



# 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

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**BACKGROUND:** Ambulatory hemodynamic monitoring with an implantable pulmonary artery (PA) sensor is approved for patients with New York Heart Association Class III heart failure (HF) and a prior HF hospitalization (HFH) within 12 months. The objective of this study was to assess the efficacy and safety of PA pressure-guided therapy in routine clinical practice with special focus on subgroups defined by sex, race, and ejection fraction.

**METHODS:** This multi-center, prospective, open-label, observational, single-arm trial of 1200 patients across 104 centers within the United States with New York Heart Association class III HF and a prior HFH within 12 months evaluated patients undergoing PA pressure sensor implantation between September 1, 2014, and October 11, 2017. The primary efficacy outcome was the difference between rates of adjudicated HFH 1 year after compared with the 1 year before sensor implantation. Safety end points were freedom from device- or system-related complications at 2 years and freedom from pressure sensor failure at 2 years.

**RESULTS:** Mean age for the population was 69 years, 37.7% were women, 17.2% were non-White, and 46.8% had preserved ejection fraction. During the year after sensor implantation, the mean rate of daily pressure transmission was  $76 \pm 24\%$  and PA pressures declined significantly. The rate of HFH was significantly lower at 1 year compared with the year before implantation (0.54 versus 1.25 events/patient-years, hazard ratio 0.43 [95% CI, 0.39–0.47],  $P < 0.0001$ ). The rate of all-cause hospitalization was also lower following sensor implantation (1.67 versus 2.28 events/patient-years, hazard ratio 0.73 [95% CI, 0.68–0.78],  $P < 0.0001$ ). Results were consistent across subgroups defined by ejection fraction, sex, race, cause of cardiomyopathy, presence/absence of implantable cardiac defibrillator or cardiac resynchronization therapy and ejection fraction. Freedom from device- or system-related complications was 99.6%, and freedom from pressure sensor failure was 99.9% at 1 year.

**CONCLUSIONS:** In routine clinical practice as in clinical trials, PA pressure-guided therapy for HF was associated with lower PA pressures, lower rates of HFH and all-cause hospitalization, and low rates of adverse events across a broad range of patients with symptomatic HF and prior HFH.

**REGISTRATION:** URL: <https://www.clinicaltrials.gov>. Unique identifier: NCT02279888.

**Key Words:** heart failure ■ hemodynamics ■ population ■ pressure ■ pulmonary artery

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### WHAT IS NEW?

- The Post-Approval Study of 1200 patients in multiple practice settings demonstrated a 57% reduction in risk of heart failure hospitalization (HFH) and a 27% reduction in all-cause hospitalizations during the year after implantation of the CardioMEMS pulmonary artery pressure sensor.
- HFH reduction was at least 50% in patients with ejection fraction >0.50 and across subgroups for race, sex, and HF cause.
- Pulmonary artery pressures declined during the year with the most significant decline for those with the highest baseline pulmonary artery pressures.
- Median pressure transmission rate was 85% daily and 100% weekly; freedom from device complications or sensor failure was over 99%.

### WHAT ARE THE CLINICAL IMPLICATIONS?

- The strategy of pulmonary artery pressure-guided HF management for patients with class III HF and prior HFH consistently reduced HFH and all-cause hospitalization when translated into clinical practice settings.
- This 1200-patient study provides generalizability that patient compliance with transmission is high and benefit to reduce HFH by 50% can be achieved, regardless of ejection fraction, sex, or race.

**H**ear failure (HF) is the primary hospital admitting diagnosis for 1 million patients and a secondary diagnosis for 2 million patients annually within the United States.<sup>1,2</sup> Despite increasingly effective medical therapy, the burden of HF remains high, predominantly driven by symptoms of worsening congestion during a progressive rise in cardiac filling pressures. Traditional disease management for reducing HFH has focused on surveillance of weight, vital signs, and clinical symptoms to detect decompensation in time to avert hospitalization. However, enhanced surveillance of these signs using telemonitoring strategies in randomized trials has consistently shown no incremental benefit over routine clinic-based care.<sup>3–5</sup> Since hemodynamic changes occur weeks in advance of the signs and symptoms that prompt HFH, implantable hemodynamic monitoring may be a superior approach to the detection of impending congestion.<sup>6</sup> Therapy guided by remote monitoring of pulmonary artery (PA) pressures in the randomized CHAMPION trial (CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in New York Heart Association Class III Heart Failure Patients) resulted in a 37% reduction in HFH rates and a 26% relative risk reduction in all-cause hospitalization (ACH).<sup>7,8</sup> In 2014, the Federal Drug Agency approved the CardioMEMS PA pressure sensor for clinical use in patients with chronic HF, New York Heart Association class III symptoms, and prior HFH

### Nonstandard Abbreviations and Acronyms

<b>ACE</b>	angiotensin-converting enzyme
<b>ACH</b>	all-cause hospitalization
<b>ARB</b>	angiotensin receptor blocker
<b>ARNI</b>	angiotensin receptor–neprilysin inhibitor
<b>AUC</b>	area under the curve
<b>CHAMP-HF</b>	Change the Management of Patients With Heart Failure
<b>CHAMPION</b>	CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in New York Heart Association Class III Heart Failure Patients
<b>COAPT</b>	Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation
<b>COMPASS-HF</b>	Chronicle Offers Management to Patients With Advanced Signs and Symptoms of Heart Failure
<b>EF</b>	ejection fraction
<b>HF</b>	heart failure
<b>HFH</b>	heart failure hospitalization
<b>HFpEF</b>	HF with preserved ejection fraction
<b>HFrEF</b>	HF with reduced ejection fraction
<b>HR</b>	hazard ratio
<b>PA</b>	pulmonary artery

within 12 months. Approval of the device for clinical use was contingent upon conduct of the CardioMEMS Post-Approval Study in 1200 patients to confirm the effectiveness and safety of PA pressure-guided therapy in clinical practice and in clinical subgroups underrepresented in the CHAMPION trial, including women, Blacks, patients with preserved ejection fraction (EF) and those with cardiac resynchronization therapy and defibrillator devices. In this article, we report the principal 1-year efficacy and safety results of the CardioMEMS Post-Approval Study.

## METHODS

### Trial Design

The CardioMEMS Post-Approval Study was a multi-center, prospective, open-label, single-arm trial evaluating the use of PA pressure-guided therapy in routine clinical practice.

### Informed Consent and Study Protocol

The trial was reviewed and approved by an institutional review board at each participating center. The trial was conducted according to the Guidelines for Good Clinical Practice in Clinical Trials<sup>9</sup> and the principles of Declaration of Helsinki.<sup>10</sup> Local investigators performed the screening and informed

consent process. All participants provided written informed consent. Patients were initially evaluated for study eligibility at a screening visit and then returned for a baseline visit where a standard right heart catheterization procedure was performed with assessment of hemodynamics and PA sensor implantation. Patients returned for study visits at 1, 6, and 12 months. Additional details about the study protocol are provided in the [Data Supplement](#). An independent clinical events committee adjudicated all hospitalizations and safety end points including associated adverse events. Hospitalizations were classified as HFH or ACH according to the definitions provided in the [Data Supplement](#).

## Participants and Eligibility Criteria

Patients with chronic HF, New York Heart Association class III symptoms and a prior HFH within 12 months, regardless of EF, were eligible for participation. Patients with HF with reduced ejection fraction (HFrEF) were required to be receiving a beta blocker for 3 months and an ACE (angiotensin-converting enzyme) inhibitor or ARB (angiotensin receptor blocker) for 1 month unless the investigator deemed the patient to be intolerant to  $\beta$ -blockers, ACE inhibitors, or ARB. Patients with body mass index  $>35$  kg/m<sup>2</sup> were required to have a chest circumference  $<65$  inches measured at the axillary level. The target PA branch for pressure sensor implantation was required to have a diameter  $\geq 7$  mm. Key exclusion criteria included active infection, history of recurrent ( $>1$ ) pulmonary embolism or deep vein thrombosis, inability to tolerate right heart catheterization, major cardiovascular event (eg, myocardial infarction, open heart surgery, stroke, etc) within the previous 2 months, cardiac resynchronization therapy implanted within the previous 3 months, glomerular filtration rate  $<25$  mL/min per 1.73 m<sup>2</sup> (obtained within 2 weeks of pressure sensor implant), nonresponsiveness to diuretic therapy or need for chronic dialysis, congenital heart disease or mechanical right heart valve, anticipated need to undergo heart transplantation or surgical ventricular assist device within the next 6 months, known coagulation disorders and hypersensitivity or allergy to aspirin, and clopidogrel.

## Setting

The participants were enrolled at 104 hospitals in the United States, 35% of which were academic medical centers. Enrollment started on September 1, 2014, and the last participant was enrolled on October 11, 2017.

## Study Population

Consent was obtained from and implants were attempted in 1214 patients (Figure 1). Unsuccessful pressure sensor implantation occurred in 14 patients, who were followed for 30 days for safety events. The 6-month visit was completed in 1013 patients and the 12-month visit was completed in 875 patients. The final patient completed 1-year follow-up in October 2018.

## Treatment

At the baseline study visit, right heart catheterization, assessment of hemodynamics, and pressure sensor implantation were performed. Patients were instructed to transmit PA pressures

daily. Physicians were instructed to use PA pressure goals to guide therapy even in the absence of change in weight or symptoms. Therapy could be further adjusted based on symptoms, weight change, or examination in clinic. Physicians were instructed to adjust medical therapy to maintain PA pressures within the euvoletic range. The euvoletic range was generally set at the following PA pressure ranges: PA systolic 15 to 35 mmHg, PA diastolic 8 to 20 mmHg, and PA mean 10 to 25 mmHg. The difference between PA diastolic and pulmonary capillary wedge pressure at the time of right heart catheterization was a factor considered in setting the target range of PA pressures. Elevation of PA pressures above the euvoletic range was considered a volume overloaded state (hypervolemic), for which physicians were advised to increase diuretics and add nitrates or other vasodilators ([Data Supplement](#)). A decrease in PA pressures below the euvoletic range was considered a volume-depletion event (hypovolemic) and physicians were advised to decrease diuretics ([Data Supplement](#)).

## Outcomes

The methods for assessment of the primary and secondary outcomes are described in the [Data Supplement](#).

### Primary Outcome

The primary effectiveness end point was the annualized HFH rate at year 1, compared with the HFH rate in the year before enrollment. Prespecified subgroups included sex, race/ethnicity, cause of cardiomyopathy, presence or absence of implantable cardiac defibrillator/cardiac resynchronization therapy defibrillator device, and EF ranges (EF  $<40\%$ ,  $40\% \leq \text{EF} \leq 50\%$ , and EF  $>50\%$ ). The primary safety end points were (1) freedom from device- or system-related complications at 2 years and (2) freedom from pressure sensor failure at 2 years. As 2-year follow-up is not yet concluded, we report here the primary effectiveness data and the corresponding primary safety end points at 1 year. A device- or system-related complication was defined as an adverse event that was related or was possibly related to the system and resulted in at least one of the following: treatment with invasive means other than intramuscular medication or right heart catheterization, death or explant of device. Pressure sensor failure was defined if no readings could be obtained from the device after troubleshooting the system to rule out problems with the external electronics.

### Secondary Outcomes

Additional end points included ACHs, mortality rate at 1 year, patient compliance with pressure transmission, and PA pressure change over time. PA pressure change over time was evaluated using the area under the curve (AUC) methodology to estimate the total increase (or decrease) in mean PA pressure (mmHg day) during the 1-year period relative to the first week of ambulatory pressures.<sup>7,11</sup> This method quantifies the frequency and duration of time that a patient spends at a pressure lower (or higher) than their baseline mean PA pressure.

### Adverse Events

Adverse events and their definitions are listed in the [Data Supplement](#). All of the adverse events were adjudicated by an independent clinical events committee.

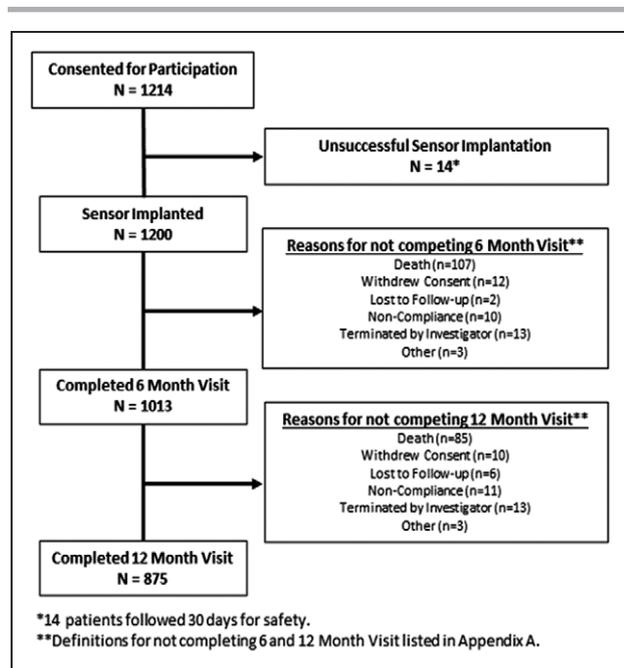


Figure 1. Screening and follow-up.

## Trial Coordination

An independent clinical events committee and steering committee coordinated the trial and communicated with the sponsor (Abbott).

## Sample Size and Statistical Methods

### Effectiveness Sample Size Determination

For the primary effectiveness end point of HFH rate during 1 year, 300 patients were estimated to provide >90% power to meet the efficacy goal (upper confidence limit less than the HF hospitalization rate in the year before enrollment), using a 1-sample, 2-sided Poisson CI with  $\alpha$  of 0.05.

### Safety Sample Size Determinations

For the 2-year primary safety end point of freedom from device- or system-related complications, using an exact 2-sided test for 1-sample binomial proportions with  $\alpha$  of 0.05, a sample size of 619 subjects was estimated to provide >90% power to detect a difference as small as 5% from the null proportion rate of 0.80 (ie, objective performance criterion of 80%). For pressure sensor failures at 2 years, a sample size of 663 subjects was estimated to provide >90% power to detect a difference as small as 3.5% from the null proportion rate of 0.90 (ie, objective performance criterion of 90%). Thus, the sample size for this study was driven by the safety end points. The 2-year attrition rate in CHAMPION was 49.1% (228/550).<sup>7</sup> To ensure sufficient patients were enrolled to adequately evaluate safety and efficacy, 1200 subjects were enrolled. Note that at least 35% of the 1200 enrolled patients (420) were planned to be women resulting in  $\approx$ 206 women completing the trial (assuming a 49% attrition rate). This sample size was planned to provide >90% power to meet the goal for effectiveness. Regarding freedom from device- or system-related complications and freedom from pressure sensor failures, 206 women would provide >90%

power to detect a difference as small as 0.06 from the null proportion rate of 0.90.

### Statistical Methods

Data were summarized using univariate statistics (eg, N, mean, SD) or frequency (eg, N, %) as appropriate. For baseline characteristics and demographics continuous variables were analyzed using 2 sample *t* test, and categorical variables were analyzed using the Fisher exact test. Enrollment was defined as having a successful pressure sensor implant. The safety population for all safety analyses was all subjects who received a pressure sensor implant or underwent the implant procedure but were never implanted, regardless of study completion status. The primary time point for safety analyses was 24 months, but 12 months were available for the 1-year analysis. Safety analysis was performed with a test of binomial proportions against performance criteria. The primary time point for effectiveness analyses was 12 months post enrollment. Unless otherwise specified, all statistical tests were 2-sided with a significance level of 0.05. The effectiveness population consists of all subjects who received a pressure sensor implant regardless of study completion status. All effectiveness analyses were performed on the effectiveness population. Effectiveness end points were analyzed using an Andersen-Gill method. Additional details regarding the statistical methods are shown in the [Data Supplement](#).

## RESULTS

### Baseline Characteristics

For the cohort of 1200 patients, mean age was  $69.4 \pm 12$  years, 37.7% were women, 14.3% were Black, 53% had HFrEF (EF <40%), 30% had HFpEF (EF >50%), and 17% had HF with mid-range EF ( $40\% \leq \text{EF} \leq 50\%$ ; Table 1). Among those with HFrEF, 94.8% were receiving a  $\beta$ -blocker, 68.0% were receiving ACE inhibitor/ARB/ARNI (angiotensin receptor–neprilysin inhibitor), and 66.4% were receiving both a  $\beta$ -blocker and ACE inhibitor/ARB/ARNI. Use of an aldosterone agonist in those with HFrEF was 54.6%. Hemodynamics in the cardiac catheterization laboratory at the time of sensor implant showed a mean PA diastolic pressure of  $20.1 \pm 7.9$  mmHg and mean cardiac index of  $2.2 \pm 0.7$  (Table 2). Ambulatory pressure readings during the first week at home were higher than at the time of sensor implant with a mean PA diastolic pressure of  $24.7 \pm 8.5$  mmHg and a mean PA mean pressure of  $34.3 \pm 10.2$  mmHg.

### Medication Changes

During the study period, 94.1% of patients had a change in medications with an average of 1.6 medication changes per patient per month. Throughout the 12-month study, 81.8% of patients had a change in medication related to an increase in PA pressure, 55.8% of patients had a change in medication that was related to a decrease in PA pressure and 82.8% of

**Table 1. Baseline Characteristics**

	All Patients*	EF <40%	40% ≤ EF ≤ 50%	EF >50%
	n=1200	n=637	n=198	n=363
Age, mean (SD), y	69 (12)	67 (13)	71 (11)	72 (10)
Men	748 (62.3)	454 (71.3)	123 (62.1)	169 (46.6)
Women	452 (37.7)	183 (28.7)	75 (37.9)	194 (53.4)
Race/ethnicity				
White	993 (82.8)	499 (78.3)	171 (86.8)	321 (88.4)
Black	172 (14.3)	114 (17.9)	26 (13.2)	32 (8.8)
Asian	12 (1.0)	8 (1.3)	0 (0)	4 (1.1)
Other	18 (1.5)	14 (2.2)	0 (0)	4 (1.1)
Body mass index, mean (SD), kg/m <sup>2</sup>	31.7 (7.9)	30.2 (7.5)	31.7 (7.7)	34.2 (8.0)
Ischemic cardiomyopathy	496 (41.3)	352 (55.3)	78 (39.4)	64 (17.6)
CRT or CRT-D device	239 (19.9)	189 (29.7)	36 (18.2)	13 (3.6)
ICD device	387 (32.3)	323 (50.7)	39 (19.7)	25 (6.9)
Comorbidities				
Hypertension	1049 (87.4)	538 (84.5)	180 (90.9)	329 (90.6)
Coronary artery disease	792 (66.0)	452 (71.0)	136 (68.7)	202(55.6)
Diabetes mellitus	655 (54.6)	338 (53.1)	108 (54.5)	207 (57.0)
Chronic obstructive pulmonary disease	422 (35.2)	201 (31.6)	74 (37.4)	146 (40.2)
Chronic kidney disease, stage 3	694 (57.8)	358 (56.2)	114 (57.6)	221 (60.9)
Chronic kidney disease, stage 4	114 (9.5)	55 (8.6)	19 (9.6)	40 (11.0)
Medical therapy				
β-blocker	1057(88.1)	604 (94.8)	174 (87.9)	277 (76.3)
ACE inhibitor/ARB/ARNI	683 (56.9)	433 (68.0)	114 (57.6)	135 (37.2)
β-blocker + ACE inhibitor/ARB/ARNI	636 (53.0)	423 (66.4)	104 (52.5)	108 (29.8)
Aldosterone agonist	529 (44.1)	348 (54.6)	77 (38.9)	103 (28.4)
Loop diuretic	1148 (95.7)	605 (95.0)	188 (94.9)	353 (97.2)
Glomerular filtration rate, mL/min per 1.73 m <sup>2</sup>	53.2 (21.1)	55.0 (22.0)	53.3 (20.9)	50.0 (19.2)

ACE indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; CRT, cardiac resynchronization therapy; CRT-D, cardiac resynchronization therapy defibrillation; EF, ejection fraction; and ICD, implantable cardiac defibrillator.

\*Two subjects had missing ejection fraction values at study entry.

subjects had a medication change that was unrelated to PA pressure, as would be appropriate for uptitration of neurohormonal modulation in stable patients. In the subgroup of patients with HFrEF (n=637), there was a significant increase the proportion of patients receiving an ARNI at baseline and at 12 months, 16.6% versus 27.5%,  $P<0.001$ .

### Pressure Transmission Compliance

A total of 286 777 pressure transmissions were collected during the study period. Mean and median daily pressure transmissions were 76±24% and 85%, respectively. Mean and median weekly pressure transmission were 93±16% and 100%, respectively. Median daily pressure transmission decreased from 97% at 1 month to 85% at 12 months. Median weekly pressure transmission remained 100% over the study period.

### Net PA Pressure Change

For the entire cohort of patients, PA pressures declined significantly from baseline during the 1 year of observation (AUC,  $-790.9\pm 2097.0$  mmHg days); however, the pattern of PA pressure change differed according to baseline mean PA pressures at the time of sensor implantation. Figure 2 shows mean PA pressure changes for patients stratified by their baseline mean PA pressures. For patients with a baseline mean PA pressure <25 mmHg (n=211), the AUC was positive ( $499.3\pm 2005.0$ ); mean PA pressure at baseline was  $20.2\pm 4.9$  mmHg, which increased by  $1.5\pm 5.8$  mmHg at the end of the first year ( $P<0.0002$ ). For patients with a baseline mean PA pressure between 25 and 35 mmHg (n=435), the AUC was negative ( $-444.1\pm 1643.7$ ); mean PA pressure at baseline was  $30.2\pm 2.8$  mmHg, which decreased by  $1.3\pm 5.0$  mmHg at the end of the first year ( $P<0.0001$ ). For patients with baseline mean PA pressure  $\geq 35$  mmHg (n=550),

**Table 2. Baseline Hemodynamics at Sensor Implant and Ambulatory Hemodynamics During First Week**

	All Patients*	EF <40%	40% ≤ EF ≤ 50%	EF >50%
	n=1200	n=637	n=198	n=363
Baseline hemodynamics at sensor implant				
Systolic blood pressure, mm Hg	126.6 (22.1)	121.2 (19.9)	129.9 (24.5)	134.1 (21.7)
Heart rate (bpm)	73.9 (12.4)	75.1 (12.2)	71.6 (12.7)	72.9 (12.5)
Pulmonary capillary wedge pressure, mm Hg	19.7 (8.4)	20.6 (9.1)	18.4 (6.8)	18.8 (7.5)
Pulmonary artery systolic pressure, mm Hg	48.0 (14.9)	48.1 (15.2)	45.2 (13.7)	49.4 (14.7)
Pulmonary artery diastolic pressure, mm Hg	20.1 (7.9)	20.5 (8.4)	18.9 (7.1)	19.8 (7.1)
Pulmonary artery mean pressure, mm Hg	31.3 (9.9)	31.6 (10.5)	29.4 (8.6)	31.9 (9.2)
Cardiac index, L/min per m <sup>2</sup>	2.2 (0.7)	2.1 (0.7)	2.3 (0.7)	2.4 (0.8)
Ambulatory hemodynamics during first week				
Pulmonary artery systolic pressure, mm Hg	49.0 (13.8)	49.0 (13.6)	47.9 (13.1)	49.7 (14.4)
Pulmonary artery diastolic pressure, mm Hg	24.7 (8.5)	25.6 (8.5)	23.8 (7.2)	23.8 (8.9)
Pulmonary artery mean pressure, mm Hg	34.3 (10.2)	34.8 (10.2)	33.4 (9.3)	34.1 (10.7)

EF indicates ejection fraction.

\*Two subjects had missing ejection fraction values at study entry.

the AUC was 3-fold more negative ( $-1560.2 \pm 2137.7$ ); mean PA pressure at baseline was  $43.0 \pm 6.8$  mm Hg, which decreased by  $4.8 \pm 6.2$  mm Hg at the end of the first year ( $P < 0.0001$ ).

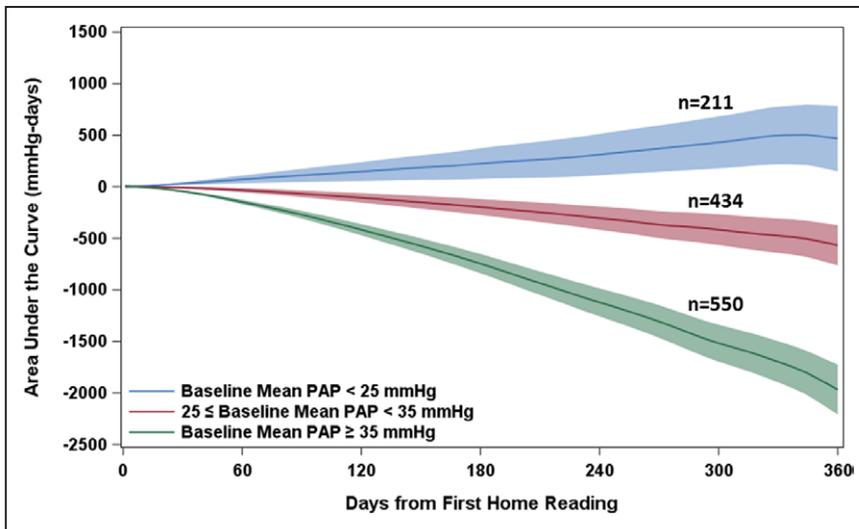
### Primary Effectiveness Outcome

The rate of HFH was significantly lower in the 1-year post-implant compared with the 1-year preimplant. There were 1600 HFH (1.25 events/patient-years before) compared with 628 HFH (0.54 events/patient-years after implant) resulting in a risk reduction of 57% (hazard ratio [HR] 0.43 [95% CI, 0.39–0.47];  $P < 0.0001$ ; Figure 3A). The rate of HFH was significantly lower in the 1-year postimplant compared with the 1-year preimplant in those who survived to 1 year (HR, 0.35 [95% CI, 0.31–0.39];  $P < 0.0001$ ). Survival at 1-year postimplant was 83.9% (95% CI, 81.7%–85.9%), and there were significant baseline differences in disease severity of patients who survived to 1 year compared with those who died (Table I in the [Data Supplement](#)). The rate of ACH was also significantly lower in the 1-year postimplant compared with the 1-year preimplant (Figure 3B). There were 2918 ACH (2.28 events/patient-years) compared with 1932 ACH (1.67 events/patient-years) resulting in a significant risk reduction of 27% (HR, 0.73 [95% CI, 0.68–0.78];  $P < 0.0001$ ). Lower HFH rates in the 1-year postimplant compared with the 1-year pre implant were consistent among all EF ranges (EF <40%, 40% ≤ EF ≤ 50%, and EF >50%; Figure 3C). Prespecified subgroups defined by gender, race (Black and White), ischemic or nonischemic cause, presence/absence of implantable cardiac defibrillator, or cardiac resynchronization therapy defibrillator all had lower HFH postimplant compared with the 1-year preimplant (Figure 4). In the subgroup of patients with HFREF, HFH postimplant compared with the year preimplant was lower, regardless of the intensity of baseline

medical therapy. For the entire HFREF cohort (n=637), there were 907 HFH (1.33 events/patient-years) before compared with 377 HFH (0.61 events/patient-years) after implant, resulting in a risk reduction of 54% (HR, 0.46 [95% CI, 0.40–0.52];  $P < 0.0001$ ). For patients with HFREF receiving both an ACE inhibitor/ARB/ARNI and  $\beta$ -blocker at study entry (n=423), there were 546 HFH (1.21 events/patient-years) before compared with 221 HFH (0.53 events/patient-years) after implant, resulting in a risk reduction of 56% (HR, 0.44 [95% CI, 0.37–0.52];  $P < 0.0001$ ). Lower HFH rates in the year postimplant compared with the year preimplant were consistent regardless of baseline PA pressures (Table II in the [Data Supplement](#)). When stratifying patients based upon the number of HFH events before study enrollment (<2, 2–4, and ≥5), all groups had fewer events in the year postimplant (Table III in the [Data Supplement](#)). It was not possible to distinguish from baseline characteristics a group of patients who were unlikely to derive benefit from PA pressure-guided therapy. PA pressures decreased from baseline after device implantation even in patients who died during the first year. Only 47 of the 1200 patients (3.9%) experienced 2 or more HFH in the year postimplant compared with their previous year, in whom the baseline characteristics were similar, including the rate of  $\beta$ -blocker use and renin-angiotensin-aldosterone system (RAAS) inhibition, compared with patients who experienced <2 HFH in the year postimplant compared with their previous year.

### Safety End Points

There were 5 device- or system-related complications (0.4%); freedom from device- or system-related complications was 99.6%. There was one pressure sensor failure (0.1%); freedom from pressure sensor failure was



**Figure 2. Change in pulmonary artery pressure over time.**

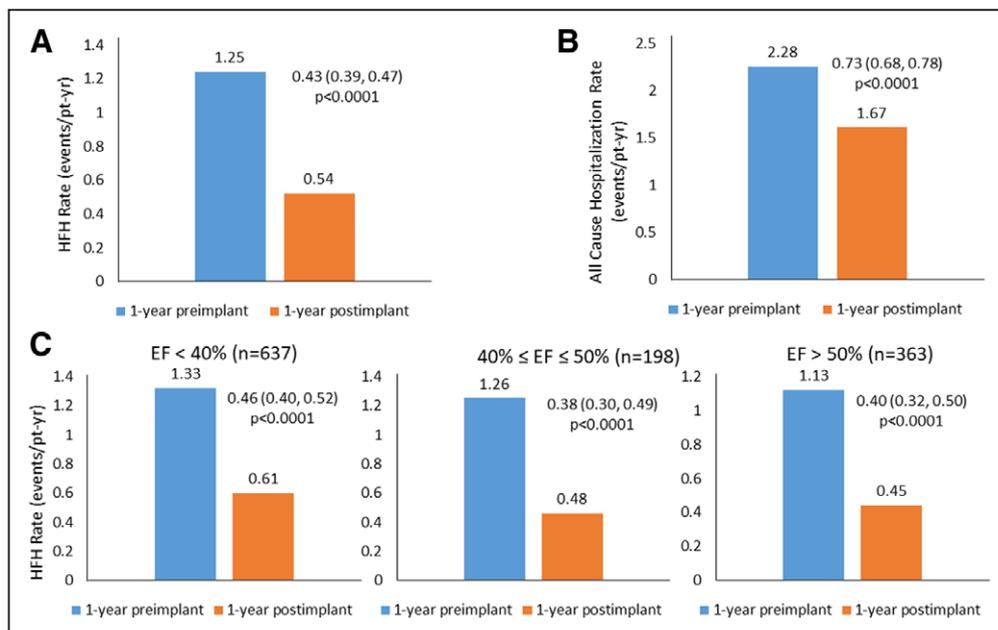
99.9%. Both rates exceeded the prespecified objective performance criteria.

### DISCUSSION

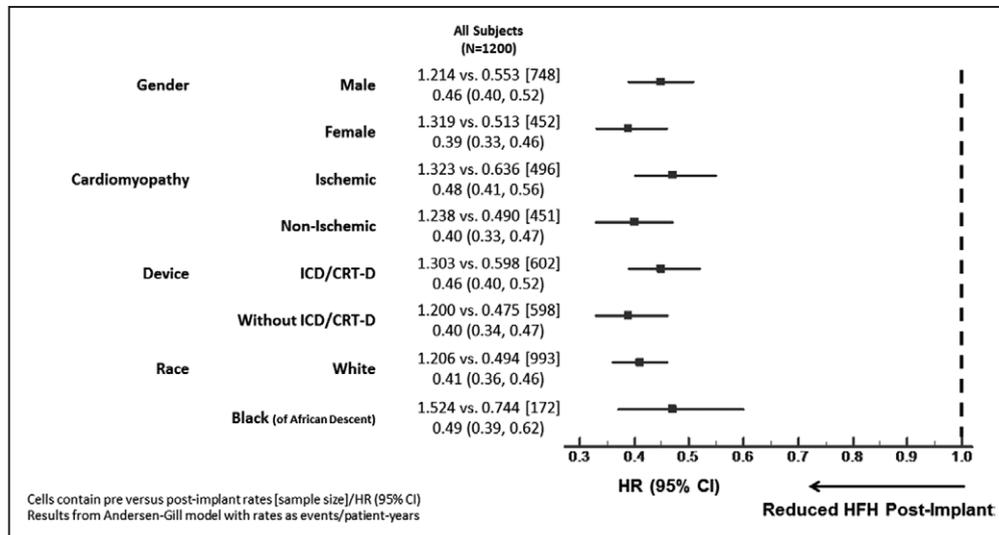
The CardioMEMS Post-Approval Study represents the largest evaluation of PA pressure-guided therapy in routine clinical practice. During the year following implantation of the PA pressure sensor, HFH and ACH were significantly lower compared with the year prior, with risk reductions comparable to those seen in the randomized trial which led to Federal Drug Agency approval of the device for commercial use.<sup>7</sup> Reductions were seen consistently across subgroups for which questions remained

after the CHAMPION trial, including those defined by sex, race, age, EF range, HF cause, and use of implanted cardiac rhythm devices. Furthermore, decreased HFH rates were seen regardless of baseline PA pressures. Rates of device related complications and pressure sensor failure were low and well below the objective performance criteria at 1-year set by the CHAMPION trial.<sup>7</sup> These data support the real-world effectiveness of PA pressure-guided therapy in clinical practice across a broad range of patients with symptomatic HF and prior HFH.

The study cohort experienced significant reductions in PA pressures, with the largest reduction seen in patients with higher baseline PA pressures. The ability to



**Figure 3. Heart failure hospitalization (HFH) and all-cause hospitalization (ACH) rates 1-year preimplant and 1-year postimplant. A,** HFH rate 1-year preimplant and 1-year postimplant. **B,** ACH rate 1-year preimplant and 1-year postimplant. **C,** HFH rate 1-year preimplant and 1-year postimplant stratified by ejection fraction (EF) ranges (EF<40%, 40%≤ EF≤50%, and EF>50%).



**Figure 4. Heart failure hospitalization (HFH) rate 1-year preimplant and 1-year postimplant in prespecified subgroups.** CRT-D indicates cardiac resynchronization therapy defibrillation; HFH, heart failure hospitalization; HR, hazard ratio; and ICD, implantable cardiac defibrillator.

continuously monitor PA pressures and adjust medical therapy allowed clinicians to optimize volume status in the ambulatory setting. Prior studies have suggested that there is a significant benefit for maintaining small reductions in cardiac pressures over extended periods of time.<sup>6</sup> The reduction in ACH in the current CardioMEMS Post-Approval Study is also consistent with prior findings from the CHAMPION study.<sup>7</sup> This may reflect the benefit of optimal volume status and lower pulmonary pressures for other major medical conditions, such as chronic obstructive pulmonary disease, a common comorbidity in patients with advanced HF.<sup>12</sup> In a subgroup of 187 patients from the CHAMPION study with chronic obstructive pulmonary disease, patients randomized to PA pressure-guided therapy had a 41% reduction in HFH and a 62% reduction in respiratory related hospitalizations.<sup>13</sup>

Similar to the CHAMPION study, we found a low rate of procedural and device related complications.<sup>7</sup> Freedom from device- or system-related complications and freedom from pressure sensor failure were high. These findings are important as the CardioMEMS Post-Approval Study was performed at 104 clinical sites within the United States and included both academic and non-academic sites. These observations are reassuring and confirm that this technology and strategy can be safely used in routine clinical practice settings.

At study entry, use of guideline-directed medical therapy for those with HFrEF was similar to contemporary HF studies of symptomatic HF including the COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation), IMPROVE-HF (Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting), and CHAMP-HF (Change the Management of Patients With Heart Failure) Registry.<sup>14–16</sup> The benefits

of PA pressure-guided therapy were seen in addition to optimal medical therapy. Prior studies of remote hemodynamic monitoring, including COMPASS-HF (Chronicle Offers Management to Patients With Advanced Signs and Symptoms of Heart Failure), found the greatest reduction in hospitalizations and also found decreased mortality when pulmonary pressure-guided therapy was used in patients already receiving optimal medical therapy.<sup>3,15</sup>

We included patients with a wide range of EF, including 17% with mid-range EF and 30% with HFpEF. Patients with mid-range EF represent a unique HF subgroup and in the current study were receiving relatively high doses of guideline-directed medical therapy and also derived benefit from PA pressure-guided therapy.<sup>17,18</sup> Treatment options for patients with HFpEF remain limited.<sup>17–19</sup> This study of 363 patients with HFpEF confirms the benefit shown for the patients with HFpEF in the CHAMPION study, PA pressure-guided therapy is the first intervention proven to decrease HFH in this growing population.<sup>7,20</sup>

The benefits of PA pressure-guided therapy in the CardioMEMS Post-Approval Study were seen across all patient subgroups, including women, Blacks, and those with or without implantable cardiac defibrillator and cardiac resynchronization therapy defibrillator devices, all of whom were better represented in this study than in the pivotal CHAMPION trial. These analyses demonstrate that this strategy, and this device can be broadly applied to improve outcomes in routine clinical practice.

## Limitations

By design, this Post-Approval Study was a single-arm study comparing patients before and after enrollment with no randomized control group. There was likely underestimation of HFH events before enrollment due

to incomplete recall of events (information bias).<sup>21</sup> This factor would have decreased the ability to detect benefit from the intervention, after which all events were prospectively reported. Censoring at the time of death may have resulted in survivor bias; however, patients who died did contribute 89 patient-years to the follow-up after device implant. The CardioMEMS Post-Approval Study enrolled high-risk patients with mortality comparable to that seen in the contemporary HF trials.<sup>4,5,22</sup> The preimplant risk of HFH in the CardioMEMS Post-Approval Study was  $\approx$ 2-fold higher than those enrolled in the open-access study<sup>8</sup> after the randomized period of the CHAMPION trial. Despite the higher baseline risk in the CardioMEMS Post-Approval Study population, we found comparable reduction in hospitalizations between this study, CHAMPION, and the open-access studies.<sup>7,8</sup>

## Conclusions

In summary, we found that both HF hospitalizations and all-cause hospitalizations were significantly lower in the year following implantation of a PA pressure sensor to guide HF management. The magnitude of decrease in PA pressures was related to baseline PA pressures, with greatest reductions in those with the highest pressures at baseline. Reductions in HF hospitalization were consistent across sex and race, across all EF ranges and in addition to best medical and rhythm device therapy. PA pressure-guided therapy was safe with few device- or system-related complications and a low rate of pressure sensor failure. These findings are consistent with the previous randomized trial data in demonstrating that PA pressure-guided therapy can effectively and safely improve outcomes in all major subgroups of HF, including patients with preserved EF, and support the efficacy of hemodynamic-guided therapy in clinical practice.

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