Long-Term Neurocognitive Outcomes in LVAD Recipients

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Disclosures

Sung-Min Cho DO MHS: None
Darlene Floden PhD: None
Nahush A. Mokadam MD: Consultant- Medtronic, Abbott, Carmat, SynCardia
Susan Joseph MD: None
Jeffrey Teuteberg MD: Consultant – Medtronic, CareDx, Abiomed, Abbott; Speaking – Medtronic, CareDx, Paragonix
David Tirschwell MD: None
Song Li MD: None
Joseph Rogers MD: None
Francis Pagani MD: None
Claudius Mahr DO: Consultant / Investigator: Abbott, Medtronic, Abiomed, Carmat, Syncardia
Ken Uchino MD: None
Randall Starling MD: None

ENDURANCE and ENDURANCE SUPPLEMENTAL: sponsored by Medtronic (formerly HeartWare Inc.)

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Background

Neurocognitive Function in LVAD Patients

- Stroke is a common adverse event (AE) following left-ventricular assist device (LVAD) implantation in destination therapy (DT) patients impacting morbidity, mortality, and quality of life (QOL)
- Cognitive impairment (with or without stroke) is not well characterized in DT LVAD population

Background

HVAD DT Trials

ENDURANCE[1]

- Prospective, randomized, multicenter trial comparing the safety and efficacy of HVAD to HMII (control) in end-stage heart failure patients who did not qualify for heart transplant.
- Enrollment included 446 patients who were randomized 2:1 to the HVAD or the HMII control (296 HVAD System, 149 HMII).

ENDURANCE Supplemental[2]

- Prospective, randomized, multicenter trial to prospectively determine the effectiveness of a blood pressure management strategy on neurological injury in DT patients receiving the HVAD System vs HMII (control).
- Enrollment included a total of 465 patients in the intent-to-treat population randomized 2:1 (308 HVAD System, 157 HMII).

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1. Rogers, et al. 2017. *N Engl J Med.*
2. Milano, et al. 2018. *JACC Heart Fail.*

Aim

To assess the short- and long-term cognitive outcomes in patients with DT LVADS

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Methods

- Post-hoc analysis of all patients enrolled in ENDURANCE and ENDURANCE Supplemental Trials (n=910)
- Patients completed a battery of neuropsychological tests at baseline, 6, 12, and 24 months post-implant
- For each cognitive test, patients were separated into “impaired” or “intact” subgroups at baseline
- Patients were then observed whether they “improved,” “declined,” or were “stable” with respect to cognitive function over 24 months

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Methods

Neuropsychological Testing

- Hopkins Verbal Learning Test – Revised (HVLT-R)[3]: A brief assessment of verbal learning and memory. We examined patient performance on total recall of 12 words over 3 learning trials (**Immediate recall**) and total recall of 12 words after a 20-minute delay (**Delayed recall**).

- Trail Making Test part B (TMT)[4] : Part B measures processing speed and the ability to mentally control simultaneous stimulus patterns (also known as mental flexibility, a type of executive/frontal lobe function). We examined total time in seconds to complete part B, capped at 240 seconds.

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3. Brandt. 1991. *Clinical Neuropsychologist*
4. Spreen et al. 1998. *A compendium of neuropsychological tests: Administration, norms, and commentary*

Methods

Neuropsychological Testing

- Short form of the Boston Naming Test (English 15-item version BNT)[5]: A measure of language where patients must explicitly name different visually presented drawings. We examined total items correctly named.
- Clock Drawing Test (CDT)[6]: CDT measures visuospatial perception and visuo-constructional function. Patient score reflected total points (maximum of 10) for accurate depiction of circle, numbers, and correct hand placement.

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5. Mack et al. 1992. *J Gerontol*
6. Freedman et al. 1994. *Clock drawing: A neuropsychological analysis*

Methods

Detection of Cognitive Change

- Using group means to examine cognitive change over time can be misleading as small improvements in test scores likely represent practice effects rather than true cognitive change
- Reliable change indices (RCI) and standardized regression-based change scores (SRB) are used to measure cognitive change while taking into account practice effects and measurement errors in follow-up

Methods

Detection of Cognitive Change

The following metrics were used to determine change outside of the 90% confidence interval

- HVLT-R and TMT: SRBs developed in an age-matched normative sample with a test-retest interval of 12 months
- BNT: RCIs developed in an age-matched normative sample with a test-retest interval of 24 months
- CDT: There are no RCIs and SRBs available for this test. We used sample-specific change scores Z > +/-1.65 based on group change at 12 months post implant for patients with no history of stroke and no stroke within 12 months of implant.

Analysis

Cognitive Tests

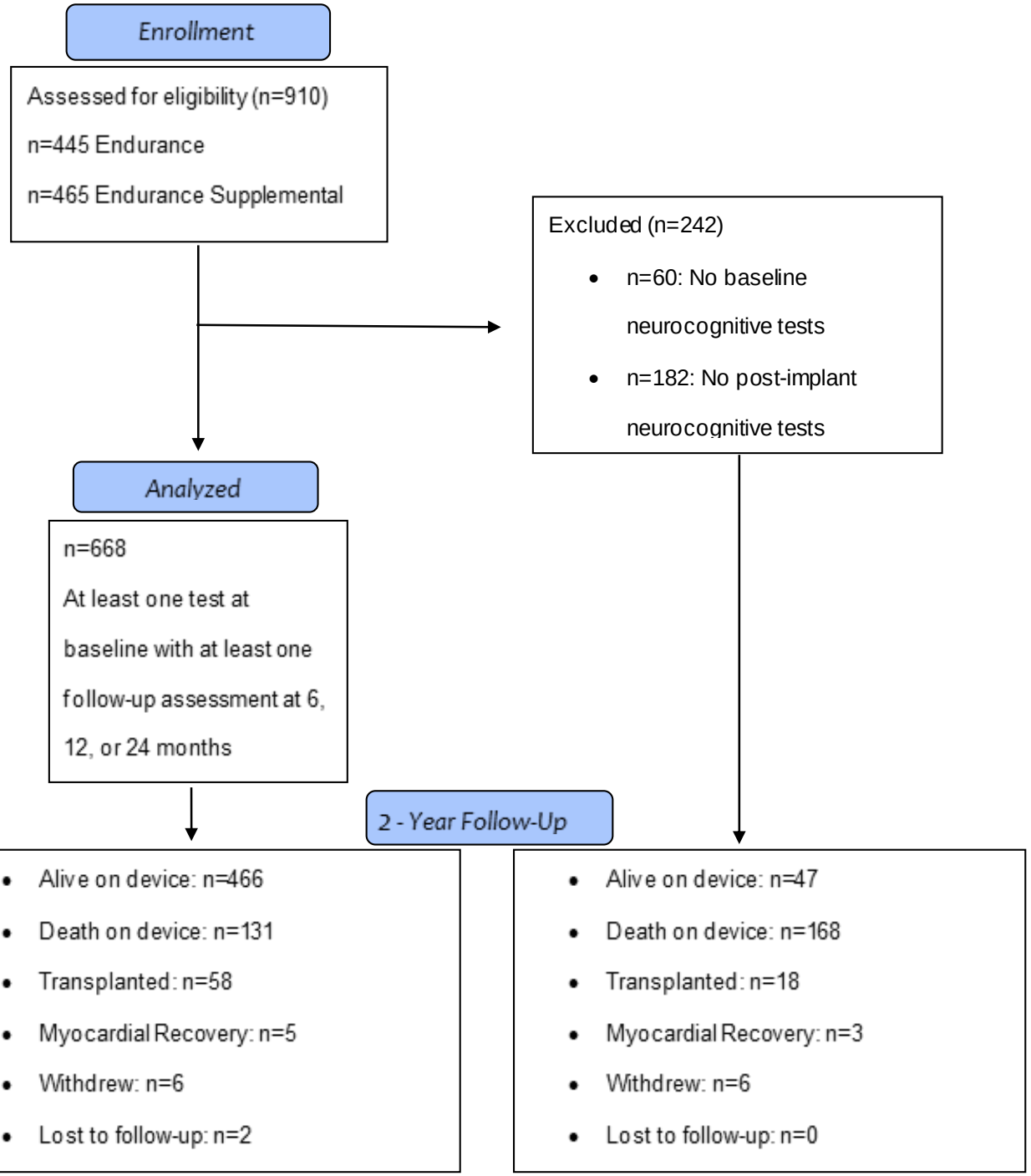
For each cognitive test, patients were separated into “impaired” or “intact” subgroups based on baseline performance for the following reasons:

1. Cognitive test performance may differ between patients who are cognitively intact or impaired at the time of LVAD implant
2. Cognitive decline is more difficult to show when scores are already impaired, and improvement is difficult to show when scores begin at the ceiling

The proportion of observed “improved,” “declined,” and “stable” patients were compared with the proportions expected by chance (5% improved/declined; 90% stable).

Results

Consort Diagram



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Results

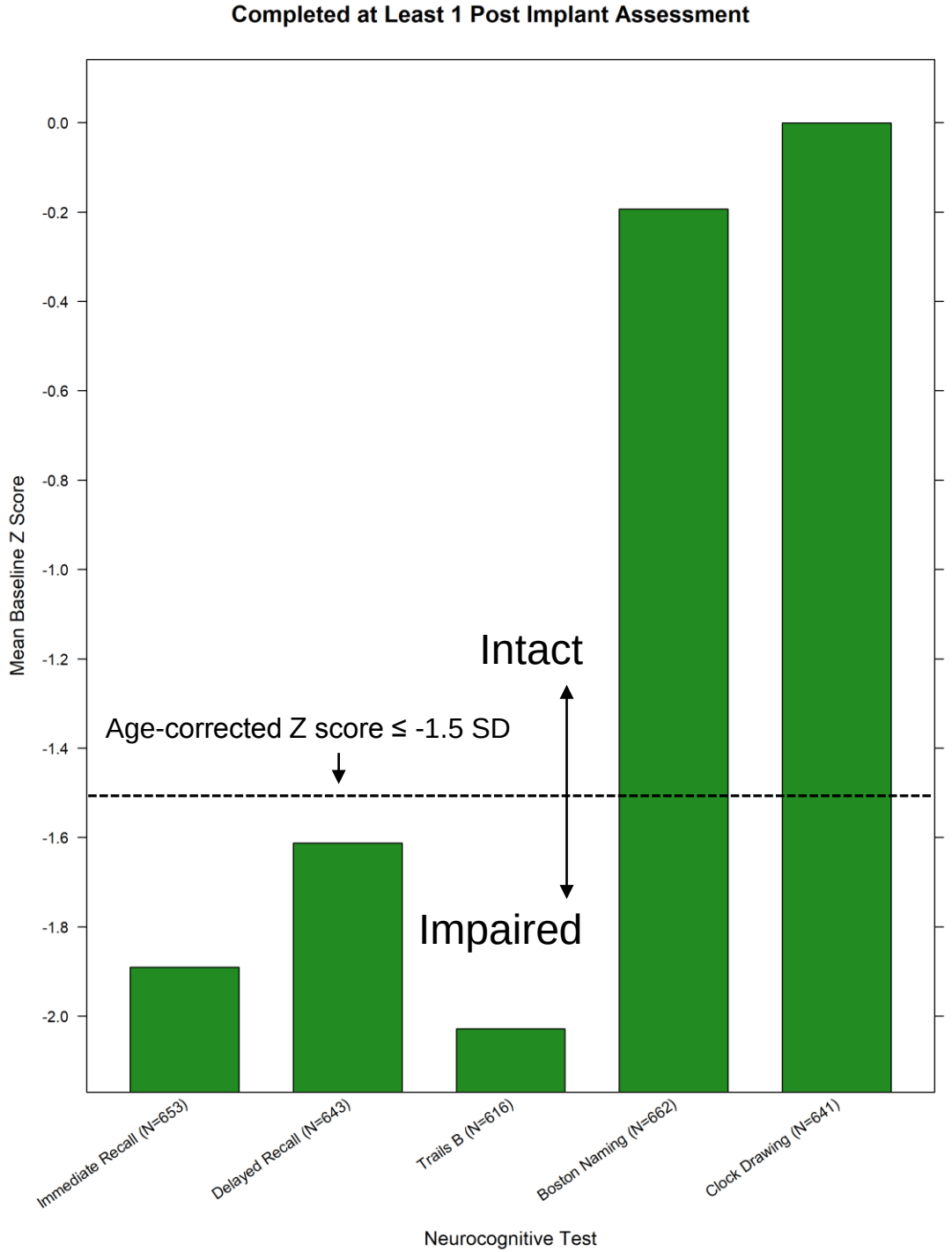
Baseline Neurocognition

Overall

- 552 (83%) patients demonstrated impairment on at least one cognitive measure at baseline.
- 38/552 (6.8%) patients demonstrated impairment on all 5 cognitive measures at baseline

Referring to figure

- Average performance on measures of memory and executive function was impaired at baseline
  - Limited ability to demonstrate decline post-implant
- Average language and visuoconstructional tests were intact at baseline
  - Limited ability to demonstrate improvement post-implant



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Results

Baseline Characteristics

Patients impaired at baseline had more diabetes, a higher pulse pressure, and were less likely to be white

Baseline Characteristics	Impaired at Baseline* (N = 552)	Intact at Baseline (N = 116)	p-value
Age (years)	63.9 ± 11.4	61.6 ± 12.1	0.07
Body Mass Index	27.7 ± 5.7	26.9 ± 5.4	0.19
Male	438 (79.3%)	91 (78.4%)	0.97
Race			
White	397 (71.9%)	100 (86.2%)	**0.004**
Non-White	155 (28.1%)	16 (13.8%)	
Smoking	375 (67.9%)	77 (66.4%)	0.94
Diabetes	275 (49.8%)	41 (35.3%)	**0.02**
Ventricular Tachycardia	244 (44.2%)	48 (41.4%)	0.87
Atrial Fibrillation	292 (52.9%)	52 (44.8%)	0.29
Chronic Obstructive Pulmonary Disease	131 (23.7%)	25 (21.6%)	0.90
Peripheral Vascular Disease	66 (12.0%)	13 (11.2%)	>0.99
Carotid Artery Disease	79 (14.3%)	16 (13.8%)	>0.99
History of Stroke	60 (10.9%)	10 (8.6%)	0.82
Ischemic Heart Failure	310 (56.2%)	63 (54.3%)	0.93
Hypertension	388 (70.3%)	80 (69.0%)	0.96
Coronary Artery Bypass Grafting	178 (32.2%)	31 (26.7%)	0.52
BUN (mg/dL)	28.5 ± 14.4	27.4 ± 14.2	0.43
Creatinine (mg/dL)	1.4 ± 0.4	1.4 ± 0.5	0.20
Intermacs 1	16 (2.9%)	1 (0.9%)	0.73
Intermacs 2	177 (32.1%)	31 (26.7%)	
Intermacs 3	238 (43.1%)	51 (44.0%)	
Intermacs 4-7	119 (21.6%)	32 (27.6%)	
NYHA III	112 (20.3%)	36 (31.0%)	0.10
NYHA IV	438 (79.3%)	79 (68.1%)	
Pulse Pressure (mmHg)	42.2 ± 13.9	39.5 ± 12.6	**0.03**
Device Type, HeartWare	365 (66.1%)	83 (71.6%)	0.53

All data are presented as n (%) for categorical variables and mean (standard deviation) for continuou variables. Bold text indicates statistical significance

* Impaired on at least one test at baseline

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Results

Baseline Intact (N=116): Change from Baseline through 24 months

HVLT – Immediate Recall
- Decline: 11%*
- Improve: 6%*
- Stable: 83%

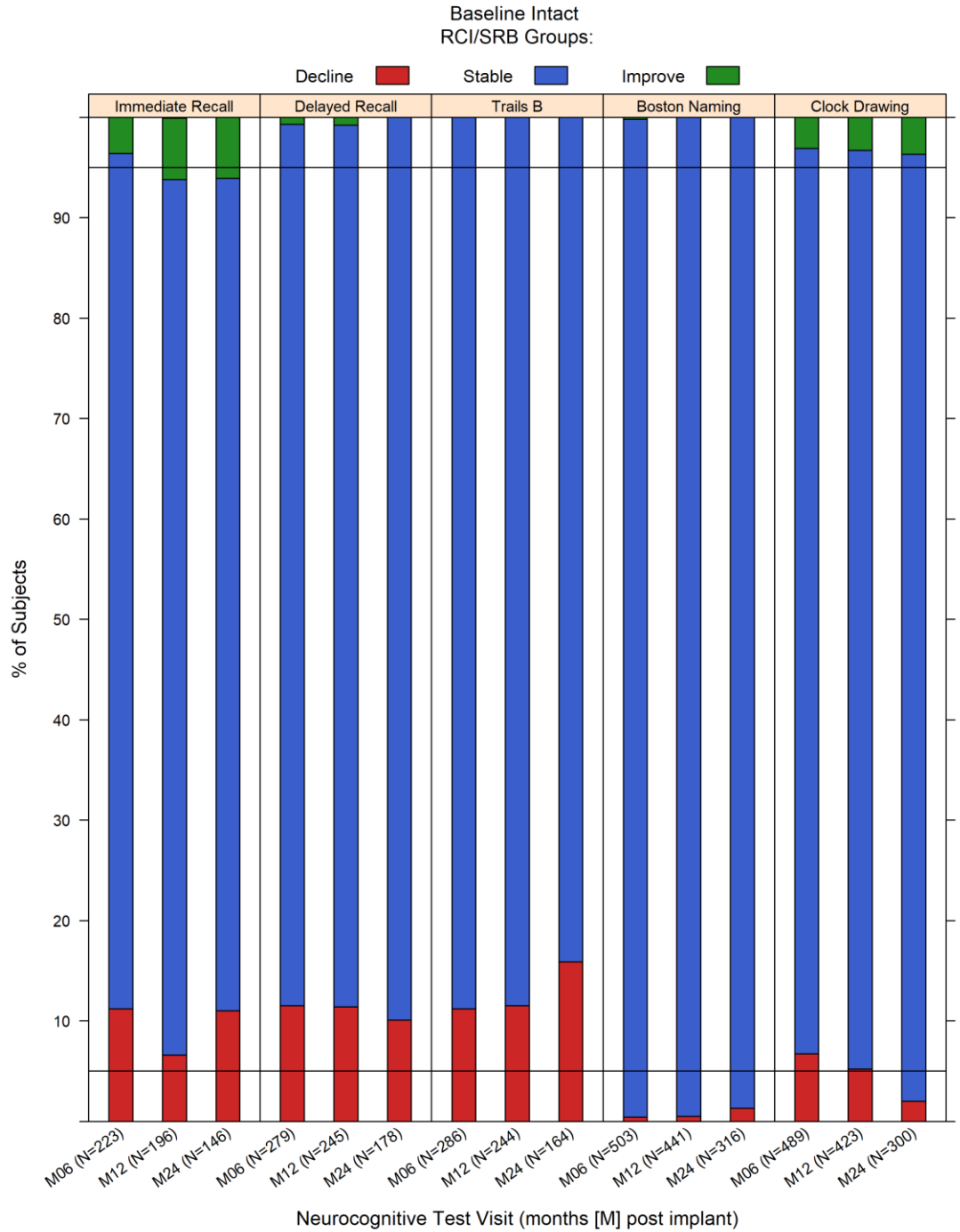
HVLT – Delayed Recall
- Decline: 10%*
- Improve: 0%
- Stable: 90%

Trails B
- Decline: 16%*
- Improve: 0%
- Stable: 84%

Boston Naming
- Decline: 1%
- Improve: 0%
- Stable: 99%

Clock Drawing
- Decline: 2%
- Improve: 4%
- Stable: 94%

*Greater than chance (the expected effect of chance is 5% improved/declined with the remaining 90% stable)



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Results

Baseline Impaired (N=552): Change from Baseline through 24 months

HVLT – Immediate Recall
- Decline: 5%
- Improve: 8%*
- Stable: 87%

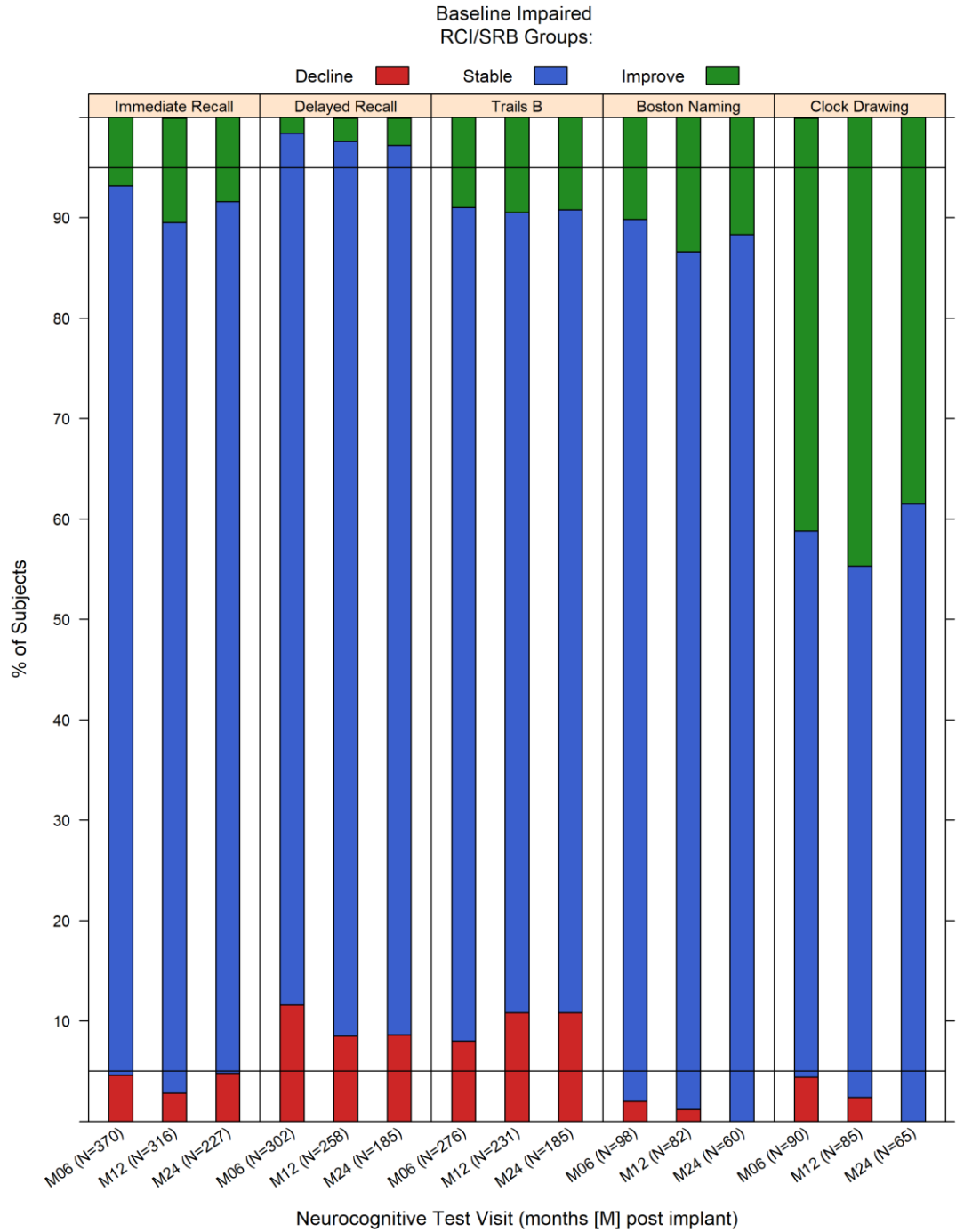
HVLT – Delayed Recall
- Decline: 9%*
- Improve: 3%
- Stable: 89%

Trails B
- Decline: 11%*
- Improve: 9%*
- Stable: 80%

Boston Naming
- Decline: 0%
- Improve: 12%*
- Stable: 88%

Clock Drawing
- Decline: 0%
- Improve: 38%*
- Stable: 62%

*Greater than chance (the expected effect of chance is 5% improved/declined with the remaining 90% stable)



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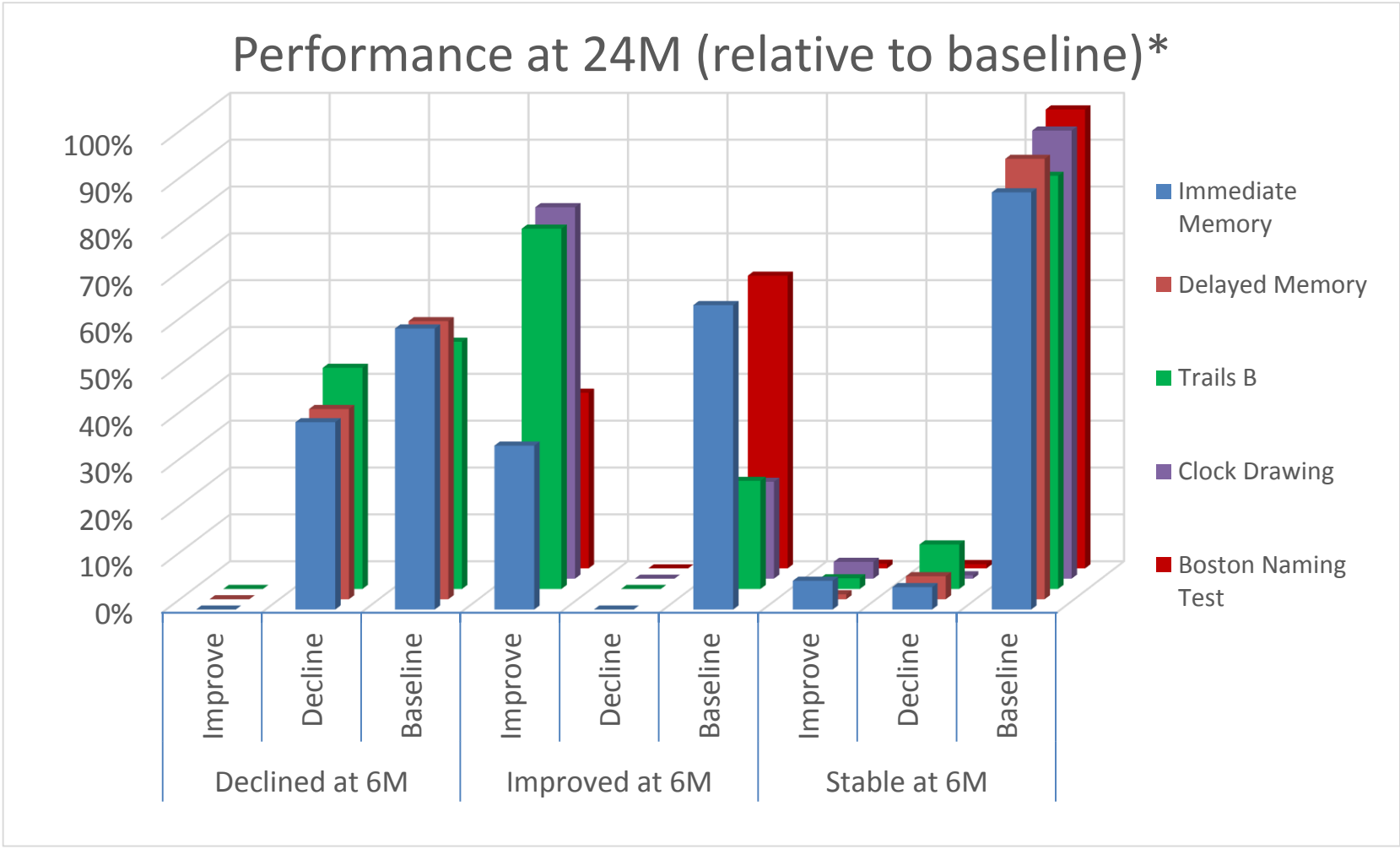
Results

Early vs Late Cognitive Change

- Of patients who showed immediate or delayed memory decline at 6 months, ~60% returned to baseline by 24 months
- Of patients who showed executive function decline at 6 months, ~50% returned to baseline by 24 months
- Of patients who showed clock drawing decline at 6 months, 85% returned to baseline by 24 months

The majority of patients* show stable cognition from baseline through 24 months



*Includes only patients tested at 6 months and 24 months

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Conclusions

- Baseline cognitive impairment is high among patients implanted with DT LVAD
- Despite this, the majority of patients showed stable neurocognitive function through 2 years across all cognitive domains tested
- Of patients who showed decline in immediate/delayed recall, executive function, and clock drawing at 6 months, 60%, 50%, and 85% respectively returned to baseline at 24 months

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Limitations

- Retrospective study
- Excluded patients (N=242) had higher rates of AEs which may bias the studied sample towards patients with less complications on LVAD support

THANK YOU

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