Baker
Heart and Diabetes Institute

REDUCE LAP HF
2 year Outcomes
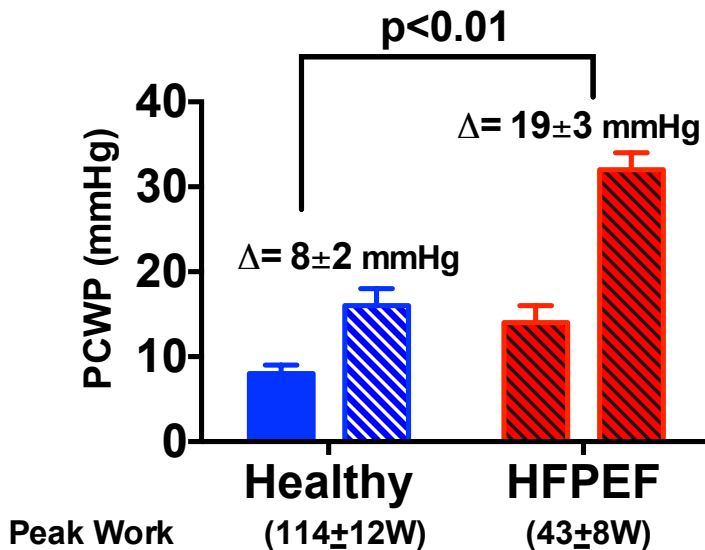
Professor David Kaye

Director, Department of Cardiology, Alfred Hospital

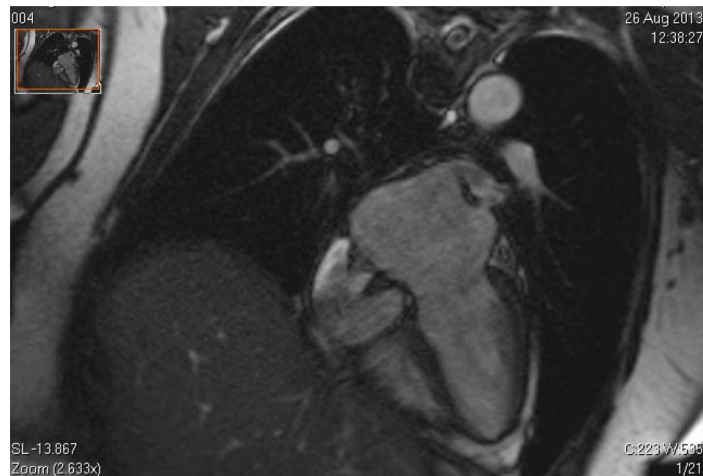*Head, Heart Failure Research Lab, BHDI*

(david.kaye@baker.edu.au)

HFpEF, Physiology and the IASD Approach

Elevated left atrial pressure (PCWP>25), especially during exercise, is a near-universal finding in patients with HFPEF.

p<0.01

Δ= 19±3 mmHg

Δ= 8±2 mmHg

PCWP (mmHg)

Healthy (114±12W)   **HFPEF** (43±8W)

Peak Work

Van Empel JAHA 2014

Inclusion/Exclusion for REDUCE LAP HF

1. Chronic symptomatic heart failure documented by one or more of the following:
a.   NYHA Class III/ambulatory functional class IV symptoms
             One hospital admission for HF within the last 12 months
             On-going management with recommended heart failure medications
2.   Age ≥ 40 years.
3.   LVEF ≥ 40% as determined by echocardiography.

4.   Hemodynamic inclusion criteria
a.   PCWP (end expiratory) or LVEDP (end expiratory) at rest ≥15 mmHg, and greater than CVP, OR
b.   PCWP (end expiratory) during supine bike exercise ≥25mm Hg.

Exclusions

Severe heart failure (stage D heart failure), CI < 2.0 L/min/m² , inotropes
Presence of significant valve disease
Right ventricular dysfunction incl. TAPSE < 1.4 cm, CVP >14 mmHg

Study End-points (6 month 1ºEPs)

DEVICE SAFETY

- Peri-procedural and 6 months MACCE & systemic embolic events
- Need for removal

DEVICE PERFORMANCE

- % of patients who have successful device implantation
- % of patients with reduction of PCWP, and left to right flow at 6 months

Study Population

Age (Y)	69±8
Gender (% Female/Male)	66 / 34
LVEF (%)	47±7
NYHA Class (n, II/III/IV)	18/46/0
Minnesota Living with HF Score	49 ± 20
BMI kg/m^2	33 ± 6
Permanent AF (%)	36
NT-Pro BNP (median, IQR pg./ml)	377 (222-925)
Hypertension (%)	81
Diabetes (%)	33
Coronary artery disease (%)	36
Diuretics at baseline (%)	91
Resting CVP (mm Hg)	9 ± 4
Resting PCWP (mm Hg)	17 ± 5

6 month and 1 year Top Line results

MACCE event	Six months %	One year %
Death	0	4.7 (3/64) MOF; stroke; unknown
Stroke	0	1.5 (1/64)* (pt died)

No MIs, device removal, systemic emboli
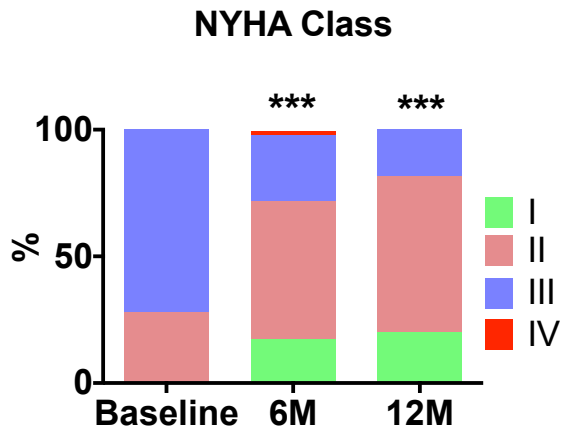
NYHA Class

MLWHF Score
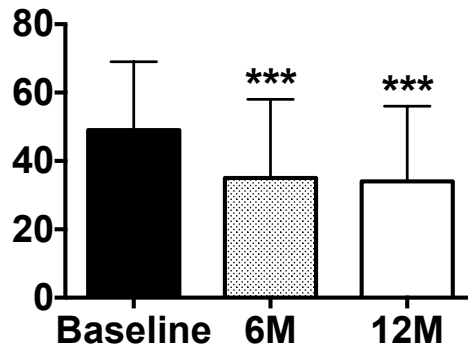
6MWD

**p<0.01, ***p<0.001 vs baseline

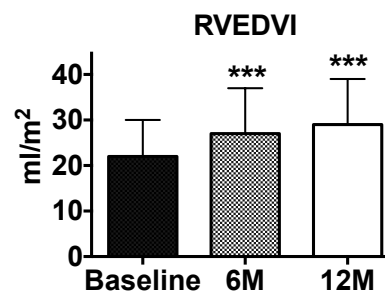Mean Δ at 1 year: 15 points
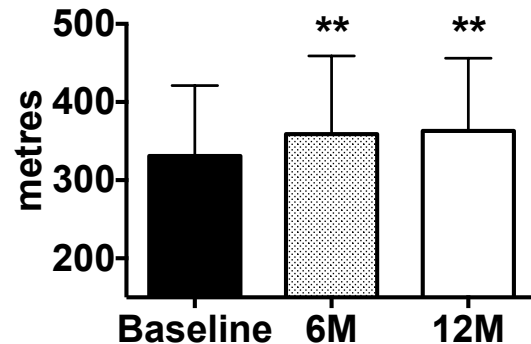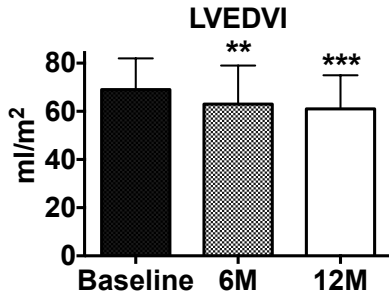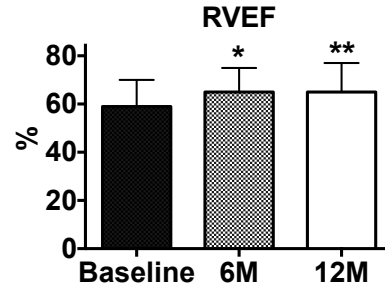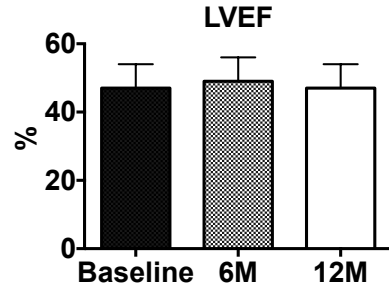
Mean Δ at 1 year: 33m

Hemodynamics to 1 Year

Exercise
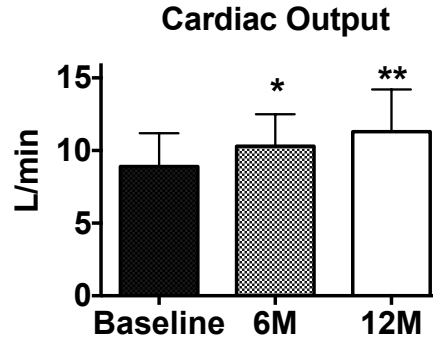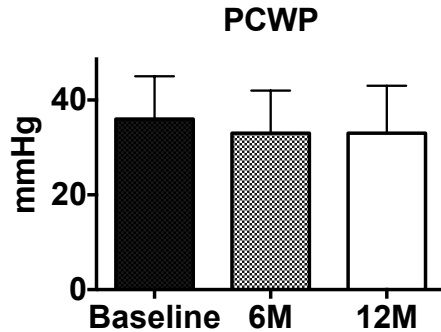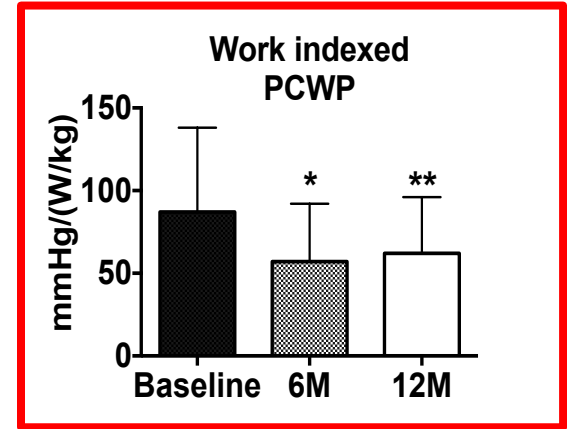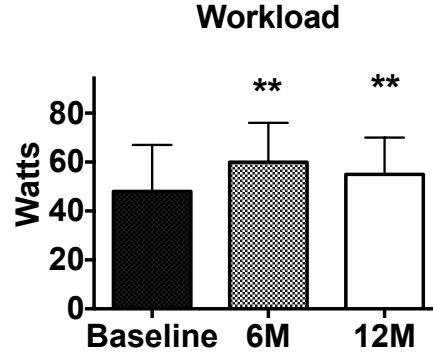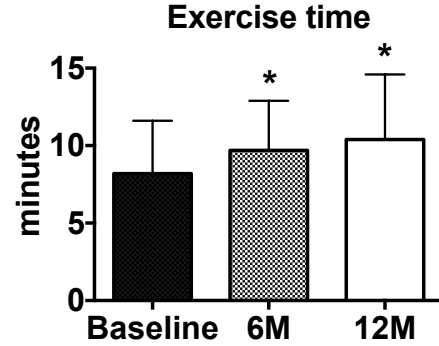
* p<0.05, ** p<0.01 vs baseline

Echo to 1 Year

No change in atrial volumes

*p<0.05, **p<0.01, ***p<0.001

2 Year Follow-up

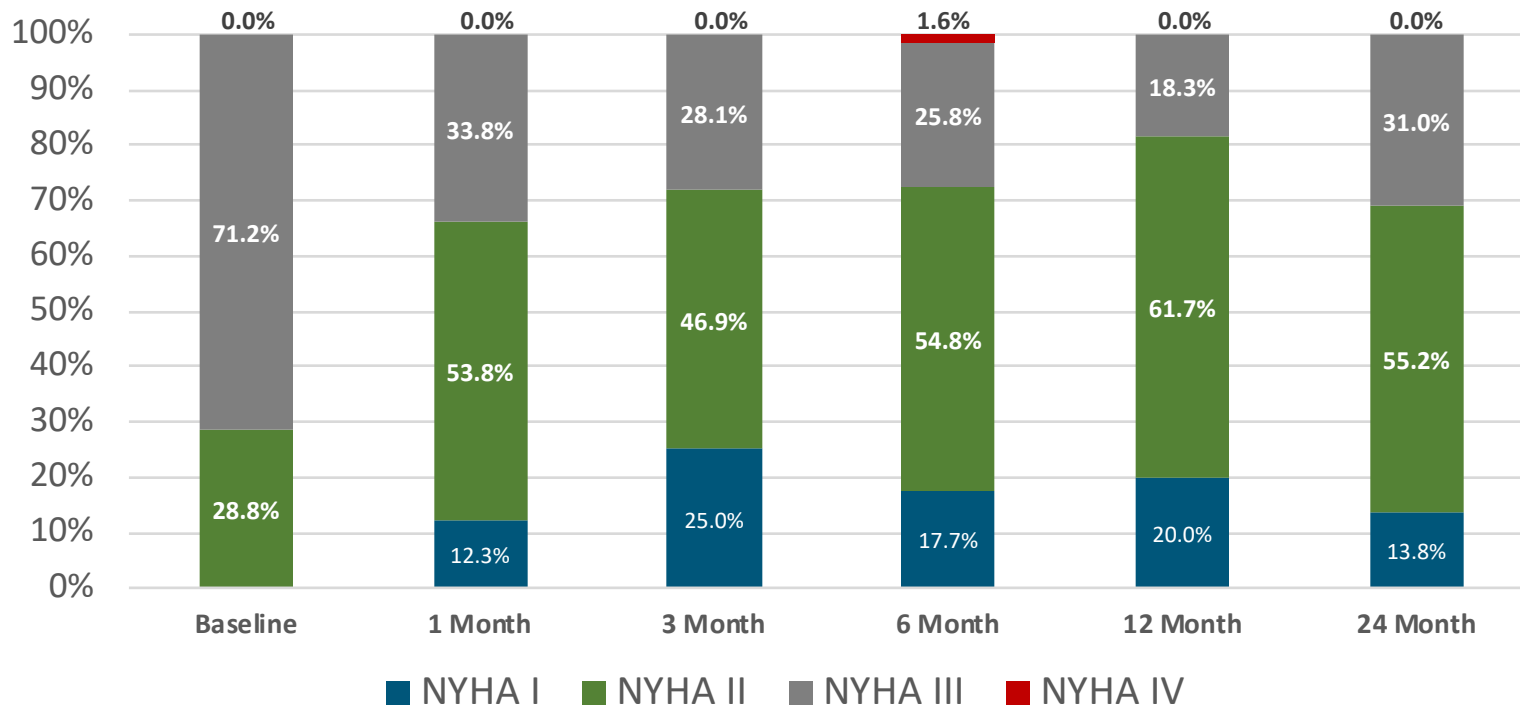**Questions: Safety and durability of effect?**

AVAILABLE
- **Safety: Death, device events**
- **Efficacy: NYHA class, HFH/other hospitalization**

NOT REQUIRED PER PROTOCOL
- **Echo**
- **Hemodynamics**
- **BNP/NT-pro BNP**

NYHA Status at >2 years

Minimum f/u 2 years, median 739 days

Outcomes summary

Outcome measure	@6M	@12M	@24M
Survival	100%	95.3% (61/64)	92.2% (59/64)
All cause mortality	0%	4.7% (3/64)	7.8% (5/64)
HF related mortality	0%	0%	3.1% (2/64)

Total follow up: Median 739 days, 177.2 pt years f/u:

- **6 deaths: = 3.4 deaths/100 yrs (3 HF, 2 non HF, 1 CVA)**
- **42 HFH events in 19 patients**

Predicting HF Outcomes – MAGGIC Scores

The survival of patients with heart failure with preserved or reduced left ventricular ejection fraction: an individual patient data meta-analysis

Meta-analysis Global Group in Chronic Heart Failure (MAGGIC)
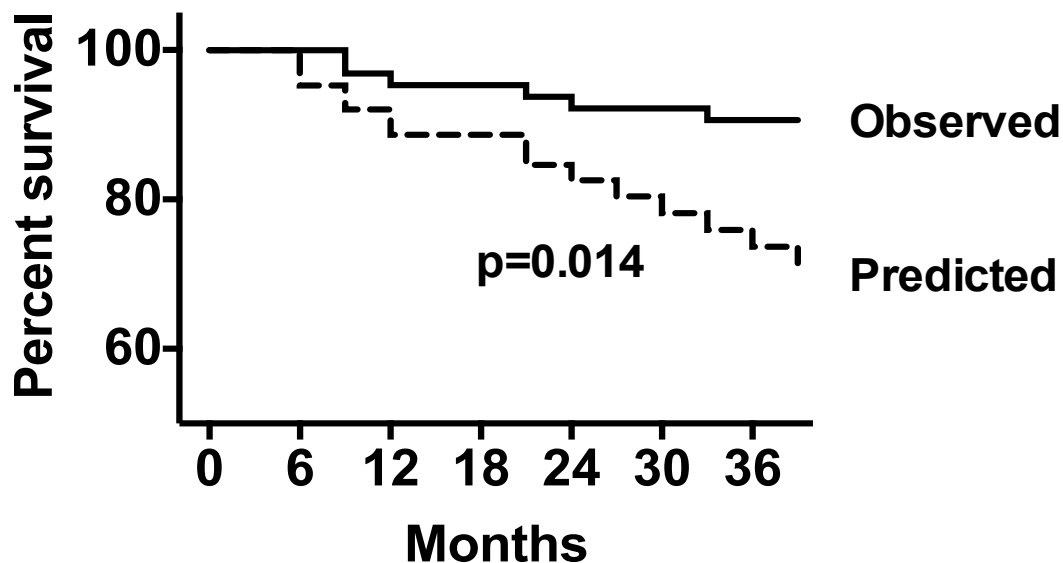
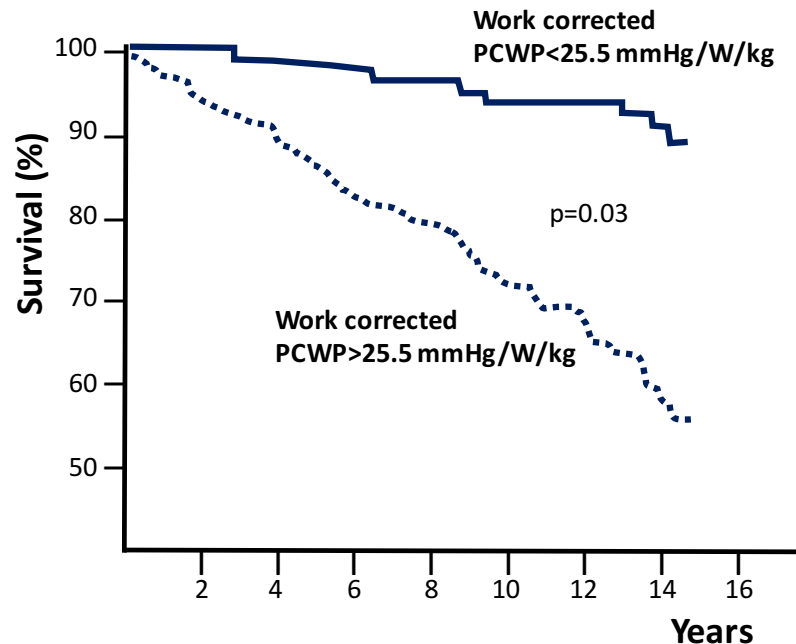| Parameter |
| --- |
| LVEF |
| Age |
| SBP |
| BMI |
| Creatinine |
| NYHA |
| Gender |
| Smoking |
| Diabetes |
| COPD |
| HF duration |
| GDMT |

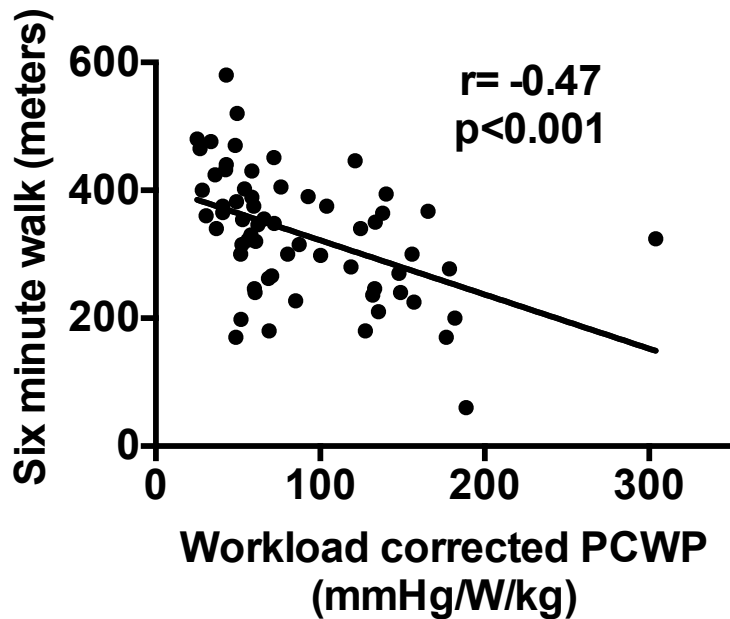**For REDUCE LAP HF population:**

Predicted mortality rate: 10.2/100pt years (95% CI 6.1-16.9).

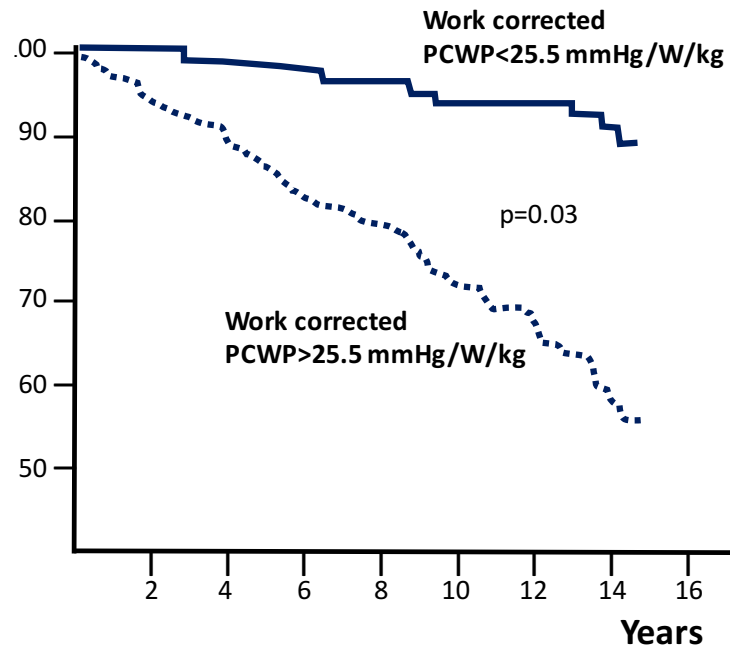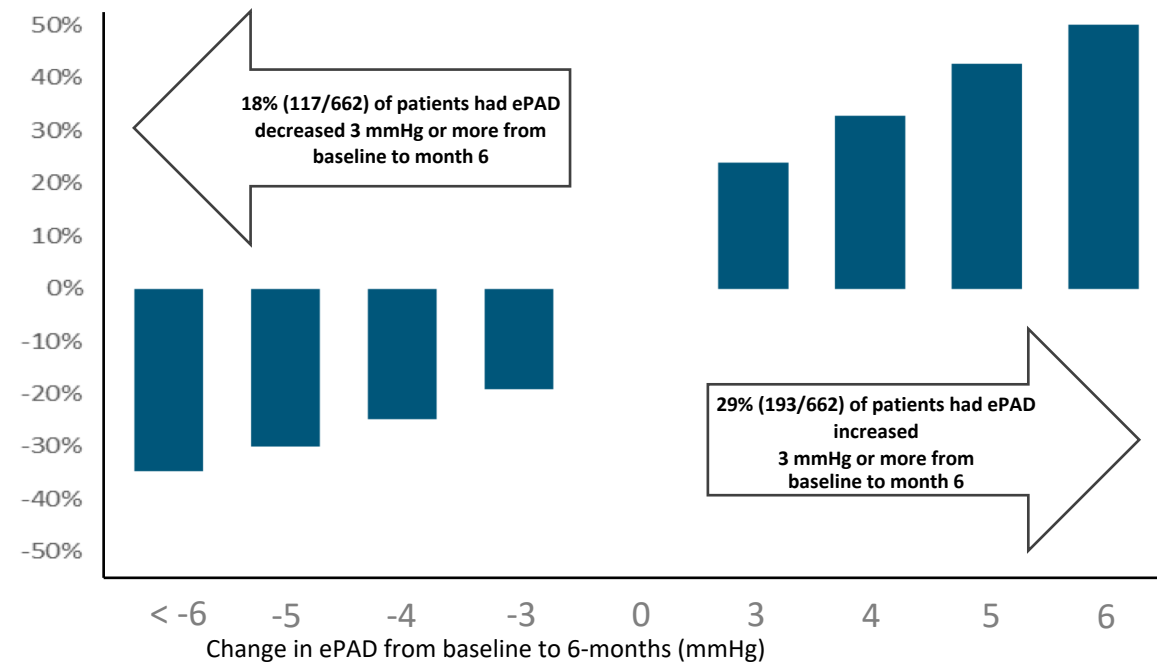**Observed rate: 33% lower mortality rate (95% CI 0.09-0.89) across the full observation period (p=0.02).**

Observed vs MAGGIC Predicted KM Curves

Survival benefit of IASD?

Survival benefit of IASD?

IASD and HF Hospitalization

TABLE 1. Baseline features according to HFH status

	No HFH (n=45)	HFH (n=19)	P value
Age (years)	69±1	71±2	0.37
Body mass index (kg/m sq)	32±1	34±2	0.27
NT-proBNP (pg/ml)	332	595	0.24
Atrial fibrillation (%)	36	37	0.92
Hypertension (%)	80	84	0.69
IHD (%)	31	32	0.97
eGFR	65±3	54±4	0.08
6 MWD (meters)	335±16	316±18	0.49
Peak exercise workload (Watts)	44±3	40±4	0.48

Echocardiography	No HFH	HFH	p value
LVEF (%)	47±1	47±1	0.66
LAVI (ml/m sq)	34±3	34±3	0.88
RAVI (ml/m sq)	35±3	35±3	0.95
TAPSE (cm)	2.0±0.1	1.9±0.1	0.52
Resting hemodynamics			
RA pressure (mmHg)	9±1	10±1	0.15
PAm pressure (mmHg)	23±1	25±1	0.39
PCWP (mmHg)	17±1	18±1	0.40
Cardiac Index (L/min/m sq)	2.7±0.1	2.7±0.2	0.78

IASD and HF Hospitalization

Resting Echo and HD at 6 months (post IASD) not associated with HFH, but: