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ORIGINAL INVESTIGATIONS

Ambulatory Hemodynamic Monitoring Reduces Heart Failure Hospitalizations in “Real-World” Clinical Practice



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ABSTRACT

BACKGROUND In the CHAMPION (CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in New York Heart Association [NYHA] Functional Class III Heart Failure Patients) trial, heart failure hospitalization (HFH) rates were lower in patients managed with guidance from an implantable pulmonary artery pressure sensor compared with usual care.

OBJECTIVES This study examined the effectiveness of ambulatory hemodynamic monitoring in reducing HFH outside of the clinical trial setting.

METHODS We conducted a retrospective cohort study using U.S. Medicare claims data from patients undergoing pulmonary artery pressure sensor implantation between June 1, 2014, and December 31, 2015. Rates of HFH during pre-defined periods before and after implantation were compared using the Andersen-Gill extension to the Cox proportional hazards model while accounting for the competing risk of death, ventricular assist device implantation, or cardiac transplantation. Comprehensive heart failure (HF)-related costs were compared over the same periods.

RESULTS Among 1,114 patients receiving implants, there were 1,020 HFHs in the 6 months before, compared with 381 HFHs, 139 deaths, and 17 ventricular assist device implantations and/or transplants in the 6 months after implantation (hazard ratio [HR]: 0.55; 95% confidence interval [CI]: 0.49 to 0.61; $p < 0.001$). This lower rate of HFH was associated with a 6-month comprehensive HF cost reduction of \$7,433 per patient (IQR: \$7,000 to \$7,884), and was robust in analyses restricted to 6-month survivors. Similar reductions in HFH and costs were noted in the subset of 480 patients with complete data available for 12 months before and after implantation (HR: 0.66; 95% CI: 0.57 to 0.76; $p < 0.001$).

CONCLUSIONS As in clinical trials, use of ambulatory hemodynamic monitoring in clinical practice is associated with lower HFH and comprehensive HF costs. These benefits are sustained to 1 year and support the “real-world” effectiveness of this approach to HF management. (J Am Coll Cardiol 2017;69:2357-65) © 2017 by the American College of Cardiology Foundation.



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ABBREVIATIONS AND ACRONYMS

CMS = Centers for Medicare
and Medicaid Services

HF = heart failure

HFH = heart failure
hospitalization

PAP = pulmonary artery
pressure

VAD = ventricular assist device

Despite considerable progress in the development of effective medical therapy, patients with chronic heart failure (HF) remain at high risk for recurrent hospitalization and death (1). In the Medicare-eligible population, roughly 1 in 4 patients are readmitted within 30 days of hospitalization, and nearly one-half are readmitted within 6 months (2). Most of these hospitalizations are related to congestive exacerbations driven by a progressive rise in intracardiac filling pressures, independent of ejection fraction or etiology (3-7).

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Data from trials of implantable hemodynamic monitoring demonstrate that in many (although not all) cases, filling pressures rise weeks in advance of symptoms sufficient to trigger clinical attention, suggesting a window of opportunity to intervene to prevent heart failure hospitalizations (HFHs) with early detection of congestion (8). Although several methods for remote monitoring of HF patients have been considered, approaches that focus on weight (9-11) and changes in device-based diagnostics (such as intrathoracic impedance [12]) have not been effective in reducing hospitalization rates. In contrast, HF management guided by longitudinal access to pulmonary artery pressures (PAPs) was associated with substantial reduction in rates of HFH in the CHAMPION (CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in New York Heart Association [NYHA] functional Class III Heart Failure Patients) trial. These benefits persisted over the full duration of randomized follow-up (13), were consistent in patients with both preserved and reduced ejection fraction (14) as well as Medicare-eligible subjects (15), and were tightly linked to the achieved reduction in PAP with diuretic agents and other guideline-directed pharmacological therapies (16). Based on these observations, in May 2014, the U.S. Food and Drug Administration (FDA) approved the CardioMEMS HF System (Abbott, Sylmar, California) as an approach to reducing HFH in patients with chronic HF, New York Heart Association functional class III functional capacity, and a hospitalization for HF management in the year prior to implantation.

Therapeutic efficacy of an intervention in select populations managed within the tightly regulated framework of a clinical trial may not accurately

represent real-world effectiveness during general use in clinical practice. The early experience of hemodynamic-guided HF management does suggest that the PAP reductions achieved with hemodynamic monitoring in the “real world” are comparable to those observed during the CHAMPION trial (17). It remains unclear, however, whether these pressure reductions have meaningfully influenced the rate of HFH in implanted patients. We examined publicly available administrative claims data from the U.S. Centers for Medicare & Medicaid Services (CMS) to compare the rates of HFH and the costs associated with HF care in the periods before and after PAP sensor implantation.

METHODS

DATA SOURCE AND IDENTIFICATION OF THE COHORT. We conducted a retrospective cohort study using CMS administrative claims data from the Standard Analytic File to evaluate health care utilization in U.S. fee-for-service Medicare beneficiaries receiving a PAP sensor implant during the period following FDA approval for commercial use (from June 1, 2014, onward). These data include Part A inpatient claims, Part B outpatient claims, and the associated denominator files (18). The inpatient and outpatient files contain institutional claims with International Classification of Diseases-Ninth or -Tenth Revision-Clinical Modification diagnosis codes, procedure codes, and reimbursement associated with inpatient stays or ambulatory visits. The denominator files include unique deidentified patient identifications, age, sex, geographic location, race or ethnicity, date of death (if present), and information about program eligibility and Medicare insurance enrollment.

PAP sensor implants were identified by inpatient claims associated with the procedure codes 38.26, 02HQ30Z, or 02HR30Z and outpatient claims associated with Current Procedural Terminology codes C9741 and C2624 (Online Table 1). As Medicare data were available through June 30, 2016, only implants on or before December 31, 2015, were included to ensure a minimum of 6 months of potential follow-up. The cohort was further limited to patients with continuous, fee-for-service (non-health maintenance organization) Medicare insurance enrollment (Parts A and B) for at least 6 months before and after implantation, retaining those who died at any time post-implant (6-month cohort). A subset of patients who received

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implants before June 30, 2015, with continuous Medicare enrollment and follow-up data available for 12 months before and after device implantation were considered in a separate analysis (12-month cohort). The analysis plan was jointly conceived by the principal author (A.S.D.) in partnership with the sponsor, with all statistical analyses performed by the outcomes research group (R.B., K.D., and N.D.) at Abbott (Sylmar, California). The claims data were extracted using Apache Spark version 2.0.1 (Apache Software Foundation, Forest Hill, Maryland) with Python version 3.5.2 (Python Software Foundation, Beaverton, Oregon), and the statistical analyses were conducted using Revolution R version 3.1.1. (Revolution Analytics, Mountain View, California). An independent review of the results was conducted by external health care economic consultants before publication. The paper was drafted by the principal author (A.S.D.), with input from all coauthors.

ANALYSIS OF EFFECTIVENESS. We compared rates of HFH (defined using the published CMS methodology [19]) and all-cause hospitalization during the 6 months before and following device implantation using the Andersen-Gill model for recurrent events, with censoring at the time of death, ventricular assist device (VAD) implantation, or cardiac transplantation. For the subset of patients with available data, we separately analyzed the same hospitalization rates during the 12 months before and following device implantation. Heart transplant or VAD implantation was identified using a Medicare severity diagnosis related groups assignment of 001 or 002 (heart transplant or implant of heart assist system without major comorbidity or complication). For all analyses, event accumulation was analyzed forward and backward from the date of PAP sensor implant. A robust variance estimate (20) was used in the Andersen-Gill model to account for possible within-participant dependence.

ANALYSIS OF COSTS. As HFH is a principal driver of health care costs, we simultaneously conducted a comparison of the comprehensive (inpatient and outpatient) costs associated with HF care during the periods before and after implantation. For patients implanted in an outpatient setting, the health care encounter containing the relevant Current Procedural Terminology code was defined as the implant encounter, with events before and after this encounter attributed to the pre- and post-implant periods, respectively. For patients who had a PAP sensor implanted in an inpatient setting, the associated hospitalization and any preceding events were counted toward the pre-implant period, whereas any encounters after hospital discharge were counted toward the

post-implant period. Classification of an encounter as being HF-related or not was made on the basis of the presence of an HF code (Online Table 2) in the primary diagnosis code position, as per the published CMS methodology (19). The principal cost comparison was between the 6 months before and after implantation, but analyses were repeated for the cohort of patients with 12-month (pre/post) data available. A nonparametric bootstrap method (21,22) was used for comparing the pre- and post-implant costs (Online Appendix).

SENSITIVITY AND SUBGROUP ANALYSES. Because some implants occurred in the midst of an HF hospitalization, sensitivity analyses restricted to outpatient implants were performed to assess consistency of the results. To further address possible confounding of the analyses by the competing risk of death, we repeated analyses in cohorts restricted to patients who survived the full analytic interval (6 or 12 months). Results in subgroups defined by sex and age ≥ 75 years were also analyzed due to concerns previously raised regarding differential efficacy of hemodynamic monitoring in these groups. Additional sensitivity analyses, consisting of generalized estimating equations (GEE) models using both Poisson and negative binomial models, further supported the findings.

RESULTS

Of 1,935 Medicare patients who underwent a PAP sensor implantation from June 1, 2014, to December 31, 2015, there were 1,114 who were continuously enrolled and had available data regarding health care utilization for at least 6 months before and after implantation, and 480 who had complete data for 12 months before and after implantation (see Figure 1 for details of patient selection). For the 6-month cohort, the majority of PAP sensor implants ($n = 832$; 74.7%) occurred in the ambulatory setting, rather than during an HF hospitalization. Among patients who underwent PAP sensor implantation in the outpatient setting, the average time from the most recent HFH to device implantation was 63.2 ± 47.5 days. Selected patient characteristics at the time of sensor implantation for the 6- and 12-month cohorts are summarized in Table 1. Overall, for both cohorts, the mean age was 71 ± 11 years, with 40% of subjects at least 75 years of age, 36% women, 14% black race, and a large burden of comorbid medical illness, including diabetes, hypertension, and chronic obstructive pulmonary disease.

Clinical outcomes for the 6 months before and after implantation are summarized in Table 2. For the entire cohort, there were 1,899 all-cause hospitalizations and 1,020 HFHs in the 6 months before implantation, compared with 1,119 all-cause

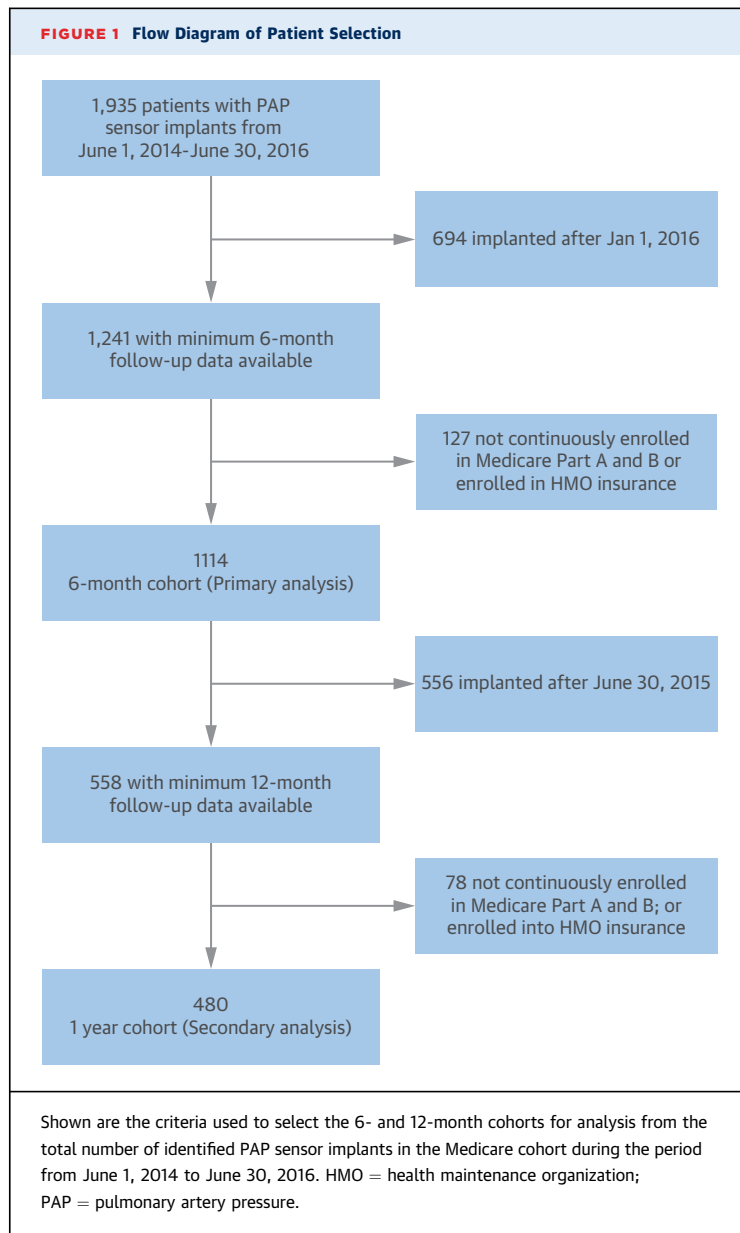


TABLE 1 Patient Characteristics (on the Basis of Medicare Claims Data) at the Time of PAP Sensor Implantation for Cohorts With 6- and 12-Month Data Available

	6-Month Cohort (n = 1,114)	12-Month Cohort (n = 480)
Age, yrs	71.3 ± 10.8	71.4 ± 11.4
Age ≥75 yrs	460 (41.3)	211 (44.0)
Female	403 (36.2)	180 (37.5)
Race		
White	902 (81.0)	396 (82.5)
Black	161 (14.5)	69 (14.4)
Other	51 (4.6)	15 (3.1)
Comorbidities*		
Diabetes	727 (65.3)	311 (64.8)
Hypertension	1,089 (97.8)	471 (98.1)
COPD	861 (77.3)	384 (80.0)

Values are mean ± SD or n (%). *Comorbidities identified using diagnosis codes from health care encounters in the 6 months before implant.

COPD = chronic obstructive pulmonary disease; PAP = pulmonary artery pressure.

confidence interval [CI]: 0.49 to 0.61; $p < 0.001$). This observation was consistent in analyses restricted to 6-month survivors (excluding those with post-implant death, VAD, or transplant), in subgroups defined by sex and age ≥ 75 years, across all Medicare administrative contractors, and in analyses restricted to outpatient implants (Figure 2, Online Figure 1). Additional sensitivity analyses using both a Poisson GEE model and negative binomial regression GEE model were performed, which further supported the robustness of the results. For the Poisson model, the incidence rate ratio was 0.60 (95% CI: 0.53 to 0.68), and for the negative binomial regression models it was 0.64 (95% CI: 0.57 to 0.73).

Reductions in HFH were associated with an estimated reduction in costs related to HF care of \$7,433/patient in the 6 months following implantation relative to the period before implantation (IQR: \$7,000 to \$7,884/patient at 6 months before implantation; $p < 0.001$). All-cause hospitalizations were also reduced in the post-implant interval (HR: 0.69; 95% CI: 0.64 to 0.75; $p < 0.001$), with associated reduction in total health care costs (Table 2).

Clinical outcomes for the subset of patients with complete 12-month data available for the period before and after implantation are summarized in Table 2. For these 480 subjects, there were 1,387 all-cause hospitalizations and 696 HFHs in the 12 months before implantation, compared with 859 all-cause hospitalizations, 300 HFHs, 15 VAD implantations or transplants, and 106 deaths after device implantation. As observed at 6 months, relative to the pre-implant interval, the cumulative incidence of HFH was also significantly lower in the

hospitalizations, 381 HFHs, 17 VAD implantations or transplants, and 139 deaths in the 6 months after device implantation. A total of 81% of patients were hospitalized at least once for any cause in the 6 months before device implantation, compared with 50% of patients in the 6 months after implant. Further, 59% of patients had at least 1 HFH pre-implant, compared with 22% of patients during the 6 months post-implant. The median number of HFHs per patient was 0.92 at 6 months before and 0.37 at 6 months after device implantation. As shown in the Central Illustration, Panel A, the cumulative incidence of HFH was significantly lower in the period following device implantation (hazard ratio [HR]: 0.55; 95%

TABLE 2 Clinical Outcomes and Health Care Costs Before and After PAP Sensor Implantation for the 6- and 12-Month Cohorts

	6-Month Cohort (n = 1,114)		12-Month Cohort (n = 480)	
	Pre-Implant	Post-Implant	Pre-Implant	Post-Implant
Follow-up, patient-yr	557	513	480	413
All-cause hospitalizations	1,899	1,119	1,387	859
HF-related	1,020	381	696	300
Non-HF-related	879	738	691	559
Days alive and out of hospital, %	93.9%	95.6%	94.8%	95.7%
VAD/Transplant	0	17	0	15
Deaths	0	139	0	106
Costs*				
HF-related	\$12,410 (\$12,050 to \$12,800)	\$4,945 (\$4,633 to \$5,300)	\$19,900 (\$19,210 to \$20,720)	\$8,690 (\$8,057 to \$9,291)
Δ cost (post – pre)	–\$7,433 (–\$7,000 to –\$7,884)		–\$11,260 (–\$10,460 to –\$12,020)	
All-cause	\$28,870 (\$28,240 to \$29,440)	\$18,360 (\$17,710 to \$18,970)	\$47,690 (\$46,370 to \$48,910)	\$34,500 (\$33,110 to \$36,000)
Δ cost (post – pre)	–\$10,510 (–\$9,703 to –\$11,330)		–\$13,190 (–\$11,590 to –\$14,740)	

Values are n unless otherwise indicated. *Costs shown are per-patient/6 months for the 6-month cohort and per patient-yr for the 12-month cohort, along with IQR (in parenthesis).
Δ = change; HF = heart failure; PAP = pulmonary artery pressure; VAD = ventricular assist device.

12-month period following device implantation (HR: 0.66; 95% CI: 0.57 to 0.76; $p < 0.001$) (**Central Illustration**, Panel B). Observed reductions in comprehensive HF costs relative to the pre-implant period were estimated at \$11,260 per patient-year (IQR: \$10,460 to \$12,020 per patient-year; $p < 0.001$). The reduction in all-cause hospitalization was also sustained at 12 months (HR: 0.77; 95% CI: 0.70 to 0.86; $p < 0.001$), as were the reductions in total costs compared with the pre-implant interval (**Table 2**).

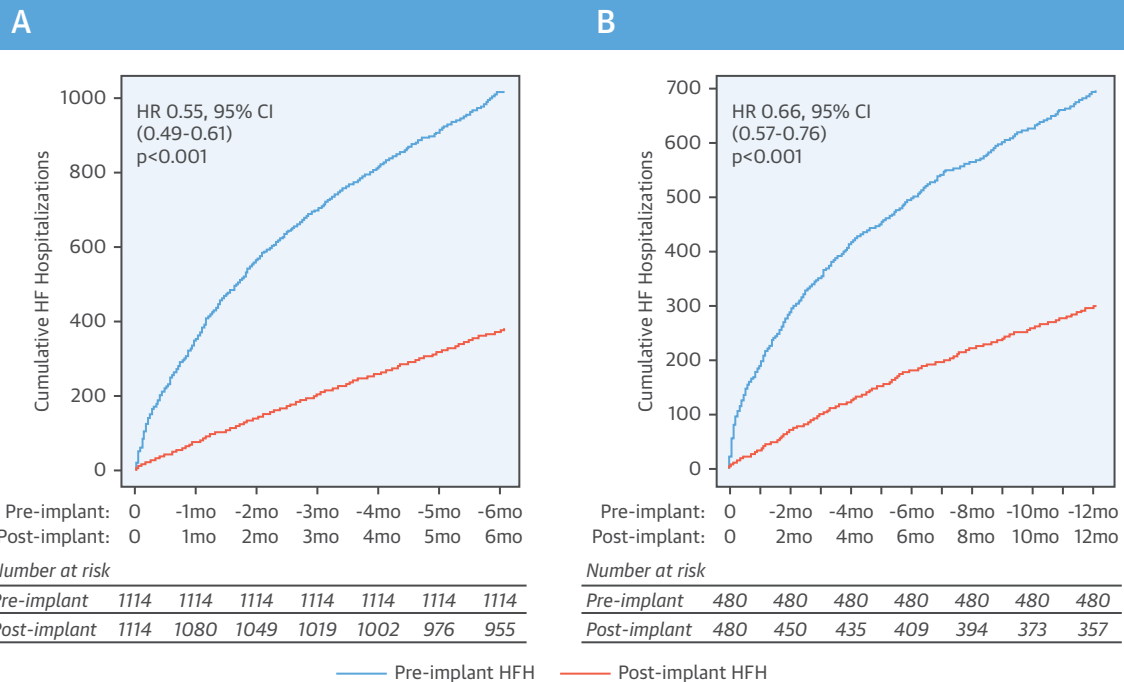
DISCUSSION

This analysis of publicly available data reflecting clinical utilization of implantable hemodynamic monitoring in Medicare patients during the commercial period post-FDA approval suggest that the reductions in HFH and cost savings seen in trial populations may also be achievable in clinical practice. The 45% lower rate of cumulative HFH observed at 6 months after PAP sensor implant versus the 6 months prior to implantation compares favorably with the 28% reduction seen with PAP-guided therapy over the same time period in the randomized CHAMPION study that supported the initial FDA approval. Moreover, the smaller cohort with 1-year pre- and post-implant data suggest that, as in the trial, these benefits may be durable over longer-term follow-up, with a 34% reduction in HFH sustained at 12 months. Concomitant reductions observed in all-cause hospitalization following device implantation suggest that reduced HFHs were not balanced by an increase in non-HF-related events. Overall reductions in health care

utilization in the post-implant period translated into substantial cost reductions at both 6 months and at 1 year compared with the pre-implant interval. These data, which are robust in competing risk models and in sensitivity analyses restricted to survivors as well as ambulatory implants, provide “real-world evidence” in an unselected population supporting the incremental value of this approach to HF management.

Although randomized clinical trials remain the gold standard for regulatory approval, regulatory agencies have increasingly acknowledged that real-world data may be used to generate valid scientific evidence regarding device safety and effectiveness in a wider patient population than that enrolled in a traditional clinical trial (23). Accordingly, FDA approval of the PAP sensor system was linked to the requirement to conduct a formal post-marketing study to demonstrate that the results achieved in the CHAMPION trial could be replicated during commercial use. Pending the results of the post-approval study (NCT02279888), these retrospective data from the Medicare population provide supportive data suggesting that the benefits of ambulatory hemodynamic monitoring seen in clinical trials may be generalizable to a broader clinical context (24). Important caveats to this analysis include the absence of Part D Medicare claims data, which precludes a detailed analysis of medication changes following device implantation, as well as the lack of linked PAP sensor data, which makes it challenging to confirm that physicians intervened to treat elevated PAPs. Accordingly, we are unable to definitively ascertain whether reduced HFH rates are related to undertreatment in the pre-implant period or improved

CENTRAL ILLUSTRATION Cumulative HFHs During the Period Before and After Pulmonary Artery Pressure Sensor Implantation



Desai, A.S. et al. *J Am Coll Cardiol.* 2017;69(19):2357-65.

(A) 6-month cohort. (B) 12-month cohort. Hazard ratios were derived using the Andersen-Gill extension of the Cox proportional hazards model, accounting for the competing risk of death, ventricular assist device, or transplant. Note that event accumulation during the pre-implant interval is counted backward from the time of implant. Data highlight significant reductions in cumulative HFHs in the period after device implantation compared with the period before implantation for both the 6- and 12-month cohorts. CI = confidence interval; HF = heart failure; HFH = heart failure hospitalization; HR = hazard ratio.

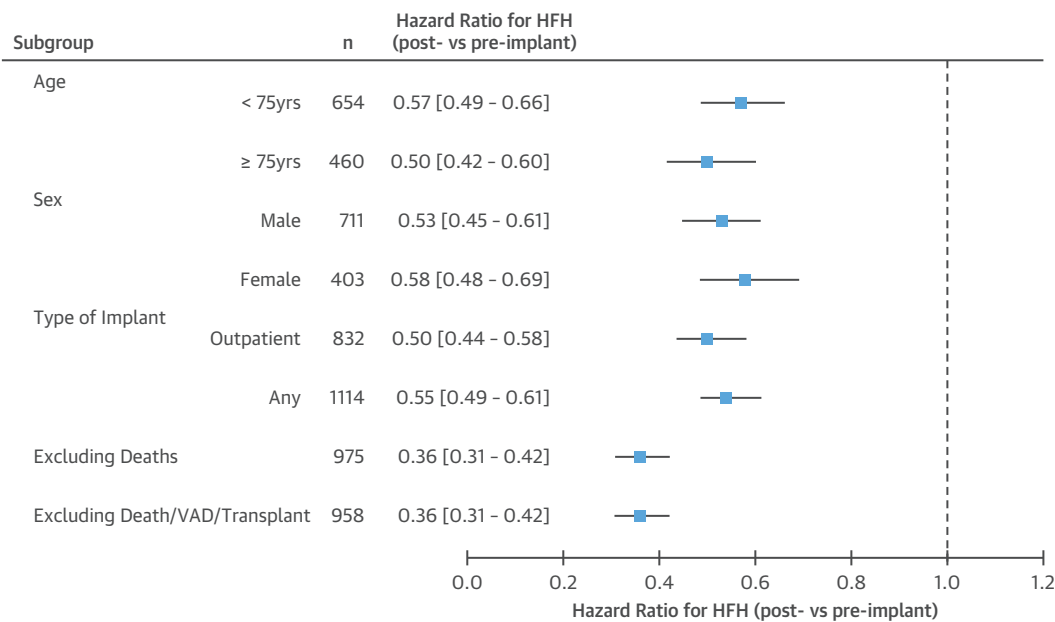
treatment in the post-implant period. Related data from the first 2,000 commercial PAP sensor implants (including both Medicare and non-Medicare patients) do suggest that PA pressure reductions achieved in clinical practice are even greater than those seen in the pivotal CHAMPION trial (17), and changes in PAP appear to be tightly linked to clinical outcomes (25). Overall, therefore, it seems reasonable to infer that the reduction in HFH is, in at least some measure, related to action taken by clinicians in response to PAP sensor data.

Despite FDA approval, there has been an ongoing dispute regarding the efficacy of hemodynamic monitoring, principally due to concerns regarding the design of the pivotal trial (26). As well, during the initial FDA review of the CHAMPION data, concerns were raised about a possible variation in the benefit of hemodynamic monitoring according to sex, as women in the treatment arm had a numerically greater (but statistically nonsignificant) rate of HFH than those in the control arm (27). The Medicare

cohort sampled for this study is nearly 4× the size of the CHAMPION trial treatment arm, and includes a larger proportion of women (40% vs. 23%) and elderly subjects (mean age 71 years vs. 61 years; 40% over 75 years of age). Data from this broader patient sample reinforce the CHAMPION results by highlighting a numerically greater reduction in HF hospitalizations at 6 months than that seen in the trial, and provide reassurance that these benefits are consistent across key subgroups of interest.

Although this is not a formal cost-effectiveness analysis, these data regarding device utilization in the commercial setting do provide some important assurances regarding the economic implications of ambulatory hemodynamic monitoring. First, observed rates of device utilization in the Medicare population are far lower than those that drove early projections of the potentially large budgetary effect of device approval (28). Second, the observed reduction in hospitalizations following device implantation is

FIGURE 2 HFHs in Subgroups of Interest During Period Before and After PAP Sensor Implant (6-Month Cohort)



Results for each subgroup reported as hazard ratios with 95% confidence intervals, adjusted for competing risk of death, VAD, or transplantation. These data demonstrate consistent reductions in HFHs in subgroups defined by age and sex, as well as in cohorts excluding post-implant deaths as well as post-implant death/VAD/transplant (to address potential survivor bias). HFH = heart failure hospitalization; PAP = pulmonary artery pressure; VAD = ventricular assist device.

numerically higher than that seen in the trial, supporting even greater cost reductions during the post-implant interval than projected from the CHAMPION data alone. Finally, the observation of sustained HFH and cost reductions out to 1 year in a real-world population supports the notion that the benefits of hemodynamic monitoring may be durable over longer-term follow-up, a factor that is essential for long-term cost-effectiveness. Based on an average Medicare reimbursement of \$23,122 ± \$16,891 for device implantation in this cohort, the reduction of \$13,190/patient in comprehensive health care costs among survivors over 1 year suggests a break-even point of roughly 2 years to recoup the initial investment.

STUDY LIMITATIONS. First, these analyses were derived from Medicare claims data, and accordingly we are unable to provide details regarding medical history, ejection fraction, the indication for PAP sensor implantation, quality of life, device safety, and the like. An objective method of identifying HFH per CMS methodology was used for this claims dataset, and there was no formal clinical event adjudication. Only Medicare charges were incorporated in the cost analyses, and accordingly, we are unable to account

for the personnel costs associated with remote management. As this was a cohort-based comparison of outcomes before and after device implantation, not a prospective randomized study, we cannot exclude the possibility that selection bias or enhancements of HF disease management in the period after device implant may also have confounded our results. However, because all patients had previously been hospitalized for HF, and because all implanting centers were selected for their experience in HF management, it is likely that background medical therapy did not differ markedly in the periods before and after implantation. Moreover, because HF is a progressive disease, with rates of hospitalization accelerating with progression toward the end stage, these results likely reflect a conservative estimate of the reductions in worsening HF, health care utilization, and cost that are likely to be seen with ambulatory hemodynamic monitoring in practice. Although censoring at the time of death, VAD, and transplant introduces the potential for survivor bias, consistent reductions in HFH in models accounting for competing risks, as well as sensitivity analyses restricted to patients at risk for the full duration of follow-up (6 or 12 months), suggest that this bias did not meaningfully influence the results.

CONCLUSIONS

These data from the “real-world” experience of Medicare implants of PAP sensors during the period following device approval suggest that the use of ambulatory hemodynamic monitoring is associated with reductions in HFH and overall costs associated with HF care. In tandem with data suggesting effective reductions in PAPs among general-use patients who had the PAP sensor system implanted since FDA approval (17), these observations support the generalizability of the CHAMPION trial results to clinical practice and argue for clinical effectiveness of ambulatory hemodynamic monitoring as a strategy for HF management.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND

PROCEDURAL SKILLS: Use of an implantable PAP sensor to guide HF management in Medicare patients managed in clinical practice is associated with reductions in HFHs and all-cause hospitalizations comparable to the rates reported in clinical trials. This suggests that, for eligible patients, the addition of ambulatory hemodynamic monitoring to standard HF care may reduce resource utilization and health care costs.

TRANSLATIONAL OUTLOOK: Additional research is needed to validate these results in other patient populations, assess the durability of the effect beyond the first year, identify patients who are most likely to benefit from a PAP sensor, confirm the consistency of benefit in patients with HF and preserved versus reduced ejection fractions, and assess the optimal clinical infrastructure needed to derive maximal benefit from ambulatory hemodynamic monitoring.

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KEY WORDS CardioMEMS, clinical effectiveness, implantable hemodynamic monitor

APPENDIX For supplemental tables and figures, please see the online version of this article.