# Pulmonary Artery Pressure-Guided Therapy for Ambulatory Heart Failure Patients in Clinical Practice: *1-Year Outcomes from the CardioMEMS Post-Approval Study*

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Registration: www.clinicaltrials.gov, NCT 02279888

# Disclosure Statement

David M. Shavelle, MD

| | |
|---|---|
| Consulting fees: | Abbott Vascular |
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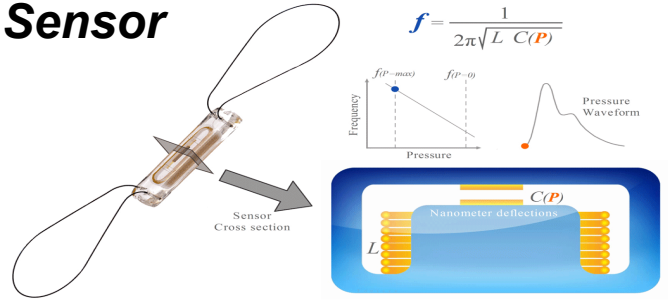
# Background

- The burden of HF hospitalization (HFH) remains high despite increasingly effective medical therapy
- Most HFH occur because of ‘congestion’ or elevated cardiac filling pressures
- Increases in pulmonary artery (PA) pressures occur weeks in advance of the signs and symptoms that prompt HFH
- Therapy guided by PA pressures in the randomized CHAMPION study[1] resulted in a 37% reduction in HFH rates and all cause hospitalization (ACH)

[1]Abraham WT, et al. *Lancet* 2011:377:658-666.

# CardioMEMS-HF system: Ambulatory Hemodynamic Monitoring with an Implantable PAP Sensor

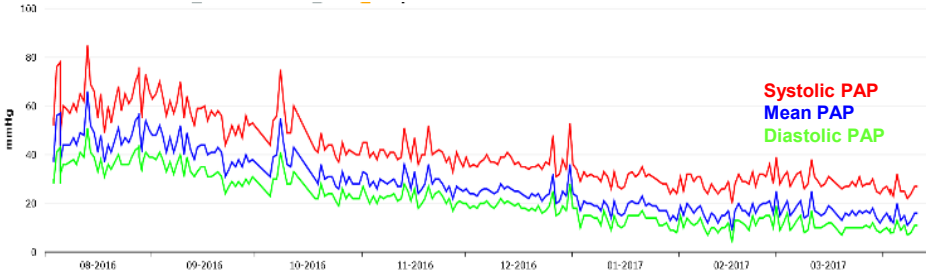
## Sensor



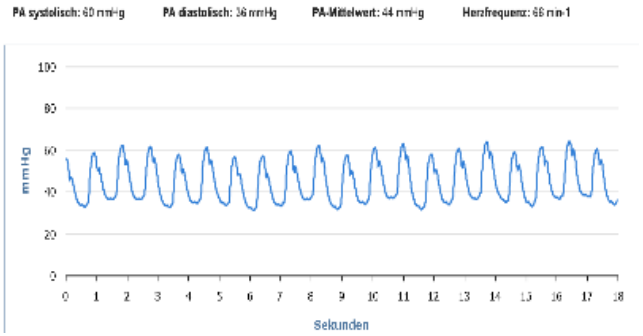

## Home electronics unit

## Database

### PA pressure trend data




### Daily PA measurement

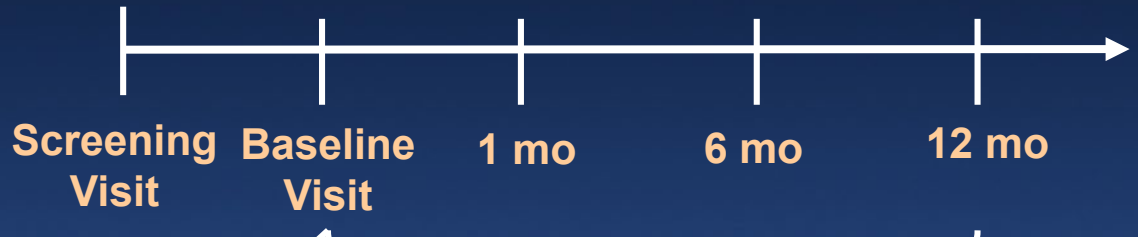


# CardioMEMS Post Approval Study (PAS): Background

- **Purpose**: To evaluate the use of the CardioMEMS HF system in patients with NYHA Class III Heart Failure in a commercial setting
- **Objective**: To confirm the safety and effectiveness in a commercial setting
- **Study Design**: Prospective, single arm, multi-center, open label trial conducted in the United States

# CardioMEMS Post Approval Study (PAS): Study Design

## A prospective, multi-center, open-label trial in ~1200 patients with NYHA Class III Heart Failure and a HFH within the prior 12 months




**Right Heart Catheterization**
**Baseline Hemodynamics**
**PA Sensor Implantation**

Scheduled Study visits

Patients instructed to transmit PA pressures daily

All hospitalizations submitted to CEC* for adjudication

**Primary Efficacy Endpoint:**
Reduction in rate of HFH at 1-year post-implant compared with the year prior to enrollment

**Primary Safety Endpoints:**
Freedom from DSRC** > 80% at 2 years
Freedom from Sensor Failure > 90% at 2 years

**Supplemental Analysis:**
HFH or death at 1 year
Death at 1 year
Patient compliance
Outcomes in subgroups

*CEC = Clinical Events Committee; **DSRC = Device and System-Related Complications; HFH = Heart Failure Hospitalization

# Inclusion Criteria

1. NYHA class III heart failure
2. At least 1 HFH within the previous 12 months
3. Patients with HFrEF should be receiving a beta blocker for 3 months and an ACE-I or ARB for 1 month unless in the investigator's opinion, the patient is intolerant to beta blocker, ACE-I or ARB
4. Patients with BMI > 35 required chest circumference (at mid axillary level) to be < 65 inches
5. PA branch diameter ≥ 7mm

# Exclusion Criteria

1. Active infection
2. History of recurrent (> 1) pulmonary embolism or deep vein thrombosis
3. Inability to tolerate right heart catheterization
4. A major cardiovascular event (e.g., myocardial infarction, open heart surgery, cerebral vascular accident) within previous 2 months
5. CRT implanted within previous 3 months
6. GFR < 25 ml/min who are non-responsive to diuretic therapy or who are on chronic renal dialysis
7. Congenital heart disease or mechanical right heart valve
8. Likely to undergo heart transplantation or VAD within the next 6 months
9. Known coagulation disorders
10. Hypersensitivity or allergy to aspirin, and/or clopidogrel

# CardioMEMS PAS: Study Flow and Follow-up

1214 pts with NYHA Class III HF and at least 1 HFH within the prior 1 year, considered for enrollment between September 1st, 2014 and March 31st, 2018 at 104 centers in the United States

**Consented for Participation**
**n = 1214**

Unsuccessful Sensor Implantation
n = 14*

**Sensor Implanted**
**n = 1200**

Reasons for not completing 6 Month Visit
Death (n=105)
Withdrew consent (n=12)
Lost to Follow-up (n=2)
Terminated by Investigator (n=21)
Other (n=2)

6 Months

**Completed Visit**
**n = 1014**

Reasons for not completing 12 Month Visit
Death (n=86)
Withdrew consent (n=10)
Lost to Follow-up (n=6)
Terminated by Investigator (n=24)
Other (n=3)

12 Months

**Completed Visit**
**n = 859**

*14 patients followed for 30 days for safety

# Baseline Characteristics

| Characteristic | All Patients* (n=1200) | EF < 40% (n=637) | EF 41-50% (n=198) | EF > 50% (n=363) |
|---|---|---|---|---|
| Age (years) | 69 ± 12 | 67 ± 13 | 70 ± 11 | 72 ± 10 |
| Female sex | 452 (38%) | 183 (29%) | 75 (38%) | 194 (53%) |
| **Race/ethnicity** | | | | |
| White | 993 (83%) | 499 (78%) | 171 (86%) | 321 (88%) |
| Black | 172 (14%) | 114 (18%) | 26 (13%) | 32 (9%) |
| Asian | 12 (1.0%) | 8 (1.3%) | 0 (0%) | 4 (1.1%) |
| Other | 18 (1.5%) | 14 (2.2%) | 0 (0%) | 2 (0.6%) |
| Ischemic CM | 496 (41%) | 352 (55%) | 78 (40%) | 64 (18%) |
| CRT/CRT-D or ICD | 600 (50%) | 488 (77%) | 73 (37%) | 38 (11%) |
| GFR (mL/min/1.73 $m^2$) | 53 ± 21 | 55 ± 22 | 53 ± 21 | 50 ± 19 |
| CKD stage 3 and stage 4 | 808 (68%) | 312 (49%) | 133 (68%) | 261 (72%) |

*Two subjects did not submit EF at baseline.

# Baseline Medical Therapy

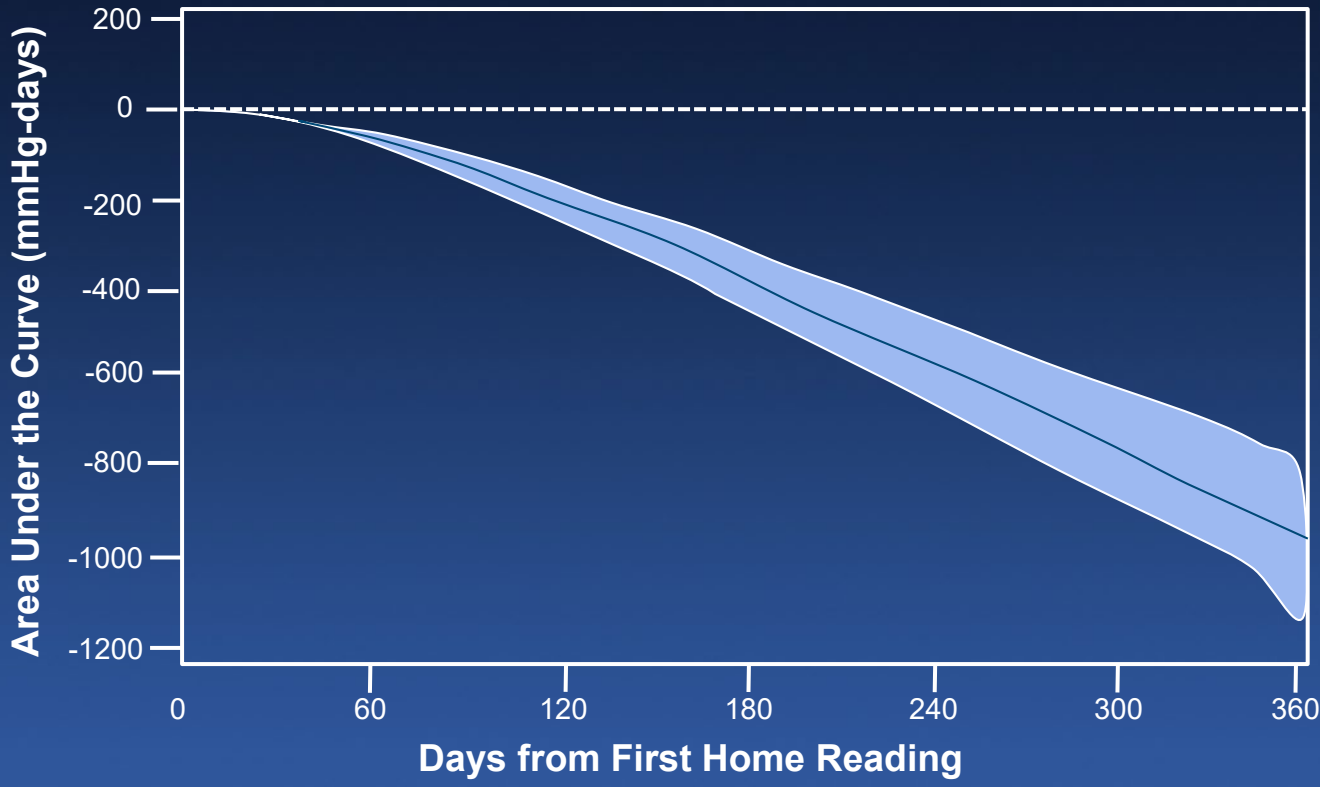
| Characteristic | All Patients (n=1200) | EF < 40% (n=637) | EF 41-50% (n=198) | EF > 50% (n=363) |
|---|---|---|---|---|
| **Medical Therapy** | | | | |
| Beta blocker | 1046 (87%) | 597 (94%) | 172 (87%) | 275 (76%) |
| ACE/ARB/ARNi | 696 (58%) | 444 (70%) | 117 (59%) | 134 (37%) |
| Beta blocker + ACE/ARB/ARNi | 626 (52%) | 416 (65%) | 103 (52%) | 106 (29%) |
| Aldosterone agonist | 673 (56%) | 426 (67%) | 113 (57%) | 133 (37%) |
| Loop diuretic | 1136 (95%) | 597 (94%) | 187 (94%) | 350 (96%) |

# Hemodynamics at PA Sensor Implant

| Characteristic | All Patients (n=1200) | EF < 40% (n=637) | EF 41-50% (n=198) | EF > 50% (n=363) |
|---|---|---|---|---|
| **Hemodynamics – Baseline** | | | | |
| Systolic blood pressure (mm Hg) | 127 ± 22 | 121 ± 20 | 130 ± 24 | 134 ± 22 |
| Pulmonary capillary wedge pressure (mm Hg) | 20 ± 8 | 21 ± 9 | 18 ± 6.8 | 19 ± 7 |
| PA systolic pressure (mm Hg) | 48 ± 15 | 48 ± 15 | 45 ± 14 | 49 ± 15 |
| PA diastolic pressure (mm Hg) | 20 ± 8 | 20 ± 8 | 19 ± 7 | 20 ± 7 |
| PA mean pressure (mm Hg) | 31 ± 10 | 32 ± 10 | 29 ± 9 | 32 ± 9 |
| Cardiac index (Lit/min/$m^2$) | 2.2 ± 0.7 | 2.1 ± 0.6 | 2.3 ± 0.7 | 2.4 ± 0.8 |

# Change in PA Pressure Over Time

## *Area Under the Curve (AUC) Method*

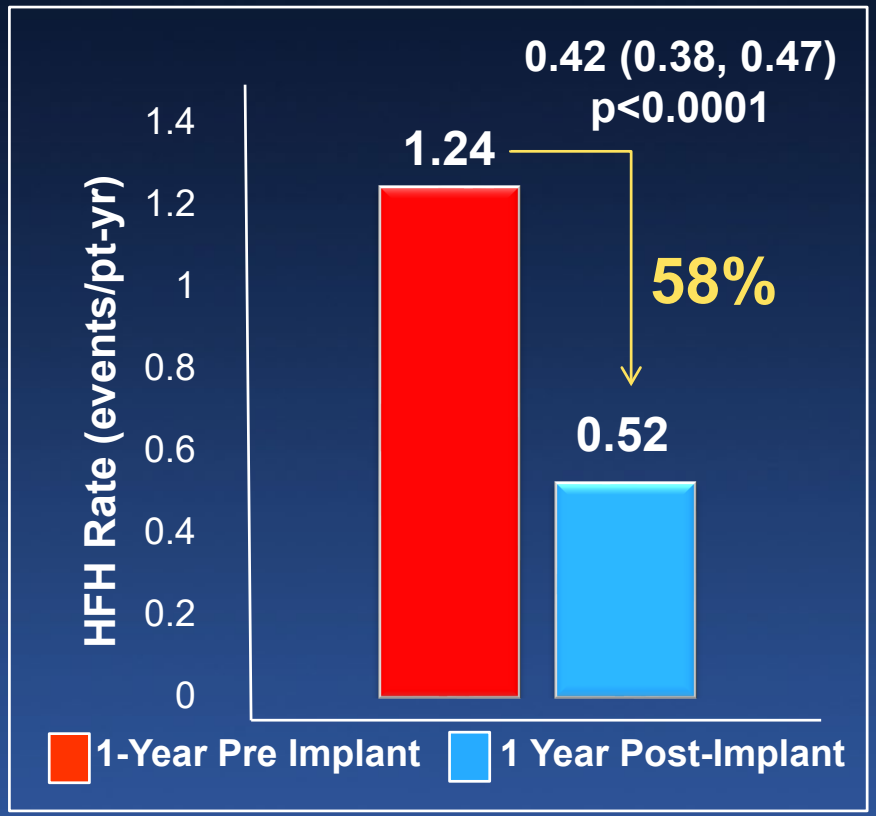



AUC method measures the frequency and duration of time that a patient spends at a pressure, lower or higher, than their baseline mean PA pressure in mmHg-days.

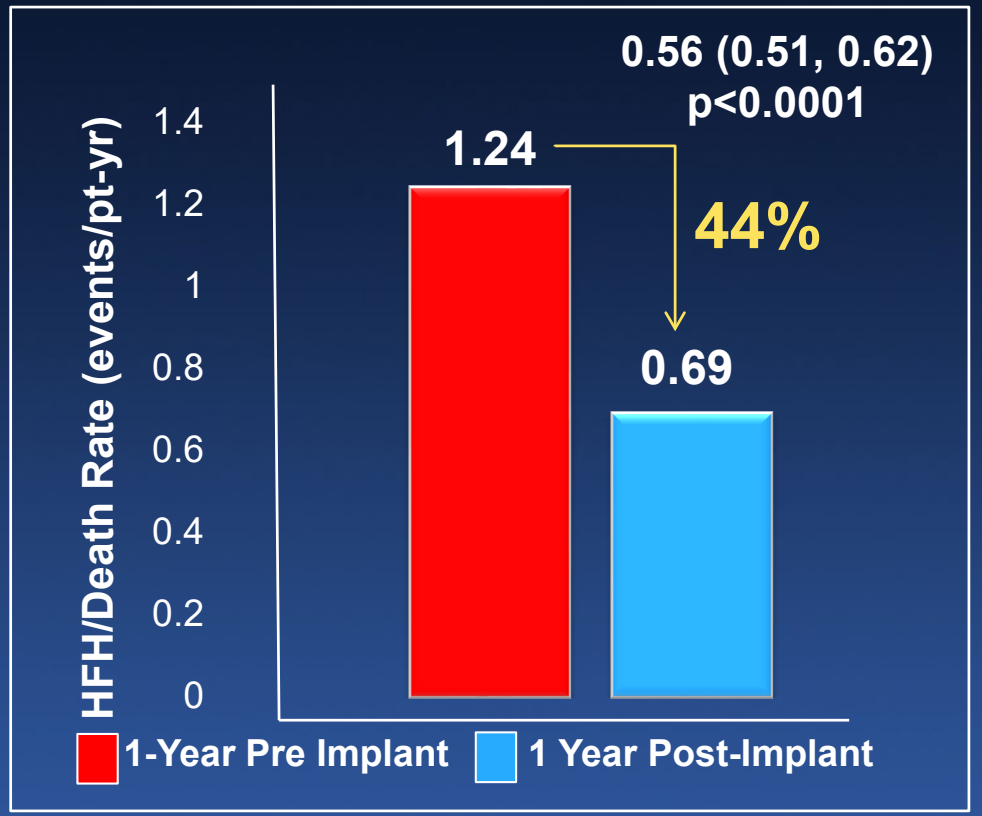
**Pressure Transmission Compliance**

| | Mean±SD | Median |
|---|---|---|
| **Daily** | 76±24% | 85% |
| **Weekly** | 92±16% | 100% |

# Hospitalizations for HF at 1 year

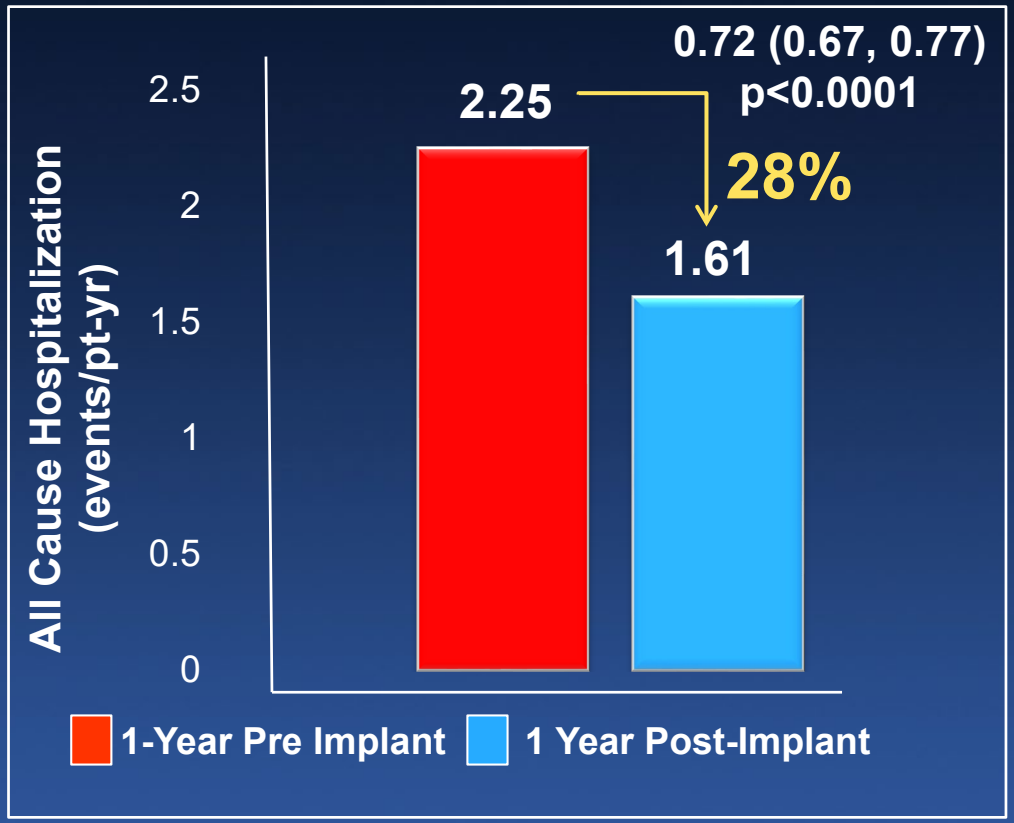



# Hospitalizations for HF/Death at 1 year



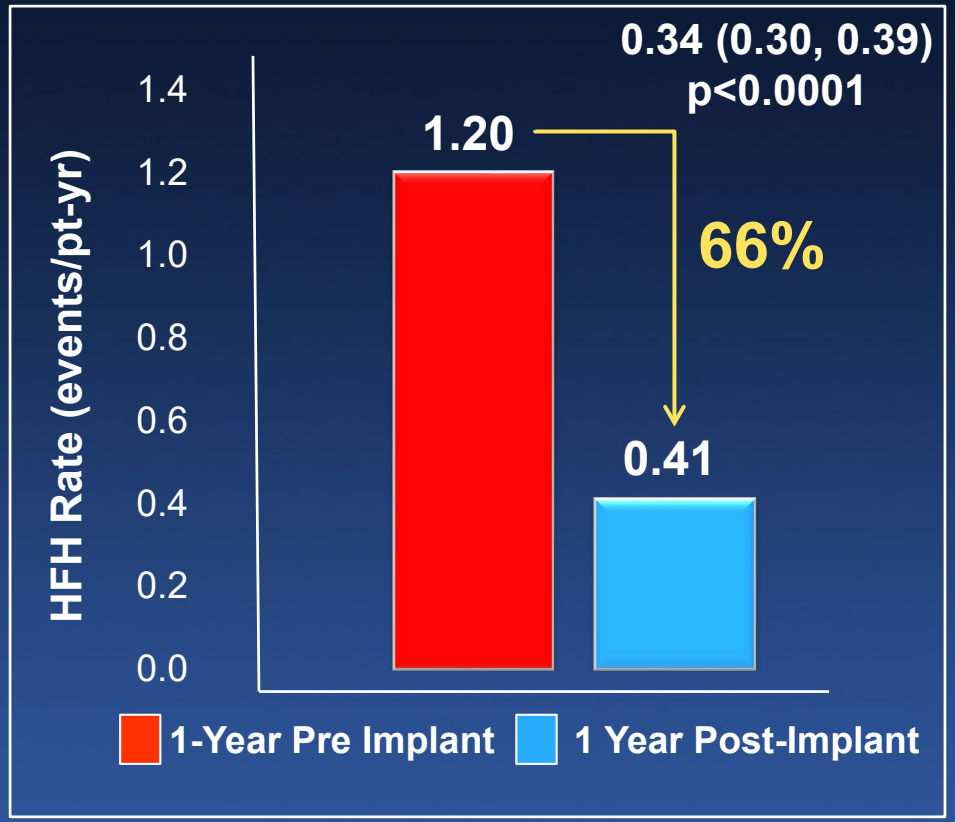

Hazard Ratio, 95% Confidence Interval and p-value estimated from the Anderson-Gill model.
All hospitalization events adjudicated by CEC.

# All Cause Hospitalizations at 1 year




Hazard Ratio, 95% Confidence Interval and p-value estimated from the Anderson-Gill model.
All hospitalization events adjudicated by CEC.

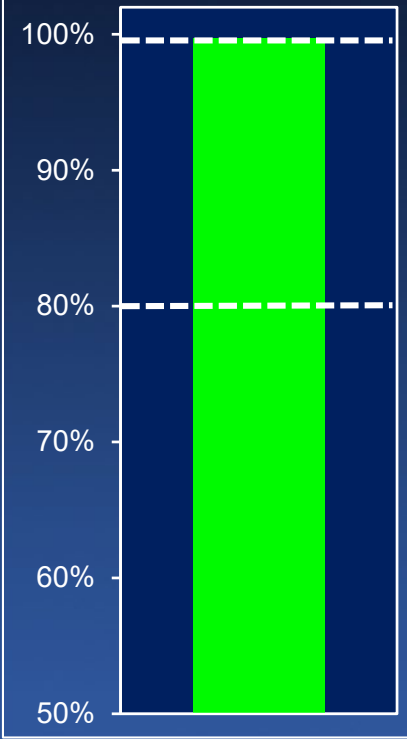
# Survivor Analysis: Hospitalizations for HF at 1 year, n=1009 (Survival 84%)




Hazard Ratio, 95% Confidence Interval and p-value estimated from the Anderson-Gill model.
All hospitalization events adjudicated by CEC.

# Primary Safety Endpoints

## Freedom from Device/System Related Complications at 1 year



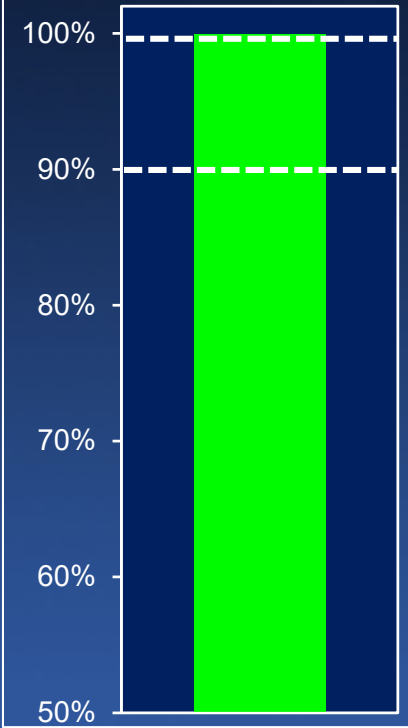

99.7%

80% OPC

**Device/System Related Complications 4/1214 (0.3%)**

DSRC: Adverse event that is possibly related to the system and has at least 1 of the following: treated with invasive means (other than IM medication or RHC), results in death of subject or results in explant of device.

## Freedom from Sensor Failure at 1 year



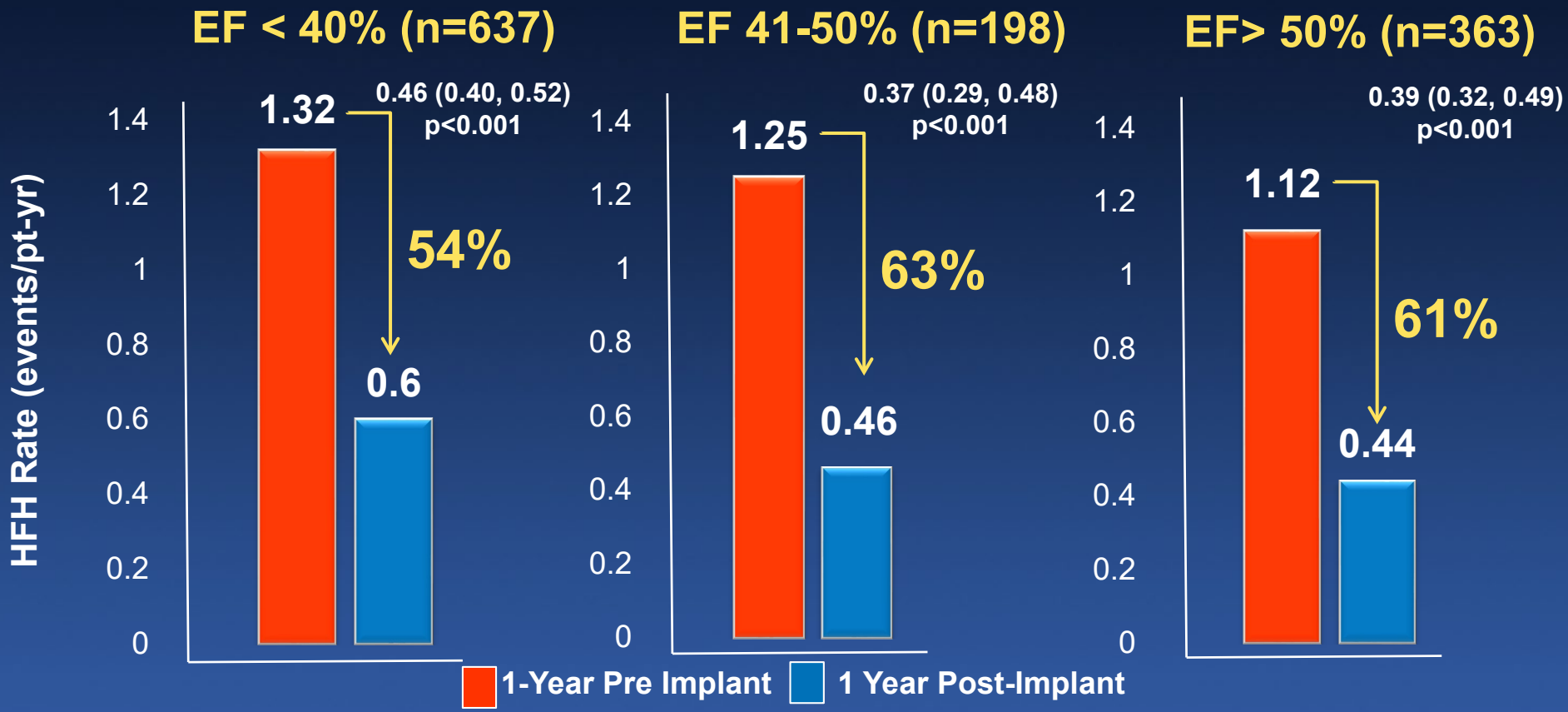

99.9%

90% OPC

**Sensor Failure 1/1200 (0.1%)**

Sensor Failure: No readings can be obtained after troubleshooting system to rule out any problems with external electronics

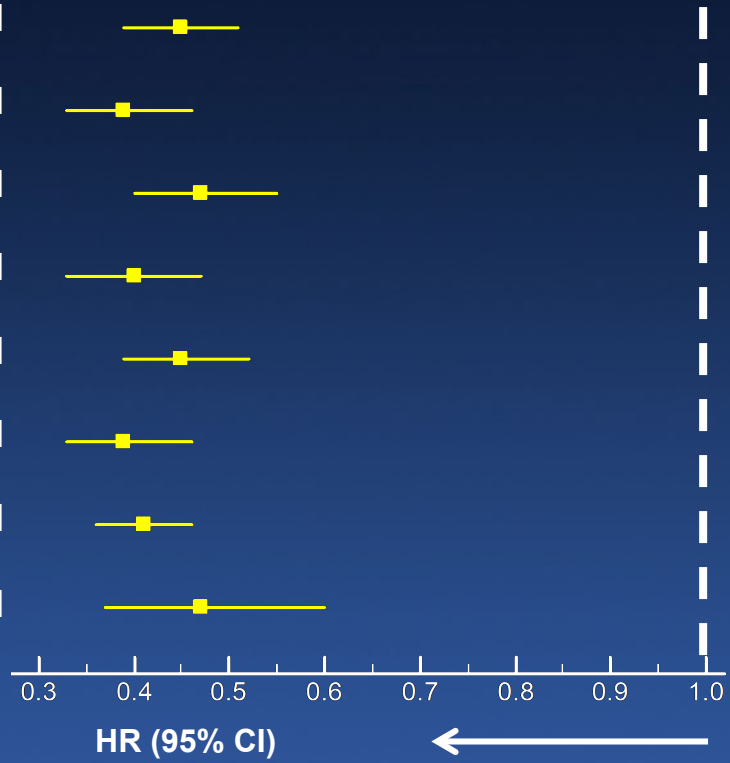
# Heart Failure Hospitalizations at 1 year
## *Stratified by Ejection Fraction*



# Heart Failure Hospitalizations: Pre-Enrollment vs Post-Enrollment

## *Stratified by Planned Sub-Groups*

| | | All Subjects (N=1200) |
|---|---|---|
| Gender | Male | 1.202 vs. 0.536 [748]<br>0.45 (0.39, 0.51) |
| | Female | 1.306 vs. 0.508 [452]<br>0.39 (0.33, 0.46) |
| Cardiomyopathy | Ischemic | 1.307 vs. 0.614 [496]<br>0.47 (0.40, 0.55) |
| | Non-Ischemic | 1.220 vs. 0.485 [449]<br>0.40 (0.33, 0.47) |
| Device | ICD/CRT-D | 1.284 vs. 0.579 [600]<br>0.45 (0.39, 0.52) |
| | Without ICD/CRT-D | 1.192 vs. 0.469 [598]<br>0.39 (0.33, 0.46) |
| Race | White | 1.192 vs. 0.483 [993]<br>0.41 (0.36, 0.46) |
| | Black (of African Descent) | 1.519 vs. 0.719 [172]<br>0.47 (0.37, 0.60) |




Cells contain pre versus post rates [sample size] / HR (95% CI)
Results from Andersen-Gill model with rates as events/patient-years

# Limitations

- Single arm study with prior to and post-enrollment comparisons
- Likely underestimation of HFH events prior to enrollment due to incomplete recall of events (information bias)
- Censoring at the time of death may have resulted in survivor bias, however:
  - HFH/death for the entire cohort reduced 44%
  - HFH for survivors reduced 66%
- PAS enrolled high risk patients: baseline event rate ~ 2x higher than CHAMPION
- Comparable efficacy to prior studies:
  - Open Access Study ‘prior control group’: HFH/death reduced 39%
  - CadioMEMS PAS: HFH/death reduced 44%

# Conclusions

- In the commercial setting, PA pressure-guided therapy for HF:
  - Decreased PA pressures
  - Decreased HF Hospitalizations
    - Across sex and race
    - Across all EF ranges
    - Amongst 1-year survivors
  - Decreased All-Cause Hospitalization
- PA pressure-guided therapy was safe with few device/system related complications and a low rate of pressure sensor failure

# CardioMEMS PAS Leadership

- **Steering Committee**
  - Lynne W. Stevenson (Chair), William T. Abraham, Robert C. Bourge, Maria Rosa Costanzo, Akshay S. Desai, J. Thomas Haywood, Lisa D. Rathman, Nirav Raval, David M. Shavelle, Richard Shlofmitz
- **Clinical Events Committee**
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  - Peter Carson — Georgetown University
  - Eugene Chung — Christ Hospital
  - Edward Michael Gilbert — University of Utah
  - Paul Hauptman — University of Tennessee
  - Wayne Levy — University of Washington
  - John Teerlink — UC San Francisco
- **Sponsor**
  - Abbott, Santa Clara, CA