Medical Policy

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Title: Cardiac Hemodynamic Monitoring for the Management of Heart Failure in the Outpatient Setting

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Populations	Interventions	Comparators	Outcomes
Individuals: • With heart failure in outpatient settings	Interventions of interest are: • Hemodynamic monitoring with an implantable pulmonary artery pressure sensor device	Comparators of interest are: • Usual care without hemodynamic monitoring	Relevant outcomes include: • Overall survival • Symptoms • Functional outcomes • Quality of life • Morbid events • Hospitalizations • Treatment-related morbidity
Individuals: • With heart failure in	Interventions of interest are:	Comparators of interest are:	Relevant outcomes include: • Overall survival • Symptoms

Populations	Interventions	Comparators	Outcomes
outpatient settings	• Hemodynamic monitoring by thoracic bioimpedance	• Usual care without hemodynamic monitoring	• Functional outcomes • Quality of life • Morbid events • Hospitalizations • Treatment-related morbidity
Individuals: • With heart failure in outpatient settings	Interventions of interest are: • Hemodynamic monitoring with inert gas rebreathing	Comparators of interest are: • Usual care without hemodynamic monitoring	Relevant outcomes include: • Overall survival • Symptoms • Functional outcomes • Quality of life • Morbid events • Hospitalizations • Treatment-related morbidity
Individuals: • With heart failure in outpatient settings	Interventions of interest are: • Hemodynamic monitoring of arterial pressure during the Valsalva maneuver	Comparators of interest are: • Usual care without hemodynamic monitoring	Relevant outcomes include: • Overall survival • Symptoms • Functional outcomes • Quality of life • Morbid events • Hospitalizations • Treatment-related morbidity

DESCRIPTION

A variety of outpatient cardiac hemodynamic monitoring devices are intended to improve quality of life and reduce morbidity for patients with heart failure by decreasing episodes of acute decompensation. Monitors can identify physiologic changes that precede clinical symptoms and thus allow preventive intervention. These devices operate through various mechanisms, including implantable pressure sensors, thoracic bioimpedance measurement, inert gas rebreathing, and estimation of left ventricular end-diastolic pressure by arterial pressure during the Valsalva maneuver.

OBJECTIVE

The objective of this evidence review is to determine whether outpatient hemodynamic monitoring improves the net health outcome in individuals with heart failure.

BACKGROUND

Chronic Heart Failure

Patients with chronic heart failure are at risk of developing acute decompensated heart failure, often requiring hospital admission. Patients with a history of acute decompensation have the additional risk of future episodes of decompensation and death. Reasons for the transition from a stable, chronic state to an acute, decompensated state include disease progression, as well as

acute events such as coronary ischemia and dysrhythmias. While precipitating factors are frequently not identified, the most common preventable cause is noncompliance with medication and dietary regimens.[1,]

Management

Strategies for reducing decompensation, and thus the need for hospitalization, are aimed at early identification of patients at risk for imminent decompensation. Programs for early identification of heart failure are characterized by frequent contact with patients to review signs and symptoms with a health care provider, education, and medication adjustments as appropriate. These encounters may occur face-to-face in the office or at home, or via cellular or computed technology.[2,]

Precise measurement of cardiac hemodynamics is often employed in the intensive care setting to carefully manage fluid status in acutely decompensated heart failure. Transthoracic echocardiography, transesophageal echocardiography, and Doppler ultrasound are noninvasive methods for monitoring cardiac output on an intermittent basis for the more stable patient but are not addressed herein. A variety of biomarkers and radiologic techniques may be used for dyspnea when the diagnosis of acute decompensated heart failure is uncertain.

The criterion standard for hemodynamic monitoring is pulmonary artery catheters and central venous pressure catheters. However, they are invasive, inaccurate, and inconsistent in predicting fluid responsiveness. Several studies have demonstrated that catheters fail to improve outcomes in critically ill patients and may be associated with harm. To overcome these limitations, multiple techniques and devices have been developed that use complex imaging technology and computer algorithms to estimate fluid responsiveness, volume status, cardiac output and tissue perfusion. Many are intended for use in outpatient settings but can be used in the emergency department, intensive care unit, and operating room. Four methods are reviewed here: implantable pressure monitoring devices, thoracic bioimpedance, inert gas rebreathing, and arterial waveform during the Valsalva maneuver. Use of the last 3 is not widespread because of several limitations including use of proprietary technology making it difficult to confirm their validity and lack of large randomized controlled trials to evaluate treatment decisions guided by these hemodynamic monitors.

REGULATORY STATUS

Noninvasive Left Ventricular End-Diastolic Pressure Measurement Devices

In 2004, the VeriCor® (CVP Diagnostics), a noninvasive left ventricular end-diastolic pressure measurement device, was cleared for marketing by U.S. Food and Drug Administration (FDA) through the 510(k) process. The FDA determined that this device was substantially equivalent to existing devices for the following indication:

"The VeriCor is indicated for use in estimating non-invasively, left ventricular end-diastolic pressure (LVEDP). This estimate, when used along with clinical signs and symptoms and other patient test results, including weights on a daily basis, can aid the clinician in the selection of further diagnostic tests in the process of reaching a diagnosis and formulating a therapeutic plan when abnormalities of intravascular volume are suspected. The device has been clinically validated in males only. Use of the device in females has not been investigated."

FDA product code: DXN.

Thoracic Bioimpedance Devices
Multiple thoracic impedance measurement devices that do not require invasive placement have been cleared for marketing by the FDA through the 510(k) process. The FDA determined that this device was substantially equivalent to existing devices used for peripheral blood flow monitoring. Table 1 presents an inexhaustive list of representative devices (FDA product code: DSB).

Table 1. Noninvasive Thoracic Impedance Plethysmography Devices

Device	Manufacturer	Clearance Date
BioZ® Thoracic Impedance Plethysmograph	SonoSite	2009
Zoe® Fluid Status Monitor	Noninvasive Medical Technologies	2004
Cheetah Starling SV	Cheetah Medical	2008
PhysioFlow® Signal Morphology-based Impedance Cardiography (SM-ICG™)	Vasocom, now NeuMeDx	2008
ReDS™ Wearable System	Sensible Medical Innovations	2015

Also, several manufacturers market thoracic impedance measurement devices integrated into implantable cardiac pacemakers, cardioverter defibrillator devices, and cardiac resynchronization therapy devices. Thoracic bioimpedance devices integrated into implantable cardiac devices are not addressed in this evidence review.

Inert Gas Rebreathing Devices
In 2006, the Innocor® (Innovision), an inert gas rebreathing device, was cleared for marketing by the FDA through the 510(k) process. The FDA determined that this device was substantially equivalent to existing inert gas rebreathing devices for use in computing blood flow. FDA product code: BZG.

Implantable Pulmonary Artery Pressure Sensor Devices
In 2014, the CardioMEMS™ Heart Failure Monitoring System (CardioMEMS, now Abbott) was approved for marketing by the FDA through the premarket approval process. This device consists of an implantable pulmonary artery (PA) sensor, which is implanted in the distal PA, a transvenous delivery system, and an electronic sensor that processes signals from the implantable PA sensor and transmits PA pressure measurements to a secure database.[3,] The device originally underwent FDA review in 2011, at which point FDA found no reasonable assurance that the monitoring system would be effective, particularly in certain subpopulations, although the FDA agreed this monitoring system was safe for use in the indicated patient population.[4,]In 2022, the CardioMEMS™ HF Monitoring System received expanded approval for the treatment of New York Heart Association (NYHA) Class II-III patients who had been hospitalized at least 1 time in the prior year and/or had elevated natriuretic peptides.

Several other devices that monitor cardiac output by measuring pressure changes in the PA or right ventricular outflow tract have been investigated in the research setting but have not received the FDA approval. They include the Chronicle® implantable continuous hemodynamic

monitoring device (Medtronic), which includes a sensor implanted in the right ventricular outflow tract, and the ImPressure® device (Remon Medical Technologies), which includes a sensor implanted in the PA.

Note: This evidence review only addresses the use of these technologies in ambulatory care and outpatient settings.

POLICY

In the ambulatory care and outpatient setting, cardiac hemodynamic monitoring for the management of heart failure using implantable direct pressure monitoring of the pulmonary artery, thoracic bioimpedance, inert gas rebreathing, and arterial pressure during the Valsalva maneuver is considered **experimental / investigational**.

POLICY GUIDELINES

This policy refers only to the use of stand-alone cardiac output measurement devices designed for use in ambulatory care and outpatient settings. The use of cardiac hemodynamic monitors or intrathoracic fluid monitors that are integrated into other implantable cardiac devices, including implantable cardioverter defibrillators, cardiac resynchronization therapy devices, and cardiac pacing devices, are not addressed in this evidence review.

Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

RATIONALE

This evidence review has been updated regularly with searches of the PubMed database. The most recent literature update was performed through. May 2, 2022.

For the first indication, because there is direct evidence from a large randomized controlled trial (RCT), we focus on it and assess the evidence it provides on clinical utility. Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The RCT is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

For indications 2, 3, and 4, we assess the evidence as a medical test. Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and

harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.

IMPLANTABLE PULMONARY ARTERY PRESSURE MONITORING

(CARDIOMEMS DEVICE)

Clinical Context and Therapy Purpose

The purpose of the CardioMEMS system in patients who have heart failure is to provide remote monitoring of pulmonary artery pressure to inform therapy modification and prevent or reduce hospitalization. Studies on the safety and/or efficacy of the CardioMEMS system consist of 2 RCTs (CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA III Heart Failure Patients [CHAMPION], Hemodynamic GUIDEd Management of Heart Failure [GUIDE-HF]) and several nonrandomized studies featuring pre-post, matched cohort comparative, and post market surveillance analyses.

The question addressed in this evidence review is: Does the use of an implantable pulmonary artery sensor device (CardioMEMS) improve net health outcomes in individuals with heart failure in the outpatient setting?

The following PICO was used to select literature to inform this review.

Populations

The relevant population(s) of interest is patients with New York Heart Association (NYHA) Class II-IV heart failure who have had a hospitalization in the past year and/or have elevated natriuretic peptides.

Interventions

Left ventricular end-diastolic pressure (LVEDP) can be approximated by direct pressure measurement of an implantable sensor in the pulmonary artery wall or right ventricular outflow tract. The sensor is implanted via right heart catheterization and transmits pressure readings wirelessly to external monitors. One device, the CardioMEMS Heart Failure Monitoring System, has approval from the U.S. Food and Drug Administration (FDA) for the ambulatory management of heart failure patients. The CardioMEMS device is implanted using a heart catheter system fed through the femoral vein and generally requires patients to have an overnight hospital admission for observation after implantation. Specific target pressure ranges provided to investigators to achieve hemodynamic stability included 10-25 mmHg for mean pulmonary artery pressure, 14-35 mmHg for systolic pressure, and 8-20 mmHg for diastolic pressure. An elevation or decrease in pulmonary artery pressure outside of a patient's individualized baseline was considered to arise from overload or depletion, respectively.

Comparators

The comparator of interest is standard clinical care without hemodynamic testing. Treatment decisions, such as medication adjustments or hospitalization, are made based on changes in clinical signs (e.g., body weight, blood pressure, laboratory parameters) and symptoms (e.g., dyspnea, fatigue, exercise intolerance) without measurement of pulmonary artery pressure.

Outcomes

The International Consortium for Health Outcomes Measurement has identified 3 domains of outcomes for a standard outcome set for patients with heart failure.[5,]

- Survival and disease control (i.e., mortality)
- Functioning and disease control (i.e., symptom control including dyspnea, fatigue and tiredness, disturbed sleep, and peripheral edema, activities of daily living including health-related quality of life, maximum physical exertion, independence and psychosocial health including depression and anxiety, confidence and self-esteem)
- Burden of care to patient (i.e., hospital visits including admissions and appointments, treatment side effects, complications)

The Heart Failure Association of the European Society of Cardiology has published a consensus document on heart failure outcomes in clinical trials.[6,] They likewise categorize important outcomes for clinical trials as mortality outcomes (all-cause and cause-specific), morbidity and clinical composites (including hospitalizations, worsening of heart failure, implantable cardioverter device shocks) and symptoms and patient-reported outcomes. The consensus document recommends that hospitalization for heart failure be defined as a hospitalization requiring at least an overnight stay caused by substantive worsening of symptoms and/or signs requiring augmentation of therapy.

Measurements of maximal oxygen consumption during exercise, the 6-minute hall walk test (6MHW), stair climb test, Short Physical Performance Battery or hand-grip strength are functional measures.

Patient-reported outcome measures may include the Kansas City Cardiomyopathy Questionnaire (KCCQ-12), the Minnesota Living with Heart Failure Questionnaire (MLHFQ), and the EuroQol 5-Dimension, 5-Level (EQ-5D-5L) Questionnaire.

Generally, demonstration of outcomes over a 1-year period is meaningful to assess outcomes for the intervention.

Study Selection Criteria

Methodologically credible studies were selected using the following principles.

- Comparative controlled prospective trials were sought, with a preference for RCTs.
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations will be considered.
- Larger sample size studies and longer duration studies are preferred.
- Studies with duplicative or overlapping populations were excluded.

Post-hoc and/or exploratory subgroup analyses of the CHAMPION trial in patients with reduced ejection fraction,[7,] preserved ejection fraction,[8,] Medicare-eligible patients,[9,] and chronic obstructive pulmonary disease[10,] are outside of the scope of this review and are therefore not discussed. Studies reporting physiological measures in the absence of clinical outcomes were also excluded.[11,]

REVIEW OF EVIDENCE

RANDOMIZED CONTROLLED TRIALS

CHAMPION

Abraham et al (2011, 2016) reported on the results of CHAMPION, a single-blind RCT enrolling patients with NYHA Class III heart failure who have had a hospitalization in the prior year. All enrolled patients were implanted with the CardioMEMS device.[12,13,] Patients were randomized to the CardioMEMS group, in which daily uploaded pulmonary artery pressures were used to guide medical therapy, or to the control group, in which investigators were blinded to daily uploaded pressures and managed patients based on clinical signs and symptoms.. An independent clinical endpoints classification (CEC) committee, blinded to the treatment groups, reviewed abstracted clinical data and determined if hospitalization was related to heart failure. It is unclear what criteria were used for adjudication of heart failure hospitalizations.[14,]

The randomized phase ended when the last patient enrolled completed at least 6 months of study follow-up (average, 18 months) and was followed in an open-access phase during which investigators had access to pulmonary artery pressure for all patients (former control and treatment group). Trial characteristics and results are summarized in Tables 2 through 4. The trial met its primary efficacy endpoint, with a statistically significant 28% relative reduction in the rate of heart failure-related hospitalizations (HFH) at 6 months. This outcome was accompanied by a significant improvement in Minnesota Living with Heart Failure Questionnaire scores at 6 and 12 months. No significant reduction in mortality was observed at 6 months or at the conclusion of the randomized phase. However, members of the FDA advisory committee in 2011 were unable to distinguish the effect of the device on HFH from the effect of nurse communications in cases where the investigator did not document a medication change in response to an abnormal pulmonary artery pressure elevation. Therefore, the FDA denied the initial approval of CardioMEMS and requested additional clarification from the manufacturer.[3,] Subsequently, the FDA held a second advisory committee meeting in 2013 to review additional data (including open-access phase) and address previous concerns related to the impact of nurse communication on the CHAMPION trial.[15,16,] Post-hoc analyses to address the impact of nurse interventions on HFH conducted by the sponsor were judged to have methodologic limitations by the FDA.[3,] However, the FDA stated that longitudinal analyses, such as those demonstrating a significant decrease in HFH when former control patients entered the treatment arm of the open-access phase, were the most useful regarding support for device effectiveness. It is important to acknowledge that all such analyses were conducted with the intent to test the robustness of potentially biased RCT results; therefore, results from these analyses should be evaluated to assess consistency and not as an independent source of evidence to support efficacy. Additional trial aspects limit the interpretation of these analyses; notably, subject dropouts were not random, and patient risk profiles could have changed from the randomized phase to the open-access phase. In the open-access phase, 93 (34%) of 270 subjects in the treatment group and 110 (39%) of 280 subjects in the control group remained in the analysis.

Importantly, the CHAMPION trial failed to demonstrate a treatment effect in women. According to FDA documents, the apparent lack of reduction in HFH in women resulted from a greater number of deaths among women in the control group early in the trial, and this early mortality resulted in a competing risk for future HFH. While both the FDA and sponsor conducted multiple analyses to understand device effectiveness in women, the FDA statisticians concluded that such analyses did clearly delineate the limited treatment effect in women.[15,] However, the overall reduction in HFH subsequently observed in the CardioMEMS post-approval study (see Tables 7 and 8) was also observed in the subgroup analysis of women, which comprised 37.7% of the study population.[17,18,]

GUIDE-HF

Lindenfeld et al (2021) reported on the results of the Hemodynamic GUIDEd Management of Heart Failure trial (GUIDE-HF), a single-blind RCT in which all patients were implanted with the CardioMEMS device.[19,] As in the CHAMPION trial, patients were randomized to control and treatment groups in which investigators were blinded or unblinded, respectively, to pulmonary artery pressures uploaded daily by all patients. The GUIDE-HF trial expanded enrollment to patients with NYHA Class II-IV heart failure with a hospitalization in the prior year and/or elevated natriuretic peptides. Patient management was composed of 2 phases: (1) an optimization phase through 3 months post-implantation and (2) a maintenance phase. The optimization phase required clinicians to monitor and manage patients more closely to optimize pulmonary artery pressures to an individualized target range, while the maintenance phase focused on maintaining optimal pulmonary artery pressures. Generally, a 3-5 mmHg persistent pressure change over 2-3 days or a change of 5 mmHg in a single day were recommended as actionable deviations. Blinded trial personnel were instructed to contact subjects with scripted language provided by unblinded study coordinators at least once every 2 weeks during the optimization phase and at least monthly during the maintenance phase. Efforts were made to balance the frequency of site-initiated communications.

Trial characteristics and results are summarized in Tables 2 through 4. The GUIDE-HF trial failed to meet its overall primary efficacy endpoint, finding a statistically insignificant 12% reduction in the composite of HFH (>24 h due to acute decompensation and requiring administration of intravenous diuretics), urgent heart failure visits (i.e., unscheduled or unplanned admission to the emergency department, hospital outpatient observation visit, or hospital inpatient visit (<24 h) due to acute decompensation and requiring administration of intravenous diuretics), and all-cause mortality at 12 months post-implantation. An independent CEC committee adjudicated all endpoints contributing to the primary outcome to confirm that they were heart failure-related. No significant improvements in individual components of the primary outcome or secondary efficacy endpoints were observed in GUIDE-HF. Subgroup analyses for the primary endpoint found a reduced treatment effect in patients with NYHA Class IV heart failure and men. The more favorable treatment effect in women observed in GUIDE-HF is inconsistent with results from the CHAMPION trial which found limited benefit. Overall, fewer patients were receiving primary classes of guideline-directed medical therapy at 12 months in both treatment and control groups. A significantly higher reduction in mean pulmonary artery pressure was observed in the treatment group; however, it is unclear whether the proportion of patients meeting target pressure ranges improved and whether absolute reductions were clinically meaningful.

With approval from the FDA in August 2020, the statistical analysis plan was updated to include sensitivity analyses with a 15% interaction significance level to evaluate the possible impact of the COVID-19 pandemic. Results of overall, pre-COVID-19, and during-COVID-19 analyses are summarized in Table 3. All patients were enrolled for at least 3 months and 71.7% of follow up occurred before the US national emergency declaration date of March 13, 2020. The CEC committee determined that there were 7 events related or possibly related to COVID-19; all occurring in the control group. Planned sensitivity analyses based on the timing of the COVID-19 pandemic included evaluation of primary endpoint events observed for subjects completing study participation prior to the pandemic and for subject follow-up occurring prior to the pandemic. The pre-COVID-19 impact analysis based on subject follow-up suggested an effect of COVID-19 on the primary endpoint (p=.11). A significant 19% reduction (p=.049) in the primary endpoint was found, driven by a 28% reduction in HFH (p=.0072). No significant improvements in heart failure visits, mortality, or secondary efficacy outcomes were observed. Additional analysis of patient data obtained during the COVID-19 pandemic as subsequently reported by Zile et al (2022)[20,] failed to find a significant reduction in the composite outcome and its individual components. Study authors noted that this was driven by an unexpected reduction in the primary event rate in the control group, potentially due to patient-dependent factors.

Study relevance, design, and conduct limitations are summarized in Tables 5 and 6. Lifestyle changes during the pandemic such as changes in physical activity, exposure to infections, willingness to seek medical care, and adherence to medications are unmeasured and add imprecision to treatment effect estimates. During COVID-19, the monthly rate of medication changes fell by 19.2% in the treatment group and 10.7% in the control group. This was accompanied by a deintensification of medication management (i.e., decreased ratio of dosage increases to decreases) by 8.8% and 17.4% in the treatment and control groups, respectively. The number of site-initiated (blinded) and overall contacts was similar pre- and during-COVID-19 after exclusion of contacts occurring in the initial 90-day optimization phase. The final 500 trial subjects enrolled had a significantly higher proportion of NYHA Class III-IV heart failure as enrollment of subjects with NYHA Class II heart failure was limited to 300 patients. Reductions in mean pulmonary artery pressure were not significantly different between groups during COVID-19 and it is unclear what proportion of medication changes were concordant with deviations in hemodynamic data over the course of the trial.

Table 2. Summary of Key RCT Characteristics

Author; Trial	**Countries**	**Sites**	**Dates**	**Participants**	**Interventions**	
					Active	*Comparator*
Abraham et al (2011, 2016);[12,13,] CHAMPION	U.S.	64	2007-2010	Main Eligibility Criteria: At least 1 previous HFH in the past 12 mo and NYHA class III HF for at least 3 mo Patient Baseline Characteristics: • Sex: 72.5%	Disease management by daily measurement of pulmonary artery pressures (via CardioMEMS) plus standard of care (n=270)	Disease management by standard of care alone (n=280)

Author; Trial	Countries	Sites	Dates	Participants	Interventions	
				male, 27.5% female • Mean Age: ~61 y • Race: 72.9% White, NR Black • NYHA Class: 100% III • Mean PAP: ~29-30 mmHg • HFpEF: 21.6%		
Lindenfeld et al (2021);[19,] Zile et al (2022);[20,] GUIDE-HF	U.S.	139	2018-2021	Main Eligibility Criteria: NYHA Class II-IV HF and at least 1 previous HFH in the past 12 mo or elevated natriuretic peptides within prior 30 days Patient Baseline Characteristics: • Sex: 62.5% male, 37.5% female • Mean Age: ~70-71 y • Race: 80.7% White, 17.9% Black • NYHA Class: 29.6% II, 65%	Disease management by daily measurement of pulmonary artery pressures (via CardioMEMS) plus standard of care (n=497)	Disease management by standard of care alone (n=503)

Author; Trial	Countries	Sites	Dates	Participants	Interventions	
				III, 5.4% IV • Mean PAP: ~28-29 mmHg		

CHAMPION: CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA III Heart Failure Patients trial; GUIDE-HF: Hemodynamic GUIDEd Management of Heart Failure trial; HF: heart failure; HFH: heart failure hospitalization; NR: not reported; NYHA: New York Heart Association; PAP: pulmonary artery pressure; RCT: randomized controlled trial.

Table 3. Summary of Key RCT Results: Main Safety and Efficacy Outcomes

Trial	N	HFH, Urgent HF Events, and Death, N (events/patient-time)	HFH, N (events/patient-time)	Urgent HF Visits, N (events/patient-time)	Death, N (%) or N (events/patient-time)	Device- or System-Related Complications, N (%)	Pressure-Sensor Failures, N (%)
Abraham et al (2011, 2016); CHAMPION [12,13,]							
At 6 months							
CardioMEMS	270	NA	84 (0.32)	NA	15 (5.6%)	3 (1)	0 (0)
Control	280	NA	120 (0.44)	NA	20 (7.1%)	3 (1)	0 (0)
HR (95% CI); p-value		NA	0.72 (0.60 to 0.85);[a] .002	NA	NR	NA	NA
At 12 months							
CardioMEMS	270	NA	182 (0.46)	NA	50 (19%)	3 (1)	0 (0)
Control	280	NA	279 (0.68)	NA	64 (23%)	3 (1)	0 (0)
HR (95% CI); p-value		NA	0.67 (0.55 to 0.80); <.0001	NA	0.80 (0.55 to 1.15); 0.23	NA	NA
Lindenfeld et al (2021); Zile et al							

Trial	N	HFH, Urgent HF Events, and Death, N (events/patient-time)	HFH, N (events/patient-time)	Urgent HF Visits, N (events/patient-time)	Death, N (%) or N (events/patient-time)	Device- or System-Related Complications, N (%)	Pressure-Sensor Failures, N (%)
(2022); GUIDE-HF[19,20,]							
At 12 Months							
Overall Analysis							
CardioMEMS	497	253 (0.563)	185 (0.410)	28 (0.065)	40 (0.094)	3 (0.6)	NA
Control	503	289 (0.640)	225 (0.497)	27 (0.063)	37 (0.086)	5 (1)	NA
HR (95% CI); p-value		0.88 (0.74 to 1.05);[b] .16	0.83 (0.68 to 1.01); .064	1.04 (0.61 to 1.77); .89	1.09 (0.70 to 1.70); 0.71	NA	NA
Pre-COVID-19 Impact Analysis							
CardioMEMS	497	177 (0.553)	124 (0.380)	23 (0.074)	30 (0.110)	NR	NA
Control	503	224 (0.682)	176 (0.525)	23 (0.073)	25 (0.088)	NR	NA
HR (95% CI); p-value		0.81 (0.66 to 1.00); .049	0.72 (0.57 to 0.92); .0072	1.02 (0.57 to 1.82); 0.95	1.24 (0.73 to 2.11); 0.42	NR	NA
During-COVID-19 Impact Analysis							
CardioMEMS	310	76 (0.597)	61 (0.490)	5 (0.048)	10 (0.067)	NR	NA
Control	307	65 (0.536)	49 (0.414)	4 (0.041)	12 (0.085)	NR	NA
HR (95% CI); p-value		1.11 (0.80 to 1.55); .53	1.18 (0.81 to 1.73); .38	1.19 (0.82 to 1.70); .80	0.79 (0.35 to 1.83); .59	NR	NA

CHAMPION: CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA III Heart Failure Patients trial; COVID: coronavirus disease; GUIDE-HF: Hemodynamic GUIDEd Management of Heart Failure trial; HF: heart failure; HFH: heart failure hospitalization; HR: hazard ratio; NA: not applicable; NR: not reported; RCT: randomized controlled trial.

[a] Primary efficacy outcome in CHAMPION trial.
[b] Primary efficacy outcome in GUIDE-HF trial.

Table 4. Summary of Key RCT Results: Secondary Outcomes

Trial	N	MLHFQ[a]	KCCQ-12[b]	EQ-5D-5L VAS[c]	6MHW Test Distance	Mean PAP Change from Baseline	Medication Changes
Abraham et al (2011, 2016); CHAMPION[12,13,]							
At 6 Months		Mean (SD)				Mean AUC Change, mmHg x days (SD)	Mean (SD)
CardioMEMS	270	45 (26)	NA	NA	NA	-156 (NR)	9.1 (7.4)
Control	280	51 (25)	NA	NA	NA	33 (NR)	3.8 (4.5)
p-value		p=.02	NA	NA	NA	p=.008	p<.0001
At 12 Months		Mean (SD)					
CardioMEMS	270	47.0 (NR)	NA	NA	NA	NR	NR
Control	280	56.5 (NR)	NA	NA	NA	NR	NR
p-value		p=.0267	NA	NA	NA	NR	NR
Lindenfeld et al (2021); Zile et al (2022); GUIDE-HF[19,20,]							
At 12 Months							
Overall Analysis			Mean Change from Baseline (SD)	Mean Change from Baseline (SD)	Mean Change from Baseline, m (SD)	Mean AUC Change, mmHg x days (SD)	Mean Changes/Month Per Patient (SD)
CardioMEMS	497	NA	5.20 (21.35) (n=421)	0.94 (20.17) (n=421)	-12.83 (100.08) (n=288)	-792.7 (1767.0)	1.031 (NR)
Control	503	NA	4.12 (22.50) (n=408)	2.90 (20.71) (N=409)	-6.46 (106.57) (n=291)	-582.9 (1698.1)	0.608 (NR)
p-value		NA	p=.48	p=.17	p=.46	p=.040	NR

Trial	N	MLHFQ[a]	KCCQ-12[b]	EQ-5D-5L VAS[c]	6MHW Test Distance	Mean PAP Change from Baseline	Medication Changes
Pre-COVID-19 Impact Analysis							
CardioMEMS	497	NA	4.19 (18.29) (n=140)	-1.28 (20.18) (n=140)	-19.46 (87.63) (n=120)	-518.0 (1327.0)	0.835 (NR)
Control	503	NA	5.05 (22.10) (n=137)	3.89 (17.73) (n=138)	-9.78 (112.70) (n=127)	-324.2 (1328.5)	0.475 (NR)
p-value		NA	p=.72	p=.024	p=.45	p=.014	p<.001

6MHW: 6 minute Hall Walk; AUC: area under the curve; CHAMPION: CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA III Heart Failure Patients trial; COVID: coronavirus disease; EQ-5D-5L VAS: EuroQOL 5-dimension 5-level Visual Analog Scale questionnaire; GUIDE-HF: Hemodynamic GUIDEd Management of Heart Failure trial; kCCQ-12: Kansas MLHFQ: Minnesota Living with Heart Failure Questionnaire; NA: not applicable; NR: not reported; RCT: randomized controlled trial; SD: standard deviation.
[a] Higher scores (range, 0-105) indicate more significant impairment in health-related quality of life.
[b] Higher scores (range, 0-100) indicate better health status.
[c] Higher scores (range, 0-100) indicate better health status.
[d] Increased distances indicate improved functional capacity.
Tables 5 and 6 display notable limitations identified in each study.

Table 5. Study Relevance Limitations

Trial	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Abraham et al (2011, 2016); CHAMPION[12,13,]		3. Delivery not similar intensity as comparator. Treatment group received additional nurse communication for enhanced protocol compliance.		5. Criteria for adjudication of heart failure hospitalizations unclear.	
Lindenfeld et al (2021); Zile et al (2022); GUIDE-HF[19,20,]		3. Unclear whether patient contacts were balanced during study optimization phase.			

CHAMPION: CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA III Heart Failure Patients trial; GUIDE-HF: Hemodynamic GUIDEd Management of Heart Failure trial.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No

CONSORT reporting of harms; 4. Not established and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 6. Study Design and Conduct Limitations

Trial	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Abraham (2011, 2016);CHAMPION[12,13,]		1. Physicians not blinded to treatment assignment but outcome adjudication (heart failure-relatedness) was independent and blinded.				
Lindenfeld et al (2021); Zile et al (2022); GUIDE-HF[19,20,]	4. COVID-19 impact analyses limited due to potential selection bias. Pre-COVID-19 analysis was enriched with patients with NYHA Class II HF.	1. Physicians not blinded to treatment assignment but outcome adjudication was independent and blinded.		1. High loss to follow-up or missing data for secondary outcomes.		5. The impact of COVID-19 on treatment effect estimates is uncertain. COVID-19-related sources of bias and imprecision may include patient lifestyle changes and altered provider behaviors.

CHAMPION: CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA III Heart Failure Patients trial; COVID: coronavirus disease; GUIDE-HF: Hemodynamic GUIDEd Management of Heart Failure trial; HF: heart failure; NYHA: New York Heart Association.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on

clinically important difference.
[f] Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated; 5. Other.

Nonrandomized Studies

As previously described in the selection criteria, studies will be included here to assess long-term outcomes and adverse effects if they capture longer periods of follow-up and/or larger populations than the RCTs. Nonrandomized studies have featured pre-post, retrospective matched cohort, and post-market surveillance analyses. Key nonrandomized study characteristics and results are summarized in Tables 7 and 8. Nonrandomized study relevance, design, and conduct limitations are summarized in Tables 9 and 10.

Cowie et al (2021) published 1-year outcomes from the prospective, international, multicenter, open-label CardioMEMS HF System for Post-Market Study (COAST).[21,] The study was designed to evaluate the safety, feasibility, and effectiveness of hemodynamic-guided heart failure management in patients with NYHA Class III heart failure in the UK, Europe, and Australia. The current report focuses on initial results from COAST-UK, which evaluated the first 100 patients who completed all follow-up in the UK before the COVID-19 pandemic emergency declaration date. The primary efficacy outcome was the change in the annualized HFH rate during the 12 months prior to implantation compared with 12 months after implantation. All clinical events were adjudicated by investigators responsible for the treatment. There were 165 HFH events (1.52 events/patient-year) before implant and 27 HFH events (0.27 events/patient-year) after implant, resulting in a significant 82% risk reduction (hazard ratio [HR], 0.178; 95% confidence interval [CI], 0.12 to 028; p<.0001). No significant improvements in EQ-5D-5L scores were observed at 6- or 12-month time points. Over 12 months, functional class improvements were noted for 41 patients reclassified as NYHA Class II and 3 patients reclassified as Class I. The primary safety endpoints of freedom from device- and system-related complications and freedom from pressure sensor failures at 2 years occurred in 100% and 99% of patients, respectively, exceeding pre-specified performance goals of 80% and 90%, respectively.

Shavelle et al (2020) reported 1-year outcomes from the open-label, observational, single-arm, post-approval study of CardioMEMS in 1200 patients (37.7% female) across 104 centers in the U.S. with NYHA Class III heart failure and a HFH even in the prior year.[17,] The primary efficacy outcome was the difference between rates of adjudicated HFH 1 year after compared to 1 year prior to device implantation. The 12-month visit was completed in 875 patients (72.9%). Prior to 1 year, 76 patients (6.3%) withdrew from the study and 186 patients (15.5%) died. The HFH rate was significantly lower at 1 year post-implantation (0.54 versus 1.25 events/patient-year; HR, 0.43; 95% CI, 0.39 to 0.47; p<.0001). The rate decrease remained significant regardless of the number of pre-enrollment HFH events, with a trend towards a more significant benefit in a small subgroup of patients (n=21) with ≥ 5 pre-enrollment HFH events. The rate of all-cause hospitalization (ACH) was also significantly lower (1.67 versus 2.28 events/patient-year; HR, 0.73; 95% CI, 0.68 to 0.78; p<.0001). During the study, 94.1% of patients had a medication change, with an average of 1.6 medication changes per month. Medication changes related to an increase or decrease in pulmonary artery pressure were implemented in 81.8% and 55.8% of patients, respectively. The primary safety outcome was defined as freedom from device- or system-related complications and pressure sensor failure at 2 years. A 2-year safety follow-up has not yet been concluded. At 1 year, freedom from device- or system-related complications

was 99.6% (5 events) and freedom from pressure sensor failure was 99.9% (1 event). The nature of these events and the frequency of procedure-related adverse events were not reported.

Angermann et al (2020) published results from the CardioMEMS European Monitoring Study for Heart Failure (MEMS-HF).[22,] This was an industry-sponsored, prospective, observational, non-randomized study designed to assess the safety and feasibility of the CardioMEMS heart failure system over a 12-month follow up in 31 centers across Germany, the Netherlands, and Ireland. A total of 239 patients (22% female) with NYHA class III heart failure and ≥ 1 HFH in the prior year were enrolled for remote pulmonary artery pressure-guided heart failure management. Co-primary outcome measures, 1-year rates of freedom from device- or system-related complications and sensor failure, were 98.3% (95% CI, 95.8 to 100.0) and 99.6% (95% CI, 97.6 to 100), respectively. Twenty-one serious adverse events (8.9%) were reported during 236 implant attempts, of which 4 were categorized as device- or system-related and 21 as procedure-related. Three procedure-related cardiac deaths were reported. The overall 12-month mortality rate was 13.8%, with no device- or system-related deaths. The secondary outcome measures included HFH rate at 12 months compared to the prior year before implantation and health-related quality of life. The HFH rate decreased 62% (0.60 versus 1.55 events/patient year; HR, 0.38; 95% CI, 0.31 to 0.48; P<0.0001). These reductions were consistent across subgroups defined by sex, age, heart failure etiology, device use, ejection fraction, baseline pulmonary artery pressure, and various comorbidities. Patient-reported health-related quality of life outcomes were assessed with the Kansas City Cardiomyopathy Questionnaire (KCCQ), 9-Item Patient Health Questionnaire (PHQ-9), and the EQ-5D-5L. All measures significantly improved at 6 months and were sustained through 12 months. Cumulative medication changes and the average rate of monthly per-patient medication changes were highest in months 0 to 3 postimplant.

Abraham et al (2019) published a retrospective matched cohort study of Medicare beneficiaries who received the CardioMEMS device between 2014 and 2016.[23,] Patients were matched to 1087 controls by demographics, history and timing of HFH, and number of ACH. Propensity scoring based on arrhythmia, hypertension, diabetes, pulmonary disease, and renal disease was used for additional matching. Follow-up was censored at death, ventricular assist device implant, or heart transplant. At 12 months post implantation, 616 and 784 HFH events occurred in the treatment and control cohorts, respectively. Study characteristics and results are summarized in Tables 7 and 8. The rate of HFH was lower in the treatment cohort at 12 months (HR, 0.76; 95% CI, 0.65 to 0.89; p<.001). Percentage of days lost to HFH (HR, 0.73; 95% CI, 0.64 to 0.84; p<.001) and ACH or death (HR, 0.77; 95% CI, 0.68 to 0.88; p<.001) were both significantly lower in the treatment group. The percentage of days lost owing to HFH or death was reduced in the treatment cohort (relative risk [RR], 0.73; 95% CI, 0.63 to 0.83).

Desai et al (2017) published a retrospective cohort study of Medicare administrative claims data for individuals who received the CardioMEMS device following the FDA approval.[24,] Of 1935 Medicare enrollees who underwent implantation of the device, 1114 were continuously enrolled and had evaluable data for at least 6 months before, and following, implantation. A subset of 480 enrollees had complete data for 12 months before and after implantation. The cumulative incidence of HFH events was significantly lower in the post implantation period than in the preimplantation period at both 6- and 12-month follow-ups.

Vaduganathan (2017) analyzed mandatory and voluntary reports of device-related malfunctions reported to the FDA to identify CardioMEMS system-related adverse events within the first 3 years of the FDA approval.[25,] From among the more than 5500 CardioMEMS implants in the first 3 years, there were 155 adverse event reports covering 177 distinct adverse events for a rate of 2.8%. There were 28 reports of pulmonary artery injury/hemoptysis (0.5%) that included 14 intensive care unit stays, 7 intubations, and 6 deaths. Sensor failure, malfunction, or migration occurred in 46 cases, of which 35 required recalibrations. Compared with a reported 2.8% event rate, the serious adverse event rate in the CHAMPION trial was 2.6% with 575 implant attempts, including 1 case of pulmonary artery injury and 2 deaths.

Table 7. Summary of Key Nonrandomized Study Characteristics

Author	Study Type	Country/Institution	Dates	Participants	Treatment	Follow-Up
Comparative Studies						
Abraham et al (2019)[23,]	Retrospective matched cohort	U.S./Medicare/Abbott	2014-2016	Individuals with CPT codes consistent with the use of procedure and at least 1 HFH within the previous 12 months	CardioMEMS implant	12 mo
Pre-post Studies						
Cowie et al (2021)[21,]	Post-approval multicenter study	U.K/Abbott	2017-2019	Individuals with NYHA class III HF and at least 1 HFH within the previous 12 months	CardioMEMS implant	12 and 24 mo
Shavelle et al (2020)[17,]	Post-approval multicenter study	U.S./Abbott	2014-2017	Individuals with a diagnosis of NYHA class III HF and at least 1 HFH within the previous 12 months	CardioMEMS implant	12 mo
Angermann et al (2020)[22,]	Prospective multicenter study	Germany, the Netherlands, Ireland/Abbott	2016-2018	Individuals with a diagnosis of NYHA class III HF and at	CardioMEMS implant; communications with trained	12 mo

Author	Study Type	Country/Institution	Dates	Participants	Treatment	Follow-Up
Comparative Studies						
				least 1 HFH within the previous 12 months	non-physician staff	
Desai et al (2017)[24,]	Retrospective cohort	U.S./Medicare	2014-2015	Individuals with inpatient CPT codes consistent with the use of the procedure	CardioMEMS implant	6 mo: preimplant and postimplant data (n=1114) 12 mo: preimplant and postimplant data (n=480)
Postmarketing Safety Studies						
Vaduganathan et al (2017)[25,]	Postmarketing surveillance study	U.S./FDA and Abbott	2014-2017	Individuals reporting Cardio-MEMS-related adverse event	CardioMEMS implant	NA

FDA: U.S. Food and Drug Administration; HF: heart failure; HFH: heart failure-related hospitalization; NA: not applicable; NYHA: New York Heart Association,

Table 8. Summary of Key Nonrandomized Study Results

Study	HFH at 6 Months	HFH at 12 Months	Safety
Comparative Studies			
Abraham et al (2019)[23,]	NR	1087	NR
HR (95% CI); p-value	NR	0.76 (0.65 to 0.89); <.001	NR
Pre-post Studies			
Cowie et al (2021)[21,]	NR	80	100
HR (95% CI); p-value	NR	0.178 (0.12 to 0.28); <.0001	Freedom from DSRC: 100% Freedom from pressure sensor failure: 99%

Study	HFH at 6 Months	HFH at 12 Months	Safety
Comparative Studies			
Shavelle et al (2020)[17,]	1013	875	NR
HR (95% CI); p-value	NR	0.43 (0.39 to 0.47); <.0001	Freedom from DSRC: 99.6% Freedom from pressure sensor failure: 99.9%
Angermann et al (2020)[22,]	198	234[a];180[b]	236
HR (95% CI); p-value	NR	0.38 (0.31 to 0.48); <.0001[a] 0.34 (0.26 to 0.44); <.0001[b]	DSRC: 1.7% Pressure sensor failure: 0.4% SAE: 21/236 (8.9%) Delivery system-related events: 4 Implant procedure-related events: 21 Pulmonary artery perforation: 1 (0.4%) Procedure-related cardiac deaths: 3 (1.3%)
Desai et al (2017)[24,]	1114	480	NR
Preimplant, n	1020	696	NR
Postimplant, n	381	300	NR
HR (95% CI); p-value	0.55 (0.49 to 0.61); <0.001	0.66 (0.57 to 0.76); <.001	NR
Postmarketing Safety Studies			
Vaduganathan et al (2017)[25,]			Estimated 5500 received CardioMEMS
AE cohort identified from MAUDE database	NR	NR	155 (2.8%) AEs; 28 pulmonary artery injury or hemoptysis (0.5%), and 2 (0.4%) deaths

AE: adverse event; CI: confidence interval; DSRC: device- or system-related complications, HFH: heart failure hospitalization; HR: hazard ratio; NR: not reported; SAE: serious adverse event.
[a] The primary efficacy analysis consisted of all 234 patients implanted with the CardioMEMS device.
[b] Results at 12-month follow-up as completed by 180 patients.

Table 9. Nonrandomized Study Relevance Limitations

Trial	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Comparative Studies					
Abraham et al (2019)[23,]	3. NYHA Class data not reported. Medicare claims data may lack complete medical history information.	1. Details regarding the frequency of nursing and/or provider communications were not described.	2. While propensity scoring was applied for several patient factors, residual confounding by unmeasured covariates remains possible. Medicare claims data may lack complete medical history data.		
Pre-post Studies					
Cowie et al (2021)[21,]		1. Details regarding the frequency of nursing and/or provider communications were not described.			
Shavelle et al (2020)[17,]		1. Details regarding the use of nursing and/or provider communications were not described.			
Angermann et al (2020)[22,]		3. Frequency of nursing communications varied based on patient NYHA Class.			
Desai et al (2017)[24,]	3. NYHA Class data not reported. Medicare claims data may lack complete medical history information.				

Trial	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Comparative Studies					
Postmarketing Safety Studies					
Vaduganathan et al (2017)[25,]					

NYHA: New York Heart Association.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not established and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 10. Nonrandomized Study Design and Conduct Limitations

Trial	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Comparative Studies						
Abraham et al (2019)[23,]	1-2. Participants were not randomly allocated and allocation was not concealed. 4. While propensity scoring was applied for several patient factors, residual confounding by unmeasured covariates remains possible. Medicare claims data may lack	1. Physicians were not blinded to treatment assignment. Events were not formally adjudicated and were limited by retrospective claims data.				

Trial	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Comparative Studies						
	complete medical history data.					
Pre-post Studies						
Cowie et al (2021)[21,]	1-2 Participants were not randomly allocated and allocation was not concealed. 4. Assessing HFH as a study entry requirement and endpoint may reflect a bias of prior hospitalization in favor of any intervention	1. Physicians were not blinded to treatment assignment. Events were adjudicated by treating physicians.	2. Only results for patients with follow-up completed before COVID-19 have been reported.			
Shavelle et al (2020)[17,]	1-2. Participants were not randomly allocated and allocation was not concealed. 4. Assessing HFH as a study entry requirement and endpoint may reflect a bias of prior hospitalization in favor of any intervention.	1. Physicians were blinded to treatment assignment. Events were adjudicated by an independent committee. Unclear whether adjudication criteria were similar to criteria used in RCTs.				
Angermann et al (2020)[22,]	1-2. Participants were not randomly allocated and allocation was	1. Physicians were blinded to treatment assignment. Outcome				

Trial	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Comparative Studies						
	not concealed. 4. Assessing HFH as a study entry requirement and endpoint may reflect a bias of prior hospitalization in favor of any intervention.	adjudication was unclear.				
Desai et al (2017)[24,]	1-2. Participants were not randomly allocated and allocation was not concealed. 4. Assessing HFH as a study entry requirement and endpoint may reflect a bias of prior hospitalization in favor of any intervention. Medicare claims data may lack complete medical history.	1. Physicians were not blinded to treatment assignment. Events were not formally adjudicated and were limited by retrospective claims data.				
Postmarketing Safety Studies						
Vaduganathan et al (2017)[25,]	1-2. Participants were not randomly allocated and allocation was not concealed.	1. Physicians were not blinded to treatment assignment. No formal outcome adjudication was used due		1. Voluntary reporting of adverse events limits the interpretation of results as all events are not captured.		

Trial	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Comparative Studies						
		to limitations with self-reports.				

COVID: coronavirus disease; HFH: heart failure hospitalization; RCT: randomized controlled trial.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated; 5. Other

Section Summary: Implantable Pulmonary Artery Pressure Monitoring (CardioMEMS Device)

The pivotal CHAMPION RCT reported a statistically significant 28% decrease in HFH in patients implanted with CardioMEMS device compared with usual care at 6 months. However, trial results were potentially biased in favor of the treatment group due to the use of additional nurse communication to enhance protocol compliance with the device. The subsequent GUIDE-HF RCT failed to meet its primary efficacy endpoint, the composite of HFH, urgent heart failure visits, and death at 1 year. With the approval of the FDA, the statistical analysis plan was updated to pre-specify sensitivity analyses to assess the impact of COVID-19 on the trial. For the 72% of patients who completed follow-up prior to the public health emergency declaration in March 2020, a statistically significant 19% reduction in the primary endpoint was reported, driven by a 28% reduction in HFH. Nonrandomized studies have also consistently reported significant reductions in HFH, but are limited by the use of historical controls, within-group comparisons, and retrospective claims data. The impact of COVID-19 on the GUIDE-HF trial met the pre-specified 15% interaction significance level. However, lifestyle changes during the COVID-19 pandemic such as changes in physical activity, exposure to infections, willingness to seek medical care, and adherence to medications are unmeasured and add imprecision to treatment effect estimates. Provider behaviors may have also been altered, partly evidenced by decreased medication changes and deintensification of medical management during COVID-19. Enrollment of NYHA Class II patients was significantly enriched in the first 500 patients enrolled, potentially impacting the pre-COVID-19 analysis.

Overall, the beneficial effect of CardioMEMS, if any, appears to be on the hospitalization outcome of the composite. Both urgent heart failure visits and death outcomes had HRs favoring the control group with wide CIs including the null value in pre-COVID-19, during-COVID-19, and overall analyses of the GUIDE-HF trial. No significant differences were observed in secondary

quality of life and functional status outcomes. While a HFH reduction of 28% found in the pre-COVID-19 analysis is consistent with findings from the CHAMPION trial, it is unclear whether physician knowledge of treatment assignment biases the decision to hospitalize and administer intravenous diuretics. In light of the absence of a demonstrated benefit on mortality and functional outcomes, lack of procedural safety data, and unclear impact of COVID-19 on remote monitoring in the GUIDE-HF trial, the net benefit of the CardioMEMS device remains uncertain. Concerns may be clarified by the ongoing GUIDE-HF RCT that proposes to enroll 2600 subjects for its open access phase and the recruiting German non-industry-sponsored PASSPORT-HF trial.

NONINVASIVE THORACIC BIOIMPEDANCE/IMPEDANCE CARDIOGRAPHY

Clinical Context and Test Purpose

The purpose of thoracic bioimpedance in patients who have heart failure in an outpatient setting is (1) to guide volume management, (2) to identify physiologic changes that precede clinical symptoms and thus allow preventive interventions, and (3) to prevent hospitalizations.

The question addressed in this evidence review is: Does the use of thoracic bioimpedance/impedance cardiography improve net health outcomes in individuals with heart failure in the outpatient setting?

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is patients with chronic heart failure who are at risk of developing acute decompensated heart failure (ADHF).

Interventions

The test being considered is thoracic bioimpedance.
Bioimpedance is defined as the electrical resistance of current flow through tissue. For example, when small electrical signals are transmitted through the thorax, the current travels along the blood-filled aorta, which is the most conductive area. Changes in bioimpedance, measured during each beat of the heart, are inversely related to pulsatile changes in volume and velocity of blood in the aorta. Cardiac output is the product of stroke volume by heart rate, thus, can be calculated from bioimpedance. Cardiac output is generally reduced in patients with systolic heart failure. Acute decompensation is characterized by worsening of cardiac output from the patient's baseline status. The technique is alternatively known as impedance cardiography.

Comparators

The comparator of interest is standard clinical care without testing. Decisions on guiding volume management are being made based on signs and symptoms.

Outcomes

The general outcomes of interest are the prevention of decompensation episodes, reductions in hospitalization and mortality, and improvements in quality of life.

Generally, demonstration of outcomes over a 1-year period is meaningful for interventions.

REVIEW OF EVIDENCE

Clinically Valid
A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Several studies were excluded from the evaluation of the clinical validity of thoracic bioimpedance testing because they did not include information needed to assess clinical validity.[26,27,28,]

Packer et al (2006) reported on the use of impedance cardiography measured by BioZ impedance cardiography monitor to predict decompensation in patients with chronic heart failure.[29,] In this study, 212 stable patients with heart failure and a recent episode of decompensation underwent serial evaluation and blinded impedance cardiography testing every 2 weeks for 26 weeks and were followed for the occurrence of death or worsening heart failure requiring hospitalization or emergent care. Results are summarized in Table 11. A composite score of 3 impedance cardiography parameters was a predictor of an event during the next 14 days ($p<0.001$).

Table 11. Clinical Validity of 3-Level Risk Score for BioZ Impedance Cardiography Monitor

Author	Initial N	Final N	Excluded Samples	Prevalence of Condition	Clinical Validity: Mean Probability of Outcome (95% CI), %		
					Low Risk	*Medium Risk*	*High Risk*
Packer et al (2006)[29,]	212	212	None	59 patients had 104 episodes of decompensated HF including 16 deaths, 78 hospitalizations, 10 ED visits	1.0 (0.5 to 1.9)	3.5 (2.4 to 4.8)	8.4 (5.8 to 11.6)

CI: confidence interval; ED: emergency department; HF: heart failure.

Section Summary: Clinically Valid
The clinical validity of using thoracic bioimpedance for patients with chronic heart failure who are at risk of developing ADHF has not been established. Association studies are insufficient evidence to determine whether thoracic bioimpedance can improve outcomes in patients with chronic heart failure who are at risk of developing ADHF. There are no studies reporting the clinical validity regarding sensitivity, specificity, or predictive value.

Clinically Useful
A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, more effective therapy, avoid unnecessary therapy, or avoid unnecessary testing.

Direct Evidence
Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

Amir et al (2017) reported on the results of a prospective study in which 59 patients recently hospitalized for heart failure were selected for remote dielectric sensing (ReDS)-guided treatment for 90 days.[30,] The number of heart failure hospitalizations during 90-day ReDS-guided therapy was compared with hospitalizations in the preceding 90 days before enrollment and the 90 days following discontinuation of ReDS monitoring. During treatment, patients were equipped with the ReDS wearable vest, which was worn once a day at home to measure lung fluid content. Study characteristics and results are summarized in Tables 12 and 13. The rate of heart failure hospitalizations was lower during the ReDS-guided follow-up compared with pre- and post-treatment periods. Interpretation of results is uncertain due to the lack of concurrent control and randomization, short-term follow-up, large CIs, and lack of clarity about lost-to-follow-up during the post-ReDS period. An RCT comparing ReDS monitoring with the standard of care (SMILE; NCT02448342) was initiated but terminated before its completion.

Table 12. Summary of Key Nonrandomized Study Characteristics

Author	Study Type	Country	Dates	Participants	Treatment	Mean FU (SD), d
Amir et al (2017)[30,]	Pre-post prospective cohort	Israel	2012-2015	Patients ≥18 y with stage C heart failure, regardless of LVEF (n=59)	ReDS Wearable System	83.0 (25.4)

FU: follow-up; LVEF: left ventricular ejection fraction; ReDS: remote dielectric sensing; SD: standard deviation.

Table 13. Summary of Key Nonrandomized Study Results

Study	HFH (events/patient/3 mo)	Deaths
Amir et al (2017)[30,]	50	50
Pre-90-day period (control)	0.04	0
90-day treatment period	0.30	2
Post-90-day period (control)	0.19	2
Hazard ratio (95% confidence interval); p	0.07 (0.01 to 0.54);.01[a] 0.11 (0.014 to 0.88);.037[b]	

HFH: heart failure-related hospitalizations.
[a] Treatment versus pretreatment period;
[b] Treatment versus posttreatment period.

Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility. Because the clinical validity of using thoracic bioimpedance has not been proved, a chain of evidence to support its clinical utility cannot be constructed.

Section Summary: Clinical Utility

The clinical utility of using thoracic bioimpedance for patients with chronic heart failure who are at risk of developing ADHF has not been established. One prospective longitudinal study reported that ReDS-guided management reduced heart failure readmissions in ADHF patients recently discharged from the hospital. However, interpretation of results is uncertain due to the lack of concurrent controls and randomization, short-term follow-up, large CIs, and lack of clarity about

lost-to-follow-up during the post-ReDS monitoring period. An RCT comparing ReDS monitoring with the standard of care was initiated but terminated before its completion.

INERT GAS REBREATHING

Clinical Context and Test Purpose

The purpose of inert gas breathing in patients who have heart failure in an outpatient setting is (1) to guide volume management, (2) to identify physiologic changes that precede clinical symptoms and thus allow preventive interventions, and (3) to prevent hospitalizations.

The question addressed in this evidence review is: Does the use of inert gas breathing improve net health outcomes in individuals with heart failure in the outpatient setting?

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is patients with chronic heart failure who are at risk of developing ADHF.

Interventions

The test being considered is inert gas breathing.

Inert gas rebreathing is based on the observation that the absorption and disappearance of a blood-soluble gas are proportional to cardiac blood flow. The patient is asked to breathe and rebreathe from a bag filled with oxygen mixed with a fixed proportion of 2 inert gases, typically nitrous oxide and sulfur hexafluoride. The nitrous oxide is soluble in blood and is therefore absorbed during the blood's passage through the lungs at a rate proportional to the blood flow. The sulfur hexafluoride is insoluble in blood and therefore stays in the gas phase and is used to determine the lung volume from which the soluble gas is removed. These gases and carbon dioxide are measured continuously and simultaneously at the mouthpiece.

This noninvasive procedure is administered by a cardiologist in an outpatient clinical setting.

Comparators

The comparator of interest is standard clinical care without testing. Decisions on guiding volume management are being made based on signs and symptoms.

Patients with heart failure are managed by cardiologists in an outpatient clinical setting.

Outcomes

The general outcomes of interest are the prevention of decompensation episodes, reduction in hospitalization and mortality, and improvement in quality of life.

Trials of using inert gas rebreathing for this population were not found. Generally, demonstration of outcomes over a 1-year period is meaningful for interventions.

Clinically Valid
A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

No studies on the clinical validity were identified that would establish how the use of inert gas rebreathing measurements helps detect the likelihood of decompensation.

Section Summary: Clinically Valid
The clinical validity of using inert gas breathing for patients with chronic heart failure who are at risk of developing ADHF has not been established.

Clinically Useful
A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy or more effective therapy, avoid unnecessary therapy, or avoid unnecessary testing.

Direct Evidence
Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No studies were identified that determined how the use of inert gas rebreathing measurements is associated with changes in patient management or evaluated the effects of this technology on patient outcomes.

Chain of Evidence
Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility. Because the clinical validity of using inert gas breathing has not been proved, a chain of evidence to support clinical utility cannot be constructed.

Section Summary: Clinically Valid
No studies of clinical utility were identified that determined how the use of inert gas breathing measurements in managing heart failure affects patient outcomes. It is unclear how such devices will improve patient outcomes.

NONINVASIVE LEFT VENTRICULAR END-DIASTOLIC PRESSURE ESTIMATION

Clinical Context and Test Purpose
The purpose of LVEDP estimation in patients who have heart failure in an outpatient setting is (1) to guide volume management, (2) to identify physiologic changes that precede clinical symptoms and thus allow preventive interventions, and (3) to prevent hospitalizations.

The question addressed in this evidence review is: Does the use of noninvasive LVEDP estimation improve health outcomes in individuals with heart failure in the outpatient setting?

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is patients with chronic heart failure who are at risk of developing ADHF.

Interventions
The test being considered is noninvasive LVEDP estimation.

LVEDP is elevated with acute decompensated heart failure. While direct catheter measurement of LVEDP is possible for patients undergoing cardiac catheterization for diagnostic or therapeutic reasons, its invasive nature precludes outpatient use. Noninvasive measurements of LVEDP have been developed based on the observation that arterial pressure during the strain phase of the Valsalva maneuver may directly reflect the LVEDP. Arterial pressure responses during repeated Valsalva maneuvers can be recorded and analyzed to produce values that correlate to the LVEDP.

This noninvasive procedure is administered by a cardiologist in an outpatient clinical setting.

Comparators
The comparator of interest is standard clinical care without testing. Decisions guiding volume management are being made based on signs and symptoms.

Patients with heart failure are managed by cardiologists in an outpatient clinical setting.

Outcomes
The general outcomes of interest are the prevention of decompensation episodes, reduction in hospitalization and mortality, and improvement in quality of life.

Trials of using noninvasive LVEDP estimation for this population were not found. Generally, demonstration of outcomes over a 1-year period is meaningful for interventions.

Clinically Valid
A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Silber et al (2012) reported on finger photoplethysmography during the Valsalva maneuver performed in 33 patients before cardiac catheterization.[31,] LVEDP was measured via a catheter placed in the left ventricle and used as the reference standard. For identifying LVEDP greater than 15 mm Hg, finger photoplethysmography during the Valsalva maneuver was 85% sensitive (95% CI, 54% to 97%) and 80% specific (95% CI, 56% to 93%).

Section Summary: Clinically Valid
Only 1 study was identified assessing the use of LVEDP monitoring in this patient population; it reported an 85% sensitivity and an 80% specificity to detect LVEDP greater than 15 mm Hg.

Clinically Useful
A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, more effective therapy, avoid unnecessary therapy, or avoid unnecessary testing.

Direct Evidence
Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

No studies were identified that determined how the use of noninvasive LVEDP estimation is associated with changes in patient management or evaluated the effects on patient outcomes.

Chain of Evidence
Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the clinical validity of using noninvasive LVEDP estimation has only been demonstrated in a small, single study, a chain of evidence to support clinical utility cannot be constructed.

Section Summary: Clinically Useful
No studies of clinical utility were identified that assessed how the use of noninvasive LVEDP estimation in managing heart failure affects patient outcomes. A chain of evidence on the clinical utility of noninvasive LVEDP estimation cannot be constructed because it is unclear how these devices will improve patient outcomes.

Summary of Evidence
For individuals who have heart failure in outpatient settings who receive hemodynamic monitoring with an implantable pulmonary artery pressure sensor device, the evidence includes RCTs and nonrandomized studies. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, morbid events, hospitalizations, and treatment-related morbidity. One implantable pressure monitor, the CardioMEMS device, has U.S. FDA approval. The pivotal CHAMPION RCT reported a statistically significant 28% decrease in HFH in patients implanted with the CardioMEMS device compared with usual care. However, trial results were potentially biased in favor of the treatment group due to the use of additional nurse communication to enhance protocol compliance with the device. The manufacturer conducted multiple analyses to address potential bias from the nurse interventions. Results were reviewed favorably by the FDA. While these analyses demonstrated the consistency of benefit of the CardioMEMS device, all such analyses have methodologic limitations. Early safety data have been suggestive of a higher rate of procedural complications, particularly related to pulmonary artery injury. While the U.S. CardioMEMS post-approval study and CardioMEMS European Monitoring Study for Heart Failure (MEMS-HF) study reported a significant decrease in HFH with few device- or system-related complications at 1 year, the impact of nursing interventions remains unclear. The subsequent GUIDE-HF RCT failed to meet its primary efficacy endpoint, the composite of HFH, urgent heart failure visits, and death at 1 year. With the approval of the FDA, the statistical analysis plan was updated to pre-specify sensitivity analyses to assess the impact of COVID-19 on the trial. For the 72% of patients who completed follow-up prior to the public health emergency declaration in

March 2020, a statistically significant 19% reduction in the primary endpoint was reported, driven by a 28% reduction in HFH. However, lifestyle changes during the COVID-19 pandemic such as changes in physical activity, exposure to infections, willingness to seek medical care, and adherence to medications are unmeasured and add imprecision to treatment effect estimates, as do alterations in provider behaviors. Enrollment of NYHA Class II patients was significantly enriched in the first 500 patients, potentially impacting the pre-COVID-19 analysis. Overall, the beneficial effect of CardioMEMS, if any, appears to be on the hospitalization outcome of the composite. Both urgent heart failure visits and death outcomes had HRs favoring the control group with wide CIs including the null value in pre-COVID-19, during-COVID-19, and overall analyses of the GUIDE-HF trial. No significant differences were observed in secondary quality of life and functional status outcomes. While the HFH reduction of 28% found in the pre-COVID-19 analysis is consistent with findings from the CHAMPION trial, it is unclear whether physician knowledge of treatment assignment biases the decision to hospitalize and administer intravenous diuretics. Given that the intervention is invasive and intended to be used for a highly prevalent condition and, in light of the absence of a demonstrated benefit on mortality and functional outcomes, the lack of periprocedural safety data, and unclear impact of COVID-19 on remote monitoring in the GUIDE-HF trial, the net benefit of the CardioMEMS device remains uncertain. Concerns may be clarified by the ongoing GUIDE-HF RCT that proposes to enroll 2600 subjects for its open access phase and the recruiting German non-industry-sponsored PASSPORT-HF trial. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have heart failure in outpatient settings who receive hemodynamic monitoring by thoracic bioimpedance, the evidence includes uncontrolled prospective studies and case series. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, morbid events, hospitalizations, and treatment-related morbidity. There is a lack of RCT evidence evaluating whether the use of these technologies improves health outcomes over standard active management of heart failure patients. The case series have reported physiologic measurement-related outcomes and/or associations between monitoring information and heart failure exacerbations, but do not provide definitive evidence on device efficacy. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have heart failure in outpatient settings who receive hemodynamic monitoring with inert gas rebreathing, no studies have been identified on clinical validity or clinical utility. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, morbid events, hospitalizations, and treatment-related morbidity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have heart failure in outpatient settings who receive hemodynamic monitoring of arterial pressure during the Valsalva maneuver, a single study was identified. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, morbid events, hospitalizations, and treatment-related morbidity. The study assessed the use of LVEDP monitoring and reported an 85% sensitivity and an 80% specificity to detect LVEDP greater than 15 mm Hg. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American College of Cardiology et al

In 2017, the American College of Cardiology (ACC), the American Heart Association (AHA), and the Heart Failure Society of America (HFSA) issued joint guidelines on the management of heart failure that offered no recommendations for the use of ambulatory monitoring devices.[32,]

In the 2022 update to the heart failure management guidelines, 2 recommendations were provided regarding remote hemodynamic monitoring in heart failure. These recommendations are summarized below in Table 14.

Table 14. 2022 ACC/AHA/HFSA Recommendation for Wearables and Remote Monitoring (including Telemonitoring and Device Monitoring)[33,]

Class of Recommendation	Level of Evidence	Recommendation
2b (Weak Evidence)	B-R (Moderate quality randomized evidence)	1. "In selected adult patients with NYHA class III HF and history of HF hospitalization in the past year or elevated natriuretic peptide levels, on maximally tolerated doses of GDMT with optimal device therapy, the usefulness of wireless monitoring of PA pressure by an implanted hemodynamic monitor to reduce the risk of subsequent HF hospitalizations is uncertain."
Value Statement: Uncertain Value (B-NR) (Moderate quality nonrandomized evidence)		2. "In patients with NYHA class III HF with a HF hospitalization within the previous year, wireless monitoring of the PA pressure by an implanted hemodynamic monitor provides uncertain value."

ACC: American College of Cardiology; AHA: American Heart Association; GDMT: guideline-directed medical therapy; HF: heart failure; HFSA: Heart Failure Society of America; NYHA: New York Heart Association; PA: pulmonary artery. Adapted from Heidenreich et al (2022).[33,]

National Institute for Health and Care Excellence

In 2021, the National Institute for Health and Care Excellence (NICE) issued a new interventional procedures guidance regarding the use of percutaneous implantation of pulmonary artery pressure sensors for monitoring the treatment of chronic heart failure. The Institute's recommendation stated that "Evidence on the safety and efficacy of percutaneous implantation of pulmonary artery pressure sensors for monitoring treatment of chronic heart failure is adequate

to support using this procedure provided that standard arrangements are in place for clinical governance, consent, and audit."

In 2018, the Institute updated their guidelines on chronic heart failure management and did not include outpatient hemodynamic monitoring as a recommendation. [34,]

Heart Failure Society of America
In 2018, the Heart Failure Society of America Scientific Statements Committee (2018) published a white paper consensus statement on remote monitoring of patients with heart failure.[35,]

The committee concluded that: "Based on available evidence, routine use of external RPM devices is not recommended. Implanted devices that monitor pulmonary arterial pressure and/or other parameters may be beneficial in selected patients or when used in structured programs, but the value of these devices in routine care requires further study."

U.S. Preventive Services Task Force Recommendations
Not applicable.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 15.

Table 15. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT04223271[a]	Heart Failure Event Advance Detection Trial (HEADstart)	165	Apr 2021 (unknown)
NCT03476590	A New Model of Medical Care With Use of Modern Methods of Non-invasive Clinical Assessment and Telemedicine in Patients With Heart Failure (AMULET)	605	Jun 2021 (ongoing)
NCT02954341[a]	CardioMEMS HF System OUS Post Market Study	300	Dec 2023 (ongoing)
NCT03387813[a]	Hemodynamic-GUIDEd Management of Heart Failure (GUIDE-HF)	3600	Feb 2024 (recruiting)
NCT04398654	Pulmonary Artery Sensor System Pressure Monitoring to Improve Heart Failure (HF) Outcomes (PASSPORT-HF)	554	May 2024 (recruiting)
NCT04441203	Patient SELF-management With HemodynamIc Monitoring: Virtual Heart Failure Clinic and Outcomes (SELFIe-HF)	150	Jun 2024 (not yet recruiting)
NCT03020043	CardioMEMS Registry of the Frankfurt Heart Failure Center	500	Dec 2025 (recruiting)

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

CPT/HCPCS	
33289	Transcatheter implantation of wireless pulmonary artery pressure sensor for long-term hemodynamic monitoring, including deployment and calibration of the sensor, right heart catheterization, selective pulmonary catheterization, radiological supervision and interpretation, and pulmonary artery angiography, when performed
93264	Remote monitoring of a wireless pulmonary artery pressure sensor for up to 30 days, including at least weekly downloads of pulmonary artery pressure recordings, interpretation(s), trend analysis, and report(s) by a physician or other qualified health care professional
93701	Bioimpedance-derived physiologic cardiovascular analysis

REVISIONS	
09-10-2010	Title revised: From: "Thoracic Bioimpedance as a Measurement of Cardiac Hemodynamics in the Ambulatory Care - Outpatient Setting" To: "Cardiac Hemodynamic Monitoring for the Management of Heart Failure in the Outpatient Setting"
	In Policy section: Added arterial pressure/Valsalva and implantable direct pressure monitoring of the pulmonary artery as mechanisms for cardiac hemodynamic monitoring for the management of heart failure in the outpatient setting.
	In Coding section: ▪ Added CPT Code: 93799 ▪ Updated wording for CPT Code: 93701
	Description section updated.
	Rationale section added.
	References section updated.
03-07-2011	In Coding section: ▪ Removed CPT codes: 0104T, 0105T
09-20-2011	Description section updated.
	Rationale section added.
	References section updated.

REVISIONS	
09-18-2012	Description section updated.
	Rationale section added.
	References section updated.
10-31-2013	Description section updated
	Rationale section updated
	References updated
04-28-2015	Updated Description section.
	Updated Rationale section.
	Updated References section.
10-13-2015	Updated Description section.
	Updated Rationale section.
	In Coding section: ▪ Revised bulleted information.
	Updated References section.
09-03-2016	Updated Description section.
	In Policy section: ▪ Removed "/" and added "during" and "maneuver" to read "In the ambulatory care and outpatient setting, cardiac hemodynamic monitoring for the management of heart failure utilizing thoracic bioimpedance, inert gas rebreathing, arterial pressure during Valsalva maneuver, and implantable direct pressure monitoring of the pulmonary artery is considered experimental / investigational."
	Updated Rationale section.
	In Coding section: ▪ Added HCPCS code: C9741. ▪ Revised bulleted information.
	Updated References section.
07-11-2017	Updated Description section.
	Updated Rationale section.
	Updated References Section.
09-12-2018	Updated Description section.
	Updated Rationale section.
	Updated References section.
01-01-2019	In Coding section: ▪ Added new CPT codes: 33289, 93264. ▪ Removed deleted HCPCS code: C9741.
06-19-2019	Updated Description section.
	Updated Rationale section.
	In Coding section: ▪ Added HCPCS code: C2624.
	Updated References section
07-02-2021	Updated Description section
	In Policy Section: ▪ Added Item A, Item B, and Item C ▪ Added "except for the CardioMEMS™ HF System," in Item D.
	Updated Rationale section
	In Coding Section ▪ Removed C2624 ▪ Added ICD-10 diagnosis codes: I50.1, I50.20, I50.21, I50.22, I50.23, I50.30, I50.31, I50.32, I50.33, I50.40, I50.41, I50.42, I50.43, I50.810, I50.811, I50.812, I50.813, I50.814, I50.82, I50.83, I50.84, I50.89, I50.9

REVISIONS	
	Updated References Section
Posted 3-14-2023 Effective 04-13-2023	Updated Description Section
	Updated Policy Section ▪ Removed: A. The CardioMEMS™ HF System may be considered medically necessary for individuals meeting ALL of the following criteria: 1. Diagnosis of NYHA Class III HF (historical assessment documented at screening visit); AND 2. Diagnosis of HF ≥ 3 months, with either preserved or reduced LVEF; AND 3. Receiving a beta blocker for 3 months with a stable dose for one month prior to the screening visit; AND 4. Receiving an ACE-I or ARB for one month unless there is a documented intolerance or contraindication present with a stable dose for one month prior to the screening visit (Beta blockers and ACE-I/ARB doses should be stable for one month prior to the screening visit); AND 5. At least 1 HF hospitalization within 12 months of the Screening Visit; AND 6. Documentation of a pulmonary artery branch diameter sized between 7mm and 15mm (implanted vessel); AND 7. Body mass index (BMI) of less than or equal to 35; or if BMI is greater than 35, a measurement of chest circumference at axillary level is required. If the chest circumference is greater than 165 cm, the sensor should not be implanted due to poor signal strength. B. The CardioMEMS™ HF System not meeting the above criteria is experimental / investigational. C. For individuals with the following contraindications the CardioMEMS™ HF System is considered experimental / investigational: 1. history of recurrent (> 1) pulmonary embolism or deep vein thrombosis 2. unable to tolerate a right heart catheterization 3. Likely to undergo heart transplantation within 6 months of Screening Visit 4. Presence of any one of the following: a. major cardiovascular event (e.g., myocardial infarction, stroke) within 2 months of the Screening Visit b. implantation of a Cardiac Resynchronization Device (CRT) ≤ 3 months prior to the screening visit c. Glomerular Filtration Rate (GFR) <25 ml/min who are non-responsive to diuretic therapy or who are on chronic renal dialysis d. congenital heart disease or mechanical right heart valve(s) e. known coagulation disorders f. hypersensitivity or allergy to aspirin, and/or clopidogrel g. Active infection D. In the ambulatory care and outpatient setting, cardiac hemodynamic monitoring for the management of heart failure utilizing thoracic bioimpedance, inert gas rebreathing, arterial pressure during Valsalva maneuver, and implantable direct pressure monitoring of the pulmonary artery except for the CardioMEMS™ HF System, is considered experimental / investigational. ▪ Added: "In the ambulatory care and outpatient setting, cardiac hemodynamic monitoring for the management of heart failure using implantable direct pressure monitoring of the pulmonary artery, thoracic bioimpedance, inert gas rebreathing, and arterial pressure during the Valsalva maneuver is considered experimental / investigational."
	Updated Policy Guidelines ▪ Added Policy Guidelines "This policy refers only to the use of stand-alone cardiac output measurement devices designed for use in ambulatory care and outpatient settings. The use of cardiac hemodynamic monitors or intrathoracic fluid monitors that are integrated into other implantable cardiac devices, including implantable cardioverter defibrillators, cardiac

REVISIONS	
	resynchronization therapy devices, and cardiac pacing devices, are not addressed in this evidence review."
	Updated Rationale Section
	Updated Coding Section ▪ Removed Coding Bullets o There is a specific CPT code for bioimpedance: 93701 o Inert gas rebreathing measurement and left ventricular end diastolic pressure should be reported using the unlisted code: 93799. ▪ Removed CPT code 93799 ▪ Removed ICD-10 codes
	Updated References Section

REFERENCES

1. Opasich C, Rapezzi C, Lucci D, et al. Precipitating factors and decision-making processes of short-term worsening heart failure despite "optimal" treatment (from the IN-CHF Registry). Am J Cardiol. Aug 15 2001; 88(4): 382-7. PMID 11545758
2. McAlister FA, Stewart S, Ferrua S, et al. Multidisciplinary strategies for the management of heart failure patients at high risk for admission: a systematic review of randomized trials. J Am Coll Cardiol. Aug 18 2004; 44(4): 810-9. PMID 15312864
3. Food and Drug Administration. Summary of Safety and Effectiveness Data (SSED): CardioMEMS HF System. 2014; https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100045b.pdf. Accessed May 2, 2022.
4. Loh JP, Barbash IM, Waksman R. 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. J Am Coll Cardiol. Apr 16 2013; 61(15): 1571-6. PMID 23352783
5. Burns DJP, Arora J, Okunade O, et al. International Consortium for Health Outcomes Measurement (ICHOM): Standardized Patient-Centered Outcomes Measurement Set for Heart Failure Patients. JACC Heart Fail. Mar 2020; 8(3): 212-222. PMID 31838032
6. Zannad F, Garcia AA, Anker SD, et al. Clinical outcome endpoints in heart failure trials: a European Society of Cardiology Heart Failure Association consensus document. Eur J Heart Fail. Oct 2013; 15(10): 1082-94. PMID 23787718
7. Givertz MM, Stevenson LW, Costanzo MR, et al. Pulmonary Artery Pressure-Guided Management of Patients With Heart Failure and Reduced Ejection Fraction. J Am Coll Cardiol. Oct 10 2017; 70(15): 1875-1886. PMID 28982501
8. Adamson PB, Abraham WT, Bourge RC, et al. Wireless pulmonary artery pressure monitoring guides management to reduce decompensation in heart failure with preserved ejection fraction. Circ Heart Fail. Nov 2014; 7(6): 935-44. PMID 25286913
9. Adamson PB, Abraham WT, Stevenson LW, et al. Pulmonary Artery Pressure-Guided Heart Failure Management Reduces 30-Day Readmissions. Circ Heart Fail. Jun 2016; 9(6). PMID 27220593
10. Krahnke JS, Abraham WT, Adamson PB, et al. Heart failure and respiratory hospitalizations are reduced in patients with heart failure and chronic obstructive pulmonary disease with the use of an implantable pulmonary artery pressure monitoring device. J Card Fail. Mar 2015; 21(3): 240-9. PMID 25541376

11. Heywood JT, Jermyn R, Shavelle D, et al. Impact of Practice-Based Management of Pulmonary Artery Pressures in 2000 Patients Implanted With the CardioMEMS Sensor. Circulation. Apr 18 2017; 135(16): 1509-1517. PMID 28219895
12. Abraham WT, Adamson PB, Bourge RC, et al. Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial. Lancet. Feb 19 2011; 377(9766): 658-66. PMID 21315441
13. Abraham WT, Stevenson LW, Bourge RC, et al. Sustained efficacy of pulmonary artery pressure to guide adjustment of chronic heart failure therapy: complete follow-up results from the CHAMPION randomised trial. Lancet. Jan 30 2016; 387(10017): 453-61. PMID 26560249
14. Adamson PB, Abraham WT, Aaron M, et al. CHAMPION trial rationale and design: the long-term safety and clinical efficacy of a wireless pulmonary artery pressure monitoring system. J Card Fail. Jan 2011; 17(1): 3-10. PMID 21187258
15. CardioMEMS ChampionTM HF Monitoring System: FDA Review of P100045/A004FDA Presentation - CardioMEMS: Oct. 9, 2013. 2013; https://wayback.archive-it.org/7993/20170111163259/http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/CirculatorySystemDevicesPanel/UCM370955.pdf. Accessed May 2, 2022.
16. CardioMEMSChampionTM Heart Failure Monitoring System: Presentation - CardioMEMS: Oct. 9, 2013. 2013; https://wayback.archive-it.org/7993/20170111163201/http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/CirculatorySystemDevicesPanel/UCM370951.pdf. Accessed May 1, 2022.
17. Shavelle DM, Desai AS, Abraham WT, et al. Lower Rates of Heart Failure and All-Cause Hospitalizations During Pulmonary Artery Pressure-Guided Therapy for Ambulatory Heart Failure: One-Year Outcomes From the CardioMEMS Post-Approval Study. Circ Heart Fail. Aug 2020; 13(8): e006863. PMID 32757642
18. DeFilippis EM, Henderson J, Axsom KM, et al. Remote Hemodynamic Monitoring Equally Reduces Heart Failure Hospitalizations in Women and Men in Clinical Practice: A Sex-Specific Analysis of the CardioMEMS Post-Approval Study. Circ Heart Fail. Jun 2021; 14(6): e007892. PMID 34129363
19. Lindenfeld J, Zile MR, Desai AS, et al. Haemodynamic-guided management of heart failure (GUIDE-HF): a randomised controlled trial. Lancet. Sep 11 2021; 398(10304): 991-1001. PMID 34461042
20. Zile MR, Desai AS, Costanzo MR, et al. The GUIDE-HF trial of pulmonary artery pressure monitoring in heart failure: impact of the COVID-19 pandemic. Eur Heart J. Mar 10 2022. PMID 35266003
21. Cowie MR, Flett A, Cowburn P, et al. Real-world evidence in a national health service: results of the UK CardioMEMS HF System Post-Market Study. ESC Heart Fail. Feb 2022; 9(1): 48-56. PMID 34882989
22. Angermann CE, Assmus B, Anker SD, et al. Pulmonary artery pressure-guided therapy in ambulatory patients with symptomatic heart failure: the CardioMEMS European Monitoring Study for Heart Failure (MEMS-HF). Eur J Heart Fail. Oct 2020; 22(10): 1891-1901. PMID 32592227

23. Abraham J, Bharmi R, Jonsson O, et al. Association of Ambulatory Hemodynamic Monitoring of Heart Failure With Clinical Outcomes in a Concurrent Matched Cohort Analysis. JAMA Cardiol. Jun 01 2019; 4(6): 556-563. PMID 31090869
24. Desai AS, Bhimaraj A, Bharmi R, et al. Ambulatory Hemodynamic Monitoring Reduces Heart Failure Hospitalizations in "Real-World" Clinical Practice. J Am Coll Cardiol. May 16 2017; 69(19): 2357-2365. PMID 28330751
25. Vaduganathan M, DeFilippis EM, Fonarow GC, et al. Postmarketing Adverse Events Related to the CardioMEMS HF System. JAMA Cardiol. Nov 01 2017; 2(11): 1277-1279. PMID 28975249
26. Kamath SA, Drazner MH, Tasissa G, et al. Correlation of impedance cardiography with invasive hemodynamic measurements in patients with advanced heart failure: the BioImpedance CardioGraphy (BIG) substudy of the Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) Trial. Am Heart J. Aug 2009; 158(2): 217-23. PMID 19619697
27. Anand IS, Greenberg BH, Fogoros RN, et al. Design of the Multi-Sensor Monitoring in Congestive Heart Failure (MUSIC) study: prospective trial to assess the utility of continuous wireless physiologic monitoring in heart failure. J Card Fail. Jan 2011; 17(1): 11-6. PMID 21187259
28. Anand IS, Tang WH, Greenberg BH, et al. Design and performance of a multisensor heart failure monitoring algorithm: results from the multisensor monitoring in congestive heart failure (MUSIC) study. J Card Fail. Apr 2012; 18(4): 289-95. PMID 22464769
29. Packer M, Abraham WT, Mehra MR, et al. Utility of impedance cardiography for the identification of short-term risk of clinical decompensation in stable patients with chronic heart failure. J Am Coll Cardiol. Jun 06 2006; 47(11): 2245-52. PMID 16750691
30. Amir O, Ben-Gal T, Weinstein JM, et al. Evaluation of remote dielectric sensing (ReDS) technology-guided therapy for decreasing heart failure re-hospitalizations. Int J Cardiol. Aug 01 2017; 240: 279-284. PMID 28341372
31. Silber HA, Trost JC, Johnston PV, et al. Finger photoplethysmography during the Valsalva maneuver reflects left ventricular filling pressure. Am J Physiol Heart Circ Physiol. May 15 2012; 302(10): H2043-7. PMID 22389389
32. Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. J Am Coll Cardiol. Aug 08 2017; 70(6): 776-803. PMID 28461007
33. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. May 03 2022; 145(18): e895-e1032. PMID 35363499
34. National Institute for Health and Care Excellence (NICE). Chronic heart failure in adults: diagnosis and management; NICE guideline NG106. September 2018. https://www.nice.org.uk/guidance/ng106. Accessed May 2, 2022.
35. Dickinson MG, Allen LA, Albert NA, et al. Remote Monitoring of Patients With Heart Failure: A White Paper From the Heart Failure Society of America Scientific Statements Committee. J Card Fail. Oct 2018; 24(10): 682-694. PMID 30308242
36. Centers for Medicare & Medicaid Services (CMS). National coverage decision for cardiac output monitoring by thoracic electrical bioimpedance (TEB) (20.16). 2006;

http://www.cms.gov/medicare-coverage- database/details/ncd-details.aspx?NCDId=267&ncdver=3&NCAId=82. Accessed May 2, 2022.

OTHER REFERENCES

1. Blue Cross and Blue Shield of Kansas Cardiology Liaison Committee, May 2015; July 2016; January 2017; May 2018; July 2019; January 2020; May 2021, February 2023.
2. Blue Cross and Blue Shield of Kansas Internal Medicine Liaison Committee, August 2018, August 2021.