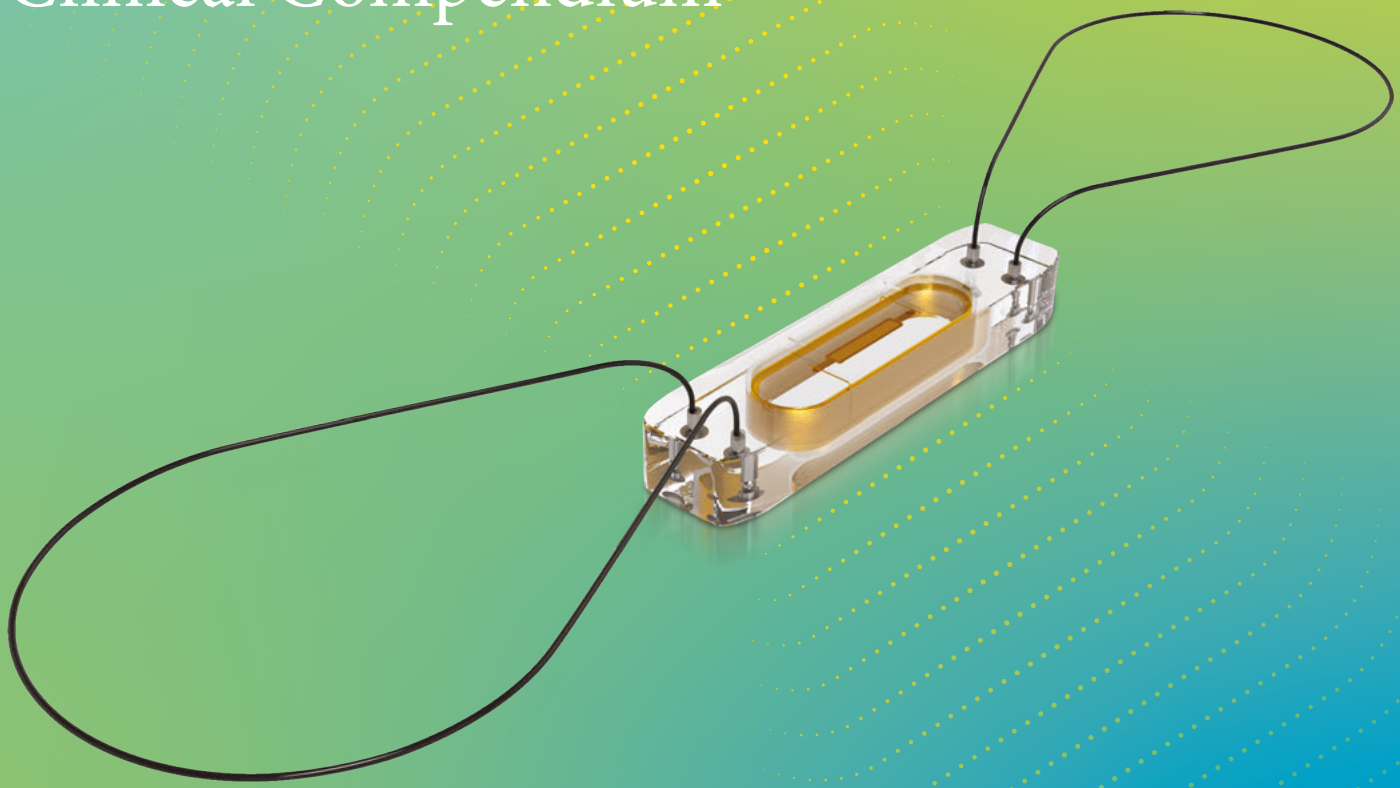
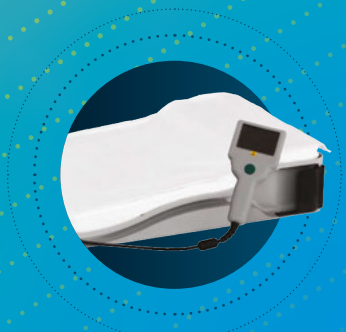
Abbott

CardioMEMS™ HF System

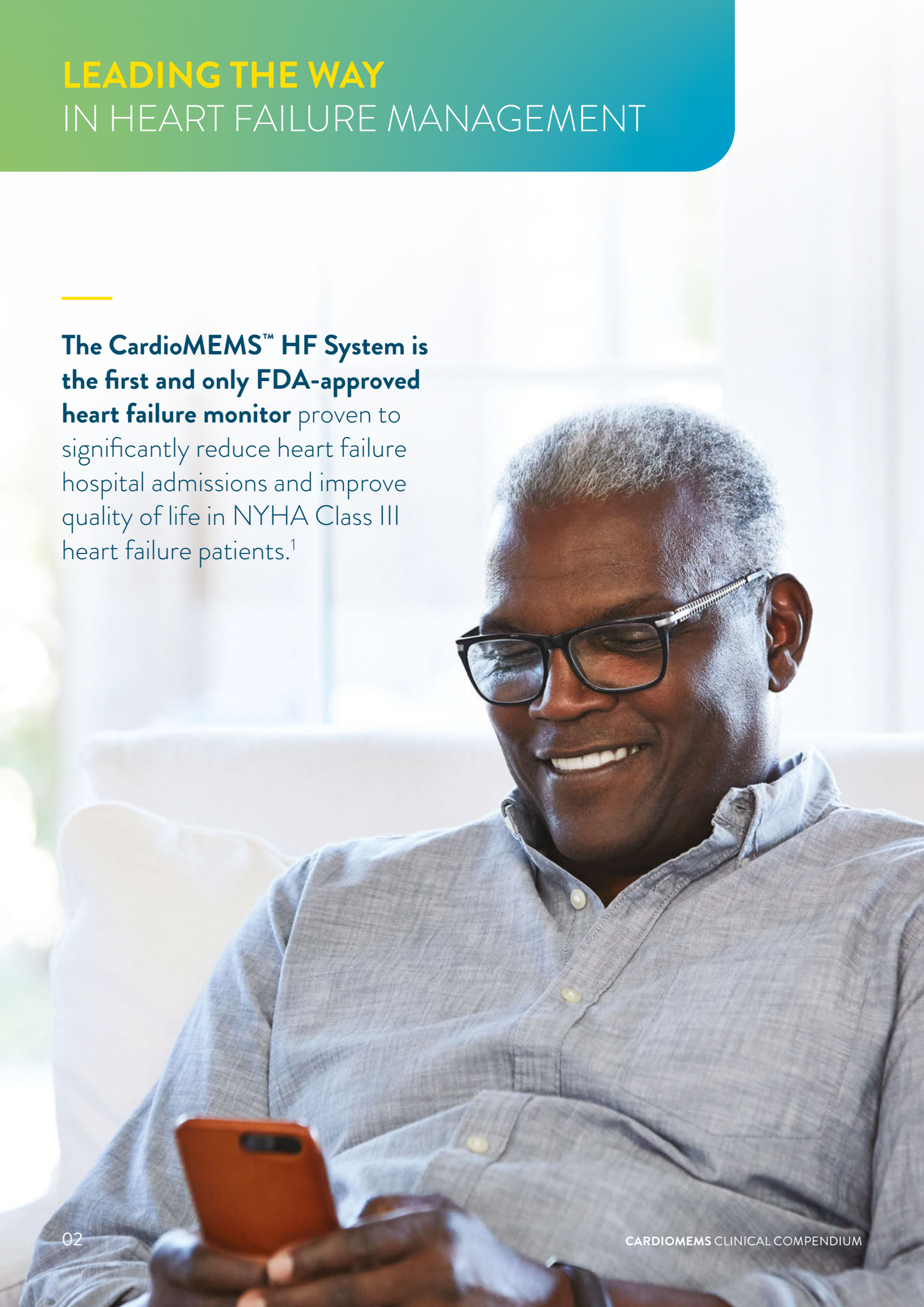
Clinical Compendium





LEADING THE WAY
IN HEART FAILURE MANAGEMENT

The CardioMEMS™ HF System is the first and only FDA-approved heart failure monitor proven to significantly reduce heart failure hospital admissions and improve quality of life in NYHA Class III heart failure patients.[1]



When used by clinicians to manage heart failure, the CardioMEMS HF System is:

- Safe and reliable — demonstrated 98.6% freedom from device- or system-related complications.[1]
- Clinically proven — reduced heart failure admissions by 33%1 and all-cause 30-day readmissions by 58%.[2]
- Proactive and personalized — patient management through direct monitoring of PA pressure and titration of medications.

Traditional physiologic markers in the development of acute decompensation in patients suffering from heart failure such as intrathoracic impedance, weight, blood pressure and symptoms are late and unreliable,[3,4] with only moderate sensitivity and specificity.[5-7] Large, randomized, controlled studies using telemonitoring of these indirect markers have failed to demonstrate a reduction in heart failure hospitalizations.[3,4,8] This clinical compendium summarizes key studies demonstrating the safety and effectiveness of the CardioMEMS HF System.

What's New since the Last Update?

Angermann C, et al. Pulmonary artery pressure-guided therapy in ambulatory patients with symptomatic heart failure: The CardioMEMS European Monitoring Study for Heart Failure (MEMS-HF). European Journal of Heart Failure. 2020. doi:10.1002/ejhf.1943.

Abraham J, et al. Management of the patient with heart failure and an implantable pulmonary artery hemodynamic sensor. Current Cardiovascular Risk Reports. 2020;14(12).

Shavelle D, et al. Lower rates of heart failure and all-cause hospitalizations during pulmonary artery pressure-guided therapy for ambulatory heart failure: One-year outcomes from the CardioMEMS Post-Approval Study. Circulation: Heart Failure. 2020;13(8):e006836.

PRE-CHAMPION

COMPARISON OF A RADIOFREQUENCY-BASED WIRELESS PRESSURE SENSOR TO SWAN-GANZ‡ CATHETER AND ECHOCARDIOGRAPHY FOR AMBULATORY ASSESSMENT OF PULMONARY ARTERY PRESSURE IN HEART FAILURE

Verdejo, et al. *J Am Coll Cardiol.* 2007;50:2375-2385.

The CardioMEMS™ HF System monitors PA pressure measurements from a sensor implanted into the PA. The safety and accuracy of the CardioMEMS™ PA Sensor have been demonstrated in previous studies.[9,10] Systolic and diastolic PA pressures were significantly correlated between the CardioMEMS PA Sensor and traditional Swan-Ganz‡ catheter measurements and between the CardioMEMS PA Sensor and standard echocardiography.[9,10]

A WIRELESS PRESSURE SENSOR FOR MONITORING PULMONARY ARTERY PRESSURE IN ADVANCED HEART FAILURE: INITIAL EXPERIENCE

Castro, et al. *J Heart Lung Transplant*. 2007;26:85-88.

Device implantation was simple and the sensor accurately measured PA pressure. No complications were observed and there was no evidence of PA thrombosis at 60 days. Diuretic and vasodilator doses were increased and the patient improved without further heart failure-related hospitalization.

CHAMPION TRIAL RATIONALE AND DESIGN: THE LONG-TERM SAFETY AND CLINICAL EFFICACY OF A WIRELESS PULMONARY ARTERY PRESSURE MONITORING SYSTEM

Adamson, et al. *J Card Fail.* 2010;17:3-10.

The CHAMPION clinical trial investigated the safety and clinical efficacy of the CardioMEMS HF System and established this management strategy as a new paradigm for the medical management of patients with symptomatic heart failure.

SAFETY AND ACCURACY OF A WIRELESS PULMONARY ARTERY PRESSURE MONITORING SYSTEM IN PATIENTS WITH HEART FAILURE

Abraham, et al. *American Heart Journal.* 2011;161:558-566.

The safety and accuracy of the CardioMEMS PA Sensor have been demonstrated in previous studies.[9,10] Systolic and diastolic PA pressures were significantly correlated between the CardioMEMS PA Sensor and traditional Swan-Ganz catheter measurements and between the CardioMEMS PA Sensor and standard echocardiography.[9,10]

A feasibility study reported the safe and successful implantation of the CardioMEMS PA Sensor in a clinical setting with no serious device-related events (n = 17).[10]

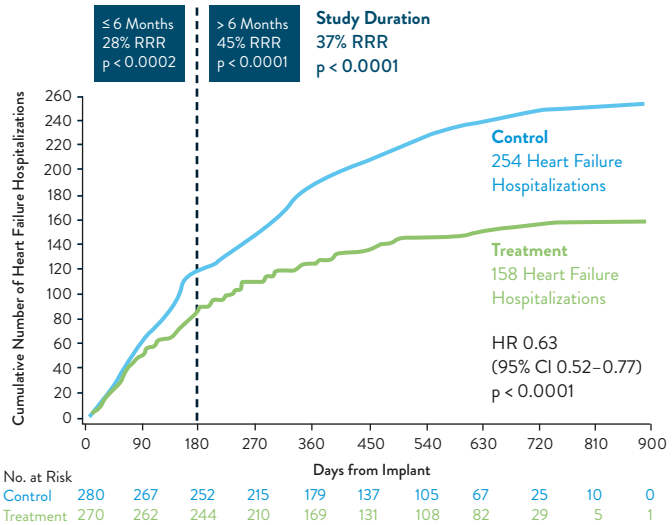
CHAMPION

WIRELESS PULMONARY ARTERY HAEMODYNAMIC MONITORING IN CHRONIC HEART FAILURE: A RANDOMIZED CONTROLLED TRIAL

Abraham, et al. *The Lancet*. 2011.[1]

- The aim of this randomized, multicenter, single-blind, controlled study was to evaluate the safety of the system and the efficacy of PA pressure-guided therapy on heart failure hospitalizations:
  - NYHA Class III heart failure patients irrespective of left ventricular EF and who had been hospitalized for heart failure within the past 12 months were implanted with the CardioMEMS PA Sensor (n = 550); patients were randomized to either the treatment group (heart failure management guided by PA pressure measurements; n = 270) or the control group (SOC management; n = 280).
- Mean follow-up time was 15 months.
- Both primary safety and efficacy endpoints were met:
  - Patients had a 98.6% freedom from device- or system-related complications (95% CI 97.3 to 99.4) with no pressure-sensor failures (95% CI 99.3 to 100.0).
  - The rate of heart failure hospitalizations at six months was reduced by 28% in the treatment group (p = 0.0002).
- During the first six months of follow-up, compared to the control group, the treatment group had:
  - A greater reduction in PA pressure (-156 vs. 33 mean AUC; p < 0.008).
  - Fewer patients admitted to the hospital for heart failure (20% treatment group vs. 29% control group; p < 0.03).
  - More days alive outside of the hospital (174.4 ± 31.1 vs. 172.1 ± 37.8 days; p < 0.02).
  - Better patient quality of life (45 ± 26 vs. 51 ± 25; p = 0.02 based on Minnesota Living with Heart Failure Questionnaire).

Figure 1. Cumulative heart failure hospitalizations during the entire period of follow-up



Abraham WT, et al. *The Lancet*. 2011.[1]

KEY RESULTS:

- The treatment group required < 1 medication change per patient per month compared to the control group (9.1 ± 7.4 vs. 3.8 ± 4.5 changes per patient during the first six months of follow-up; p < 0.0001).
- During the entire follow-up (mean 15 months), PA pressure-guided therapy (treatment group) significantly reduced heart failure hospitalizations by 37% compared to the control group (p < 0.0001; **Figure 1**).
- The treatment group had a lower risk of death or freedom from first heart failure hospitalization during the entire follow-up period compared to the control group (p = 0.0086).

SUSTAINED EFFICACY OF PULMONARY ARTERY PRESSURE TO GUIDE ADJUSTMENT OF CHRONIC HEART FAILURE THERAPY (CHAMPION): COMPLETE FOLLOW-UP RESULTS FROM THE CHAMPION RANDOMIZED TRIAL

Abraham, et al. *The Lancet*. 2016.[11]

- This CHAMPION clinical trial analysis evaluated the impact on heart failure hospitalizations of the introduction of PA pressure monitoring in the control group (n = 170) of patients and continued PA monitoring in the treatment group (n = 177) during the open access phase of the trial.
- Following completion of the randomized access period (mean follow-up of 18 months), all patients were managed utilizing PA pressure monitoring with the CardioMEMS™ HF System (mean follow-up of 13 months) and evaluated in a longitudinal analysis.
- New access to PA pressures in the control group resulted in a 48% reduction in heart failure hospitalization rates (0.36 vs. 0.68; HR 0.52; 95% CI 0.40 to 0.69; p < 0.0001; **Figure 2**).
- The low heart failure hospitalization rate in the treatment group during the randomized access period was maintained in the open access period (0.45 vs. 0.48; HR 0.93; 95% CI 0.70 to 1.22; p = 0.5838; **Figure 2**).

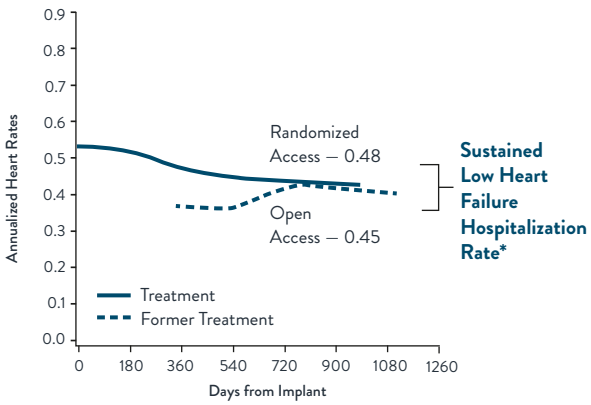
KEY RESULTS:

- The longitudinal analysis confirms the effectiveness of the CardioMEMS HF System and supports the findings from the randomized portion of the CHAMPION clinical trial.
- Even after adjustment for longitudinal confounders, new access to PA pressure monitoring for the formerly blinded control group resulted in a significant reduction in heart failure hospitalizations.

Randomized and open access periods also led to significant reduction in heart failure hospitalization

Figure 2. Part 1: Randomized access

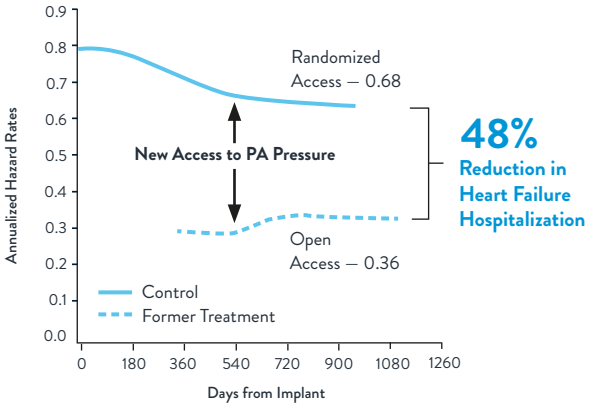
TREATMENT AND FORMER TREATMENT



*Over 31 months, despite termination of sponsor communications.
Abraham W, et al. *The Lancet*. 2016.

Figure 2. Part 2: Open access

CONTROL AND FORMER CONTROL



Results from the open access period **confirm the effectiveness** of the CardioMEMS™ HF System observed during the random access period.

PREPLANNED (PROSPECTIVE) CHAMPION SUBGROUP ANALYSES

EFFECTS OF PA PRESSURE MONITORING ON HFpEF SUBGROUP

WIRELESS PULMONARY ARTERY PRESSURE MONITORING GUIDES MANAGEMENT TO REDUCE DECOMPENSATION IN HEART FAILURE WITH PRESERVED EJECTION FRACTION

Adamson, et al. *Circulation Heart Fail.* 2014.[12]

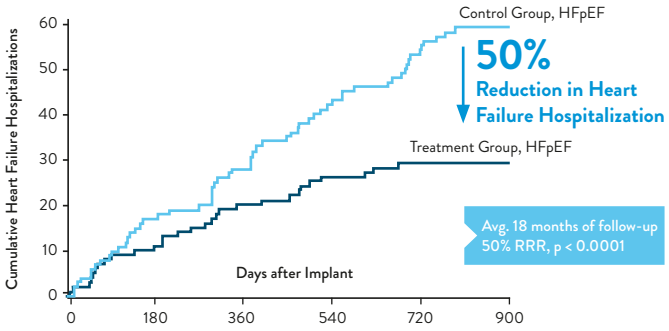
- This subanalysis of the CHAMPION clinical trial evaluated the effect of PA pressure-guided therapy with the CardioMEMS™ HF System in NYHA Class III patients with preserved ejection fraction (HFpEF).
- Of the HFpEF patients (n = 119), 62 were randomized to the treatment group (PA pressure-guided therapy) and 57 to the control group (SOC).

KEY RESULT:

- PA pressure-guided therapy significantly reduced heart failure hospitalizations for HFpEF patients in the treatment group by 50% compared to those patients in the control group, with an average follow-up time of 30 months ($p < 0.0001$). Results were associated with a rate of 0.43 events/patient-year in the treatment group vs. 0.86 events/patient-year in the control group **(Figure 3)**.

Prospective Subgroup Analysis: HFpEF Patients Managed with the CardioMEMSTM HF System Show Significant Reduction in Heart Failure Hospitalization

Figure 3



EFFECTS OF PA PRESSURE MONITORING ON HFrEF SUBGROUP, HFrEF SUBGROUP ALREADY ON GDMT

PULMONARY ARTERY PRESSURE-GUIDED MANAGEMENT OF PATIENTS WITH HEART FAILURE AND REDUCED EJECTION FRACTION

Givertz, et al. *J Am Coll Cardiol.* 2017.[13]

Initiation of a PA pressure-guided heart failure management strategy, even in HFrEF patients receiving optimal background medical and device therapy, was able to achieve large, consistent reductions in heart failure hospitalization and mortality in HFrEF patients enrolled in the CHAMPION trial.

Prospective Subgroup Analysis: HFrEF Patients Show Significant Reduction in Heart Failure Hospitalization and Strong Trend Toward Improved Survival

Figure 4. Clinical outcomes

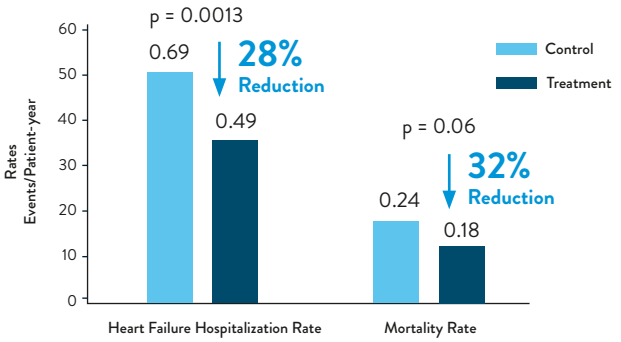
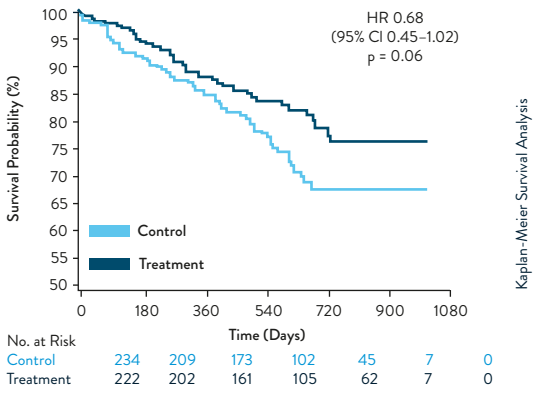


Figure 5. Survival probability



KEY RESULTS:

Prospective Study Results

- In the CHAMPION HFrEF cohort, heart failure hospitalization rates were **28% lower** than control **(p = 0.0013)**; mortality was **32% lower**, trending toward significance **(p = 0.06)** at 18 months **(Figure 4 and Figure 5)**.

RETROSPECTIVE STUDY DESCRIPTION:

This paper also included a retrospective analysis of the CHAMPION HFrEF cohort (n = 456), based on strong indicators for reduced heart failure hospitalization and mortality in the prospective subgroup analysis of HFrEF patients.

This study addresses the hypothesis that hemodynamic-guided care benefits patients even if they are already on maximum GDMT.

Evaluated heart failure hospitalizations and mortality based on patients' ability to tolerate full GDMT vs. incomplete medical therapy.

CONCLUSION:

- A pressure-guided heart failure management strategy resulted in significant reductions in hospitalizations and mortality in patients receiving prior optimal GDMT.
- Maximally tolerated GDMT at target doses is very important to control heart failure disease progression. There is apparent synergy between GDMT and hemodynamic monitoring in the control of heart failure disease progression.
- This retrospective analysis suggests the impact of GDMT on mortality and heart failure progression is significantly enhanced by avoiding decompensation events using guidance from the CardioMEMS™ HF System.

KEY RESULTS:

- In the CHAMPION HFrEF population (prospective subgroup analysis), heart failure hospitalization rates were 28% lower than control (p = 0.0013) and mortality was 32% lower, trending toward significance (p = 0.06).
- Because there was such a strong signal for improved survival in the prospective study, a retrospective study was done on the CHAMPION HFrEF subgroup, splitting them into groups based on the ability to tolerate GDMT:
  - **Group 1** (n = 455)**: tolerated at least one ACEI/ARB and/or BB.**
  - **Group 2** (n = 337)**: tolerated both ACEI/ARB and BB.**
- Heart failure hospitalization in Group 1 was 33% lower than control (p = 0.0002) (left panel, left points).
- Heart failure hospitalization in Group 2 was 43% lower than control (p < 0.0002) (left panel, right points).
- Mortality in Group 1 was 37% lower than control (p = 0.0293) (right panel, left points).
- Mortality in Group 2 was 57% lower than control (p = 0.0052) (right panel, right points).

Figure 6. Partial GDMT

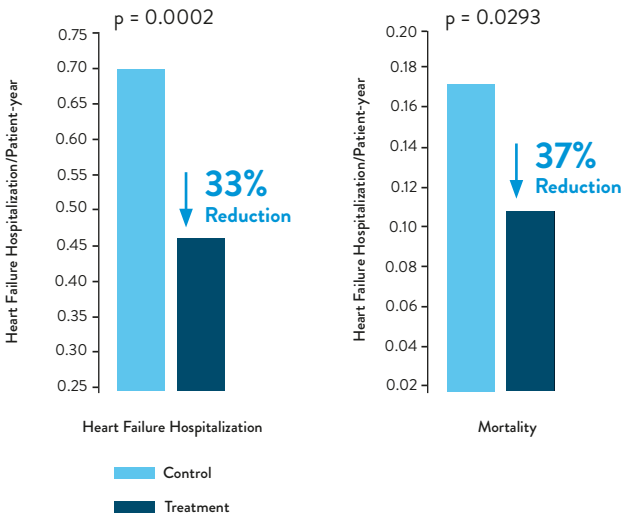
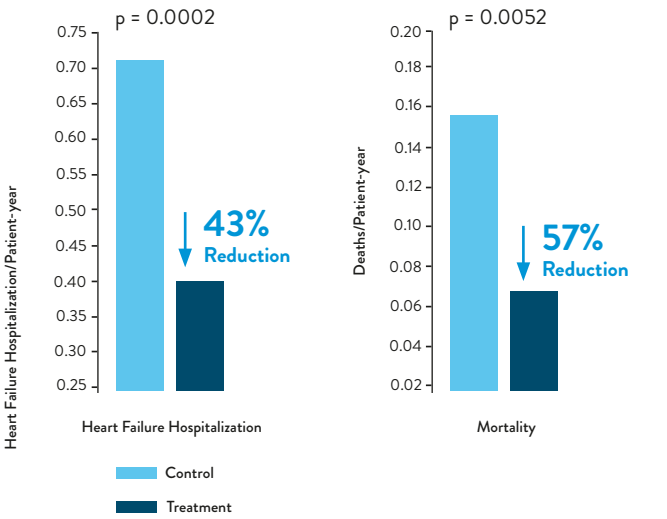


Figure 7. "Max" GDMT



RETROSPECTIVE SUBANALYSES

CARDIOMEMS™ HF SYSTEM-GUIDED PA PRESSURE MONITORING PROVIDED ACTIONABLE INFORMATION AND A MORE PERSONALIZED PHARMACOLOGICAL APPROACH, SO CLINICIANS COULD BETTER MANAGE HF

EFFECT OF CRT ON HEART FAILURE RELATED HOSPITALIZATIONS IN PATIENTS WITH REDUCED EF UTILIZING REMOTE PULMONARY ARTERY PRESSURES IN THE CHAMPION TRIAL

Weiner S, et al. *Heart Rhythm*. 2011.[14]

- This subanalysis of the CHAMPION clinical trial evaluated the effect of PA pressure-guided therapy with the CardioMEMS™ HF System in patients with rEF (rEF < 40%; n = 430) with and without a CRT device.
- 40% (171 of 430) of rEF patients had CRT devices; of this cohort, 82 patients were in the treatment group and 89 in the control group.
- 60% (259 of 430) of rEF patients did not have CRT devices; of this cohort, 126 patients were in the treatment group and 42 in the control group.

KEY RESULTS:

- Remote PA pressure data in the treatment group resulted in similar reductions in heart failure hospitalization in patients with and without a CRT device, suggesting that heart failure management guided by PA pressures may provide additive benefits to CRT therapy:
  - For patients in the rEF-CRT group, those who received PA pressure-guided therapy had significantly fewer heart failure hospitalizations (RRR = 24%; p = 0.0264).
  - For patients in the rEF-no CRT group, PA pressure-guided therapy resulted in a RRR = 23%.

THE UTILITY OF REMOTE WIRELESS PULMONARY ARTERY PRESSURE MONITORING IN PATIENTS WITH OR WITHOUT A HISTORY OF MYOCARDIAL INFARCTION: EXPERIENCE FROM THE CHAMPION TRIAL

Strickland WL, et al. *JACC*. 2011.[15]

- This subanalysis of the CHAMPION clinical trial determined whether PA pressure monitoring affected the clinical outcomes of patients with and without a history of MI.
- 271 of the 550 NYHA Class III heart failure patients enrolled in the CHAMPION clinical trial had a history of MI and were randomized to either the control (n = 137) or treatment (n = 134) groups.
- At six months, there was a 2.2-day benefit of days alive outside the hospital for patients in the treatment group; at 15 months, this increased to 30.1 days.

KEY RESULT:

- At six months and for the full study duration (mean 15 months), remote PA pressure monitoring had a significant reduction in heart failure hospitalizations for patients with and without a history of MI in the treatment group vs. control **(Table 1)**.

Table 1. RRR of heart failure hospitalizations

	RRR at 6 Months for Treatment Group	RRR at 15 Months for Treatment Group
History of MI	30% (p < 0.0039 vs. control)	46% (p < 0.0001 vs. control)
No MI	25% (p = 0.016 vs. control)	23% (p = 0.021 vs. control)

IMPACT OF REMOTE, WIRELESS PULMONARY ARTERY HEMODYNAMIC MONITORING IN PATIENTS WITH ATRIAL FIBRILLATION AND CHRONIC HEART FAILURE: INSIGHTS FROM THE CHAMPION TRIAL

Miller, et al. *JACC*. 2012.[16]

- This CHAMPION clinical trial subanalysis compared the baseline characteristics and impact of PA pressure-guided therapy on hospitalization rates in patients with a history of AF (n = 255) compared to those with normal sinus rhythm (n = 200).
- The AF cohort had significant baseline differences compared to the sinus rhythm cohort (older: 65 vs. 59; more often male):
  - 80% vs. 66%, more frequently had CRT or CRT-D devices.
  - 44% vs. 27%, higher mean PA pressures: 30.2 vs. 28.5 mmHg, etc.

KEY RESULTS:

- AF patients in the treatment group had a significantly lower heart failure hospitalization rate than those in the control group at six months (37%; p = 0.0004) and 15 months (41%; p < 0.0001).
- AF patients had a 57% higher heart failure hospitalization rate vs. non-AF patients (0.47 vs. 0.30 events/patient; p < 0.0001).

TARGETING PULMONARY ARTERY PRESSURES IN THE TREATMENT OF CHRONIC HEART FAILURE: INSIGHTS FROM THE CHAMPION TRIAL

Adamson, et al. *European Heart Journal*. 2012.[17]

- This CHAMPION clinical trial subanalysis determined whether remote access to PA pressure data may provide a method to identify and treat high filling pressures in heart failure patients at increased risk for decompensation (n = 550).
- At implant, the mean PA pressure was similar in both control and treatment groups (31.8 ± 10.7 mmHg and 31.3 ± 11.1 mmHg, respectively).

- Average PA pressures increased during the six weeks prior to heart failure hospitalizations in both groups ($p < 0.0001$) and decreased significantly after successful in-hospital decongestion ($p < 0.0001$).
- Treatment patients with heart failure hospitalizations had lower pressures compared to control patients with heart failure hospitalizations at all time points prior to hospitalization:
  - Treatment patients also had lower PA pressures compared to the control patients regardless of hospitalization type (heart failure related or non-heart failure related).

KEY RESULTS:

- Higher PA pressures and increases in PA pressure were both associated with increased risk for heart failure hospitalizations.
- Heart failure treatment strategies that target both high PA pressure and increases in PA pressures may be effective strategies for lowering the risk of decompensation in chronic heart failure patients.

BENEFITS OF PULMONARY ARTERY PRESSURE MONITORING IN PATIENTS WITH NYHA CLASS III HEART FAILURE AND CHRONIC KIDNEY DISEASE: RESULTS FROM THE CHAMPION TRIAL

Abraham, et al. *J Card Failure*. 2014.[18]

This subgroup data analysis from the CHAMPION clinical trial compared heart failure hospitalizations between NYHA Class III heart failure patients with CKD monitored (mean follow-up of 18 months) with PA pressure (n = 150) to those managed with SOC (n = 147):

- When CKD patients were managed with PA pressures, heart failure hospitalization rates were significantly reduced (42%) compared to patients with CKD managed according to SOC (0.48 vs. 0.83; HR 0.58; $p < 0.001$).
- Changes in CKD indicators (creatinine and glomerular filtration rates) were not adversely affected in the PA pressure-monitored group.

KEY RESULTS:

- CKD in patients with heart failure is a frequent comorbidity that is associated with worse clinical outcomes, including higher heart failure hospitalization rates.
- For heart failure patients with CKD, PA pressure monitoring reduced heart failure hospitalizations by 42% compared to SOC heart failure management.
- Intensified heart failure medical therapy as a result of PA pressure monitoring was safe and did not adversely affect renal function.

PULMONARY HYPERTENSION RELATED TO LEFT HEART DISEASE: INSIGHT FROM A WIRELESS IMPLANTABLE HEMODYNAMIC MONITOR

Benza, et al. *JHLT*. 2015.[19]

This CHAMPION clinical trial subanalysis evaluated the effect of PA pressure monitoring in heart failure patients with comorbid PH (mean PA pressure > 25 mmHg):

- Data were obtained for 314 patients (59%) who had WHO Group II PH. Patients in the PH cohort were further stratified by TPG and pulmonary vascular resistance.
- 67% (213 out of 314) of PH patents had a TPG ≤ 15.
- Patients without PH were at significantly lower risk for mortality than PH patients (HR 0.31; 95% CI 0.19 to 0.52; $p < 0.0001$).
- PH patients had higher heart failure hospitalization rates than non-PH patients (0.77/year vs. 0.37/year; HR 0.49; 95% CI 0.39 to 0.61; $p < 0.001$).
- In patients with and without PH, ongoing knowledge of hemodynamic data resulted in a reduction in heart failure hospitalization for PH patients (HR 0.64; 95% CI 0.51 to 0.81; $p = 0.002$) and for non-PH patients (HR 0.60; 95% CI 0.41 to 0.89; $p = 0.01$).
- Among PH patients, there was a reduction in the composite endpoint of death and heart failure hospitalization with ongoing knowledge of hemodynamics (HR 0.74; 95% CI 0.55 to 0.99; $p = 0.04$), but no difference in survival (HR 0.78; 95% CI 0.50 to 1.22; $p = 0.28$).

KEY RESULT:

- PH patients are at a high risk for adverse outcomes. Ongoing knowledge of hemodynamic variables may allow more effective treatment strategies to reduce the morbidity of the disease.

HEART FAILURE AND RESPIRATORY HOSPITALIZATIONS ARE REDUCED IN HEART FAILURE SUBJECTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE USING AN IMPLANTABLE PULMONARY ARTERY PRESSURE MONITORING DEVICE

Krahnke, et al. *J Card Fail*. 2015.[20]

The purpose of this CHAMPION clinical trial subanalysis was to evaluate whether PA pressure-guided therapy reduced heart failure hospitalizations and REHs in a cohort of patients with comorbid COPD (n = 187).

KEY RESULTS:

- There was an overall reduction in PA pressures; patients in the treatment group (n = 91) had an average AUC reduction of 202 mmHg days compared to the increase of 107 mmHg days in the control group (n = 96; $p = 0.03$).
- At 15 months, there was a 41% reduction in heart failure hospitalization rates in the treatment group vs. the control group (0.55 vs. 0.96; HR 0.59; 95% CI 0.44 to 0.81; $p = 0.0009$).
- At 15 months, patients in the treatment group (n = 91) had a 62% reduction in REH (0.12 vs. 0.31; HR 0.38; 95% CI 0.21 to 0.71; $p = 0.0023$).

LIMITATIONS OF RIGHT HEART CATHETERIZATION IN THE DIAGNOSIS AND RISK STRATIFICATION OF PATIENTS WITH PULMONARY HYPERTENSION RELATED TO LEFT HEART DISEASE: INSIGHTS FROM A WIRELESS PULMONARY ARTERY PRESSURE MONITORING SYSTEM

Raina, et al. *JHLT*. 2015.[21]

- This CHAMPION sub-study compared the use of the CardioMEMS™ HF System with RHC to diagnose and stratify risk in patients with PH.
- RHC identified 320 patients with PH (defined as mean PA pressure > 25 mmHg) and among these patients mean PA pressure obtained from RHC was similar to the CardioMEMS HF System's first-week PA pressure.
- RHC also identified 217 patients without PH (defined as mean PA pressure readings ≤ 25 mmHg) and 51% of them met this definition according to data obtained from the CardioMEMS HF System (18.5 for the RHC vs. 18.4 for the CardioMEMS HF System, p = 0.9208).
- The other 49% of patients identified by RHC as not having PH had first-week mean PA pressure readings > 25 mmHg with the CardioMEMS HF System, indicating PH.
- Among the 217 patients using the CardioMEMS HF System diagnosed by RHC as non-PH, the 49% with first-week mean PA pressure readings > 25 mmHg had significantly higher heart failure hospitalization rates than the 51% of patients with readings ≤ 25 mmHg (0/49 vs. 0.25/year, p = < 0.0001).

KEY RESULTS:

- This analysis suggests that using RHC alone may result in PH underdiagnoses in patients with heart failure.
- In this study, the more frequent PA pressure monitoring with the CardioMEMS HF System provided better diagnostic and risk stratification compared with single RHC.

THERAPY GUIDED BY PA PRESSURE ALONE VS. SIGNS AND SYMPTOMS

PRESSURE FOR ACTION: IMPLANTABLE PULMONARY ARTERY PRESSURE SENSOR MEASUREMENTS ALONE BEAT CLINICAL SIGNS TO GUIDE PREVENTION OF HEART FAILURE HOSPITALIZATIONS

Goldberg LR, et al. HRS 2015 Abstract AB36-02.[22]

- Data analysis from the CHAMPION clinical trial during the six-month primary endpoint period:
  - 550 patients: 270 in the treatment group and 280 in the control group.
- All interventions for patients in the PA pressure-managed group were characterized prospectively by investigators as triggered primarily by clinical findings OR by changes in PA pressure.
- Heart failure hospitalization rates were lowest in patients for whom all diuretic interventions were triggered by PA pressure (0.39 events/patient-year), despite this cohort having the highest baseline PA pressure **(Figure 8)**.
- There was a statistically significant 67% RRR of heart failure hospitalizations if a patient's diuretic interventions were managed with PA pressure alone vs. clinical signs only (HR 0.33; 95% CI 0.16 to 0.59; p = 0.0007).
- Medication changes based on PA pressure information were more effective in reducing heart failure hospitalizations than using signs and symptoms alone.

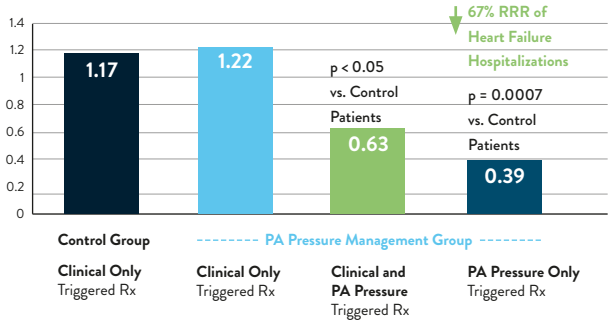
KEY RESULTS:

- Heart failure hospitalization rates (events/patient-year) were significantly reduced if a patient's diuretic management therapies were managed by:
  - PA pressure only compared to clinical signs (67% reduction).
  - PA pressure and clinical signs compared to clinical signs (46% reduction).
- Heart failure hospitalization rates were most effectively reduced by a management strategy based on PA pressures without reliance on clinical changes.
- This supports the strategy of early intervention prior to clinical signs to avert clinical decompensation and heart failure readmissions.[1,2]

CONCLUSION:

Managing medical therapy based on PA pressures, along with follow-up lab and patient assessments, led to significantly better outcomes than managing based on clinical signs and symptoms.

Figure 8. Heart failure hospitalization rate (events/year)



Managing medical therapy based on PA pressures, along with follow-up lab and patient assessments, led to **significantly better outcomes than managing based on clinical signs and symptoms.**

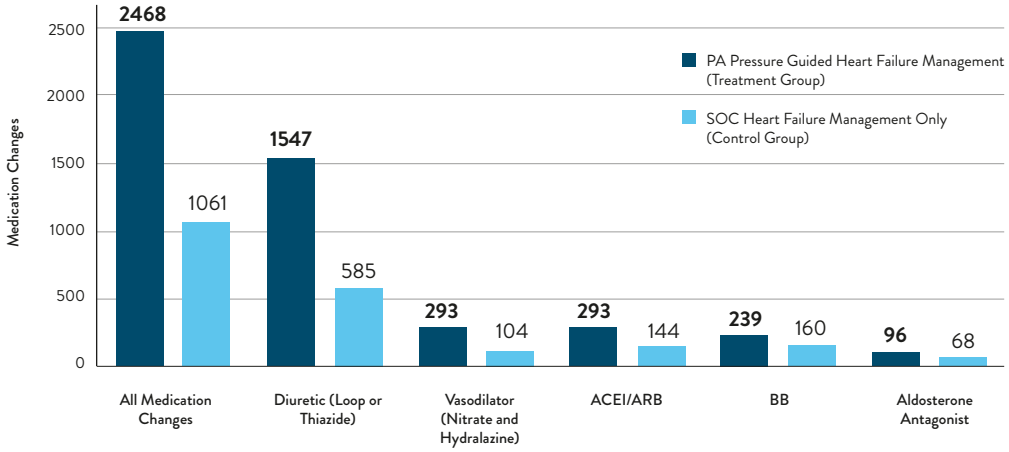
INTERVENTIONS LINKED TO DECREASED HEART FAILURE HOSPITALIZATIONS DURING AMBULATORY PULMONARY ARTERY PRESSURE MONITORING

Costanzo, et al. *J Am Coll Cardiol Heart Fail.* 2016.[23]

MEDICATION INCREASES AND DECREASES IN RESPONSE TO PA PRESSURE:

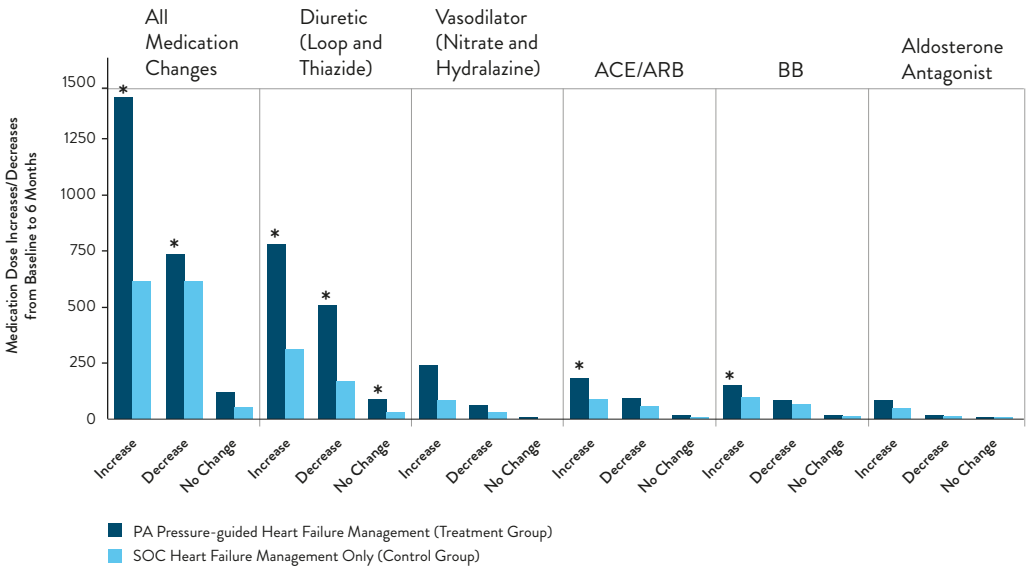
- Knowledge of ambulatory PA pressures leads to more interventions that reduce heart failure events compared with standard clinical assessment.
- The current study is focused on the degree and nature of the interventions made.
- Most medication interventions in CHAMPION were adjustments in diuretics.
- It is not known when vasodilators would be more effective than diuretics to maintain lower filling pressures. Neither is it known how titration of ACEIs/ARBs and BBs should be modulated by knowledge of ambulatory filling pressures that are too high or too low.
- The current analysis validates the target pressure ranges and the algorithm for intervention that can be used as a starting point to reduce heart failure hospitalizations and improve patient outcomes in previously hospitalized NYHA Functional Class III patients.

Figure 9. Frequency of medication changes by drug class



- Medication changes based on PA pressure information were more effective in reducing heart failure hospitalizations than using signs and symptoms alone.

Figure10.



*p < 0.05 PA Pressure-guided Heart Failure Management vs. SOC Heart Failure Management.
No change represents where a medication was changed (e.g., dose frequency, route) that resulted in no net dose equivalent change.

MEDICARE-ELIGIBLE POPULATIONS

PULMONARY ARTERY PRESSURE-GUIDED HEART FAILURE MANAGEMENT REDUCES 30-DAY READMISSIONS

Adamson, et al. *Circulation: Heart Failure.* 2016.[2]

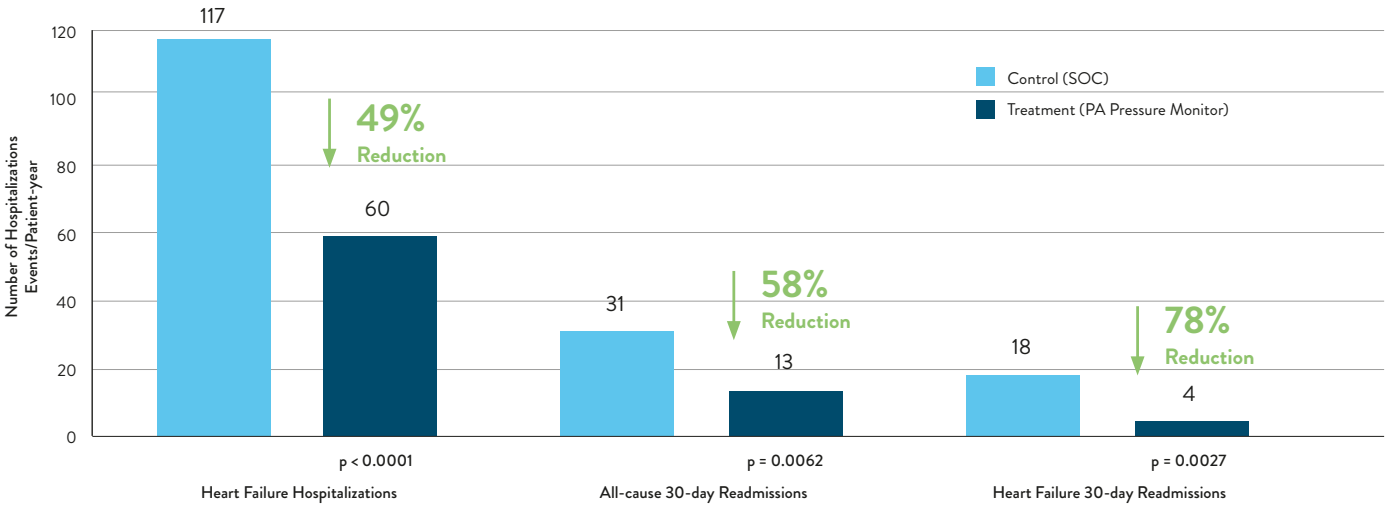
- This data analysis from the CHAMPION clinical trial evaluated 30-day readmissions and heart failure hospitalizations between patients monitored with the CardioMEMS™ HF System and those not monitored over a period of 18 months.
- 245 patients were included in the analysis: 120 in the PA pressure treatment group and 125 in the SOC control group.
- In this analysis, patients managed with PA pressure compared to those managed according to SOC experienced:
  - 58% reduction in all-cause 30-day readmissions (0.07 vs. 0.18; HR 0.42; p = 0.0062).*
  - 78% reduction in heart failure 30-day readmissions (0.02 EPPY vs. 0.10 EPPY; HR 0.22; p = 0.0027).*
  - 49% reduction in heart failure hospitalizations (0.34 EPPY vs. 0.67 EPPY; HR 0.51; p < 0.0001).*

*Event rates are based on events/patient-year.

KEY RESULTS:

- This retrospective analysis of the CHAMPION clinical trial demonstrated that PA pressure-guided management of Medicare-eligible heart failure patients significantly reduced 30-day readmissions, which may help to alleviate the economic burden associated with heart failure readmissions.
- This analysis supports results from the CHAMPION clinical trial demonstrating a 37% reduction in heart failure hospitalizations and improved quality of life with PA pressure-guided heart failure management in NYHA Class III heart failure patients irrespective of Medicare eligibility.[1]

Figure 11. Subgroup analysis: Medicare-eligible population shows significant reduction in 30-day readmissions



Statistically significant reductions in 30-day readmission and heart failure hospitalization in Medicare-eligible patients 65 years or older (n = 245), when PA pressures are monitored using the CardioMEMS™ HF System.

Adamson, et al. *Circ Heart Fail.* 2016.

ALSO, SEE GIVERTZ, ET AL, IN PROSPECTIVE SUBGROUP ANALYSES SECTION:

PULMONARY ARTERY PRESSURE-GUIDED MANAGEMENT OF PATIENTS WITH HEART FAILURE AND REDUCED EJECTION FRACTION

Givertz, et al. *J Am Coll Cardiol*. 2017.[13]

HEART FAILURE PATIENTS WITH COMMON COMORBIDITIES

PA Pressure-guided Therapy Has Been Shown to Consistently Reduce Heart Failure Hospitalizations in Patients with Common Heart Failure Comorbidities

Heart failure is often associated with a variety of comorbidities such as respiratory disease, coronary artery disease and AF. These comorbidities contribute to disease progression and may alter the response to treatment.[24] This section highlights additional subanalyses from the CHAMPION clinical trial that consistently show that PA pressure-guided therapy reduces heart failure hospitalizations in patients with common heart failure comorbidities. **Table 2** summarizes the rate of heart failure hospitalizations across the different studies.

The CHAMPION Trial Subgroup Analyses: Reduction of Heart Failure Hospitalization in Patient Groups with Common Comorbidities

Table 2. Patients with common heart failure comorbidities have consistent reduction in heart failure hospitalizations with PA pressure-guided therapy

Subgroup or Comorbidity	n (control)	n (treatment)	Follow-up Period (months)	Reduction of Heart Failure Hospitalization Rate in Treatment Group vs. Control Group
Medicare population[2]	125	120	18	49%, p < 0.0001
HFpEF[12]	56	59	18	50%, p < 0.0001
HFrEF following GDMT[13]	174	163	17	43%, p < 0.0001
CRT-D or ICD following GDMT[25]	146	129	18	43%, p < 0.0001
History of MI[20]	137	134	15	46%, p < 0.001
COPD[26,27]	96	91	15	41%, p = 0.0009
Pulmonary hypertension[28]	163	151	15	36%, p = 0.0002
AF[18]	135	120	15	41%, p < 0.0001
CKD[19]	150	147	15	42%, p = 0.0001

Patients with common heart failure comorbidities and patents in important subgroups **have consistent reduction in heart failure hospitalizations** with PA pressure-guided therapy.

THE UTILITY OF A WIRELESS IMPLANTABLE HEMODYNAMIC MONITORING SYSTEM IN PATIENTS REQUIRING MECHANICAL CIRCULATORY SUPPORT

Feldman D, et al. *ASAIO*. 2018.[28]

- This subanalysis of the CHAMPION clinical trial evaluated the effect of PA pressure-guided therapy on optimizing medications, pump parameters and timing of VAD intervention and transplantation in patients receiving an LVAD (n = 27).

KEY RESULT:

- LVAD patients who received PA pressure-guided therapy (15 out of 27 patients) had significantly shorter times to VAD intervention (p = 0.001), more changes to medical therapy based on hemodynamic information (p = 0.025) and shorter times between VAD intervention and heart transplantation (p = 0.001).

THE CARDIOMEMS™ HF SYSTEM COMMERCIAL EXPERIENCE: RESULTS FROM REAL-WORLD STUDIES

HEMODYNAMIC-GUIDED HEART-FAILURE MANAGEMENT USING A WIRELESS IMPLANTABLE SENSOR: INFRASTRUCTURE, METHODS, AND RESULTS IN A COMMUNITY HEART FAILURE DISEASE-MANAGEMENT PROGRAM

Jermyn R, et al. *Clin Cardiol.* 2016.[29]

KEY RESULT:

- Hemodynamic-guided heart failure management leads to significant improvements in NYHA Class and heart failure hospitalization rate in a small single-center study in a real-world setting, compared with usual care delivered in a comprehensive disease-management program:
  - Three-fold greater improvement in KCCQ scores.
  - Increase in 6MWD: Average increase of 96 meters at 90 days vs. no increase in the SOC group.

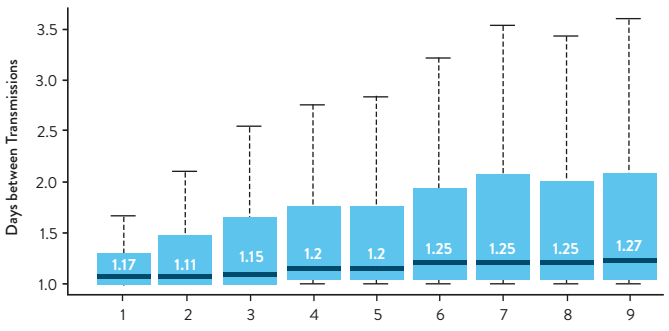
IMPACT OF PRACTICE-BASED MANAGEMENT OF PA PRESSURES IN 2000 PATIENTS IMPLANTED WITH THE CARDIOMEMS SENSOR

Heywood, et al. *Circulation.* 2017.[30]

Observational Study from the First 2000 Commercially Implanted Patients from the **Merlin.net™** Patient Care Network Database

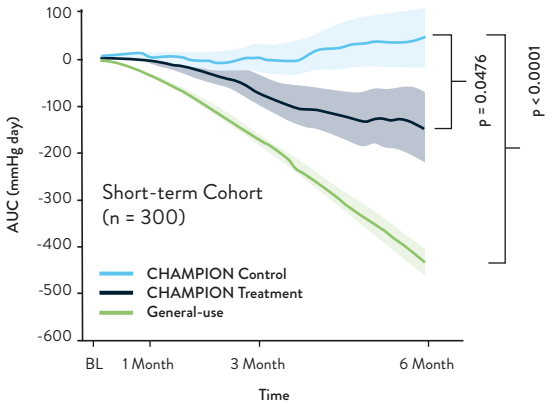
Post-approval Observational Study of the CardioMEMS™ HF System Large (N = 2000) Observational Study from the First 2000 Commercially Implanted Patients

Figure 12. Transmissions compliance



Patients consistently upload pressures:
Median 1.2 days between transmissions

Heywood JT, Jermyn R, Shavelle D, et al. *Circulation.* 2017;135:1509-17.

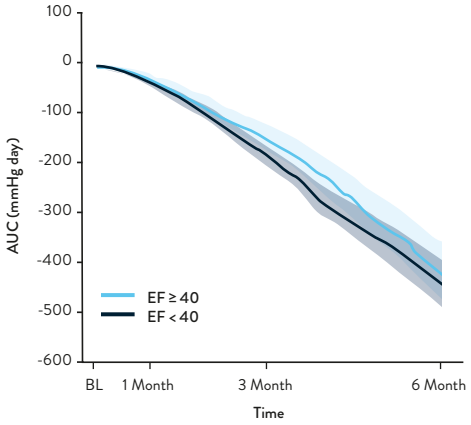


Providers consistently treat pressures:
Larger treatment effect in the real-world than CHAMPION

PATIENTS' PRESSURE REDUCTION STRATIFIED BY EF AND BY GENDER

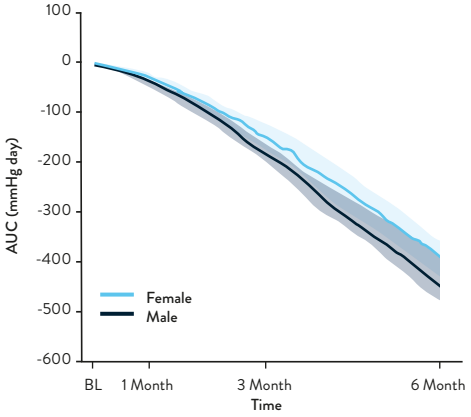
Pressures Are Reduced Equally Well in HFrEF and HFpEF, as Well as Male and Female

Figure 13. AUC mean PA pressure stratified by EF



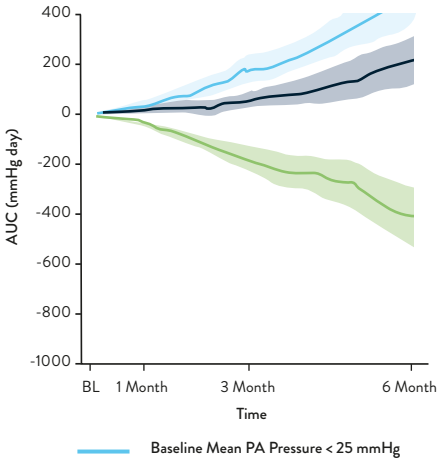
Heywood JT, Jermyn R, Shavelle D, et al. *Circulation*. 2017;135:1509-17.

Figure 14. AUC mean PA pressure stratified by gender



Pressure Changes Stratified by Baseline PA Pressure

Figure 15. CHAMPION control cohort



KEY RESULTS:

- High transmission compliance.
- Data drove appropriate patient care.
- Same results in HFpEF and HFrEF.
- "Long-term patient acceptance and adherence is clearly demonstrated."
- "The magnitude of pressure lowering … was significantly larger than was seen in the pivotal clinical trial."

Figure 16. CHAMPION treatment cohort

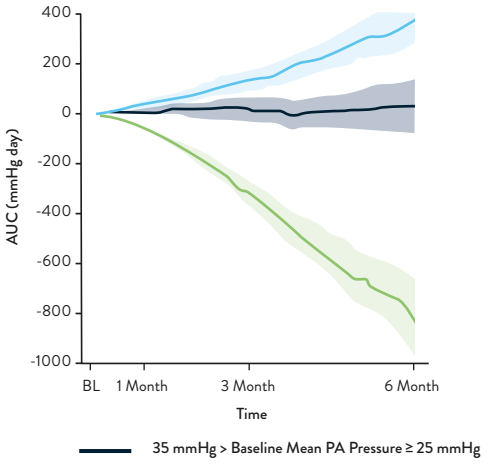
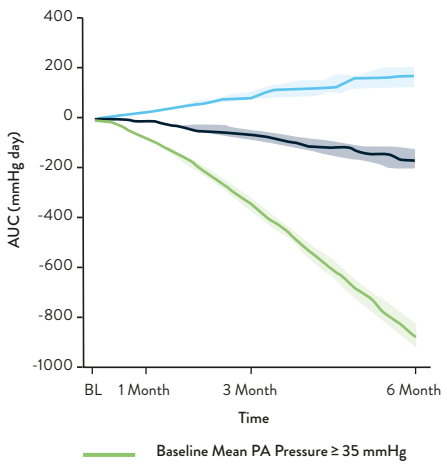


Figure 17. General-use cohort



Greatest reduction in mean PA pressure observed for CardioMEMS™ HF System patients with higher baseline PA pressure. Patients in the treatment group with baseline PA pressure at goal, remained at goal over time.

Heywood JT, Jermyn R, Shavelle D, et al. *Circulation*. 2017;135:1509-17.

AMBULATORY HEMODYNAMIC MONITORING REDUCES HEART FAILURE HOSPITALIZATIONS IN "REAL-WORLD" CLINICAL PRACTICE

Desai AS, et al. *JACC.* 2017.[31]

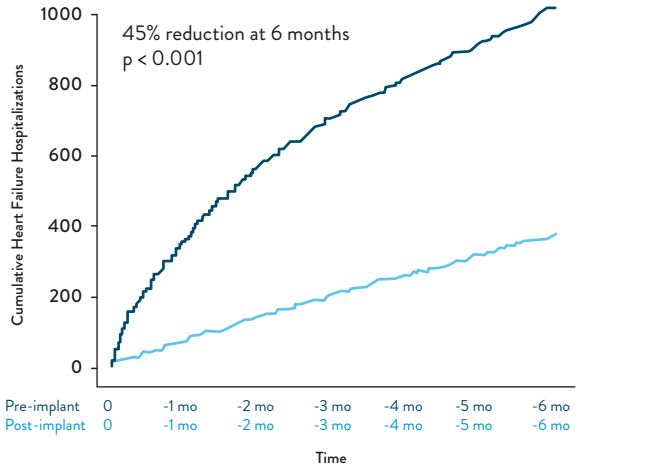
Real-world Use of the CardioMEMS™ HF System: Reduced Heart Failure Hospitalization and Associated Costs in a Large Retrospective Cohort (n = 1114) from a Medicare Claims Database — 6 and 12 Months of Follow-up

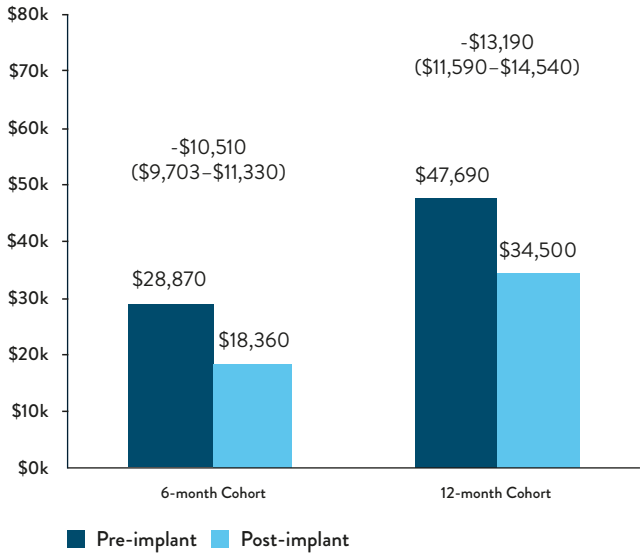
KEY RESULTS:

- Real-world reduction in heart failure hospitalization after CardioMEMS™ PA Sensor implant:
  - 45% reduction at six months.
- Significant cost reductions for hospitalization:
  - $10,510 per patient — six months.
  - $13,190 per patient — year.

These benefits support the real-world effectiveness of this approach to heart failure management.

Figure 18. Cumulative heart failure hospitalization during period before and after CardioMEMS™ PA Sensor implant





ASSOCIATION OF AMBULATORY HEMODYNAMIC MONITORING WITH CLINICAL OUTCOMES IN A CONCURRENT MATCHED COHORT ANALYSIS

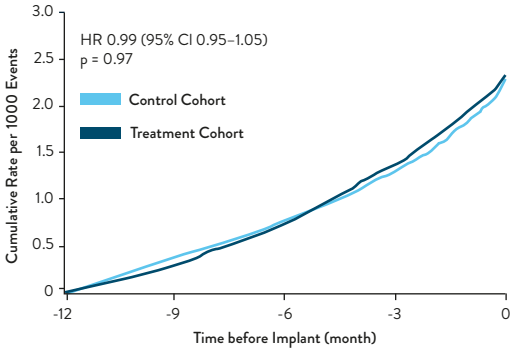
Abraham J, et al. *JAMA Cardiology.* 2019.[32]

STUDY OBJECTIVE:

This study examined the impact of ambulatory hemodynamic monitoring on clinical outcomes in patients with heart failure, asking the following questions:

- Is ambulatory hemodynamic monitoring associated with differences in rates of survival or heart failure hospitalization in a non-trial setting?
- Are results sustained at 12 months?

Figure 19. Time series of heart failure hospitalizations in the 12 months before PA pressure sensor implant



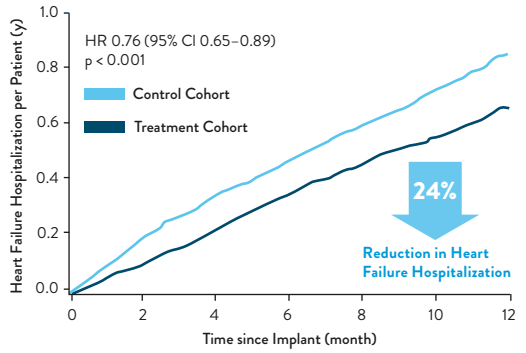
No. at Risk

Control Cohort	1087	1087	1087	1087	1087
Treatment Cohort	1087	1087	1087	1087	1087

The cumulative pre-implant heart failure hospitalization events clearly show similar trajectories for both arms of the study leading up to CardioMEMS PA Sensor implantation for the treatment group.

Figure 20. Cumulative events after PA pressure sensor implant

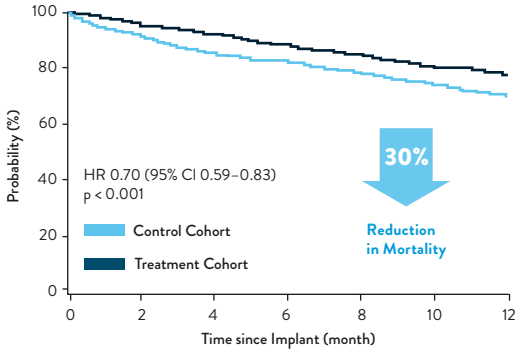
A. Cumulative heart failure hospitalizations after PA pressure sensor implantation



No. at Risk							
Control Cohort	1087	1000	931	891	850	805	764
Treatment Cohort	1087	1037	991	944	908	862	830

Cumulative incidence of heart failure hospitalization during 12-month follow-up shows a **24% reduction in heart failure hospitalization rate** in the treatment (CardioMEMS PA Sensor) arm, p < 0.001.

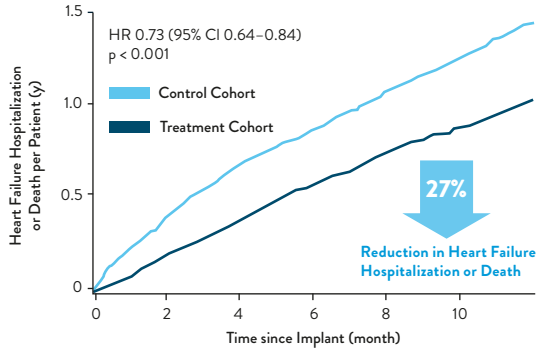
B. Kaplan-Meier survival analysis in the matched population



No. at Risk							
Control Cohort	1087	1000	931	891	850	805	764
Treatment Cohort	1087	1037	991	944	908	862	862

Kaplan-Meier survival analysis during the 12-month follow-up period shows a **30% reduction in mortality** in the treatment (CardioMEMS™ PA Sensor) arm, p < 0.001.

C. Combined outcome of heart failure hospitalization or death



No. at Risk							
Control Cohort	1087	1000	931	891	850	805	764
Treatment Cohort	1087	1037	991	944	908	862	830

Combined outcomes during the 12-month follow-up period show a **27% reduction in heart failure hospitalizations or death** in the treatment (CardioMEMS PA Sensor) arm, p < 0.001.

A. Heart failure hospitalizations. **B.** Deaths **C.** Combined heart failure hospitalizations and death

CONCLUSION:

In this large, retrospective, Medicare administrative claims analysis, the authors observed:

- Significantly lower rates of all-cause mortality (30%) and heart failure hospitalization (24%) among heart failure patients implanted with a CardioMEMS™ PA Sensor versus a contemporary cohort of matched controls (p < 0.001 for each).
- Reduced rates of heart failure hospitalization and mortality for CardioMEMS™ HF System patients are similar to outcomes from the CHAMPION trial, even though patients in this study are significantly older.
- Meaningful reductions in the number of days lost to death or hospitalization (17.5–18.5 days), a metric that is meaningful to patients, physicians and payers.

MONITORING PULMONARY ARTERIAL HYPERTENSION USING AN IMPLANTABLE HEMODYNAMIC SENSOR

Benza, et al. *Chest*. 2019.[33]

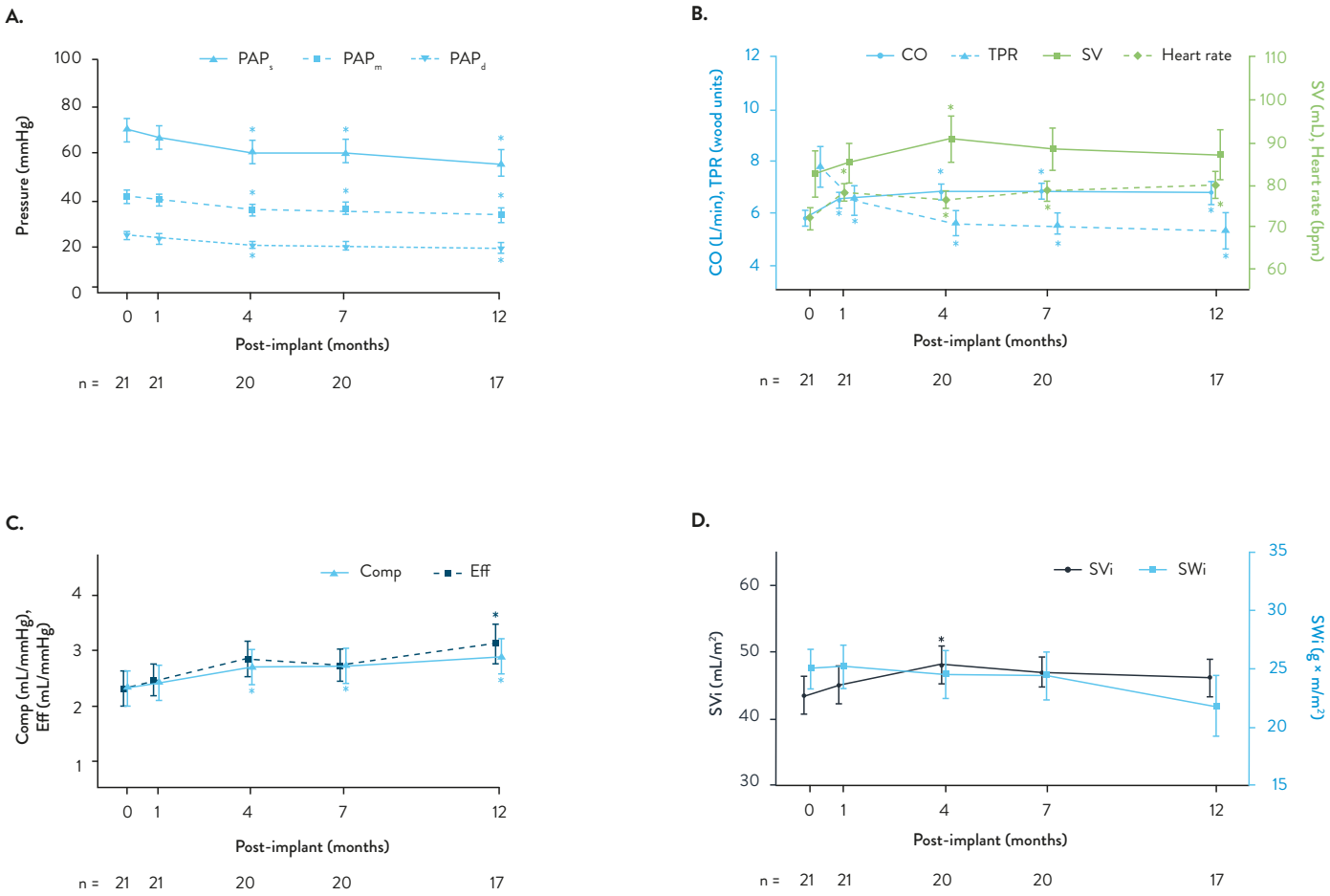
STUDY OBJECTIVE:

Pilot study (N = 26) designed to evaluate the feasibility and early safety of monitoring patients with PAH and right-sided heart failure using the CardioMEMS™ HF System. **Note:** The objective of this pilot study was to test the feasibility of monitoring therapy, not necessarily to use the CardioMEMS HF System to guide the therapy.

KEY RESULTS:

Significant reductions in PA pressures (PAP_m, 42 ± 13 to 34 ± 14 mmHg) and elevations in CO (5.8 ± 1.5 to 6.8 ± 1.8 L/min) were observed over one year of CardioMEMS HF System-monitored therapy. There were also observed elevations in SV, vascular compliance, SVi and Eff, as well as reductions in SW and TPR.

Figure 21. Hemodynamic response measured by the CardioMEMS™ HF System for patients at Allegheny General Hospital. Plots show mean ± SE. Asterisks show statistically significant differences ($p < 0.05$) from 0-month baseline. Number of patients at each time point is shown below the x-axes.

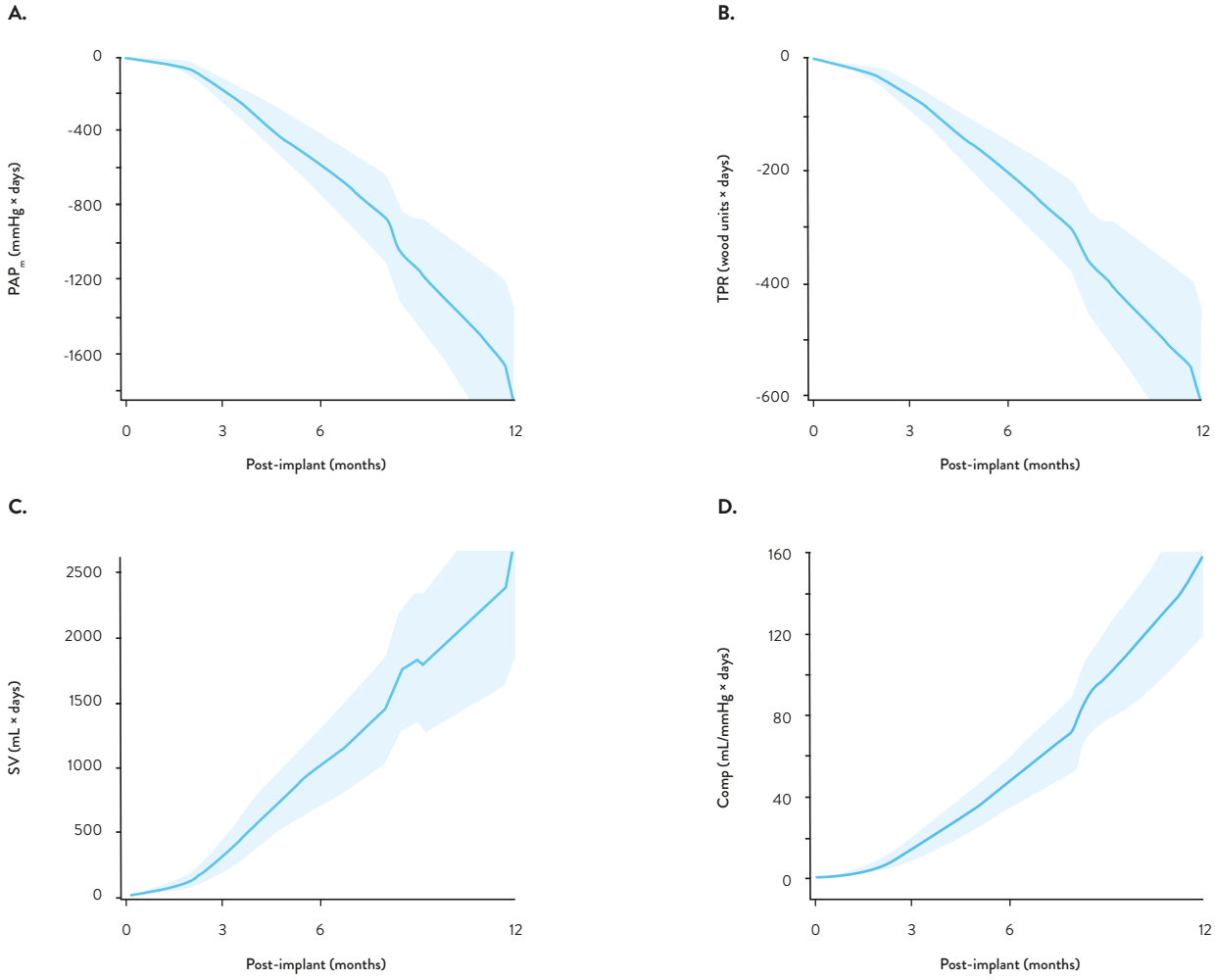


In the AUC analyses shown below, SV, TPR and compliance all exhibited significant changes at 12 months relative to baseline ($p < 0.05$). In patients that were highly managed (nine or more medication changes) within the first 4 months (most with serial changes in parenteral prostacyclins, based on knowledge of hemodynamics), early hemodynamic changes were well-visualized and captured using the CardioMEMS™ HF System. Therefore, home monitoring and capturing significant changes in hemodynamic responses to changes in drug therapy over time are feasible.

Changes in NYHA Class from baseline ($p < 0.001$), natriuretic peptides ($p < 0.01$) and Minnesota Living with Heart Failure Questionnaire quality of life score ($p < 0.001$) for the implanted cohort with at least one-month follow-up post-implant ($n = 24$) were all encouraging. These improvements mirrored the hemodynamic changes illustrated in the figures above. In addition, 6MWD correlated with CardioMEMS HF System-determined hemodynamics.

These changes were analyzed to demonstrate potential alternative efficacy endpoints that could be used in future trials of the device in PAH and to visualize the parallel between patterned hemodynamic changes obtained through monitoring with the CardioMEMS HF System and other outcomes assessed in clinic.

Figure 22. Cumulative hemodynamic response illustrated by AUC analyses across 365 days for patients at Allegheny General Hospital
PAP_m, TPR, SV and compliance are shown as mean (solid line) ▌SE of the cumulative change over time. All $p < 0.05$ at 12 months, relative to baseline.



KEY RESULTS:

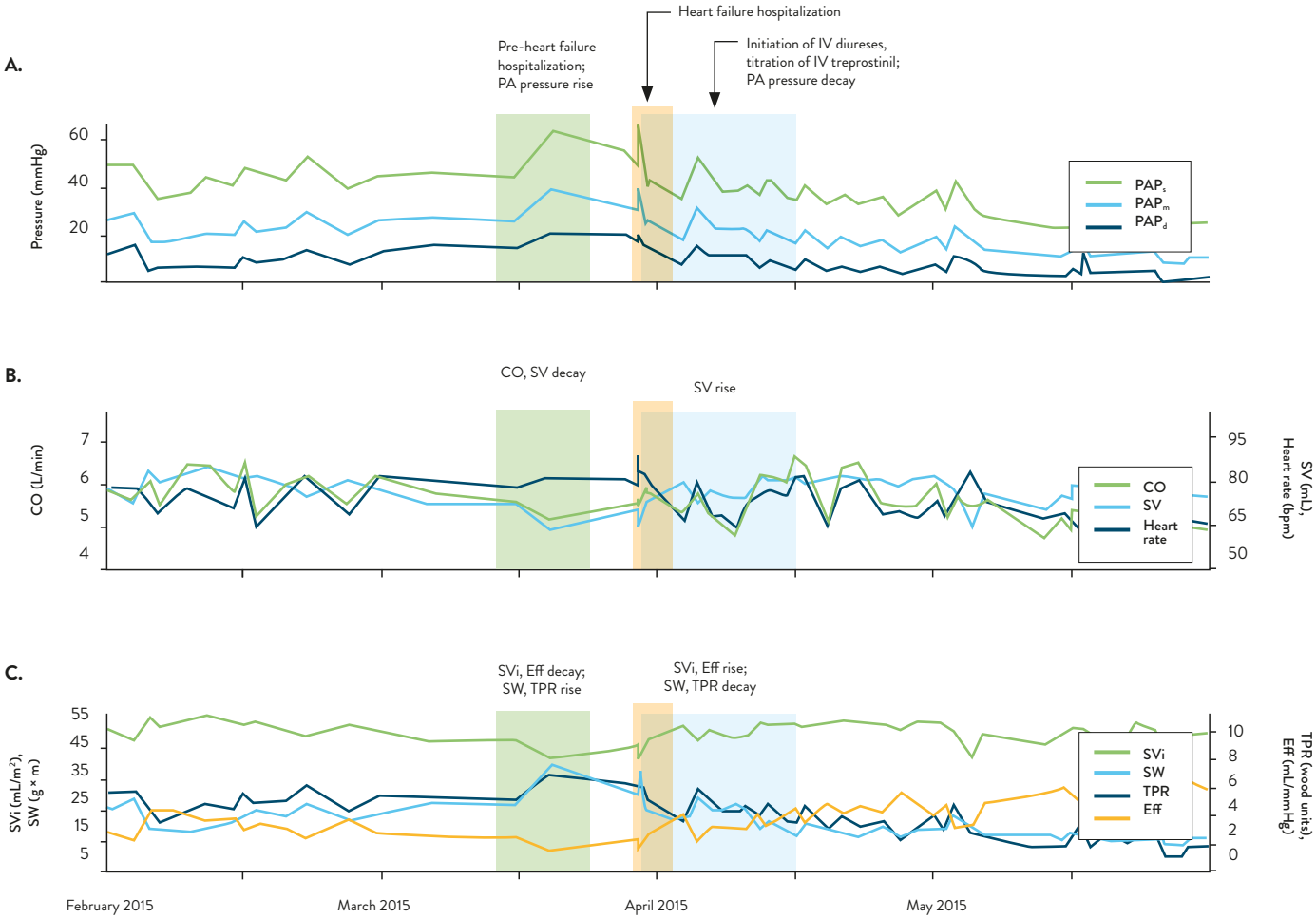
- PAH is a progressive chronic disease that ultimately progresses to right heart failure and death.
- This feasibility study of 26 patients with PAH indicates that the CardioMEMS™ HF System can be used to monitor and effect favorable changes in hemodynamics, and may help guide medical therapy in these patients, resulting in improved outcomes.
- Improvements in patients' hemodynamics correlated with improvements in NYHA functional class, natriuretic peptide levels, quality of life and 6MWD.
- Use of the CardioMEMS HF System in this pilot study was associated with short- and long-term safety.

CONCLUSION:

The CardioMEMS HF System provided useful information to monitor PAH therapy, and demonstrated short- and long-term safety. Larger clinical trials are needed before its widespread use to guide therapy in patients with severe PAH with right-sided heart failure.

The case example below shows early clinical worsening for a patient weeks prior to a heart failure hospitalization and subsequent hemodynamic recovery.

Figure 23. Example of acute right ventricular failure because of medication noncompliance. Patient medication noncompliance (blue shading) resulted in rise in deteriorating hemodynamics and heart failure hospitalization (orange shading). IV diuresis and reinstitution of medications (red shading) resulted in an improvement in all parameters.

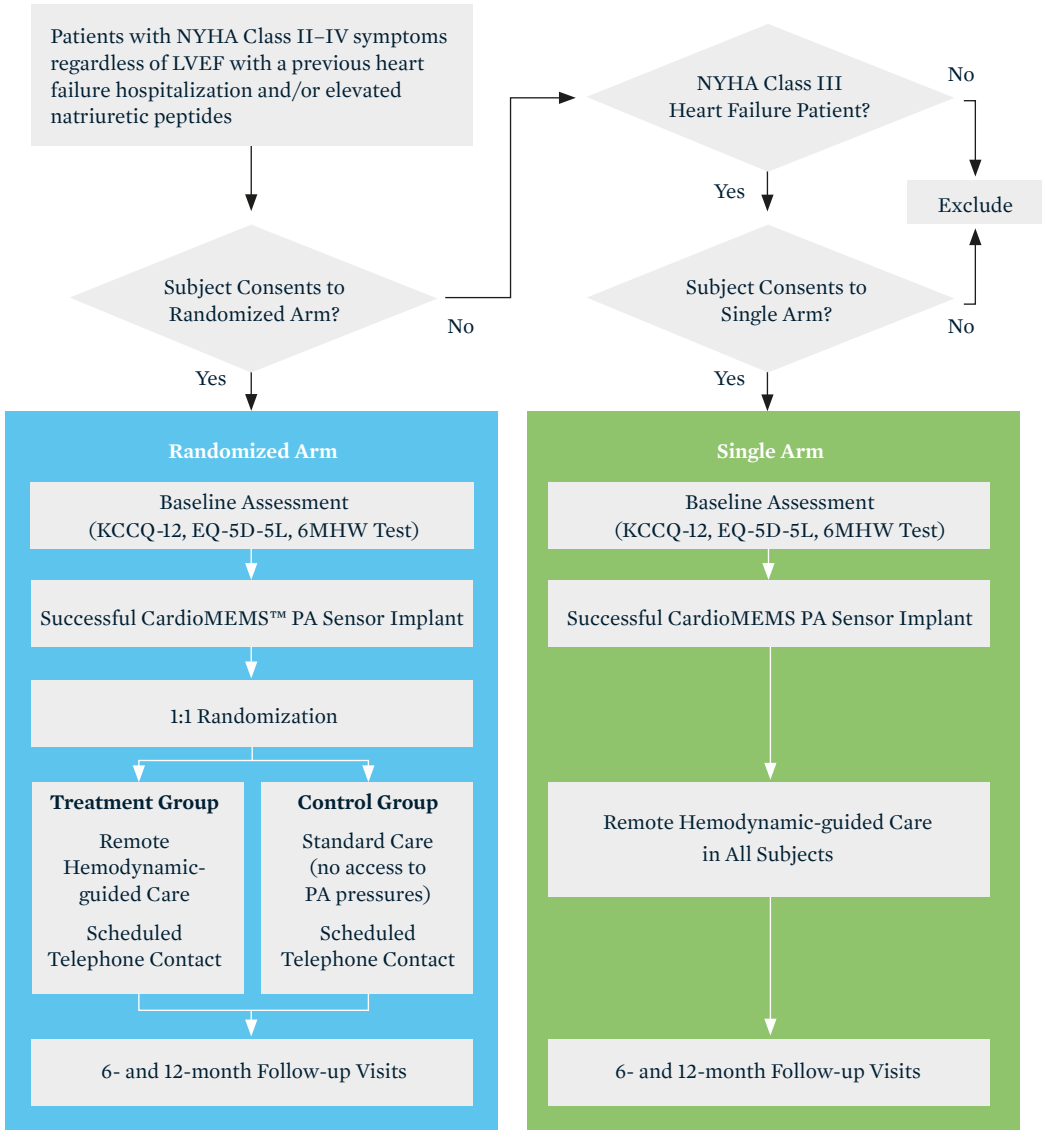


HEMODYNAMIC-GUIDED MANAGEMENT OF HEART FAILURE (GUIDE-HF)

Lindenfeld, et al. *Am Heart J.* 2019.[34]

- Largest trial ever (N = 3600) to study hemodynamic-guided heart failure management.
- Includes patients currently indicated for the CardioMEMS™ HF System, as well as heart failure patients with NYHA Class II and IV, and heart failure patients with elevated natriuretic peptides without recent heart failure hospitalization.
- Randomized arm (N = 1000) to evaluate the effects of the CardioMEMS HF System on heart failure hospitalization and death, as well as quality of life and functional capacity in NYHA Class II–IV patients with a heart failure hospitalization in the past 12 months or elevated natriuretic peptide levels in the previous 30 days, regardless of left ventricular ejection fraction.
- Single arm (N = 2600) to determine whether PA pressure-guided care is as effective in NYHA Class III patients enrolled based on elevated natriuretic peptide levels as it is in those with a prior heart failure hospitalization.
- Secondary endpoints: Cumulative heart failure event rates 12 months post-implant versus heart failure event rates 12 months pre-implant.
- Positive results will help lead to entry into ACC and AHA heart failure guidelines and obtain CMS National Coverage Determination.

Figure 24.



GUIDE-HF Trial Schematic

THE CARDIOMEMS EUROPEAN MONITORING STUDY FOR HEART FAILURE (MEMS-HF)

Angermann, et al. *European Journal of Heart Failure*. 2020.[35]

STUDY OBJECTIVE:

A prospective, single-arm, multicenter, open-label study (N = 234) to evaluate the safety and efficacy of the CardioMEMS™ HF System in routine clinical practice outside the United States, with special focus on subgroups defined by gender, race and EF. Sites included Germany, the Netherlands and Ireland.

KEY RESULTS:

- **98.3% freedom from DSRC** (4/236) and **99.6% freedom from pressure sensor failure** (1/234).
- **62% heart failure hospitalization reduction** at one-year post-implant compared to one-year pre-implant.
- Consistent results supporting the only proven management tool for HFpEF patients, demonstrating a **63% heart failure hospitalization reduction at one year in HFpEF patients** (EF ≥ 40%).
- Excellent adherence to data transmission, with 78% mean daily transmission and 90% mean weekly transmission.
- Significant improvements across all patient-reported quality of life outcomes (including PHQ-9 for depression).
- Significant reduction in NT-proBNP levels at 6 and 12 months (n = 82).
- 36% of cohort saw improved NYHA classification at 12 months.

Figure 25. Overall annualized heart failure hospitalization rate

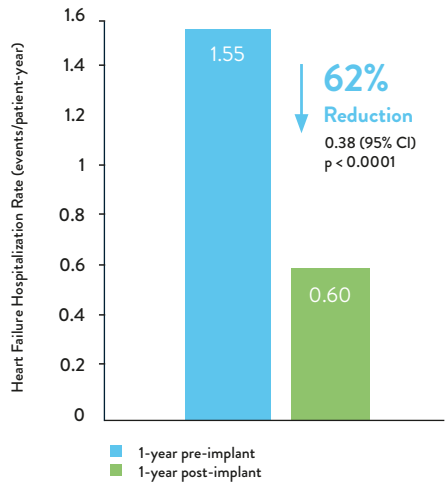
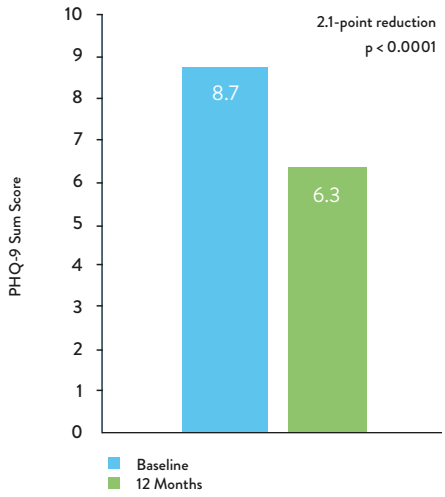


Figure 26. PHQ-9 change from baseline to 12 months



MANAGEMENT OF THE PATIENT WITH HEART FAILURE AND AN IMPLANTABLE PULMONARY ARTERY HEMODYNAMIC SENSOR (HF2 PAPER)

Abraham, et al. *Current Cardiovascular Risk Reports*. 2020.[36]

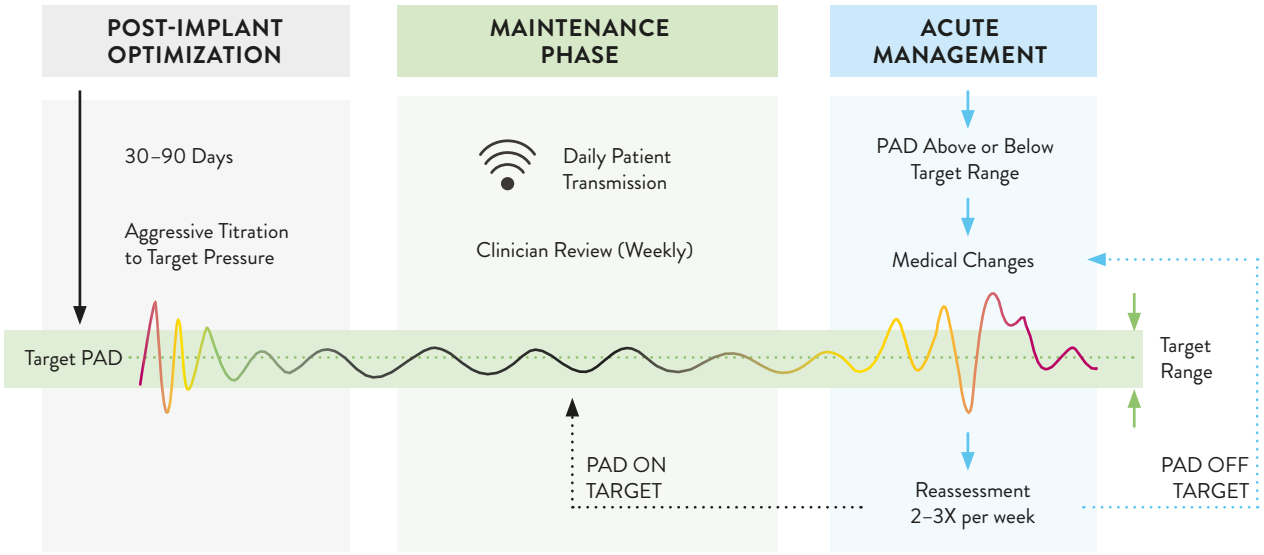
STUDY OBJECTIVE:

A summary of pulmonary vascular physiology and a single center's experience utilizing a phased approach in the management of patients with the CardioMEMS HF System. The publication also addresses key differences in the treatment algorithms of HFrEF and HFpEF patients and details for a successful program structure (staff, communication, etc.)

KEY RESULTS:

- A goal of management with the CardioMEMS HF System must be to treat indications of increased afterload to preserve the right heart and avoid the associated, markedly worse clinical outcomes.
- Initial hemodynamics and calibration:
  - Accurate PAD pressure and PCWP must be achieved at implant. This can help identify precapillary involvement associated with worse outcomes.
  - Establish a target PAD pressure and proactively treat out- of-range values.
- Goals for three phases of management:
  - Post-implant (0–7 days): Review data and set threshold (10 mmHg range).
  - Optimization (up to 90 days): Establish and achieve optimal goal with clinical stability.
  - Maintenance (> 90 days): Narrow threshold (5 mmHg), and maintain and treat by exception/notification from the Merlin.net™ Patient Care Network.

Figure 27.



ONE-YEAR OUTCOMES FROM THE CARDIOMEMS POST-APPROVAL STUDY (U.S. PAS)

Shavelle, et al. *Circulation: Heart Failure.* 2020.[37]

STUDY OBJECTIVE:

- Large (N = 1200) prospective, multicenter, single-arm, open-label study to evaluate the safety and efficacy of the CardioMEMS™ HF System in routine clinical practice in the United States, with special focus on subgroups defined by gender, race and EF.

KEY RESULTS:

- **99.6% freedom from DSRC** (5/1200) and **99.9% freedom from sensor failure** (1/1200) at one year (final safety endpoint at two years).
- **57% heart failure hospitalization** reduction one-year post-implant compared to one-year pre-implant.
- **27% all-cause hospitalization** reduction one-year post-implant compared to one-year pre-implant.
- Consistent results to support the only proven management tool in HFpEF patients, with 60% heart failure hospitalization reduction at one year for patients with an EF > 50%.
- Excellent adherence to data transmission, with 76% mean daily transmission and 93% mean weekly transmission.

Figure 28. Heart failure hospitalizations (1-year pre-implant vs. 1-year post-implant)

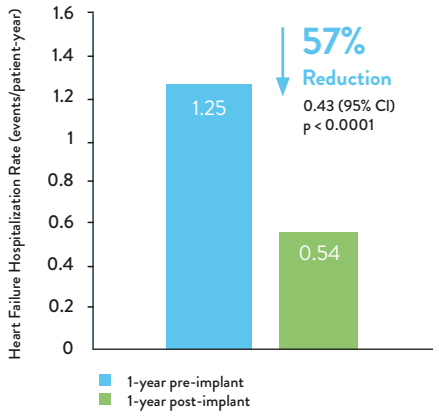
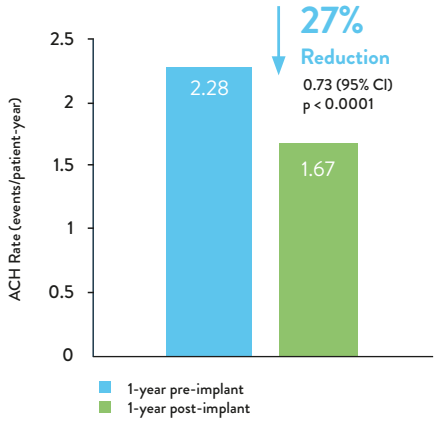


Figure 29. All-cause hospitalizations (1-year pre-implant vs. 1-year post-implant)



HEALTHCARE ECONOMICS

HEALTH ECONOMIC IMPACT OF A PULMONARY ARTERY PRESSURE SENSOR FOR HEART FAILURE TELEMONITORING: A DYNAMIC SIMULATION

Kolominsky-Rabas PL, et al. *Telemedicine and e-Health*. 2016.[38]

SUMMARY:

This simulation estimated the reductions of heart failure hospitalizations with PA guided care, the improvement on quality of life and the economic savings as a result of implementation in the German healthcare system. This simulation also showed the rise of heart failure prevalence numbers in the context of an aging population, and given the considerable burden of heart failure, the potential of a PA pressure monitoring system to improve the management of heart failure patients and enable cost savings at the same time is substantial.

PULMONARY ARTERY PRESSURE-GUIDED HEART FAILURE MANAGEMENT: US COST-EFFECTIVENESS ANALYSES USING THE RESULTS OF THE CHAMPION CLINICAL TRIAL

Martinson M, et al. *European J Heart Failure*. 2017.[39]

KEY RESULTS:

The primary effectiveness endpoint was the ICER comparing the costs and QALYs of heart failure hospitalization outcomes in the CHAMPION treatment and control groups. The model was used to extrapolate this endpoint to five years.

Over the five-year projections, patients in the treatment group had average QALYs of 2.56 with a total cost of $140,966; patients in the control group had QALYs of 2.16 with a total cost of $133,681. The ICER was $18,515 per QALY **(Table 3)**.

CONCLUSION:

This study, based on the results of the CHAMPION clinical trial, used standard economic modelling to show that PA pressure-guided management of heart failure using the CardioMEMS™ HF System is cost-effective from the perspective of U.S. payers. The ICERs, when considered for heart failure management or comprehensive management, were well below the conventional U.S. acceptability threshold of $50,000.

Table 3. Cost-effectiveness analysis base case and survival over a five-year time horizon

	Primary CEA Endpoint: Heart Failure Hospitalization Outcomes		All-cause Hospitalization Outcomes		Comprehensive Patient Management Outcomes	
	Treatment Group	Control Group	Treatment Group	Control Group	Treatment Group	Control Group
Cumulative average cost	U.S. $56,974	U.S. $52,149	U.S. $140,966	U.S. $133,681	U.S. $212,004	U.S. $200,360
Cumulative QALYs	2.56	2.16	2.56	2.16	2.56	2.16
Cumulative average years of survival	3.70	3.47	3.70	3.47	3.70	3.47
ICER (U.S. $/QALY)	U.S. $12,262		U.S. $18,515		U.S. $29,592	
Cost reduction for each patient under treatment post implant (U.S. $/year)[a]	U.S. $4,443		U.S. $5,261		U.S. $5,296	

a. Costs saving per life year for the treatment group.

COST-EFFECTIVENESS OF REMOTE CARDIAC MONITORING WITH THE CARDIOMEMS HEART FAILURE SYSTEM

Schmier, et al. *Clinical Cardiology*. 2017.[40]

KEY RESULTS:

Mortality trends are lower for the CardioMEMS™ HF System vs. SOC:

- Based on the model's base case, half (50.4%) of the original CardioMEMS HF System patients were dead at 60 months vs. 50% mortality at 40 months for patients on SOC.
- At the end of the 60 months, 49.6% of CardioMEMS HF System patients remained alive vs. 23.8% of SOC patients.

Cost/QALY was in the high-value space:

- Device cost/QALY was well below $50,000, remaining in the high-value space (based on ACC and AHA guidelines).

CONCLUSION:

- The CardioMEMS HF System was found to be cost-effective, with an ICER of $44,832 per QALY.
- This places the CardioMEMS HF System in the high-value category compared to LVADs ($128K–$209K/QALY) and CRT-D ($62K/QALY).
- "For heart failure patients meeting current indications, the CardioMEMS HF System may represent an important clinical advance, while at the same time being a cost-effective treatment for heart failure."

Table 4. Model results: base case

	CardioMEMS	SOC
Five-year costs and outcomes		
Total costs	$188,880	$162, 772
Implant: device, procedure, complications	$19,111	$0
Inpatient costs	$108,124	$113,199
Outpatient costs (including monitoring)	$61,645	$49,573
Total accumulated QALYs	2.509	1.926
ICER (cost per QALY gained)	$44,832	

Table 5. Base case input parameters: costs

Parameter	Cost (USD)[a]	Source(s)
CardioMEMS™ device (per device)	$17,750	Average sales price
Implantation procedure	$1,280	Medicare: $1,138; CPT‡ 93451, 93568, 33210, 2016 MFS; Commercial: $1,707 (MFS × 1.5)
Complications, each	$5,770	Martinson et al[39] inflated to 2016
Hospitalizations		Takes into account % Medicare vs. commercial
Heart failure hospitalization	$21,007	Martinson et al[39] inflated to 2016
Non-heart failure hospitalization	$24,367	Martinson et al[39] inflated to 2016
Monthly monitoring	$47	Martinson et al[39] inflated to 2016
Outpatient costs, routine care (per year)	$19,576	Martinson et al[39] inflated to 2016

a. Costs are presented in 2016 dollars and were inflated or discounted as described in the methods. All costs are weighted based on the assumption that 75% of patients are covered by Medicare and 25% have commercial coverage.

THE COST-EFFECTIVENESS OF REAL-TIME PULMONARY ARTERY PRESSURE MONITORING IN HEART FAILURE PATIENTS: A EUROPEAN PERSPECTIVE

Cowie MR, et al. *European Journal of Heart Failure*. 2017.[41]

METHODS:

A Markov model was developed to estimate the cost-effectiveness of PAP-guided treatment of heart failure using the CardioMEMS HF System compared with usual care. Cost-effectiveness was measured as the incremental cost per QALY gained.

STUDY OBJECTIVE:

Heart failure treatment guided by physicians using the CardioMEMS HF System has been shown to reduce heart failure hospitalizations, but uncertainty remains regarding the value of the CardioMEMS HF System in European health systems where healthcare costs are significantly lower than in the United States.

KEY RESULTS:

- In the base case analysis over a time horizon of 10 years, PAP-guided heart failure therapy increased cost compared with usual care by £10,916 (€14,030) (i.e., from £6,189 in usual care to £17,104 in PAP-guided heart failure therapy).
- QALYs per patient for usual care and PAP-guided patients were 2.57 and 3.14, respectively, an increase of 0.57 QALY with PAP-guided treatment.
- The resultant ICER is £19,274 (€24,772) per QALY gained.
- The base case analysis did not include staff time due to a lack of data.
- Running the model with estimated staff time included resulted in an increased ICER of between £22,342 and £25,464 per QALY gained (€28,709–€32,721).

CONCLUSION:

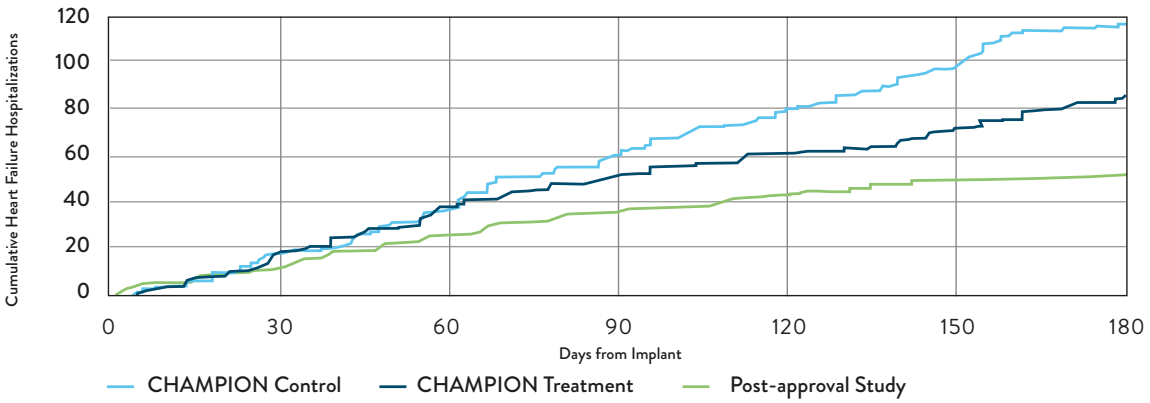
The analysis indicates that the CardioMEMS HF System could provide a cost-effective means for heart failure physicians to manage and treat patients outside of face-to-face clinic appointments, shifting care from the hospital/clinic to the home, reducing resource-intensive hospitalizations and improving the quality of life of patients suffering from heart failure.

POST-APPROVAL STUDY

REDUCTION OF HF HOSPITALIZATION IN THE CARDIOMEMS™ HF SYSTEM POST-APPROVAL STUDY

Raval, et al. Presented at: HFSA 2017.[42]

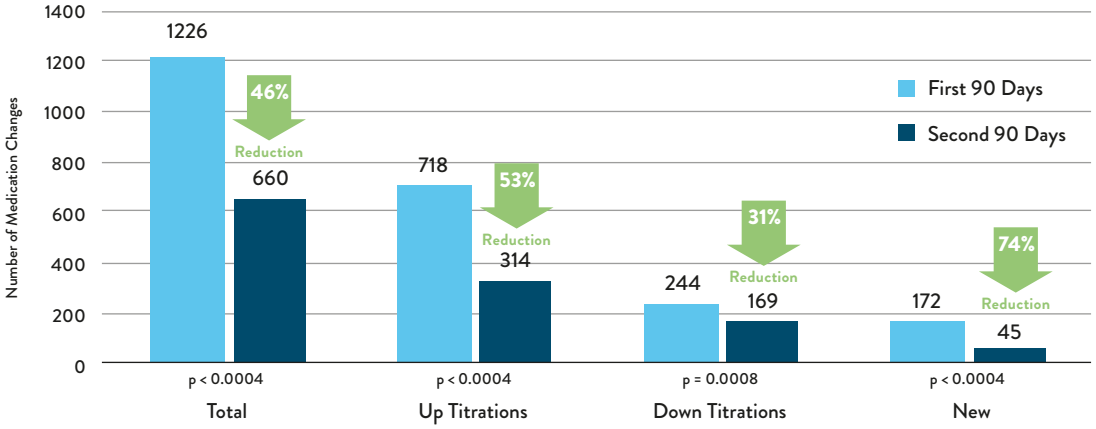
Figure 30.



In the post-approval study, there were 56 heart failure hospitalizations (0.20 events/pt-6m) in 43 pts.

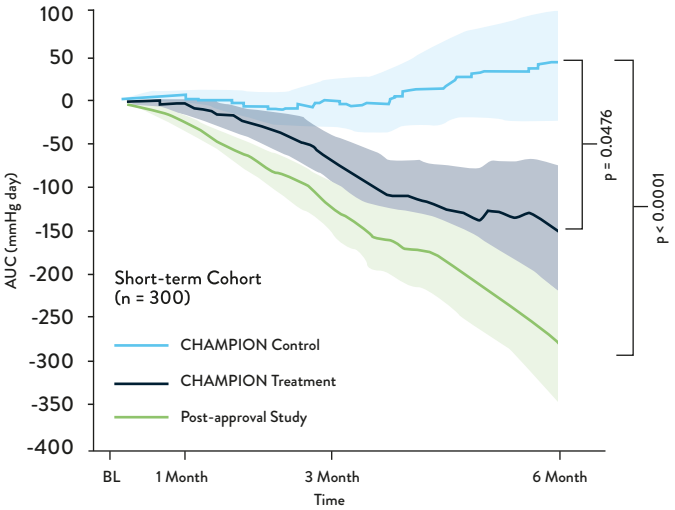
MEDICATION CHANGES SIGNIFICANTLY REDUCED IN FIRST 90 DAYS VS. SECOND 90 DAYS IN THE PAS

Figure 31. Medication changes — first 90 days vs. second 90 days



65% of the overall heart failure medication changes were made in the first 90 days, with trends of stabilization and significantly fewer medication changes during the second 90 days.

Figure 32. The CardioMEMS™ HF System PAS short-term results: REDUCED heart failure hospitalization and MEAN PA pressure



AUC (mmHg day)			
	1 Month	3 Months	6 Months
CHAMPION control (275 pts)	3.1 ± 6.7 (270 pts)	-5.5 ± 24.7 (251 pts)	42.2 ± 65.0 (228 pts)
CHAMPION treatment (270 pts)	-7.0 ± 7.7 (266 pts)	-59.3 ± 27.6 (257 pts)	-150.1 ± 71.0 (236 pts)
PAS (300 pts)	-27.7 ± 7.0 (291 pts)	-112.6 ± 26.0 (275 pts)	-281.0 ± 63.5 (262 pts)

Significantly greater reductions in mean PA pressure for the PAS cohort relative to the CHAMPION control group after six months, and **qualitatively greater reductions** compared to the CHAMPION treatment group.

CLINICAL RESEARCH PAPERS BY TOPIC

IMPROVED QUALITY OF LIFE AND FUNCTIONAL CAPACITY

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DECREASED HEART FAILURE HOSPITAL ADMISSIONS AND READMISSIONS

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DECREASED PA PRESSURES

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THE CARDIOMEMS™ HF SYSTEM IS PROACTIVE AND ACTIONABLE; GDMT IS REACTIVE AND INEXACT

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ACRONYM DEFINITIONS

6MHW	six-minute hall walk
6MWD	six-minute walk distance
ACC	American College of Cardiology
ACEI	angiotensin-converting enzyme inhibitor
AF	atrial fibrillation
ARB	angiotensin receptor blocker
AUC	area under curve
BB	beta blocker
BL	baseline
bpm	beats per minute
CEA	cost-effectiveness analyses
CI	confidence interval
CKD	chronic kidney disease
CMS	Centers for Medicare & Medicaid Services
CO	cardiac output
comp	compliance
COPD	chronic obstructive pulmonary disease
CPT‡	Current Procedural Terminology
CRT	cardiac resynchronization therapy
CRT-D	cardiac resynchronization therapy defibrillator
DSRC	device-/system-related complication
EF	ejection fraction
Eff	right ventricular efficiency
EPPY	events per patient-year
GDMT	guideline-directed medical therapy
GDP	gross domestic product
GUIDE-HF	Hemodynamic-GUIDEd Management of Heart Failure
HF	heart failure
HFpEF	heart failure with preserved ejection fraction
HFrEF	heart failure with reduced ejection fraction
HR	hazard ratio
ICD	implantable cardioverter defibrillator
ICER	incremental cost-effectiveness ratio
IDE	investigational device exemption
IV	intravenous
KCCQ	Kansas City Cardiomyopathy Questionnaire
LVAD	left ventricular assist device
LVEF	left ventricular ejection fraction
MFS	Medicare Fee Schedule
MI	myocardial infarction
mmHg	millimeter of mercury
NT-pro BNP	N-terminal pro b-type natriuretic peptideBNP
NYHA	New York Heart Association
PA	pulmonary artery
PAD	pulmonary artery diastolic
PAH	pulmonary arterial hypertension
PAP	pulmonary artery pressure
PAP_d	diastolic pulmonary artery pressure
PAP_m	mean pulmonary artery pressure
PAP_s	systolic pulmonary artery pressure
PAS	post-approval study
PCWP	pulmonary capillary wedge pressure
PH	pulmonary hypertension
PHQ-2	Patient Health Questionnaire-2
pts	points
QALY	quality-adjusted life year
RA	randomized access
rEF	reduced ejection fraction
REH	respiratory event hospitalization
RHC	right heart catheterization
RRR	relative risk reduction
SE	shaded envelope
SOC	standard of care
SV	right ventricular stroke volume
SVi	stroke volume index
SW	right ventricular stroke work
SWi	stroke work index
TPG	transpulmonary gradient
TPR	total pulmonary resistance
VAD	ventricular assist device
WHO	World Health Organization

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CardioMEMS™ HF System

Clinical Compendium

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BRIEF SUMMARY: Prior to using these devices, please review the Instructions for Use for a complete listing of indications, contraindications, warnings, precautions, potential adverse events and directions for use.

INDICATIONS AND USAGE: The CardioMEMS™ HF System is indicated for wirelessly measuring and monitoring pulmonary artery (PA) pressure and heart rate in New York Heart Association (NYHA) Class III heart failure patients who have been hospitalized for heart failure in the previous year. The hemodynamic data are used by physicians for heart failure management and with the goal of reducing heart failure hospitalizations.

CONTRAINDICATIONS: The CardioMEMS™ HF System is contraindicated for patients with an inability to take dual antiplatelet or anticoagulants for one month post implant.

POTENTIAL ADVERSE EVENTS: Potential adverse events associated with the implantation procedure include, but are not limited to, the following: Infection, Arrhythmias, Bleeding, Hematoma, Thrombus, Myocardial infarction, Transient ischemic attack, Stroke, Death, and Device embolization.

Limitations: Patients must use their own Apple‡ or Android‡ mobile device to receive and transmit information to the myCardioMEMS™ mobile app. To do so the device must be powered on, app must be installed and data coverage (cellular or Wi-Fi‡) available. The myCardioMEMS™ app can provide notification of medication adjustments and reminders, requests for lab work and acknowledgement that the PA pressure readings have been received. However there are many internal and external factors that can hinder, delay, or prevent acquisition and delivery of the notifications and patient information as intended by the clinician. These factors include: patient environment, data services, mobile device operating system and settings, clinic environment, schedule/configuration changes, or data processing.

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