Health Evidence Review Commission (HERC)

Coverage Guidance: CardioMEMS™ for Heart Failure Monitoring

Approved 10/4/2018

HERC Coverage Guidance

CardioMEMS™ is not recommended for coverage for heart failure monitoring *(weak recommendation).*

Note: Definitions for strength of recommendation are in Appendix A. *GRADE Table Element Descriptions*.

Rationales for each recommendation appear below in the GRADE table.

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Rationale for development of coverage guidances and multisector intervention reports

Coverage guidances are developed to inform coverage recommendations for public and private health plans in Oregon as plan administrators seek to improve patients' experience of care, population health, and the cost-effectiveness of health care. In the era of public and private sector health system transformation, reaching these goals requires a focus on maximizing the benefits and minimizing the harms and costs of health interventions.

HERC uses the following principles in selecting topics for its reports to guide public and private payers:

- Represents a significant burden of disease or health problem
- Represents important uncertainty with regard to effectiveness or harms
- Represents important variation or controversy in implementation or practice
- Represents high costs or significant economic impact
- Topic is of high public interest

HERC bases its reports on a review of the best available research applicable to the intervention(s) in question. For coverage guidances, which focus on diagnostic and clinical interventions, evidence is evaluated using an adaptation of the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology. For more information on coverage guidance methodology, see Appendix A.

Multisector interventions can be effective ways to prevent, treat, or manage disease at a population level. In some cases, HERC has reviewed evidence and identified effective interventions, but has not made formal coverage recommendations when these policies are implemented in settings other than traditional health care delivery systems because effectiveness could depend on the environment in which the intervention is implemented.

GRADE Table

HERC develops recommendations by using the concepts of the GRADE system. GRADE is a transparent and structured process for developing and presenting evidence and for performing the steps involved in developing recommendations. The table below lists the elements that determine the strength of a recommendation. HERC reviews the evidence and assesses each element, which in turn is used to develop the recommendations presented in the coverage guidance box. Estimates of effect are derived from the evidence presented in this document. Assessments of confidence are from the published systematic reviews and meta-analyses, where available and judged to be reliable.

In some cases, no systematic reviews or meta-analyses encompass the most current literature. In those cases, HERC may describe the additional evidence or alter the assessments of confidence in light of all available information. Such assessments are informed by clinical epidemiologists from the Center for Evidence-based Policy. Unless otherwise noted, statements regarding resource allocation, values and preferences, and other considerations are the assessments of HERC, as informed by the evidence reviewed, public testimony, and subcommittee discussion.

Recommendations for coverage are based on the balance of benefit and harms, resource allocation, values and preferences, and other considerations. See Appendix A for more details about the factors that constitute the GRADE table.

GRADE Table

Should CardioMEMS™ be recommended for coverage for heart failure monitoring?

Outcomes	Estimate of Effect for Outcome/ *Confidence in Estimate*	Resource Allocation	Values and Preferences	Other Considerations
All-cause mortality *(Critical outcome)*	19% for CardioMEMS™ vs. 23% for control HR 0.80 (95% CI 0.55 to 1.15, p = 0.23) ●○○○ *(Very low confidence, based on 1 RCT, n = 550)*	The cost of the CardioMEMS™ device is substantial. The cost of the device, implantation, and complications in 2016 dollars is reportedly close to $19,000. Ongoing monitoring is necessary and would increase costs associated with the device. If this device were effective at reducing hospitalizations and further morbidity and mortality, it has the potential to be cost-effective.	We would assume that patients would strongly prefer to avoid heart failure exacerbations and repeated heart failure hospitalizations. However, this preference would be tempered by the serious adverse event rate of 15/550 that includes events such as arrhythmias, bleeding, and shock. More rare but plausible concerns include infection, thrombosis, and device migration; the study might have been underpowered to detect these events. Given the noninvasiveness of alternatives (e.g., using a scale and communication with clinic staff), we would expect high variability in preferences.	All of the reports are derived from a single trial (CHAMPION) for which there are concerns about bias. There are concerns about external validity given that the monitoring and recommendations of the data obtained through CardioMEMS™ was interpreted by specialty heart failure centers (with assistance of device manufacturer consultation). It is unclear how adoption of this technology within non-specialty centers may modify its potential effectiveness.

GRADE Table

Should CardioMEMS™ be recommended for coverage for heart failure monitoring?

Outcomes	Estimate of Effect for Outcome/ *Confidence in Estimate*	Resource Allocation	Values and Preferences	Other Considerations
Cardiovascular mortality *(Critical outcome)*	Not reported			
Heart failure-related hospitalization *(Critical outcome)*	0.46 events per patient-year for CardioMEMS™ vs. 0.68 events per patient year for control HR 0.67 (95% CI 0.55 to 0.80, p < 0.001) Approximate NNT = 5 ●●○○ *(Low confidence, based on 1 RCT, n = 550)*			
Quality of life *(Important outcome)*	Improved Minnesota Living with Heart Failure Questionnaire score in the CardioMEMS™ group (45) vs. the control group (51), (105 point scale, p = 0.02) ●○○○ *(Very low confidence, based on 1 RCT, n = 550)*			

GRADE Table

Should CardioMEMS™ be recommended for coverage for heart failure monitoring?

Outcomes	Estimate of Effect for Outcome/ *Confidence in Estimate*	Resource Allocation	Values and Preferences	Other Considerations
Harms *(Important outcome)*	15 serious procedure-related or device-related adverse events were reported (4 bleeding events, 3 events related to interruption of anticoagulation, 2 exacerbations of atrial arrhythmias, 2 febrile illnesses, 1 in-situ pulmonary thrombus, 1 episode of cardiogenic shock, 1 episode of atypical chest pain, and 1 delivery-system failure that required snare retrieval) Approximate NNH = 37 ●○○○ *(Very low confidence, based on 1 RCT, n = 550)*			

Balance of benefits and harms: We have low confidence that CardioMEMS™ decreases the rate of heart failure-related hospitalization, very low confidence that it improves quality of life, and very low confidence that there is a mortality benefit. We have very low confidence that it is associated with serious adverse events. While the balance of benefits and harms weighs in favor of the intervention, based on the limited evidence it is unclear that the benefit outweighs the risk.
Rationale: The balance of benefits and harms weighs in favor of the intervention, but it is very expensive and invasive, and preferences would likely be highly variable. Given that the evidence is derived from only one trial that has concern of bias, a confirmatory trial is necessary to improve the confidence regarding the potential benefit of this intervention.
Recommendation: CardioMEMS™ is not recommended for coverage for heart failure monitoring *(weak recommendation).*

Note: GRADE table elements are described in Appendix A. A GRADE Evidence Profile is in Appendix B.

Background

Heart failure occurs when the heart muscle is damaged to the extent that it cannot meet the body's needs for blood and oxygen (American Health Association, 2018). About 5.7 million adults in the U.S. have heart failure, and heart failure is a contributing cause to one in nine deaths (Heidenreich et al., 2013). About half of people who develop heart failure die within five years of diagnosis (Heidenreich et al., 2013). The annual economic costs of heart failure in the U.S. are estimated at $30.7 billion, including the costs of health care services, medications, and missed days of work (Mozaffarian et al., 2016).

Risk factors for heart failure include coronary heart disease, myocardial infarction, hypertension, and diabetes. Behavioral risk factors include cigarette smoking; a diet high in fat, cholesterol, and sodium; physical inactivity; and being obese (Centers for Disease Control and Prevention [CDC], 2016). Early diagnosis and treatment can improve outcomes for patients with heart failure, and treatment usually involves medications, behavioral interventions focusing on diet and physical activity, and daily monitoring of symptoms (CDC, 2016).

Heart failure symptoms and disease progression can be difficult to monitor because of subtle onset of decompensation, medication regimens, the complexities of lifestyle changes, and interactions with comorbid conditions (Bui & Fonarow 2012). Interventions to monitor ambulatory heart failure patients include increased self-care and self-management; home visitations by providers; structured telephone support; telemonitoring; and remote monitoring through the use of implantable devices, such as CardioMEMS™ (Bui & Fonarow 2012). Because of penalties imposed by the Centers for Medicare and Medicaid Services (CMS) for heart failure readmissions, preventing rehospitalization has become a major focus of health insurers and hospital systems (Boccuti & Casillas, 2017).

Indications

CardioMEMS™ is indicated for wirelessly measuring and monitoring pulmonary artery 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. CardioMEMS™ is contraindicated for patients who are unable to take dual antiplatelet or anticoagulants for one month after implant of the device (Abbott, 2018).

Technology Description

CardioMEMS™ measures pulmonary artery hemodynamic data that physicians can use to initiate or modify treatments for heart failure. The CardioMEMS™ heart failure monitoring system includes the implantable wireless sensor with delivery catheter, a patient-based or clinic-based electronics system, and a patient database. The wireless sensor is permanently implanted into the distal pulmonary artery (CardioMEMS, 2014). The manufacturer lists the potential adverse events from implanting CardioMEMS™ as infection, arrhythmias, bleeding, hematoma, thrombus, myocardial infarction, transient ischemic attack, stroke, device embolization, and death (Abbott 2018).

The data provided by CardioMEMS™ are heart rate; pulmonary artery waveform; and systolic, diastolic, and mean pulmonary artery pressure. These data are transmitted to the patient database on a secure website (CardioMEMS, 2014). CardioMEMS™ received premarket approval from the U.S. Food and Drug Administration (FDA) in May 2014 (FDA, 2014a).

Evidence Review

Abraham et al., 2011

The pivotal trial examining the effectiveness of the implantable hemodynamic monitoring system (IHMS) is known as the CardioMEMS™ Heart Sensor Allows Monitoring of Pressures to Improve Outcomes in NYHA III Heart Failure Patients (CHAMPION) trial. Its initial results were published in February 2011.

The CHAMPION trial enrolled adults with a diagnosis of heart failure for at least three months with NYHA functional Class III symptoms and at least one heart failure-related hospitalization in the preceding 12 months. Patients were eligible without respect to the left ventricular ejection fraction. To be eligible, patients must have been on optimal or best-tolerated guideline-directed heart failure therapies. Major exclusion criteria were a history of recurrent pulmonary embolism or deep venous thrombosis, Stage IV or V chronic kidney disease, implantation of cardiac resynchronization device in the three months prior to enrollments, recent major adverse cardiovascular events, and hypersensitivity to aspirin or clopidogrel.

CHAMPION was designed as a randomized, single-blind, multicenter trial and was conducted at 64 sites in the United States. The study enrolled 550 patients who all underwent implantation of the CardioMEMS™ device and were admitted to the hospital overnight for observation. Prior to discharge from the hospital, patients were randomized (1:1) to an experimental arm (in which treating clinicians could access readings from the device) and to a control arm (in which treating clinicians could not access readings from the device). All patients were instructed to take pressure readings every day to ensure that patients were blinded to their treatment allocation. In the experimental group, invasive hemodynamic data were reviewed at least weekly, and more often if changes were made in the treatments. Patients in both groups were seen by their treating clinician at one, three, and six months, then every six months. Each study site was required to balance the number of patient contacts between the experimental and control groups. The primary outcomes were the rate of heart failure-related hospitalizations, freedom from device-related complications, and freedom from pressure sensor failure, all measured at six months. The secondary outcome measures were change in mean pulmonary artery pressure, proportion of patients with heart failure-related hospitalization, days alive outside the hospital, and quality of life as measured by the Minnesota Living with Heart Failure Questionnaire (MLHFQ), all measured at six months. Outcomes assessment and adjudication were performed by an independent, blinded committee.

The trial was conducted between September 2007 and October 2009. Overall, 550 patients were enrolled and had the device implanted. There were 270 patients randomized to the experimental arm and 280 patients randomized to the control arm. The mean age of patients was 61 years, roughly 72% of patients were men, and roughly 80% had a left ventricle (LV) ejection fraction of < 40%. Approximately 75% of patients were on ACE inhibitors, 90% were on beta blockers, and 40% were on aldosterone antagonists at baseline. The two groups were generally comparable with respect to baseline characteristics, but there were small differences with respect to the following:

- Proportion of patients with LV ejection fraction > 40% (62 [23%] in the experimental group vs. 57 [20%] in the control group)
- Proportion of patients with coronary artery disease (182 [67%] in the experimental group vs. 202 [72%] in the control group)

- Proportion of patients with atrial flutter or atrial fibrillation (120 [44%] in the experimental group vs. 135 [48%] in the control group)
- Proportion of patients on nitrates (64 [24%] in the experimental group vs. 56 [20%] in the control group).

All patients remained in their assigned treatment group until the six month follow-up period was completed for every enrollee; the mean follow-up duration during the randomized portion of the trial was 15 months. Six month follow-up was available for 244 patients in the experimental arm and 254 patients in the control arm. The overall rate of attrition was approximately 10% and was non-differential. The study authors used intention-to-treat analysis.

For the primary efficacy outcome of heart failure-related hospitalizations at up to six months, there were fewer events in the experimental arm (84 events, 0.32 events per patient per six months) compared with the control arm (120 events, 0.44 events per patient per six months); this equated to a statistically significant reduction of 28% (HR 0.72, 95% CI 0.60 to 0.85, p = 0.0002, number needed to treat [NNT] 8). The authors found a statistically significant reduction in events in the experimental arm (HR 0.63, 95% CI 0.52 to 0.77, p < 0.0001, NNT 4) for the pre-specified supplemental efficacy endpoint of heart failure-related hospitalizations during the complete randomized follow-up period. For the safety-related primary endpoints, there were no pressure sensor failures, and there were 15 serious procedure-related or device-related adverse events (four bleeding events, three events related to interruption of anticoagulation, two exacerbations of atrial arrhythmias, two febrile illnesses, one in-situ pulmonary thrombus, one episode of cardiogenic shock, one episode of atypical chest pain, and one delivery-system failure that required snare retrieval).

Relevant secondary outcomes were a lower proportion of patients admitted to the hospital at six months in the experimental group (20% vs. 29% in the control group, RR 0.71, 95% CI 0.53 to 0.96, p = 0.03), small but statistically significant improvements in days alive outside the hospital at six months (174.4 vs. 172.1, p = 0.02), and MLHFQ score at six months (45 vs. 51, p = 0.02). There was no statistically significant difference in survival at six months (HR 0.77, 95% CI 0.40 to 1.51, p = 0.45). In a pre-specified subgroup analysis by LV systolic function, the rate of heart failure-related hospitalizations was lower in the experimental arm in both subgroups (0.16 per patient per six months vs. 0.33 per patient per six months for patients with preserved ejection fraction; 0.36 per patient per six months vs. 0.47 per patient per six months for patients with reduced ejection fraction).

The authors also conducted an incompletely reported cost-effectiveness analysis. Using a hypothetical cohort of patients with a five-year time horizon, the authors estimated that the treatment group gained 0.306 quality-adjusted life years (QALY) at an incremental cost of $4,282, leading to an incremental cost-effectiveness ratio of $13,979 per QALY gained. The authors did not specify the perspective, clearly outline all assumptions or report sensitivity analyses, and did not state whether a customary discounting rate was applied.

Potential sources of bias in the initial report of the CHAMPION trial were that study clinicians (who were ultimately responsible for decisions regarding hospitalization) were not blinded to the treatment group (performance bias), that the device manufacturer sponsored the trial and was involved in data collection and management, and that all authors disclosed conflicts of interest (including consultancies, research grants, or employment).

At the initial FDA Circulatory System Devices Panel meeting at which CardioMEMS™ was discussed in 2011, several criticisms of the design, conduct, and reporting of the CHAMPION trial were leveled (Loh, Barbash, & Waksman, 2013). Three major concerns were outlined. First, FDA statisticians questioned the robustness of the statistical models used in the analysis of heart failure admissions. As an example, if an alternative bootstrap model was applied, as few as two additional hospitalizations in the experimental arm would have increased the likelihood of a type I error to greater than 10% (i.e., p value in excess of 0.1). Second, an FDA Division of Bioresearch Monitoring audit found evidence that unblinded representatives of the sponsor or principal investigators communicated with study sites to make specific treatment recommendations for some patients in the experimental group. Third, in a post-hoc subgroup analysis by gender, the putative efficacy of the device was not observed in women for whom the hazard ratio for heart failure-related hospitalization was 1.15 (95% CI 0.83 to 1.59, p = 0.3953). Partly on the basis of these concerns, the advisory panel voted (7 to 3) that there was not reasonable assurance that the device was effective.

The manufacturer and principal investigators responded to these criticisms at a subsequent FDA advisory panel meeting. They provided additional analyses emphasizing that the number of communications with specific recommendations to treating clinicians was small and that a propensity score analysis comparing experimental group patients whose clinicians did not receive investigator communications to a matched group of controls found a similar reduction in heart failure-related hospitalizations. They also contended that the absence of efficacy in women stemmed from a small number of women in the trial and an excess number of deaths in the control group (which reduced their time in the study); using a combined endpoint of mortality or heart failure-related hospitalization, there was not a treatment-by-gender interaction at a p value of 0.05 (although the FDA pointed out that under a more customary p value cutoff of 0.15 for tests of interaction, the observed subgroup difference remained). Despite the additional information and analyses, the advisory panel again voted (7 to 4) that there was not "reasonable assurance" that the device was effective. The FDA disagreed with the advisory panel's determination, noting that:

> When considering the totality of effectiveness data, the consistency of the results indicate a positive treatment effect in reducing HFR hospitalizations. This positive treatment effect seen in the Open Access (Part 2) of the study also agrees with the positive treatment effect seen in the Randomized Access (Part 1). However, because of the confounding effect of the nurse communications from Part 1 and the limitations of the ancillary analyses from Part 2, there remains some uncertainty regarding the magnitude of that positive effect. (FDA, 2014b, p. 89)

Adamson et al., 2014

This study, derived from the previously described CHAMPION trial, reported the effectiveness of CardioMEMS™ in patients with preserved left ventricular function. Of the 550 patients enrolled in the CHAMPION trial, 119 had a left ventricular ejection fraction (EF) > 40% (mean EF 50.6%). Because the American Heart Association and American College of Cardiology consensus definition for heart failure with preserved ejection fraction changed in 2013, the authors also provided a subgroup analysis based on the newer EF cutoff of 50% (n = 66 patients). In general, within the subgroup of patients with preserved ejection fraction, the baseline patient characteristics were similar between the experimental and control groups. Compared to those with reduced EF, patients with preserved EF were more likely to

have comorbid diabetes and cerebrovascular disease and less likely to have a history of myocardial infarction or hypotension.

In the preserved EF group (> 40%), for the primary efficacy endpoint of heart failure-related hospitalization at six months, there were 11 hospitalizations in the experimental arm (0.18 events per patient per six months) and 19 hospitalizations in the control arm (0.33 events per patient per six months) (incidence rate ratio [IRR] 0.54, 95% CI 0.38 to 0.70, p < 0.0001). Among the group of patients with EF > 50%, for the primary efficacy endpoint of heart failure-related hospitalization at six months, there were nine hospitalizations in the experimental arm (0.18 events per patient per six months) and 10 hospitalizations in the control arm (0.35 events per patient per six months) (IRR 0.50, 95% CI 0.29 to 0.86, p = 0.0129). The authors stated that the greater event rate in the control group, despite a numerically similar number of events, derived from a shorter combined follow-up period in the control group.

During the complete randomized follow-up period (mean 17.6 months), for patients with preserved EF (> 40%) there were 29 hospitalizations in the experimental arm (0.43 events per patient per year) and 59 hospitalizations in the control arm (0.86 events per patient per year) (IRR 0.50, 95% CI 0.35 to 0.70, p < 0.0001). Among the group of patients with EF > 50%, there were 13 hospitalizations in the experimental arm (0.41 events per patient per year) and 31 hospitalizations in the control arm (1.39 events per patient per year) (IRR 0.30, 95% CI 0.18 to 0.48, p < 0.0001).

At the six-month follow-up, the proportion of patients with preserved EF (> 40%) who were hospitalized was 12.9% in the experimental arm and 22.8% in the control arm. During the complete randomized follow-up period, the proportion of patients with preserved EF (> 40%) who were hospitalized was 29% in the experimental arm and 38.6% in the control arm. The authors did not report the proportion of patients with EF > 50% who were hospitalized during either timeframe.

Adamson et al., 2016

This study, derived from the previously described CHAMPION trial, reported the effectiveness of CardioMEMS™ in reducing the risk of 30-day readmissions among a subgroup of Medicare-eligible participants. Of the 550 patients enrolled in the trial, 245 were older than 65 at the time of device implantation. Compared to the overall study population, this group was largely composed of white men with ischemic cardiomyopathy and reduced LV ejection fraction. Within the subgroup, the mean LV ejection fraction was lower in the control group (30.4% vs. 34.6%), and the baseline pulmonary artery pressures were slightly higher in the control group. The reason for hospitalization was prospectively adjudicated by an independent group of cardiologists, although the authors did not state that these adjudicators were blinded to the treatment group.

The mean follow-up time in the subgroup was 515 days. During this follow-up period, there were 175 total heart failure-related hospitalizations, of which 155 were considered index admissions that contributed to the analysis. Overall, there were 44 all-cause readmissions, of which 21 were heart failure-related. The overall rate of heart failure-related hospitalizations was 0.34 events per patient per year in the experimental group, compared to 0.67 events per patient per year in the control group (HR 0.51, 95% CI 0.37 to 0.70, p < 0.0001). The rate of 30-day all-cause readmission was 0.07 events per patient per year in the experimental group, compared to 0.18 events per patient per year in the control group (HR 0.42, 95% CI 0.22 to 0.80, p = 0.008). The rate of 30-day heart failure readmission was 0.02

events per patient per year in the experimental group, compared to 0.10 events per patient per year in the control group (HR 0.23, 95% CI 0.08 to 0.68, p = 0.008).

During the open access period, 63 control arm patients were followed for a mean of 13 months. After these patients had entered the open access period (and clinicians had access to hemodynamic measurements), the heart failure-related hospitalization rate was 0.35 events per patient per year compared to a rate of 0.67 events per person per year during the randomized phase of the trial. More than half (n = 135) of the originally randomized patients in this subgroup completed the full randomized portion of the trial.

Abraham et al., 2016

This report, derived from the previously described CHAMPION trial, reported complete results of the trial after the open access period. As patients enrolled in the trial, they remained in their randomly allocated treatment group until the last patient completed six months of follow-up. At that point, pressure measurements for patients in the control arm during the randomized portion of the trial were made available to the treating clinicians. Patients were followed for an average of 13 months in the open access period. No communications between the sponsor and study clinicians occurred during the open access period. The statistical analysis plan was developed in conjunction with the FDA.

Of the original 550 patients enrolled in the trial, 347 patients completed the full randomized access period (177 in the experimental group and 170 in the control group). The study withdrawals that occurred during the randomized access portion of the trial were most commonly due to death. During the open access period, an additional 43 patients in the former control group and 58 patients in the former experimental group withdrew.

Complete outcomes from the randomized access portion of the trial at a mean follow-up duration of 18 months were reported as follows:

	Randomized access experimental group	Randomized access control group	Statistical analysis
Heart failure admissions	n = 182 0.46 events per patient-year	n = 279 0.68 events per patient-year	HR 0.67 (0.55 to 0.80) p < 0.0001
Deaths and heart failure admissions	n = 232 0.58 events per patient-year	n = 343 0.84 events per patient-year	HR 0.69 (0.59 to 0.82) p < 0.0001
Death	n = 50 (19%)	n = 64 (23%)	HR 0.80 (0.55 to 1.15) p = 0.23
Death or first admission for heart failure	n = 121 (45%)	n = 145 (52%)	HR 0.77 (0.60 to 0.98) p = 0.033
All-cause admissions	n = 554	n = 672	HR 0.84 (0.75 to 0.95) p = 0.0032

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	Randomized access experimental group	Randomized access control group	Statistical analysis
	1.38 events per patient-year	1.65 events per patient-year	
Deaths and all-cause admissions	n = 604 1.51 events per patient-year	n = 736 1.80 events per patient-year	HR 0.84 (0.76 to 0.94) p = 0.0017

Outcomes comparing the randomized access control group to the open-access former control group were reported as follows:

	Randomized access control group	Open-access former control group	Statistical analysis
Heart failure admissions	n = 279 0.68 events per patient-year	n = 64 0.36 events per patient-year	HR 0.52 (0.40 to 0.69) p < 0.0001
Deaths and heart failure admissions	n = 343 0.84 events per patient-year	n = 85 0.51 events per patient-year	HR 0.61 (0.48 to 0.78) p < 0.0001
Death	n = 64 (23%)	n = 21 (12%)	HR 0.71 (0.43 to 1.17) p = 0.17
Death or first admission for heart failure	n = 145 (52%)	n = 49 (29%)	HR 0.53 (0.38 to 0.73) p < 0.0001
All-cause admissions	n = 672 1.65 events per patient-year	n = 230 1.30 events per patient-year	HR 0.35 (0.67 to 0.92) p = 0.0034
Deaths and all-cause admissions	n = 736 1.80 events per patient-year	n = 251 1.52 events per patient-year	HR 0.85 (0.72 to 0.99) p = 0.0351

Outcomes comparing the randomized access experimental group to the open-access former experimental group were reported as follows:

	Randomized access experimental group	Open-access former experimental group	Statistical analysis
Heart failure admissions	n = 182	n = 78	HR 0.93 (0.70 to 1.22) p = 0.58

	Randomized access experimental group	Open-access former experimental group	Statistical analysis
	0.48 events per patient-year	0.45 events per patient-year	
Deaths and heart failure admissions	n = 232 0.61 events per patient-year	n = 109 0.67 events per patient-year	HR 1.09 (0.86 to 1.39) p = 0.46
Death	n = 50 (19%)	n = 31 (18%)	HR 1.40 (0.89 to 2.23) p = 0.15
Death or first admission for heart failure	n = 121 (45%)	n = 55 (31%)	HR 0.85 (0.61 to 1.17) p = 0.32
All-cause admissions	n = 554 1.51 events per patient-year	n = 218 1.32 events per patient-year	HR 0.87 (0.74 to 1.03) p = 0.10
Deaths and all-cause admissions	n = 604 1.65 events per patient-year	n = 249 1.61 events per patient-year	HR 0.97 (0.83 to 1.14) p = 0.75

Givertz et al., 2017

This study, derived from the previously described CHAMPION trial, reported the effectiveness of CardioMEMS™ in reducing the risk of hospitalization for heart failure or death among patients with reduced ejection fraction who were on at least one guideline-directed medical therapy at baseline. This analysis by baseline tolerance of angiotensin-converting enzyme inhibitor (ACEi)/angiotensin receptor blocker (ARB) and β-Blockers (BB) was not pre-specified. Of the 550 trial participants, 456 had a reduced LV ejection fraction (< 40%). Among patients with reduced EF, 445 patients were on either an ACEi/ARB or a BB at baseline (Group 1), and 337 patients were on ACEi/ARB and BB at baseline.

In the overall group of patients with reduced EF at mean follow-up of 18 months, the rate of hospitalization for heart failure was 0.49 events per patient-year in the experimental group and 0.69 events per patient-year in the control group (HR 0.72, 95% CI 0.59 to 0.88, p = 0.013), and death occurred in 17.6% of experimental group patients compared to 24.4% of the control group patients (HR 0.68, 95% CI 0.45 to 1.02, p = 0.06). Using a Cox proportional hazards model that accounted for changes in the doses of ACEi/ARB and BB, or nitrates and hydralazine, the hazard ratios for mortality were similar and remained statistically nonsignificant.

Among Group 1 patients (those on at least one ACEi/ARB or BB at baseline), the rate of hospitalization for heart failure was 0.45 per patient-year in the experimental group and 0.68 per patient-year in the control group (HR 0.67, 95% CI 0.54 to 0.82, p = 0.0002), and the all-cause mortality rate was 0.171 per patient-year in the control group and 0.107 per patient-year in the experimental group (HR 0.63, 95% CI 0.41 to 0.96, p = 0.0293). Among Group 2 patients (those on both an ACEi/ARB or BB at baseline), the

rate of hospitalization for heart failure was 0.69 per patient-year in the control group and 0.39 per patient-year in the experimental group (HR 0.57, 95% CI 0.45 to 0.73, p = 0.0002), and the all-cause mortality rate was 0.155 per patient-year in the control group and 0.067 per patient-year in the experimental group (HR 0.43, 95% CI 0.24 to 0.76, p = 0.0052). Using a Cox proportional hazards model that accounted for changes in the doses of ACEi/ARB and BB, or nitrates and hydralazine, the hazard ratios for mortality were similar and remained statistically significant.

Evidence Summary

There is low-quality evidence from a single, seriously flawed randomized controlled trial (RCT) that CardioMEMS™ reduces the risk of heart failure-related hospitalization in patients with NYHA Class III heart failure who have had a previous admission for heart failure. This finding was consistent in patients with both preserved and reduced LV function, but in the initial trial, this result was not significant among women. The evidence for a reduction in all-cause mortality, improved quality of life, and harms is very low because it is further limited by imprecision in the estimates. The trial was mainly limited by its single-blind design, manufacturer funding and involvement, and concerns (raised by an FDA advisory panel) related to the statistical analysis plan and improper communications between the sponsor and study investigators in the experimental group.

Policy Landscape

Payer Coverage Policies

Medicaid

No coverage policy for was identified for CardioMEMS™ for the Washington State Medicaid Program.

Medicare

No Medicare National Coverage Determinations were found for CardioMEMS™. One Local Coverage Determination (L36419) was found for CardioMEMS™, which considers this device investigational and non-covered unless in an approved clinical trial.

Private Payers

Coverage policies were searched for four private payers: Aetna, Cigna, Moda, and Regence. The Cigna policy (effective 10/15/2017) and the Regence policy (effective: 1/1/2018) do not cover CardioMEMS™. No coverage policies for CardioMEMS™ were found for Aetna or Moda.

Recommendations from Others

The 2017 Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment published by the American College of Cardiology summarized the evidence on CardioMEMS™ and then concluded: "This suggests that in well-selected patients with recurrent congestion, this highly specialized monitoring strategy may guide therapeutic decision making. The impact on mortality is unknown. A team-based approach may be necessary to best deploy this monitoring strategy" (Yancy et al., 2017, p. 215).

The poor-quality 2016 guidelines from the European Society of Cardiology on diagnosis and treatment of acute and chronic heart failure state that CardioMEMS™ could be considered in symptomatic heart failure patients who have had a previous hospitalization for heart failure (Ponikowski et al., 2016). The guidelines rate this recommendation as Class IIb, meaning that there is conflicting evidence or a divergence of opinion about the usefulness or efficacy of CardioMEMS™.

Quality Measures

No quality measures were identified when searching the National Quality Measures Clearinghouse for CardioMEMS or heart failure monitoring. The Clearinghouse lists a number of quality measures related to hospital admissions and health outcomes for patients with heart failure. One example of a measure, developed by CMS, is the 30-day risk-standardized mortality rate for patients discharged from the hospital with a principal diagnosis of heart failure (mortality defined as death from any cause within 30 days of the start of the index admission). Another measure developed by CMS is the 30-day risk-standardized hospital readmission rate for patients with heart failure. This measures unplanned hospital readmissions within 30 days of the original discharge date.

References

Evidence Sources

Abraham, W. T., Adamson, P. B., Bourge, R. C., Aaron, M. F., Costanzo, M. R., Stevenson, L. W., . . . Yadav, J. S. (2011). Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: A randomised controlled trial. *Lancet, 377*(9766), 658-666. doi: 10.1016/s0140-6736(11)60101-3

Abraham, W. T., Stevenson, L. W., Bourge, R. C., Lindenfeld, J. A., Bauman, J. G., & Adamson, P. B. (2016). Sustained efficacy of pulmonary artery pressure to guide adjustment of chronic heart failure therapy: Complete follow-up results from the CHAMPION randomised trial. *Lancet, 387*(10017), 453-461. doi: 10.1016/s0140-6736(15)00723-0

Adamson, P. B., Abraham, W. T., Bourge, R. C., Costanzo, M. R., Hasan, A., Yadav, C., . . . Stevenson, L. W. (2014). Wireless pulmonary artery pressure monitoring guides management to reduce decompensation in heart failure with preserved ejection fraction. *Circulation: Heart Failure, 7*(6), 935-944. doi: 10.1161/circheartfailure.113.001229

Adamson, P. B., Abraham, W. T., Stevenson, L. W., Desai, A. S., Lindenfeld, J. A., Bourge, R. C., & Bauman, J. (2016). Pulmonary artery pressure-guided heart failure management reduces 30-day readmissions. *Circulation: Heart Failure, 9*(6), e002600. doi: 10.1161/circheartfailure.115.002600

Givertz, M. M., Stevenson, L. W., Costanzo, M. R., Bourge, R. C., Bauman, J. G., Ginn, G., & Abraham, W. T. (2017). Pulmonary artery pressure-guided management of patients with heart failure and reduced ejection fraction. *Journal of the American College of Cardiology, 70*(15), 1875-1886. doi: 10.1016/j.jacc.2017.08.010

Other Citations

Abbott. (2018). *CardioMEMS™ HF System*. Retrieved from https://www.sjm.com/en/patients/heart-failure/our-solutions/pulmonary-artery-pressure-monitoring/cardiomems-hf-system/important-safety-information

American Heart Association. *High blood pressure guidelines*. Retrieved from http://www.heart.org/HEARTORG/Conditions/HeartFailure/Heart-Failure_UCM_002019_SubHomePage.jsp

Boccuti, C., & Casillas, G. Aiming for fewer hospital u-turns: The Medicare hospital readmission reduction program. Retrieved from https://www.kff.org/medicare/issue-brief/aiming-for-fewer-hospital-u-turns-the-medicare-hospital-readmission-reduction-program/

Bui, A. L., & Fonarow, G. C. (2012). Home monitoring of heart failure management. *Journal of the American College of Cardiology, 59*(2), 97-104. doi: 10.1016/j.jacc.2011.09.044

CardioMEMS, Inc. (2014). *CardioMEMS™ HF System: User's Manual*. Retrieved from: https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100045d.pdf

Centers for Disease Control and Prevention. (2016). *Heart failure fact sheet*. Retrieved from https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_heart_failure.htm

Heidenreich, P. A., Albert, N. M., Allen, L. A., Bluemke, D. A., Butler, J., Fonarow, G. C., . . . Trogdon, J. G. (2013). Forecasting the impact of heart failure in the United States: A policy statement from the American Heart Association. *Circulation: Heart Failure, 6*(3), 606-619. doi: 10.1161/HHF.0b013e318291329a

Loh, J. P., Barbash, I. M., & Waksman, R. (2013). Overview of the 2011 Food and Drug Administration Circulatory System Devices Panel of the Medical Devices Advisory Committee Meeting on the CardioMEMS Champion Heart Failure Monitoring System. *Journal of the American College of Cardiology, 61*(15), 1571-1576. doi: 10.1016/j.jacc.2012.08.1035

Mozaffarian, D., Benjamin, E. J., Go, A. S., Arnett, D. K., Blaha, M. J., Cushman, M., . . . Turner, M. B. (2016). Heart disease and stroke statistics--2016 update: A report from the American Heart Association. *Circulation, 133*(4), e38-360. doi: 10.1161/cir.0000000000000350

Ponikowski, P., Voors, A. A., Anker, S. D., Bueno, H., Cleland, J. G., Coats, A. J., . . . van der Meer, P. (2016). 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: The task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). *European Journal of Heart Failure, 18*(8), 891-975. doi: 10.1002/ejhf.592

U.S. Food and Drug Administration. (2014a). *Premarket approval (PMA)*. Retrieved from https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm?id=P100045

U.S. Food and Drug Administration. (2014b). S*ummary of safety and effectiveness data (SSED).* Retrieved from https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100045b.pdf

Yancy, C. W., Januzzi, J. L., Jr., Allen, L. A., Butler, J., Davis, L. L., Fonarow, G. C., . . . Wasserman, A. (2018). 2017 ACC expert consensus decision pathway for optimization of heart failure treatment: Answers to 10 pivotal issues about heart failure with reduced ejection fraction. *Journal of the American College of Cardiology, 71*(2), 201-30. doi: 10.1016/j.jacc.2017.11.025

Suggested citation: Obley, A., Mosbaek, C., King, V., & Livingston, C. (2018). *Coverage guidance: CardioMEMS™ for heart failure monitoring*. Portland, OR: Center for Evidence-based Policy, Oregon Health & Science University

Appendix A. GRADE Table Element Descriptions

Element	Description
Balance of benefits and harms	The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. An estimate that is not statistically significant or has a confidence interval crossing a predetermined clinical decision threshold will be downgraded.
Quality of evidence	The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted
Resource allocation	The higher the costs of an intervention—that is, the greater the resources consumed in the absence of likely cost offsets—the lower the likelihood that a strong recommendation is warranted
Values and preferences	The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted
Other considerations	Other considerations include issues about the implementation and operationalization of the technology or intervention in health systems and practices within Oregon.

Strong recommendation

In Favor: The subcommittee concludes that the desirable effects of adherence to a recommendation outweigh the undesirable effects, considering the balance of benefits and harms, resource allocation, values and preferences and other factors.

Against: The subcommittee concludes that the undesirable effects of adherence to a recommendation outweigh the desirable effects, considering the balance of benefits and harms, resource allocation, values and preferences and other factors.

Weak recommendation

In Favor: The subcommittee concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, considering the balance of benefits and harms, resource allocation, values and preferences and other factors., but further research or additional information could lead to a different conclusion.

Against: The subcommittee concludes that the undesirable effects of adherence to a recommendation probably outweigh the desirable effects, considering the balance of benefits and harms, cost and resource allocation, and values and preferences, but further research or additional information could lead to a different conclusion.

Confidence in estimate rating across studies for the intervention/outcome

Assessment of confidence in estimate includes factors such as risk of bias, precision, directness, consistency and publication bias.

High: The subcommittee is very confident that the true effect lies close to that of the estimate of the effect. Typical sets of studies are RCTs with few or no limitations and the estimate of effect is likely stable.

Moderate: The subcommittee is moderately confident in the estimate of effect: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Typical sets of studies are RCTs with some limitations or well-performed nonrandomized studies with additional strengths that guard against potential bias and have large estimates of effects.

Low: The subcommittee's confidence in the estimate of effect is limited: The true effect may be substantially different from the estimate of the effect. Typical sets of studies are RCTs with serious limitations or nonrandomized studies without special strengths.

Very low: The subcommittee has very little confidence in the estimate of effect: The true effect is likely to be substantially different from the estimate of effect. Typical sets of studies are nonrandomized studies with serious limitations or inconsistent results across studies.

Appendix B. GRADE Evidence Profile

No. of Studies	Study Design(s)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Factors	Quality
Quality Assessment (Confidence in Estimate of Effect)							
All-cause mortality							
1	RCT	High	N/A	None	Serious		Very low ●○○○
Cardiovascular mortality							
0	RCT	High	N/A	N/A	N/A		Insufficient evidence
Heart failure-related hospitalization							
1	RCT	High	N/A	None	Not serious		Low ●●○○
Quality of life							
1	RCT	High	N/A	None	Serious		Very low ●○○○
Harms							
1	RCT	High	N/A	None	Serious		Very low ●○○○

Appendix C. Methods

Scope Statement

Populations

Adults with chronic heart failure

Population scoping notes: None

Interventions

CardioMEMS™ heart failure monitoring system

Intervention exclusions: None

Comparators

Usual care (e.g., daily weight measurements, symptom reporting, frequent encounters), heart rate variability monitors, intrathoracic impedance monitors

Outcomes

Critical: All-cause mortality, cardiovascular mortality, heart failure-related hospitalizations

Important: Quality of life, harms

Considered but not selected for the GRADE table: None

Key Questions

KQ1: What is the comparative effectiveness of CardioMEMS™ for the management of patients with chronic systolic heart failure?

KQ2: How does the comparative effectiveness of CardioMEMS™ vary by:
  a. Age
  b. Gender
  c. Race/ethnicity
  d. Comorbid medical conditions
  e. Prior and current treatments
  f. Previous hospitalization for acute decompensated heart failure
  g. Heart failure etiology
  h. Preserved vs. reduced ejection fraction.
  i. Treatment setting (inpatient/outpatient)
  j. Patient adherence to prior treatment and monitoring plans
  k. New York Heart Association class/American College of Cardiology stage

KQ3: What are the harms of CardioMEMS™?

Search Strategy

A full search of the core sources was conducted to identify systematic reviews, meta-analyses, and technology assessments that meet the criteria for the scope described above. Searches of core sources were limited to citations published after 2010.

The following core sources were searched:

Agency for Healthcare Research and Quality (AHRQ)
Canadian Agency for Drugs and Technologies in Health (CADTH)
Cochrane Library (Wiley Online Library)
Institute for Clinical and Economic Review (ICER)
Medicaid Evidence-based Decisions Project (MED)
National Institute for Health and Care Excellence (NICE)
Tufts Cost-effectiveness Analysis Registry
Veterans Administration Evidence-based Synthesis Program (ESP)
Washington State Health Technology Assessment Program

A MEDLINE® search was also conducted to identify systematic reviews, meta-analyses, and technology assessments, using the search terms for CardioMEMS. The search was limited to publications in English published since 2010. In addition, a MEDLINE® search was conducted for randomized controlled trials published since 2010.

Searches for clinical practice guidelines were limited to those published since 2010. A search for relevant clinical practice guidelines was also conducted using MEDLINE® and the following sources:

Australian Government National Health and Medical Research Council (NHMRC)
Canadian Agency for Drugs and Technologies in Health (CADTH)
Centers for Disease Control and Prevention (CDC), Community Preventive Services
National Guidelines Clearinghouse
National Institute for Health and Care Excellence (NICE)
Scottish Intercollegiate Guidelines Network (SIGN)
United States Preventive Services Task Force (USPSTF)
Veterans Administration/Department of Defense (VA/DoD) Clinical Practice Guidelines

Inclusion/Exclusion Criteria

Studies were excluded if they were not published in English, did not address the scope statement, or were study designs other than systematic reviews, meta-analyses, technology assessments, randomized controlled trials, or clinical practice guidelines.

Appendix D. Applicable Codes

CODES	DESCRIPTION
CPT Codes	
93451	Right heart catheterization including measurement(s) of oxygen saturation and cardiac output, when performed
93568	Injection procedure during cardiac catheterization including imaging supervision, interpretation, and report; for pulmonary angiography (List separately in addition to code for primary procedure)
93799	Unlisted cardiovascular service or procedure
93297	Interrogation device evaluation(s), (remote) up to 30 days; implantable cardiovascular monitor system, including analysis of 1 or more recorded physiologic cardiovascular data elements from all internal and external sensors, analysis, review(s) and report(s) by a physician or other qualified health care professional
93299	Interrogation device evaluation(s), (remote) up to 30 days; implantable loop recorder system, including analysis of recorded heart rhythm data, analysis, review(s) and report(s) by a physician or other qualified health care professional
HCPCS Level II Codes	
C9741	Right heart catheterization with implantation of wireless pressure sensor in the pulmonary artery, including any type of measurement, angiography, imaging supervision, interpretation, and report
C2624	Implantable wireless pulmonary artery pressure sensor with delivery catheter, including all system components

Note: Inclusion on this list does not guarantee coverage.