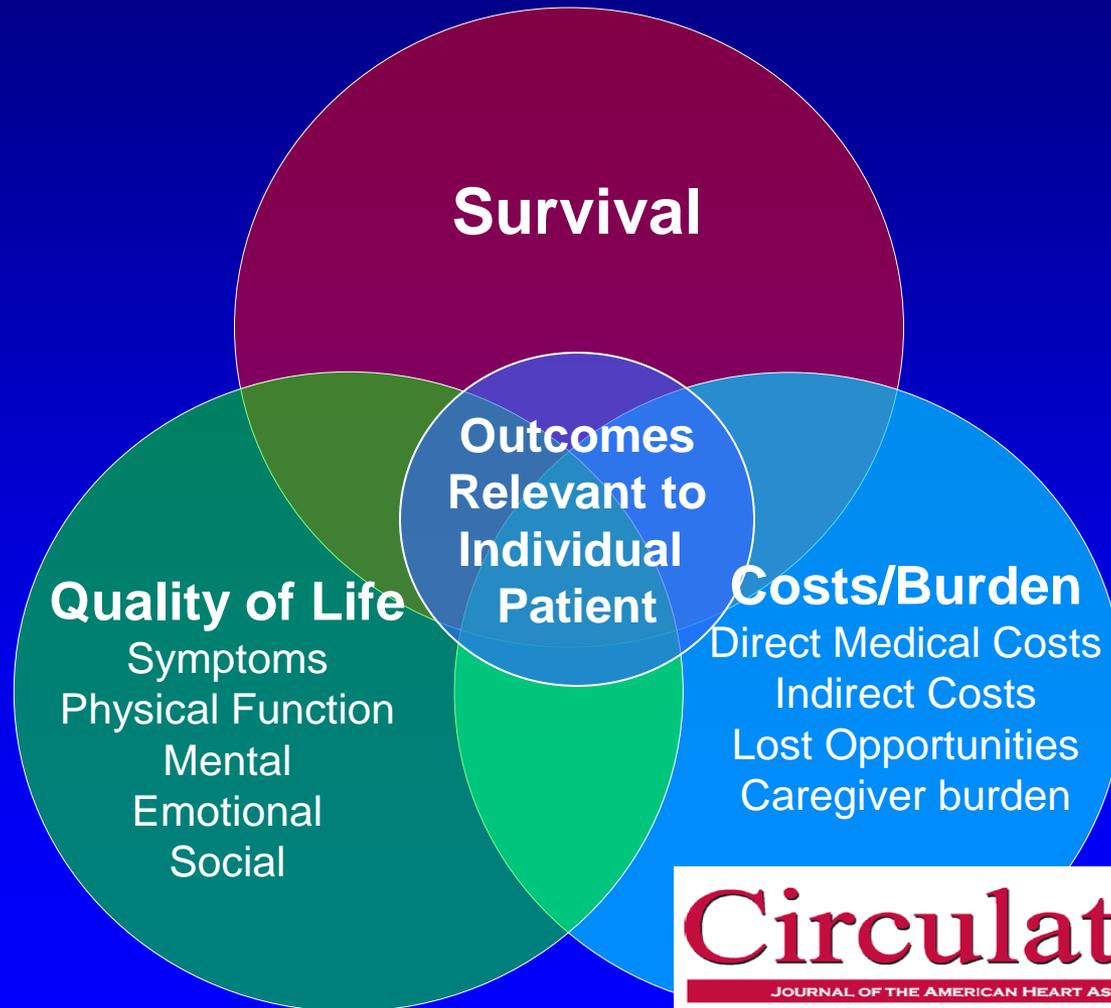
Courtesy of D. Naftel: 2006-2012

Making Decisions

One Patient At A Time

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- **Summary of present knowledge gaps**

Dimensions of VAD Decision Making for Destination “Lifetime” Therapy



Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association
Learn and

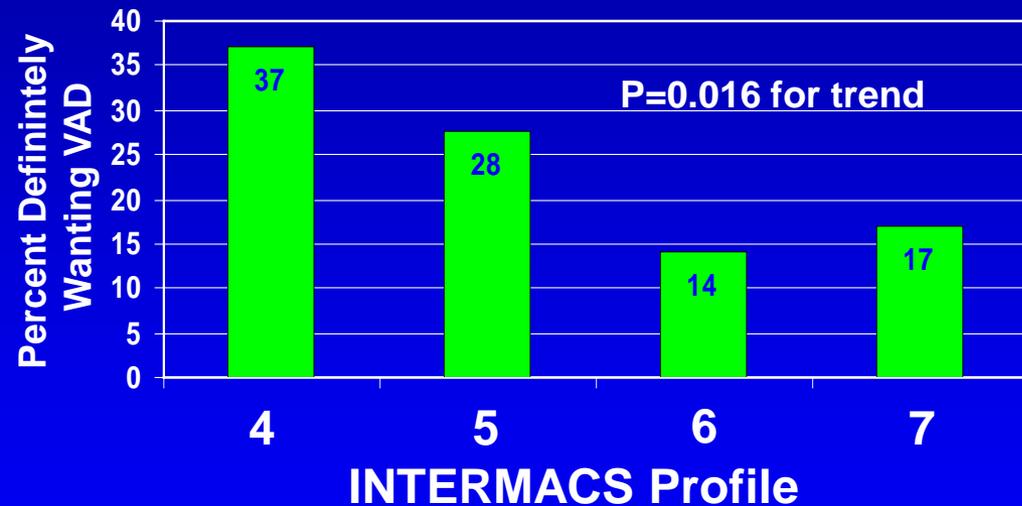
Decision Making in Advanced Heart Failure : A Scientific Statement From the American Heart Association

Larry A. Allen, Lynne W. Stevenson, Kathleen L. Grady, Nathan E. Goldstein, Daniel D. Matlock, Robert M. Arnold, Nancy R. Cook, G. Michael Felker, Gary S. Francis, Paul J. Hauptman, Edward P. Havranek, Harlan M. Krumholz, Donna Mancini, Barbara Riegel and John A. Spertus

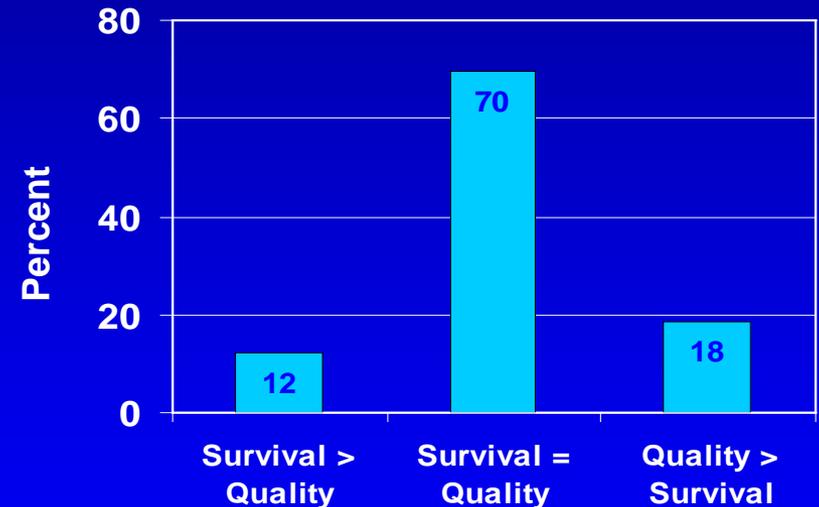
Engaging Patients about The VAD Decision

MedaMACS Screening Pilot

Cautious Enthusiasm for LVAD



Patient Priorities



37% of pts in Profile 4

indicated definite preference for VAD

Standardize Informed Consent for Advanced HF Procedures

- Background/indications
- Procedure
- Potential Benefits
- Potential Risks
- **Alternative strategies**

- Experience of your health care team

- \$ Costs – initial
- \$ Costs – per year

*Adapted from Krumholz,
Informed Consent to
Promote Patient-Centered Care.
JAMA 2010;303:1190*

Translation to patients should include examples :

- *“Of 100 patients like you, ----- lived two years longer with...”*
- *“Of 100 patients like you, ----- had strokes that limited their ability to speak/walk/care for themselves*
- *“Of 100 patients like you, ----- rated their daily activity as “near normal”*
- *Because of your special conditions of -----, we may expect your outcomes to be better / worse than previous experiences.*

- **Expected duration of hospitalization**
- **Likelihood of discharge home vs to rehabilitation**
- **Months to full functional recovery**

- **Family and caregiver experience**

Major Adverse Events Impacting Quality and Length of Life

- **Stroke – about 1 in 10**
- **GI bleed – about 1 in 3**
- **Infection – frequent mild infection, severe infection less common**
- **Pump thrombosis –**

When are quality of life and outlook for survival sufficiently poor to accept risks of these adverse events?

Knowledge Gaps Regarding Function and Quality of Life and Patient Satisfaction With Therapy

- **Traditionally has not been a central focus of funded data collection**
- **Most useful data for the ambulatory population is the change from before to after LVAD**
- **Bias of missing data in patients who are more ill, both before and after LVAD**
- **New impetus in INTERMACS 2.0 to better inform on quality of life**
- **New policy standard for collecting QOL data**
- **Carrot or stick required to insert this task into multi-tasking Advanced Heart Disease centers**

Vital Role of Palliative Care Members of LVAD Heart Team

- **Help patient to make decision consistent with lifestyle, preferences, and goals.**
- **Provide patient with support to state “No” as decision, with understanding of the alternative care to be offered to alleviate symptoms and improve quality of life until the end of life.**
- **If “Yes”, review with patients the possibility of undesired outcomes, with discussion to include family regarding “What if” decisions.**
- **Recognize that many patients receiving LVAD to enhance quality and length of life will still have LVAD at the time of death.**

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Knowledge Gaps

Limiting Shared Decision-Making

- **What is the anticipated survival for ambulatory patients at home on optimal oral therapy for HF?**
 - **With VAD**
 - **Without VAD**
- **What are the quality of life and satisfaction with therapy for all eligible patient profiles?**
 - **With VAD**
 - **Without VAD**
- **How can we re-define the intent of VAD therapy to emerge from the shadows cast by a “bridge to decision”?**

