



Relevant Financial Relationship Disclosure Statement

Pre-Implant Patient Triage Using Patient Status with INTERMACS Patient Profiles: Can We Refine Selection Strategy for MCS?

- I will not discuss the investigational use of devices or medications.
- The following relevant financial relationships exist related to my role in this session:
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Pre-Implant Patient Triage Using Patient Status with INTERMACS Patient Profiles: Can We Refine Selection Strategy for MCS?

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Background and Purpose

- INTERMACS is a US national registry for patients receiving durable mechanical circulatory support (MCS) device therapy to treat advanced heart failure.
- Implantable MCS is an established therapy when other forms of treatment for advanced heart failure are ineffective.
- The risk of MCS therapy significantly correlates with the acuity and severity of illness.

Background and Purpose

- Traditional hemodynamic and laboratory parameters used to assess risk are modifiable through the use of inotrope therapy or short-term circulatory support.
- To refine patient selection and maximize MCS outcomes, a series of 7 descriptive patient profiles reflecting acuity and severity of illness were created for the INTERMACS registry.

Hypothesis

- A descriptive profile of the patient's status at the time of MCS implantation would simplify and improve the assessment of implant risk for MCS.

Methods

- A total of 420 patients from 74 sites were entered into the INTERMACS registry from 6/23/2006 to 12/31/2007.
- Registry data was prospectively entered electronically in the INTERMACS, web-based, data entry system maintained by the United Network for Organ Sharing (UNOS).
- Pre-implant *Patient Profile* assignment was based upon the degree of inotrope support and hemodynamic stability at the time of MCS implant.

Methods

- Data analysis was performed at the University of Alabama (DCC).
- IRB approval was obtained at each participating INTERMACS center.
- Statistical Methods:
 - *Patient Profile* groups were compared using chi-square or one way analysis of variance for dichotomous and continuous variables, respectively.
 - Outcomes were compared using the log rank test.
 - Competing outcomes methodology was used for estimating the time course of multiple, mutually exclusive events
 - For the purposes of data analysis, *Patient Profiles* 5, 6, and 7 were combined due to the low number of patients

Patient Profiles

- **Profile 1:** “Crashing and burning” - critical cardiogenic shock.
- **Profile 2:** “Progressive decline” – inotrope dependence with continuing deterioration.
- **Profile 3:** “Stable but inotrope dependent” - describes clinical stability on mild-moderate doses of intravenous inotropes.
- **Profile 4:** “Recurrent advanced heart failure” - “recurrent” rather than “refractory” decompensation.

Patient Profiles

- **Profile 5:** “Exertion intolerant” - describes patients who are comfortable at rest but are exercise intolerant.

- **Profile 6:** “Exertion limited” – a patient who is able to do some mild activity but fatigue results within a few minutes or any meaningful physical exertion.

- **Profile 7:** “Advanced NYHA III” - describes patients who are clinically stable with a reasonable level of comfortable activity, despite history of previous decompensation that is not recent.
 - Arrhythmia modifier (A) - Recurrent ventricular tachyarrhythmias may dominate the clinical picture (repeated shocks from ICD or external defibrillator, usually more than 2 weekly). The A-modifier may be added to any INTERMACS level except level 7, (e. g. Level 4-A).

Distribution of Patients Among Profiles

| INTERMACS <i>Patient Profile</i> <i>(Pre-Implant)</i> | Ventricular Arrhythmia Modifier | | | Total | |
|--|--|------------|--------------|--------------|-----------------|
| | No. | Yes | % | No. | % 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 | 100% | 420 | 100% |

Patient Characteristics

| INTERMACS Patient Profile (Pre-Implant) | Age (years- mean) | Male (%) | NYHA Class IV (%) | Etiology: Ischemic (%) | Inotrope Support (%) | LVEF <20% (%) | Pre- Implant Ascites (%) |
|--|----------------------------------|---------------------|----------------------------------|---------------------------------------|-------------------------------------|---------------------------------|---|
| Profile 1 | 49.3 | 74% | 93% | 45% | 89% | 56% | 15% |
| Profile 2 | 51.2 | 77% | 90% | 42% | 96% | 61% | 16% |
| Profile 3 | 49.8 | 89% | 78% | 51% | 97% | 60% | 9% |
| Profile 4 | 55.6 | 91% | 68% | 48% | 37% | 58% | 12% |
| Profile 5, 6, and 7 | 58.0 | 83% | 53% | 44% | 47% | 24% | 0% |
| P Values | .02 | .11 | <.0001 | 0.86 | <.0001 | .07 | .05 |

Hemodynamic Variables

| INTERMACS Patient Profile (Pre-Implant) | Heart Beat (beats / minute) | Systolic Blood Pressure (mmHg) | Mean Pulmonary Artery Pressure (mmHg) | Pulmonary Capillary Wedge Pressure (mmHg) | Cardiac Index (L/min/m²) |
|--|--|---|--|--|--|
| Profile 1 | 101 | 95 | 33.9 | 26.3 | 2.1 |
| Profile 2 | 94 | 100 | 34.8 | 25.1 | 2.3 |
| Profile 3 | 92 | 98 | 38.4 | 24.5 | 2.0 |
| Profile 4 | 85 | 99 | 36.8 | 28.4 | 1.9 |
| Profiles 5, 6, and 7 | 87 | 110 | 35.1 | 21.5 | 1.9 |
| P Values | <.0001 | .004 | .2 | .4 | .2 |

(numbers represent mean values)

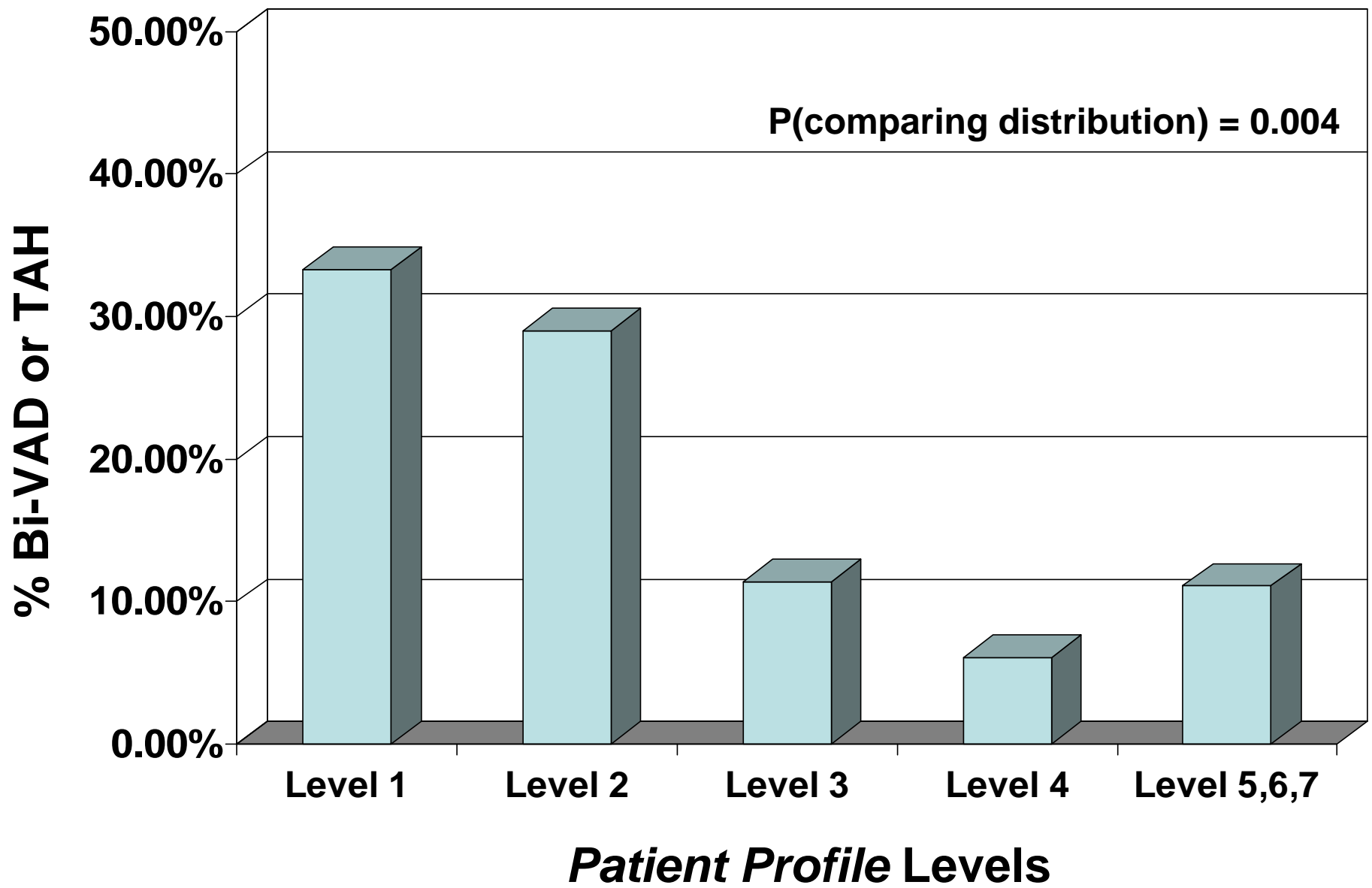
Laboratory Variables

| INTERMACS Patient Profile (Pre-Implant) | Na (mEq/L) | Creat (mg/dl) | Blood Urea Nitrogen (mg/dl) | White Blood Count (thousand/ mm³) | Albumin (g/dl) |
|--|-----------------------|--------------------------|--|---|---------------------------|
| Profile 1 | 133.6 | 1.8 | 34.6 | 12.4 | 3.0 |
| Profile 2 | 133.6 | 1.6 | 31.9 | 9.8 | 3.2 |
| Profile 3 | 133.6 | 1.3 | 26.1 | 8.9 | 3.2 |
| Profile 4 | 137.0 | 2.1 | 36.3 | 9.2 | 3.6 |
| Profiles 5, 6, and 7 | 136.1 | 1.7 | 35.5 | 8.5 | 3.5 |
| P Values | .02 | .01 | .2 | <.0001 | <.0001 |

Laboratory Variables

| INTERMACS Patient Profile (Pre-implant) | Total Bilirubin (mg/dl) | SGOT (AST) (IU/L) | SGPT (ALT) (IU/L) | INR |
|--|--|------------------------------|------------------------------|------------|
| Profile 1 | 2.0 | 441.4 | 380.3 | 1.6 |
| Profile 2 | 1.7 | 61.8 | 100.9 | 1.4 |
| Profile 3 | 1.3 | 47.7 | 73.8 | 1.4 |
| Profile 4 | 1.0 | 88.4 | 104.7 | 1.3 |
| Profiles 5, 6, and 7 | 1.2 | 29.6 | 34.0 | 1.4 |
| P Values | .03 | .0002 | .003 | .02 |

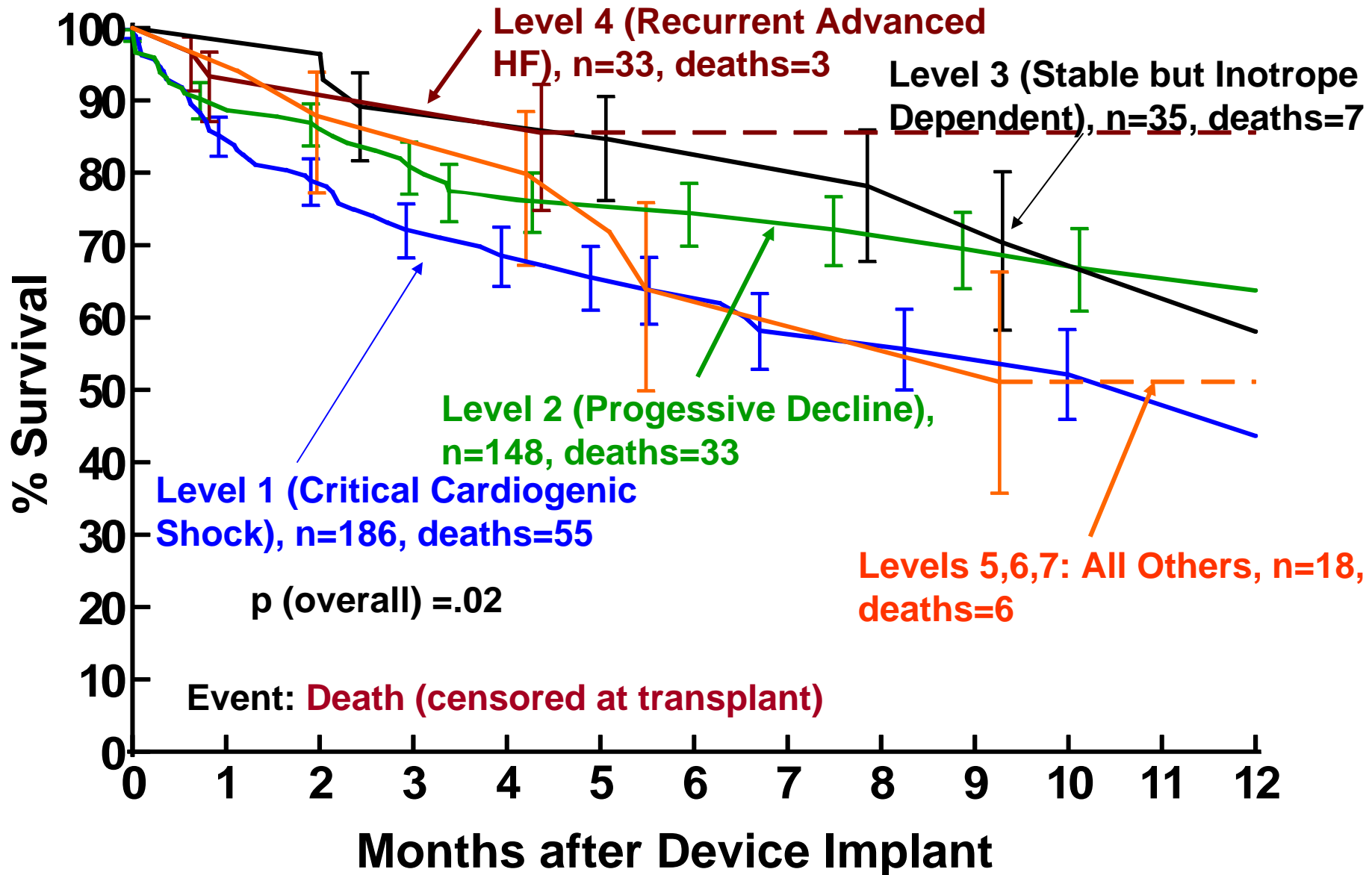
Device Support by *Patient Profile*



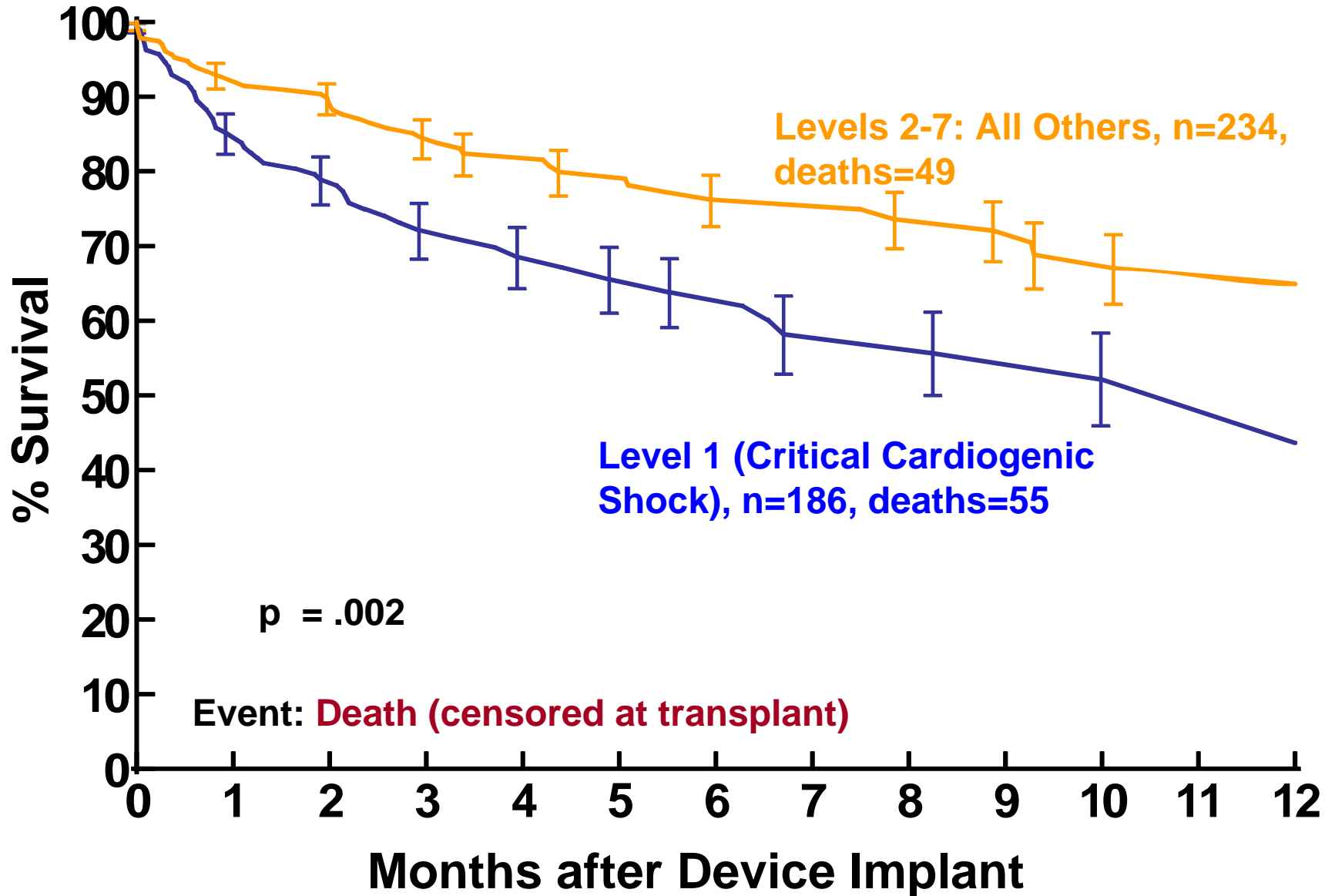
Outcomes

| INTERMACS <i>Patient Profile</i> <i>(Pre-Implant)</i> | Patient No. | Survival at 6 Months (%) | Percent Alive with Device In Place at 6 Months (%) |
|--|------------------------|-------------------------------------|---|
| Profile 1 | 186 | 64% | 26% |
| Profile 2 | 148 | 74% | 43% |
| Profile 3 | 35 | 85% | 65% |
| Profile 4 | 33 | 86% | 48% |
| Profile 5 | 5 | -- | -- |
| Profile 6 | 6 | -- | -- |
| Profile 7 | 7 | -- | -- |
| P Values | | 0.02 | |

Patient Survival Among Profiles



Patient Survival Among Profiles



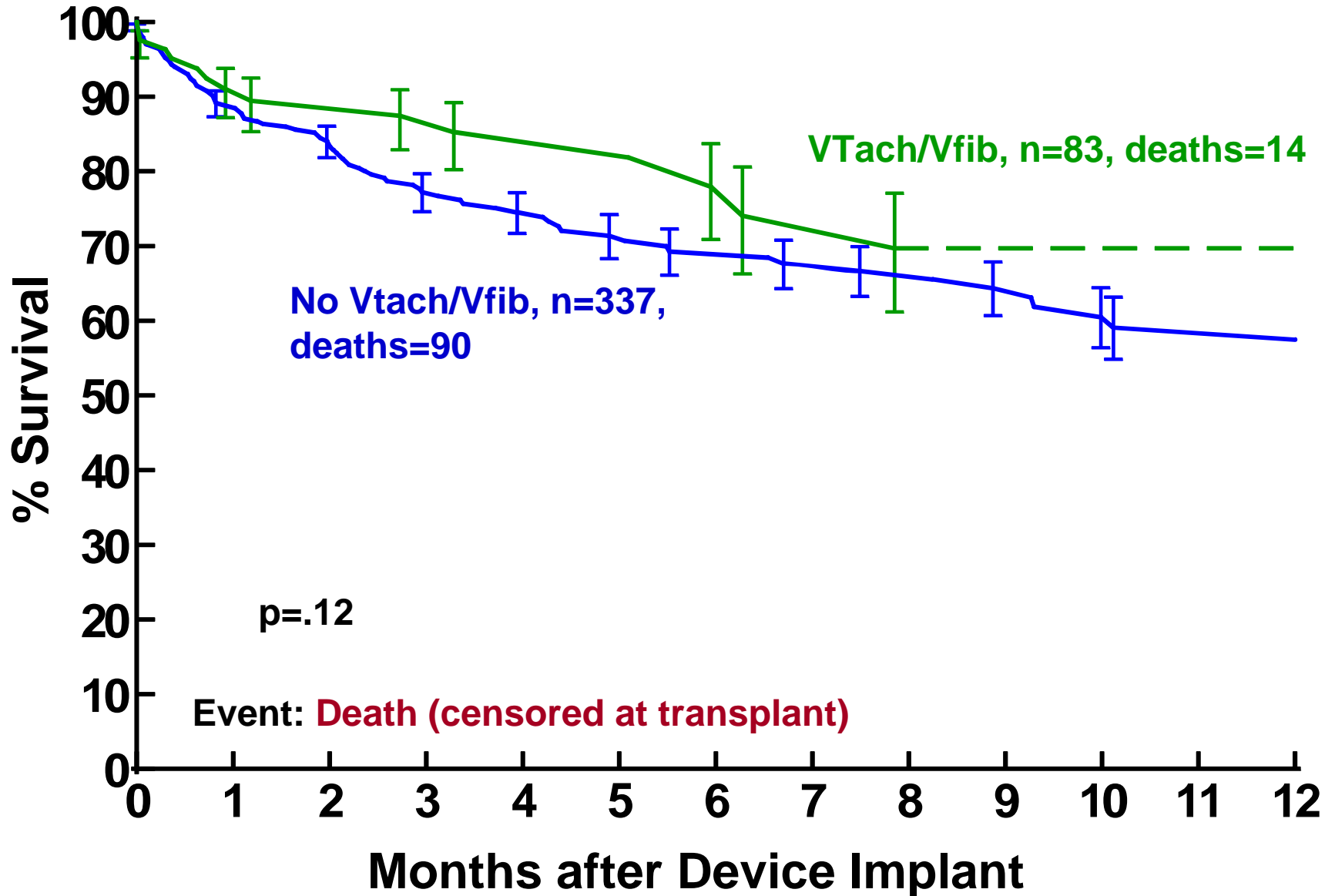
Levels 2-7: All Others, n=234, deaths=49

Level 1 (Critical Cardiogenic Shock), n=186, deaths=55

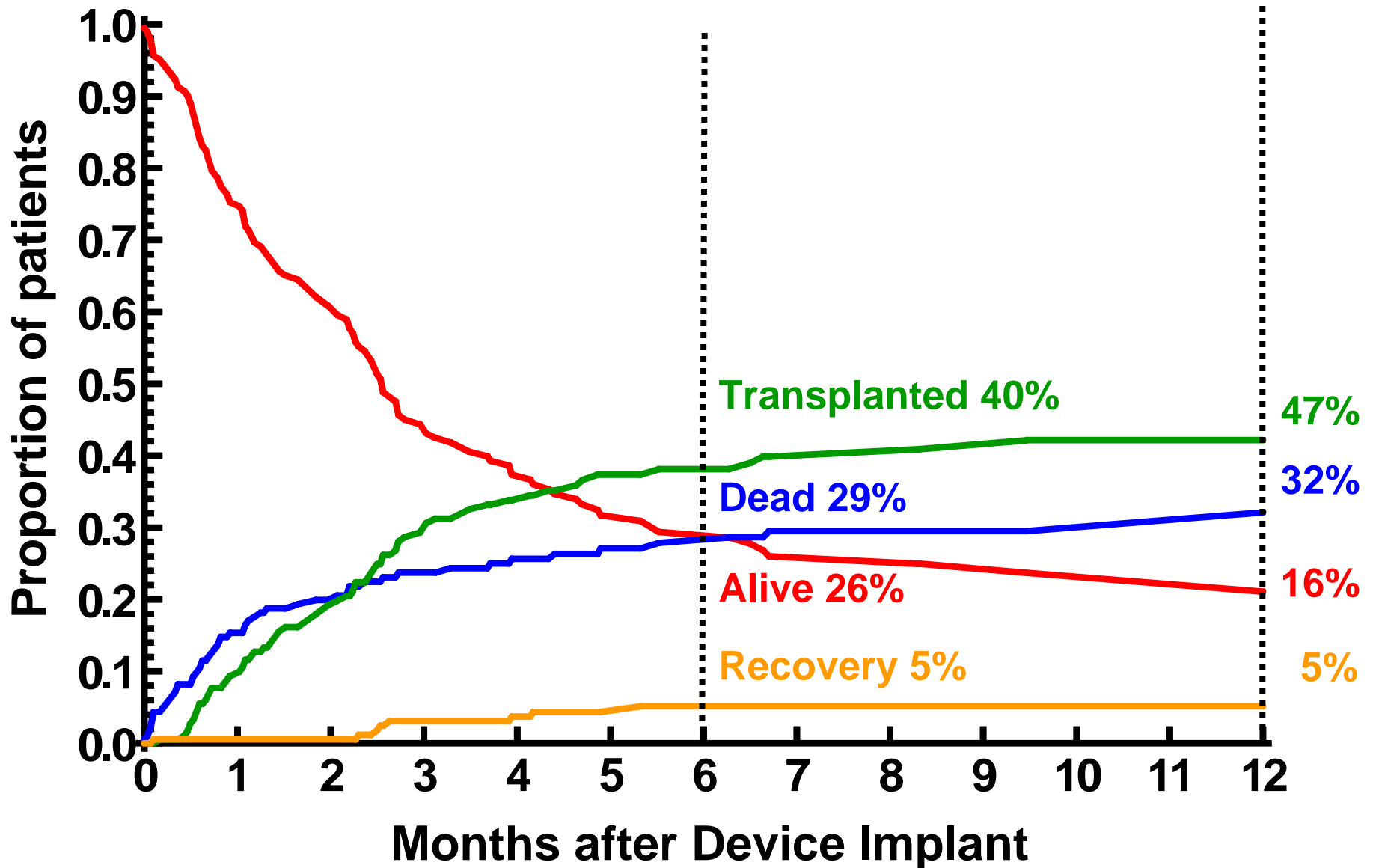
p = .002

Event: Death (censored at transplant)

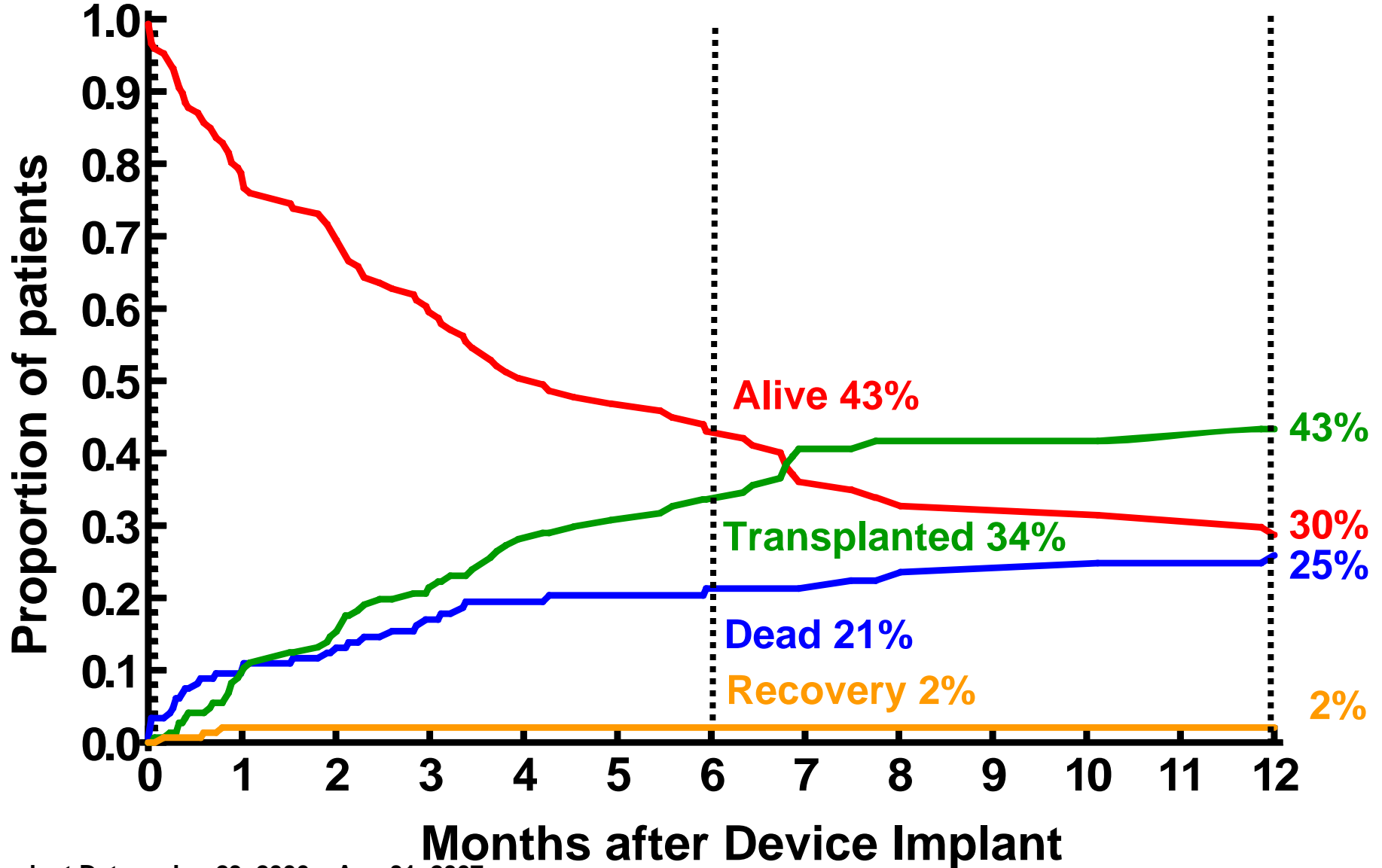
Influence of Arrhythmia Modifier on Patient Survival



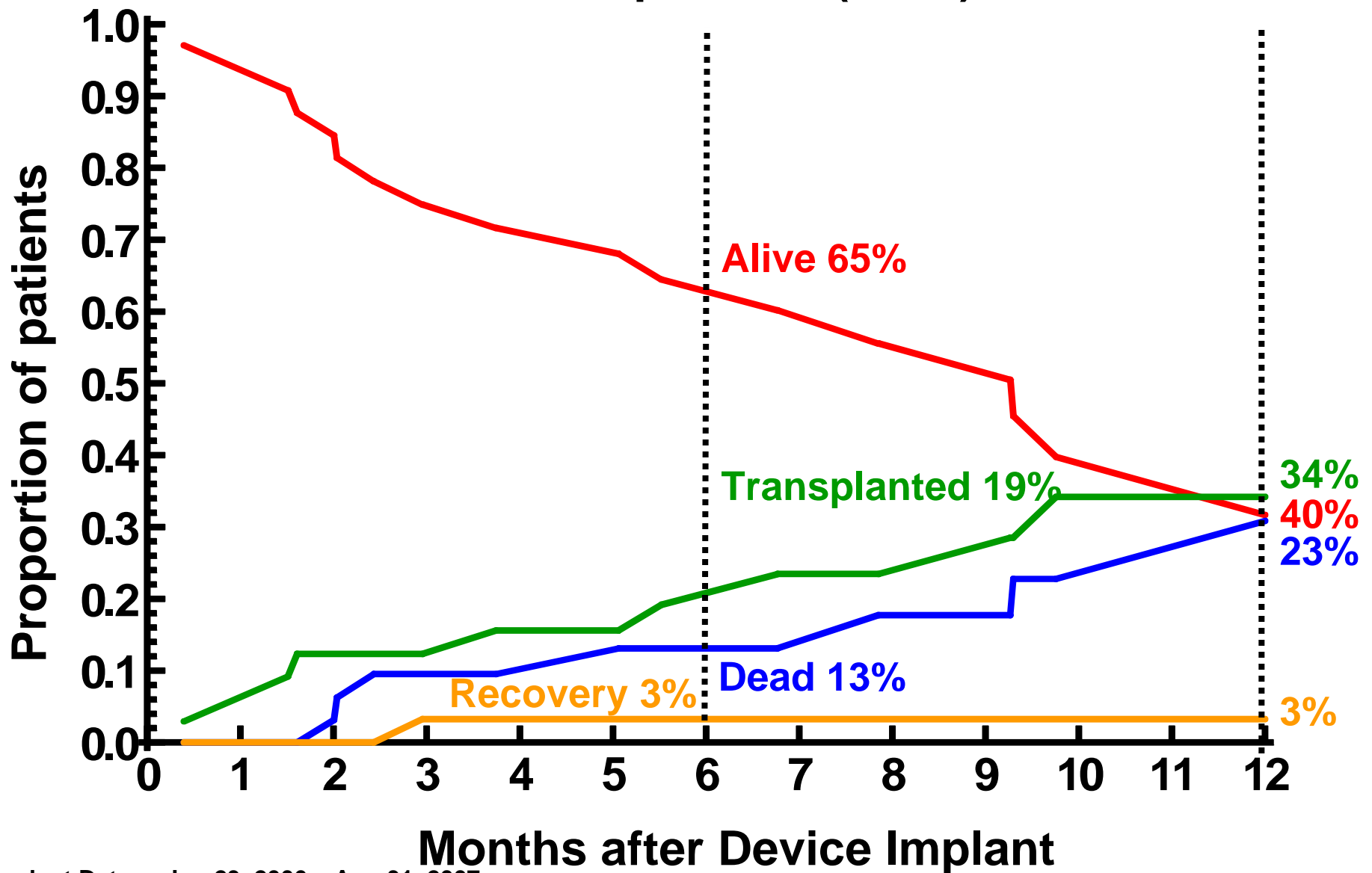
Competing Outcomes – Level 1: Critical Cardiogenic Shock (n=186)



Competing Outcomes – Level 2: Progressive Decline (n=148)



Competing Outcomes – Level 3: Stable but Inotrope Dependent (n=35)



RESULTS SUMMARY

- Most patients were assigned to *Patient Profiles* 1 and 2 at the time of MCS implantation.
- Patients in more ill *Patient Profiles* manifest a higher prevalence of biventricular failure (more liver dysfunction and presence of ascites) and were more likely to require biventricular support or TAH.
- Patient survival was significantly greater for *Patient Profiles* 2 through 7 compared to *Patient Profile* 1.
- Patients in Profile 1 were more likely to undergo heart transplantation at 6 months compared to *Patient Profiles* 2 and 3.

Conclusions

- Descriptive *Patient Profiles* identify important differences in patient characteristics and laboratory variables.
- Implantation of MCS in the terminal phases of heart failure, *Patient Profile 1* (Critical cardiogenic shock) is associated with a significantly decreased survival compared to *Patient Profiles 2* through 7.
- The use of Patient Profiles simplifies the assessment of MCS implant risk.
- Further development of *Patient Profiles* may help refine selection and timing for MCS devices.