NICE National Institute for Health and Care Excellence

**HIGHLY CONFIDENTIAL**

## Diagnostics Advisory Committee (DAC)

## Pulmonary artery pressure technologies for remote monitoring of chronic heart failure – 1st meeting

**16 September 2025**

| | |
|---|---|
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| **Link to SCM list for this topic** | Specialist Committee Members |

The following documents are made available to the Committee:

1. Cover sheet
2. Scope (noCON)
3. Assessment report overview (REDACTED)
4. External assessment report (noCON)
5. External assessment report comments table (noCON)
6. Register of interests (see topic page)

NICE National Institute for Health and Care Excellence

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Diagnostics Assessment Programme

# Pulmonary artery pressure technologies for remote monitoring of chronic heart failure

## Final scope

February 2025

## 1 Introduction

The topic selection oversight panel selected pulmonary artery pressure technologies for remote monitoring of heart failure for guidance development by the Diagnostics Assessment Programme based on a medical technology selection briefing. NICE published an Interventional Procedures Guidance (IPG711) on percutaneous implantation of pulmonary artery pressure sensors for monitoring treatment of chronic heart failure in November 2021, and there is enough evidence in relation to the safety and efficacy of this procedure for clinicians to consider it as an option.

A glossary of terms is provided in appendix A.

## 2 Description of the technology

This section describes the properties of the technology based on information provided to NICE by manufacturers and experts and information available in the public domain. NICE has not carried out an independent evaluation of this description.

### 2.1 Purpose of the medical technology

Pulmonary artery pressure monitoring systems use sensors to collect data on pulmonary artery pressure in people with chronic heart failure to allow for ongoing remote monitoring. A pulmonary artery pressure sensor is implanted into a suitable branch of the pulmonary artery via a large vein (usually the femoral vein). Data on pulmonary artery pressure (PAP), such as pressure trend information and PAP

waveforms, is transmitted from the sensor to an external monitor in the patient's home. The monitor securely transmits the data to a remote database that can be accessed by the heart failure team. The patient usually initiates the PAP measurement daily, or more often if needed by the heart failure team. The system is not intended to make or confirm any diagnosis, but it is used to guide the ongoing monitoring and management of chronic heart failure. PAP trends are observed, this enables intervention with a change of medication to address fluid accumulation at an early stage, potentially reducing hospital admissions and improving outcomes and quality of life. The aim of this is avoiding decompensation (sudden deterioration in heart function and worsening of symptoms) and hospitalisation for heart failure. Monitoring takes place at home without the need for outpatient appointments or home visits.

## 2.2 Product properties

- CardioMEMS HF System (Abbott)

  The CardioMEMS HF System provides pulmonary artery (PA) haemodynamic data used for monitoring in the management of heart failure (HF). The system measures PAP, and the data is used by the physician to initiate or modify heart failure treatment and manage heart failure.

  The system includes the following components:

  - Implantable wireless sensor with delivery catheter
  - Patient or hospital electronics system
  - Patient database website

  The wireless sensor is designed for permanent implantation into the distal pulmonary artery. Once implanted, the CardioMEMS PA Sensor provides non-invasive haemodynamic data that is collected in the physician’s office, clinic, hospital, or patient’s home. The data provided by the system includes:

  - PAP waveform
  - Systolic, diastolic, and mean PAP

- Heart rate

This haemodynamic data is transmitted to a secure website that serves as the patient database so that PAP monitoring information is available at all times through the internet. Changes in PAP can be used in conjunction with heart failure signs and symptoms to guide adjustments to medications.

| **Technology (manufacturer)** | **Classification** | **Intended use** |
|---|---|---|
| CardioMEMS HF System (Abbott) | CE class III | In UK, the CardioMEMS HF System is indicated for patients with a New York Heart Association (NYHA) class III symptoms and a prior HF hospitalisation within the last 12-months regardless of ejection fraction. The GUIDE-HF publication expanded U.S. Food and Drug Administration (FDA) indication to include NYHA class II and III patients with a prior HF hospitalisation within the last 12-months and/or elevated BNP or NT pro-BNP 2 years ago.<br><br>The CardioMEMS HF System is used by the physician in the hospital or office setting to obtain and review PAP measurements. The CardioMEMS HF System is used by the patient in the home to wirelessly obtain and send haemodynamic and PA pressure measurements to a secure database for review and evaluation by the patient's physician.<br><br>The CardioMEMS HF System is contraindicated for patients with an inability to take dual antiplatelet or anticoagulants for one month post implant. |

## 2.3 Potential alternative technologies

One alternative technology has been identified and its regulatory status and availability for use in the NHS are currently uncertain:

- Cordella Pulmonary Artery Sensor System and Cordella Heart Failure System (Endotronix/Edwards Lifesciences)

  The Cordella Pulmonary Artery Sensor System is intended to measure, record and transmit pulmonary artery pressure (PAP) data from NYHA Class III heart failure patients who are at home on diuretics and guideline-directed medical therapy (GDMT), and have been stable for 30 days on GDMT. The device output is meant to aid clinicians in the assessment and management of heart failure, with the goal of reducing hospitalisations for heart failure. It is contraindicated for patients with an inability to take dual antiplatelet or anticoagulants for one month post implant.

  The technology is currently not available for use in the NHS. Launch is expected to take place after the relevant regulatory approvals have been granted. A dossier has been submitted for CE mark review and a decision on European market access is expected in 2025.

# 3 Population

## 3.1 Heart failure

Heart failure is a clinical syndrome caused by any structural or functional cardiac disorder that impairs the heart's ability to function efficiently and pump blood around the body. The most common symptoms of heart failure are breathlessness, fatigue, and oedema. Conditions that cause heart failure include coronary heart disease, high blood pressure, heart rhythm or valve abnormalities, and conditions affecting the heart muscle (cardiomyopathies and myocarditis). The European Society of Cardiology (ESC) guidelines for the diagnosis and treatment of acute and chronic heart failure highlight that atrial fibrillation and heart failure frequently co-exist, and they can cause or exacerbate each other.

Heart failure may present as acute or chronic, depending on whether a person has an established diagnosis of heart failure and speed of symptom onset. Acute heart failure may be the first occurrence of heart failure in people without a heart failure

diagnosis (new onset) or, more frequently, be in people with a chronic heart failure diagnosis who experience sudden deterioration in heart function and worsening of symptoms, which is known as decompensated heart failure.

The British Heart Foundation website explains that heart failure can be grouped into different categories depending on the strength of the heart, that is, the left ventricular ejection fraction (LVEF), which is the amount of blood squeezed out of the main chamber of the heart with every beat. Depending on the percentage ejection fraction (where 50% or greater is considered normal), heart failure may be classed as the following:

- HFpEF – heart failure with preserved ejection fraction (50% and over)
- HFmrEF – heart failure with mildly reduced ejection fraction (between 40% and 49%)
- HFrEF – heart failure with reduced ejection fraction (below 40%).

Heart failure may also be grouped by symptom severity and limitation of physical activity according to the New York Heart Association (NYHA) functional classification of heart failure, ranging from class I (no limitations) to class IV (inability to carry out any physical activity without discomfort and symptoms which may be present at rest).

Heart failure mainly affects people over the age of 65, with an average age of diagnosis of 77, and risk increases significantly with age. Around 1 in 35 people aged 65 - 74 years have heart failure, which increase to 1 in 15 people aged 75 – 84 years, and to just over 1 in 7 people of those aged 85 years and above (NICE 2018).

Around 920,000 people in the UK were living with heart failure in 2018 with an estimated 200,000 new diagnoses each year (NHS England 2022). The incidence of heart failure in the UK is 140 per 100,000 men and 120 per 100,000 women (NICE TA314). The prevalence of heart failure is increasing over time because of population ageing and a rise in the prevalence of associated comorbidities.

Heart failure has a poor prognosis – estimates of 1 year mortality vary, but a long term registry of people with heart failure found a mortality rate of 6.4% for those with

chronic heart failure across Europe (Crespo-Leiro, 2016). A UK-based population study conducted between 2000 and 2017 found that patients diagnosed with heart failure had a 1 year survival rate of 81%, 5 year survival of 48% and 10 year survival of 26% (Taylor, 2019).

Heart failure accounts for a total of 1 million inpatient bed days each year – 2% of all NHS inpatient bed days – and 5% of all emergency medical admissions to hospital. The figures from NHS Hospital Episode Statistics indicate that there were 98,884 hospital admissions for heart failure in 2021/22 compared with 86,474 in 2018/19. This is at significant cost to the NHS – a 2016 All Party Parliamentary Group report on heart failure found that the condition costs the NHS around £2 billion per year, or approximately 2% of the total NHS budget (All-Party parliamentary Group report published in 2016).

## 3.2 Diagnostic and care pathway

### 3.2.1. Diagnosis, assessment and monitoring of chronic heart failure

The NICE guideline for diagnosis and management of chronic heart failure in adults published in 2018 and the NICE Clinical Knowledge Summary for chronic heart failure published in August 2024 provide guidance on diagnosis and assessment of heart failure. Taking a clinical history, performing a clinical examination and testing, including NT pro-BNP and an ECG are recommended. Some people may also require other tests, such as echocardiography, chest x-ray, and blood, urine and lung function tests.

The NICE guideline for diagnosis and management of chronic heart failure in adults recommends that monitoring of people with chronic heart failure should include a clinical assessment of functional capacity, fluid status, cardiac rhythm, cognitive status and nutritional status, a review of medication, and an assessment of renal function. Clinical experts highlighted that in practice a combination of the ESC guideline for diagnosis and treatment of acute and chronic heart failure and the NICE guidelines are followed in the NHS. The ESC guideline adds that heart failure management may involve in person services or home-based telemonitoring, and

that the COVID-19 pandemic has highlighted some of the potential advantages of the latter. While care is usually followed up by heart failure clinics, suitable patients may be followed up by healthcare professionals including community heart failure nurses, GPs with special interest in heart failure and specialist pharmacists. Clinical experts emphasised that there is no standard heart failure service model and current practice is highly varied.

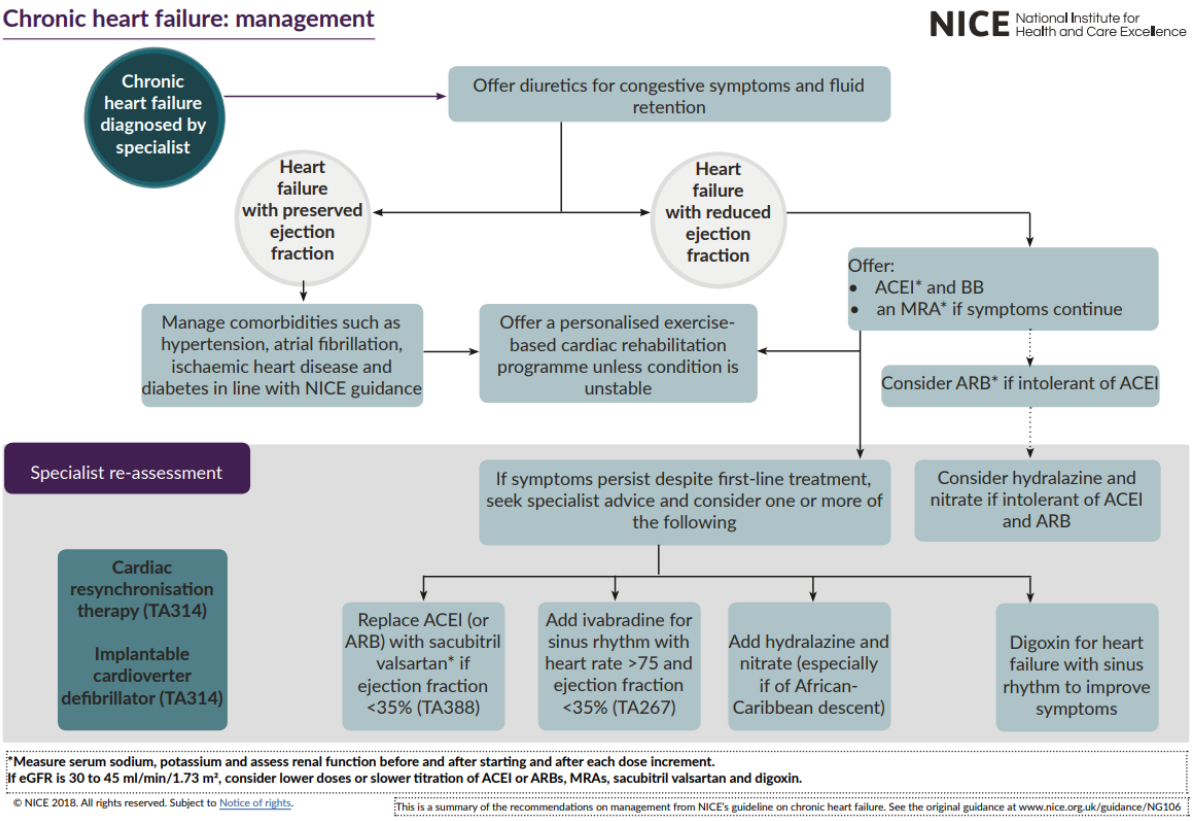
People should have additional monitoring if they have co-morbidities, are taking co-prescribed medications or if their condition has deteriorated since their last review. The frequency of monitoring is dependent on the clinical status and stability of the person's condition. For people whose condition is unstable, monitoring may be offered as frequently as every few days, up to every 2 weeks. The NICE guideline for diagnosis and management of chronic heart failure in adults recommends that reviews are offered every 6 months for people whose condition is stable, but clinical experts highlighted that in practice most people would be reviewed annually whilst some people with a stable condition may not have a review at all. Early follow up visits are recommended at 1 to 2 weeks following hospital discharge to assess signs of congestion and drug tolerance. Levels of serum natriuretic peptide may be monitored as a surrogate biomarker for heart failure in people under 75 who have heart failure with reduced ejection fraction and an estimated glomerular filtration rate above 60 ml per minute per 1.73 $m^2$.

Signs of heart failure can also be monitored using cardiac implantable electronic devices (CIEDs), some of which may also deliver a therapeutic intervention (such as pacemakers, implantable cardioverter defibrillators (ICDs), and cardiac resynchronisation therapy (CRT) devices) whilst others only monitor metrics over time.

### 3.2.3 Treatment for chronic heart failure

The NICE guideline for diagnosis and management of chronic heart failure in adults recommends the use of pharmacological treatments including routine use of diuretics for the relief of congestive symptoms. People with heart failure should also be offered a personalised, exercise-based cardiac rehabilitation programme if their condition is stable and they are able to participate.

Figure 1: Visual summary of the current NICE guideline on chronic heart failure management




In the case of heart failure with reduced ejection fraction, the NICE guideline for diagnosis and management of chronic heart failure in adults recommends that an angiotensin-converting enzyme (ACE) inhibitor, or angiotensin II receptor blockers (ARBs) licensed for heart failure if the person is intolerant to ACE inhibitors, should be offered as a first line treatment in combination with a beta-blocker licensed for heart failure.

If people are continuing to experience symptoms, mineralocorticoid receptor antagonists (MRAs) may be used in addition to first line therapies.

The ESC guideline for diagnosis and treatment of acute and chronic heart failure recommend the use of sodium-glucose cotransporter-2 (SGLT2) inhibitors as a first line therapy in people with reduced ejection fraction. The NICE technology appraisal Dapagliflozin for treating chronic heart failure with reduced ejection fraction and the NICE technology appraisal Empagliflozin for treating chronic heart failure with

reduced ejection fraction also support the use of an SGLT2 inhibitor in these people, as an add-on to optimised standard care with:

- angiotensin-converting enzyme (ACE) inhibitors or angiotensin-2 receptor blockers (ARBs), with beta blockers, and, if tolerated, mineralocorticoid receptor antagonists (MRAs), or
- sacubitril valsartan, with beta blockers, and, if tolerated, MRAs.

The NICE technology appraisal dapagliflozin for treating chronic heart failure with preserved or mildly reduced ejection fraction and NICE technology appraisal empagliflozin for treating chronic heart failure with preserved or mildly reduced ejection fraction recommend dapagliflozin and empagliflozin as options for treating symptomatic heart failure with preserved or mildly reduced ejection fraction.

The ESC guideline for diagnosis and treatment of acute and chronic heart failure states that intravenous iron supplementation with ferric carboxymaltose should be considered in symptomatic people with heart failure who have recently been hospitalised for heart failure, who have left ventricular ejection fraction below 50% and an iron deficiency to reduce the risk of heart failure hospitalisation.

A person should be referred to a specialist multidisciplinary heart failure team (where available) or cardiology service for specialist treatment if a person has:

- Severe heart failure (NYHA class IV).
- Heart failure that does not respond to treatment in primary care or can no longer be managed in the home setting.
- Heart failure resulting from valvular heart disease.
- Left ventricular ejection fraction of 35% or less.
- A NT pro-BNP level above 2000 ng/L (236 pmol/L). These people should be referred urgently for specialist assessment and transthoracic echocardiography within 2 weeks.
- A NT pro-BNP level between 400 and 2000 ng/L (47–236 pmol/L). These people should be referred to have specialist assessment and transthoracic echocardiography within 6 weeks.

Specialist pharmacological treatments for heart failure with reduced ejection fraction may include ivabradine, sacubitril valsartan, hydralazine in combination with nitrate and digoxin.

Specialist referral for transplantation should be considered for heart failure patients with severe refractory symptoms or refractory cardiogenic shock. People suitable for transplantation may also be offered a left ventricular assist device (LVAD) to support pumping of blood around the body either while waiting for a suitable transplant to become available or as a permanent intervention.

The NICE guideline for diagnosis and management of chronic heart failure in adults was published in 2018, and is currently being updated to reflect changes in medical management. Publication of the updated guidance is expected in 2025. The ESC guideline for diagnosis and treatment of acute and chronic heart failure is also being updated.

### 3.2.3 Devices for heart failure

As the condition becomes more severe, cardiac function and symptoms may no longer be controlled by pharmacological treatment alone. The NICE Technology appraisal TA314 recommends the use of implantable cardioverter defibrillators (ICDs), cardiac resynchronisation therapy (CRT) with defibrillator (CRT-D) or CRT with pacing (CRT-P) as treatment options for people with heart failure or people at risk of heart failure (people with previous serious ventricular arrhythmia). People with heart failure include those who have left ventricular dysfunction with a left ventricular ejection fraction of 35% or less (according to NYHA functional class, QRS duration and presence of left bundle branch block (LBBB)).

## 3.3 Patient issues and preferences

Heart failure is a long-term condition with no cure. People with the condition have many symptoms including breathlessness, fatigue and oedema which may make it difficult for them to attend hospital appointments. There is often anxiety associated with having the condition and this can impact on an individual's daily activities. Remote monitoring could decrease patient anxiety by providing reassurance to

patients that their condition is being monitored regularly by their clinical care team. Remote monitoring could reduce the number of face-to-face appointments, and the potential stress and travel costs associated with these appointments. It could improve access to specialist heart failure care for people living in geographically remote areas.

Remote monitoring aims to detect an increase in pulmonary artery pressure associated with worsening heart failure. The increase in pulmonary artery pressure indicates that fluid is beginning to accumulate, and this can be detected before the patient notices a change in symptoms. This enables intervention with a change of medication to address the fluid accumulation at an early stage, potentially reducing hospital admissions for heart failure and improving outcomes and quality of life.

The patient undergoes a procedure to implant the sensor into the pulmonary artery, as outlined in NICE guidance on percutaneous implantation of pulmonary artery pressure sensors for monitoring treatment of chronic heart failure. Once the sensor has been implanted and calibrated, patients use a system at home to initiate measurements. Patients are required to either lie down in a specific position or sit up in a chair and use a handheld control to initiate the measurement. Measurements must be initiated daily (or most days) to provide complete trend data. Patients must be willing and able to fit this into their routine. Patients must also be willing and able to comply with requests to visit the clinic and make changes to their medication to benefit from PAP monitoring.

Heart failure patients who meet the criteria for CIEDs may be able to benefit from algorithm-based remote monitoring, which is incorporated into their device, as outlined in NICE guidance on heart failure algorithms for remote monitoring in people with cardiac implantable electronic devices. Heart failure patients who do not meet the criteria for CIEDs are unable to access algorithm-based remote monitoring. PAP monitoring could address an unmet need for heart failure patients who do not have CIEDs and could benefit from remote monitoring. Having a CIED implanted does not preclude a person from having a PAP monitoring device.

# 4 Comparator

The comparator is usual care for monitoring chronic heart failure, as outlined in 3.2.

# 5 Scope of the assessment

### Table 1: Scope of the assessment

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| **Decision question** | Does remote pulmonary artery pressure monitoring for chronic heart failure represent a clinically and cost-effective use of NHS resources? |
| **Populations** | Adults who have chronic heart failure of any cause with NYHA class III symptoms at the time of assessment who are at high risk of hospital admission for their heart failure.<br><br>If evidence allows, the following subgroups may be considered:<br>• People with renal impairment<br>- eGFR 30 - 60 mL/min/1.73m$^2$<br>- eGFR < 30 mL/min/1.73m$^2$<br>• Baseline pulmonary artery pressure (at time of sensor implantation)<br>• Age<br>- <75 years<br>- 75 years and over |
| **Intervention** | Pulmonary artery pressure systems for remote monitoring of chronic heart failure<br>• CardioMEMs HF System (Abbott)<br>• Cordella Pulmonary Artery Sensor System and Cordella Heart failure System (Endotronix/Edwards) |
| **Other alternative interventions** | • None identified |
| **Comparator** | Usual care for monitoring of heart failure (see 3.2) |
| **Healthcare setting** | Pulmonary artery monitoring devices are used at home. The readings are sent remotely to a database which can be accessed by the patient's care team, usually based at a hospital. |
| **Outcomes: clinical** | Clinical outcomes for consideration may include:<br><br>• Hospitalisation for heart failure |

| | |
|---|---|
| | • Urgent care for heart failure (hospital attendance for i.v. diuretics)<br>• Worsening of heart failure (e.g., decompensation, change of NYHA symptom class)<br>• Changes to clinical management (including medication changes)<br>• Mortality due to heart failure<br>• All-cause mortality<br>• Failure of sensor implantation or sensor<br>• Adverse events<br>  ○ Complications associated with sensor implantation (including hospitalisation, complications associated with vascular procedures, infection, complications associated with anticoagulant/dual antiplatelet therapy post-implantation)<br>• Improvement in co-morbidities<br>• Functional capacity (for example, 6 minute walk test, incremental shuttle walking test)<br>• Patients lost to follow-up |
| **Outcomes: patient-reported** | Patient-reported outcomes for consideration may include:<br>• Health-related quality of life<br>• Adherence to using the technology<br>• Adherence to treatment (adherence to adjusted medication triggered by changes in PAP trend data, adherence to usual heart failure medication)<br>• Qualitative data on patient experience of using the technology |
| **Outcomes: costs** | Costs will be considered from an NHS and Personal Social Services perspective. Costs for consideration may include:<br>• Cost of procedure to implant the sensor, including the catheter, sensor and staff time<br>• Cost of system, including the patient system and hospital system and software<br>• Downstream costs associated with use of the technology |
| **Measuring cost-effectiveness** | The cost-effectiveness of interventions should be expressed in terms of incremental cost per quality-adjusted life year. |
| **Time horizon** | The time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.<br><br>Outcomes will be assessed at 1, 2 and 5 years |

# 6 Other issues for consideration

## 6.1 Sustainability

Use of remote monitoring systems could reduce the number of unnecessary hospital appointments, reducing travel for people with heart failure and reducing carbon emissions.

The implanted sensor is designed to remain in use for a lifetime. The catheter used to insert the sensor is disposable. The equipment used by the patient at home needs to be disposed of in accordance with regional regulations for disposal of electronic waste.

## 6.2 Emerging technologies for remote monitoring of heart failure

### 6.2.1 NORM System

The NORM system (FIRE1) comprises an implantable sensor, an externally worn belt and an app/web portal. The sensor is implanted into the inferior vena cava (IVC) and works by continuously measuring the cross-sectional areas of the IVC. The patient wears a belt for a few minutes each day. The belt activates the sensor and records expansions and contractions of the IVC, which corresponds to the amount of fluid in the body. The wireless belt sends the sensor data to the cloud. The NORM System's algorithms process the data to generate information on the patients IVC. These algorithms monitor the patient's condition and identify when the care team need to get involved. Information is accessible via clinician and patient apps. NORM is outside of the scope for this guidance, as it does not measure pulmonary artery pressure.

## 6.3 Ongoing studies

### 6.3.1 CardioMEMs HF System

The PASSPORT-HF study is an ongoing open-label, prospective, RCT across 50 centres in Germany. 554 patients with chronic heart failure, predominantly in NYHA class III within the last 30 days and hospitalised for heart failure at least once in the 12 months prior to enrolment irrespective of the ejection fraction. Patients are on stable guideline-directed pharmacotherapy and are randomised to receive the CardioMEMs sensor or control group. The expected completion date is December 31, 2026.

TEAM-HF is an international study across 75 sites that comprises an RCT and a single-arm registry 850 patients with chronic heart failure, NYHA IIIB/IV who had prior HF hospitalisation and an elevated mean PAP secondary to left ventricular failure are followed 2 to 5 years. The RCT aims to determine: a) if HeartMate 3, the left ventricular assist device (LVAD) can demonstrate an improvement in survival compared to GDMT in patients who have elevated ambulatory PAP and are not dependent on intravenous inotrope medication; b) to establish disease-state criteria to trigger referral for a HeartMate 3.

Patients who do not meet the PAP threshold for the RCT are entered into a single arm registry. The objective is to follow patients with lower mean PAP to evaluate how their HF progresses and if a delayed HeartMate 3 implantation would benefit these patients.

The CardioMEMS HF System is used to measure ambulatory PAP in patients participating in the trial. The expected completion date is September 2032.

### 6.3.2. Cordella Pulmonary Artery Sensor System and Cordella Heart Failure System

The PROACTIVE-HF trial is designed to assess the benefit of personalised and proactive management of patients with class III heart failure guided by daily measurement of pulmonary artery pressures in combination with weight, blood pressure heart rate, blood oxygen saturation and symptoms. PROACTIVE-HF was

originally designed as a single-blind RCT. Patients with heart failure (NHYA class III) and at high risk of congestion (previous hospitalisation for heart failure or elevated NTproBNP) were entered into the trial. All patients received the Cordella pulmonary artery sensor and were randomised to intervention or control groups. PAP readings were visible to clinicians in the intervention group and were not visible to clinicians in the control group. In December 2021, the trial design was changed to a single arm unblinded trial in consultation with the FDA. The expected completion date is September 2029.

At the scoping workshop, the company highlighted another ongoing study, PROACTIVE-HF 2. PROACTIVE-HF 2 is an ongoing open label prospective RCT across 100 centres in the USA, UK and Europe, designed to assess the safety and effectiveness of the Cordella PA Sensor System in patients with NYHA Class II and III heart failure.

### 6.3.3 Right-sided heart failure

Clinical experts advised that pulmonary artery pressure monitoring devices are also used for monitoring right-sided heart failure (including pulmonary hypertension and genetic conditions). Assessment of pulmonary artery monitoring devices for monitoring right-sided heart failure is out of scope for this guidance, as this is an emerging area of practice and trial data are not yet available.

## 7 Potential equality issues

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with protected characteristics and others.

The risk of heart failure is related to older age and family history. Both the incidence and prevalence of heart failure increases steeply with age, and the average age at diagnosis is 77 (NICE 2018). Heart failure with reduced ejection fraction is more common in men, due to the link with increased coronary artery disease in men,

whereas heart failure with preserved ejection fraction is more common in women. People with heart failure may be covered by the Equality Act 2010 under disability if their condition has a substantial and adverse effect on ability to carry out normal day-to-day activities and lasts at least 12 months. Many people with heart failure are older and have multiple co-morbidities.

People with cognitive impairment, problems with manual dexterity, and learning disabilities may need additional support to use the technology at home.

The devices are pre-programmed with a number of languages. If the required language is not pre-programmed, it would need to be added to the device.

No potential equality issues were identified in relation to pregnancy, ethnicity, religion, sexual orientation and gender reassignment.

# 8 Potential implementation issues

Potential enablers and barriers to implementation include:

## 8.1 Training and staffing

Training and appropriate staffing is required to facilitate sensor implantation and PAP monitoring. Patients and/or their carers will need training on how to initiate the measurement. Training on PAP trends and escalation processes should be provided to the healthcare professional who access patient PAP data. A clinical expert mentioned that heart failure specialist nurses are well placed to access and monitor the data, as a heart failure specialist nurse would be able to read and interpret PAP trend data and prescribe medications if required.

## 8.2 Costs

Costs may differ between technologies. Beyond the cost of the sensor implant, healthcare professionals are needed for ongoing monitoring and management. Therefore, the cost of the staffing models would form a key part of the cost.

# 9 Authors

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# Appendix A Glossary of terms

### Acidaemia

Abnormal acidity of the blood

### Ambulatory monitoring

Ambulatory monitoring devices can be used by the patient at home or as an outpatient, without the need to be in a clinic or hospital setting.

### BNP (B-type Natriuretic Peptide)

A hormone released by the heart when the ventricles are stretched. Levels of BNP in the blood increase when heart failure develops or worsens and decrease when the condition is stable. It is an important clinical marker for the diagnosis of heart failure in patients with unexplained shortness of breath.

### Cardiac implantable electronic devices

Cardiac implantable electronic devices (CIEDs) are used to manage slow and fast heart rates, and in the treatment of selected patients with heart failure. CIEDs are usually implanted under the skin, with 1 to 3 leads threaded down a vein to connect to the heart. Types of CIED include permanent pacemakers, implantable cardioverter defibrillators (ICDs), and cardiac resynchronisation therapy (CRT) devices.

### Cardiac resynchronisation therapy

Cardiac resynchronisation therapy (CRT) is a treatment used to help the heart pump more effectively. It is recommended for some patients with poor ventricular function (when the heart is not pumping as well as it should). A CRT pacemaker (CRT-P) is used to treat heart failure when the two sides of the heart lose their coordination and become less efficient at pumping blood around the body. A CRT defibrillator (CRT-D) does the same as a CRT-P but has additional defibrillation therapy to correct abnormal heart rhythms.

### Cardiomyopathy

A general term for disease of the heart muscle, where the walls of the heart chambers have become stretched, thickened or stiff, affecting the heart's ability to pump blood around the body.

**Dyspnoea**

Shortness of breath.

**Echocardiogram**

An ultrasound scan of the heart which visualises the structure and function of the heart and surrounding blood vessels.

**Electrocardiogram**

A test that records the rhythm, rate and electrical activity of the heart.

**Femoral**

Femoral refers to the thigh. The femoral vein is a deep vein located in the thigh.

**Haemodynamic**

Relating to the flow of blood through arteries and veins and the forces that affect blood flow.

**Heart failure decompensation**

A rapid worsening of symptoms and/or signs of heart failure that warrants immediate medical intervention. It typically includes difficulty breathing (dyspnoea), leg or feet swelling, and fatigue.

**Implantable cardioverter defibrillator**

An implantable cardioverter defibrillator (ICD) is a device implanted in the chest to detect and control irregular heart rhythms by sending electric shocks to the heart.

**Left bundle branch block**

A heart block occurs when electrical signals in the heart are blocked or delayed. A left bundle branch block (LBBB) occurs when signals to the left ventricle get blocked or delayed.

**Left ventricular assist device**

A left ventricular assist devices (LVAD) is a device which acts like an artificial heart pump. It is used to treat severe heart failure, with the aim of restoring blood flow around the body. LVADs may be given to people waiting for a heart transplant.

**Myocarditis**

Inflammation of the heart muscle, usually caused by a viral infection.

**Natriuretic peptide**

Proteins made by the heart and blood vessels (see brain natriuretic peptide and N-terminal pro b-type natriuretic peptide)

**NT pro-BNP (N-terminal pro-B-type Natriuretic Peptide)**

A non-active prohormone that is released from the same molecule that produces BNP. NT pro-BNP levels in the blood also rise with heart failure.

**NYHA class**

The New York Heart Association (NYHA) classification is system which classifies the severity of heart failure based on symptoms.

**Oedema**

A build-up of fluid in the ankles, feet and legs that causes swelling.

**Pacemaker**

A pacemaker sends electrical pulses to the heart to control the pace at which it beats. It consists of a pulse generator, which has a battery and a tiny computer circuit, and 1 or more wires known as pacing leads, which attach to the heart.

**Percutaneous**

A percutaneous procedure is a procedure where access to the target tissue is achieved via needle puncture of the skin. Percutaneous access is commonly used in vascular procedures, including implantation of devices.

**Pulmonary artery**

The blood vessel that carries blood from the right ventricle of the heart to the lungs

**QRS**

The QRS complex is part of an electrocardiogram (ECG) measurement. It represents depolarisation of the ventricles.

# Appendix B References


All-Party Parliamentary Groups. Focus on Heart Failure [online; accessed 17 January 2025]

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## Routine use assessment

# DG10087 Pulmonary artery pressure technologies for remote monitoring of chronic heart failure

## Assessment report overview

This overview summarises key information from the assessment and sets out points for discussion in the committee meeting. It should be read together with the final scope and the external assessment report (EAR). List of abbreviations used in this overview is in appendix A.

## 1. The technology

Pulmonary artery pressure (PAP) monitoring systems use implantable sensors to collect data on PAP in people with chronic heart failure to allow for ongoing remote monitoring. The technologies aim to detect increases in PAP (which indicate that fluid is beginning to accumulate due to worsening heart failure) at an early stage. Earlier detection allows for medication to be optimised so that decompensation (worsening of heart failure symptoms due to the heart's inability to maintain adequate circulatory function) and hospitalisation can be avoided.

A PAP sensor is implanted into the pulmonary artery (the artery that carries deoxygenated blood from the right side of the heart to the lungs) via a right heart catheterisation procedure. NICE previously recommended that the evidence on safety and efficacy is adequate to support the procedure for percutaneous implantation of pulmonary artery pressure sensors for monitoring treatment of chronic heart failure.

The patient initiates daily measurements at home. Data on PAP, including pressure trends and waveforms, is collected and transmitted to an external monitor in the patient's home. The monitor securely forwards this information to a remote database which can be accessed by the patient's care team. PAP

monitoring is used as part of ongoing monitoring to guide management of chronic heart failure. PAP monitoring is not intended to make or confirm diagnosis of heart failure.

## Technologies

Two technologies were in scope for the assessment: CardioMEMS HF System (Abbott) and Cordella Pulmonary Artery Pressure Sensor System and Cordella Heart Failure System (referred to as CardioMEMs and Cordella).

**Table 1 Summary of technologies for monitoring pulmonary artery pressure included in the assessment**

| | **CardioMEMS HF System (Abbott)** | **Cordella Pulmonary Artery Sensor System and Cordella Heart Failure System (Endotronix/Edwards Life Sciences** |
|---|---|---|
| **Intended use** | CardioMEMS is indicated for wirelessly measuring and monitoring PAP and heart rate in patients with chronic heart failure. In the UK. CardioMEMS is indicated for patients with NYHA class III symptoms and a prior hospitalisation for heart failure within the last 12 months, regardless of ejection fraction status. | Cordella is intended to measure, record and transmit PAP data in patients with NYHA class III heart failure who are at home on diuretics and guideline-directed medical therapy, and have been stable for 30 days. The device output is intended to aid clinicians in the assessment and management of heart failure with the goal of reducing heart failure hospitalisations. Cordella is currently an investigational device and is not yet approved for use on the UK. |
| **Contraindications** | CardioMEMS is contraindicated for people who are unable to take dual antiplatelet therapy or anticoagulants following implantation. | Cordella is contraindicated for people who are unable to take dual antiplatelet therapy or anticoagulants following implantation. |
| **CE mark status** | Class III CE mark | Class III CE mark |

| | | |
|---|---|---|
| **Description** | CardioMEMs includes a small pressure sensor that is permanently implanted in the distal pulmonary artery during a minimally invasive right heart catheterisation procedure. The sensor is secured with nitinol wire loops. It measures PAP changes, which reflect fluid retention in the lungs due to worsening chronic heart failure.<br><br>At home, patients use a portable electronics unit and a pillow with an embedded antenna. By lying down on the pillow and activating the device, patients initiate daily pressure readings by pressing a button. The data are wirelessly transmitted to a secure database for clinicians to review. Clinicians can observe trends and adjust medications and treatments as needed, and often before symptoms appear, reducing the risk of decompensation and hospitalisation. | The sensor is implanted in the pulmonary artery, and readings can be initiated at home by holding a wireless handheld device against the right pectoral region for 20 seconds. In addition to PAP data, the Cordella Heart Failure System measures vital signs including blood pressure, heart rate, weight, and oxygen saturation.<br><br>Collected data is sent to the myCordella Hub, which guides patients in using the system, asks health-related questions, and transmits information to the myCordella Patient management Portal for clinicians to access. This system aims to assist healthcare providers in assessing and managing heart failure potentially reducing hospitalisations. |
| **Usage within NHS** | In the NHS in England, CardioMEMs has mostly been used in a trial setting and is not currently routinely used. | Not currently used in NHS |

# 2. The condition

Heart failure is a clinical syndrome caused by any structural or functional cardiac disorder that impairs the heart's ability to function efficiently and pump blood around the body. The most common symptoms of heart failure are breathlessness, fatigue, and oedema.

Heart failure may be classed by ejection fraction as follows:

- HFpEF – heart failure with preserved ejection fraction (50% and over)
- HFmrEF – heart failure with mildly reduced ejection fraction (between 40% and 49%)
- HFrEF – heart failure with reduced ejection fraction (below 40%).

Heart failure may also be classed by symptom severity and limitation of physical activity according to the New York Heart Association (NYHA) ranging from class I (no limitations) to class IV (inability to carry out any physical activity without discomfort and symptoms which may be present at rest).

Heart failure mainly affects people over the age of 65, with an average age of diagnosis of 77, and risk increases significantly with age.

## 3. Current practice

### Diagnosis, assessment and monitoring of chronic heart failure

The NICE guideline for diagnosis and management of chronic heart failure in adults recommends that monitoring of people with chronic heart failure should include a clinical assessment of functional capacity, fluid status, cardiac rhythm, cognitive status and nutritional status, a review of medication, and an assessment of renal function.

The ESC guideline for diagnosis and treatment of acute and chronic heart failure adds that heart failure management may involve in person services or home-based telemonitoring. While care is usually followed up by heart failure clinics, suitable patients may be followed up by healthcare professionals including community heart failure nurses, GPs with special interest in heart failure and specialist pharmacists.

People should have additional monitoring if they have co-morbidities, are taking co-prescribed medications or if their condition has deteriorated since their last review.  The frequency of monitoring is dependent on the clinical status and stability of the person's condition.

Further information on heart failure management is available in the final scope and in section 1.3 of the assessment report.

# 4. Unmet need

Heart failure accounts for a total of 1 million inpatient bed days each year (2% of all NHS inpatient bed days) and 5% of all emergency medical admissions to hospital. Hospitalisations for heart failure are a significant cost to the NHS and have a big impact on the quality of life of the individual patients.

PAP monitoring technologies offer remote monitoring of chronic heart failure and aim to reduce hospitalisations for heart failure. PAP monitoring technologies would be used as an add-on test in the care pathway to supplement standard clinical management for NYHA class III patients. PAP monitoring technologies would need to be integrated into a specialist multidisciplinary heart failure service, with alerts and trend data monitored and managed by specialist healthcare professionals.

Further details, including descriptions of the interventions, comparator, care pathway and outcomes, are in the final scope.

# 5. Clinical effectiveness

Comprehensive literature searches identified relevant published clinical evidence, supplemented by company responses to requests for information from NICE.

Search and selection methods are described in section 4.2 of the assessment report.

## 5.1 Overview of key studies

11 studies (60 reports) were included in the clinical effectiveness review. Eligible evidence comprised of 3 randomised controlled trials (RCTs), 3 single arm prospective studies and two studies on patient experience for CardioMEMS and 3 prospective single arm studies for Cordella. Two of the single arm Cordella trials included patient surveys that contributed data on patient experience and satisfaction.

Only one study was conducted in the UK, other studies were conducted in the USA, Canada, Belgium, Ireland and Germany. Sample sizes varied widely from 12 participants to 1214 participants in a large prospective single arm study. Study populations typically included older adults (mean or median ages between 61 to 71 years) with a higher proportion of male and white participants. Where reported, baseline mean PAP and kidney function were similar across studies.

## Studies that provided quantitative outcome data for CardioMEMS

3 RCTs evaluated CardioMEMS: CHAMPION, MONITOR-HF and GUIDE-HF. In CHAMPION and MONITOR-HF, trial participants had NYHA class III heart failure. In the GUIDE-HF trial, participants had NYHA class II-IV heart failure. Participants in the intervention arms of these trials received the standard of care heart failure management guided by the hemodynamic information from the implanted sensors. All 3 trials used standard care as the comparator, which was defined as guideline-directed medical therapy or standard heart failure management. In CHAMPION and GUIDE-HF, randomisation occurred after sensor implantation. In MONITOR-HF, randomisation occurred before sensor implantation. Duration of follow-up ranged from 12 to 48 months for the RCTs and 3 to 12 months for the single arm studies.

**Table 2: Study design and characteristics of studies reporting quantitative outcome data for CardioMEMs**

| Study name/ Technology | Study design & Country | Population | Country |
|---|---|---|---|
| CHAMPION<br><br>CardioMEMs | RCT,<br><br>Intervention group N=270, 72% male, mean age (SD) 61 (3) years. | NHYA class III heart failure and HHF within past 12 months | USA |

| | | | |
|---|---|---|---|
| | Control group N=280, 73% male, mean age (SD) 62 (13) years. | | |
| GUIDE-HF<br><br>CardioMEMs | RCT,<br><br>Intervention group N= 497, 62% male, median age (lower/upper range) 71 (64,76) years.<br><br>Control group N= 503, 63% male, median age (lower/upper range) 70 (64,77) years | NYHA class II-IV heart failure and HHF within past 12 months or elevated natriuretic peptides of NT-pro-BNP | USA, Canada |
| MONITOR-HF<br><br>CardioMEMs | RCT<br><br>Intervention group N=176, 78% male, median age (upper/lower range) 69 (61,75) years)<br><br>Control group N=172, 73% male, median age (upper/lower range) 70 (61,75) years | NYHA class III heart failure and HHF or urgent visit within past 12 months | Netherlands |

### Studies that provided quantitative outcome data for Cordella

3 single arm studies with 597 participants in total evaluated Cordella: SIRONA, SIRONA 2 and PROACTIVE-HF. Participants in these trials had NYHA class III heart failure. All participants in these studies received daily

PAP measurement and vital sign monitoring, which was used to guide heart failure management.

PROACTIVE-HF was originally designed as an RCT but was changed to a single-arm study as a result of emerging evidence supporting PAP-guided HF management in NYHA class III patients, increased access to reimbursed PAP technology (in the USA), and disruptions from the COVID-19 pandemic.

**Table 3: Study design and characteristics of studies reporting quantitative outcome data for Cordella**

| Study name/ Technology | Study design & Country | Population | Country |
|---|---|---|---|
| PROACTIVE-HF (RCT phase)<br><br>Cordella | RCT<br><br>Intervention group N= 88, % male not reported, age not reported.<br><br>Control group N=72, 58% male, mean age (SD) 66 (11) years | NYHA class III heart failure and HFH, HF treatment in a day setting or urgent visit for HF care within past 12 months and/or elevated NT-pro-BNP. | USA, Ireland, Belgium |
| PROACTIVE-HF (single arm phase)<br><br>Cordella | Single arm plus survey<br><br>N=456, 61% male, mean age (SD) 64 (13) years | NYHA class III heart failure and HFH, HF treatment in | USA, Ireland, Belgium |

| | | | |
|---|---|---|---|
| | | a day setting or urgent visit for HF care within past 12 months and/or elevated NT-pro-BNP. | |
| SIRONA<br><br>Cordella | Prospective single arm<br><br>N=15, 67% male, mean age 71 years | NYHA class III heart failure with reduced or preserved ejection fraction and HFH or equivalent within past 12 months | Belgium, Ireland |
| SIRONA 2<br><br>Cordella | Prospective single arm<br><br>N=70, 71% male, mean (SD) age 71 (10) years | NYHA class III heart failure with reduced or preserved ejection fraction and HFH or equivalent | Belgium, Germany, Ireland |

| | | | |
|---|---|---|---|
| | | within past 12 months | |

## Studies included for device related outcomes only

Studies included for device related outcomes were prospective single-arm, multicentre, open-label study evaluations of CardioMEMS. Participants had NYHA class III heart failure. The COAST study aimed to enrol 800 patients from 85 sites across the UK, Europe and Australia. Results are currently available for the UK and French cohorts. MEMS-HF was conducted in Germany, the Netherlands and Ireland, and CardioMEMS-PAS in the USA.

**Table 4: Study design and characteristics of studies reporting device related outcomes for CardioMEMS**

| Study name | Study design | Country | Population |
|---|---|---|---|
| MEMS-HF | Prospective, non-randomised, multi centre<br><br>N=234, 78% male, mean age (SD) 68 (11) years | Germany, Netherlands, Ireland | NYHA class III heart failure and HFH within past 12 months |
| COAST-UK | Prospective, non-randomised, multi centre<br><br>N=100, 70% male, mean age (SD) 69 (12) years | UK | NYHA class III heart failure and HFH within past 12 months |

| | | | |
|---|---|---|---|
| COAST-FRANCE | Prospective, non-randomised, multi centre<br><br>N=103, 78% male, mean age (SD) 67 (12) years | France | NYHA class III heart failure and HFH within past 12 months |
| CardioMEMS-PAS | Prospective, non-randomised, multi centre<br><br>N=1214, 62% male, mean age (SD) 70 (12) years | USA | NYHA class III heart failure and HFH within past 12 months |

## Qualitative studies

Two qualitative studies assessed patients' experience of using CardioMEMs. Assad et al conducted a web-based survey and Hynes et al carried out semi-structured interviews with patients. The SIRONA-2 and PROACTIVE-HF studies also carried out patient surveys to evaluate patient experience with the Cordella system and engagement with PAP measurement.

**Table 5: Study design and characteristics of included qualitative studies for CardioMEMS**

| Study name | Study design | Country | Population |
|---|---|---|---|
| Assad et al | Survey<br><br>N=30, % male not reported, mean age not reported | USA | Heart failure patients with CardioMEMS device implanted |

| | | | |
|---|---|---|---|
| Haynes et al | Semi-structured interviews<br><br>N=12, 67% male, mean age (SD) 71 (13) years | USA | Heart failure patients with CardioMEMS implanted |

Full details of study design and characteristics are in section 5.3 and appendix 3 of the EAR.

## 5.2 Results

Full details of the outcomes of the clinical effectiveness review are in section 5.5 and appendix 4 of the EAR. A summary of data across key outcomes is presented here.

### Heart Failure Hospitalisation (HFH)

Six studies reported HFH and all suggested beneficial effects of the PAP monitoring technologies in reducing hospitalisation at between 3- and 48-month follow-up. Definitions of HFH were similar across studies. There was high certainty evidence from 3 RCTs that CardioMEMS was associated with reduced HFH compared to standard care (summary HR was 0.66 (95% CI 0.57, 0.76)).

There was lower certainty evidence suggesting that Cordella was associated with a reduction in HFH. Data supplied by the manufacturer of Cordella for the randomised phase of PROACTIVE-HF suggested a similar improvement associated with Cordella (HR 0.61, 95% CI 0.36, 1.04), although confidence intervals were wide.

Two of the three single arm studies that evaluated Cordella reported a reduction in HFH following sensor implantation. PROACTIVE-HF reported that the average HFHs per patient in the 6 months before implant was 0.6 (SD= 0.7) compared to 0.1 (SD=0.4) in the 6 months after implant in the single-arm phase of the study ($p< 0.0001$). SIRONA 2 reported that the event rate decreased from 1.26 events per patient-year (EPPY), in the 12 months prior to

device implantation to 0.27 EPPY in the 12 months post-implantation (p< 0.0001). The SIRONA study was very small and it was not possible to determine the impact of the Cordella device in this study.

Indirect comparison of Cordella with CardioMEMS conducted using comparative evidence from the RCT phase of PROACTIVE-HF and the RCTs of CardioMEMS suggested no difference in HFH between the two technologies [redacted].

### All-cause mortality

All-cause mortality was reported by all 3 RCTs that evaluated CardioMEMS and for the comparative and single arm phases of the PROACTIVE-HF Cordella study and the SIRONA 2 study. Overall, there was a suggestion for a small decrease in mortality across the 3 CardioMEMS RCTs and from data provided by the manufacturer of Cordella for the comparative phase of the PROACTIVE HF trial. Confidence intervals were wide and consistent with both an increased and decreased risk of death for CardioMEMS (HR 0.91, 95% CI 0.70, 1.17) and for Cordella (HR 0.51, 95% CI 0.20, 1.32). Indirect comparison of Cordella with CardioMEMS suggested no evidence of a difference in all-cause mortality between the two technologies [redacted], although the estimate is very imprecise.

### Failure of sensor implantation

All studies provided data on failure of sensor implantation. The proportion of participants in whom the device failed to implant ranged from 0 to 7.5% across studies, with a summary estimate of 1.7% (95% CI 0.8%, 2.9%) in the CardioMEMS studies and 4.9% (95% CI 3.1%, 7.0%) in the Cordella studies. Further details are reported in section 5.5.1.3 of the EAR.

### Sensor failure

All studies except GUIDE-HF reported on sensor failure at between 3 and 48 months of follow-up. The proportion of participants with a sensor implanted in whom the sensor subsequently failed was low (0 to 1.2%) with a summary estimate 0.1% (95% CI 0.0, 0.6%) and 0% (95% CI 0,0.1%) for Cordella. Further details are reported in section 5.5.1.4 of the EAR.

### Device/system or procedure-related complications (DSRC) and procedure related complications

All studies provided data on device or system related complications. Definitions of a DSRC were broadly similar across studies. The proportion of DSRC were very low across studies for both CardioMEMS and Cordella (range 0.8 to 2.4%). The summary proportion of DSRC across trials was 0.7% (95% CI 0.3, 1.3%) for CardioMEMS and 0.1% (0.0, 0.09%) for Cordella. Further details are reported in section 5.5.1.5 of the EAR.

### Health-related quality of life

All studies provided data on health-related quality of life (HRQoL) measured using either the EQ-5D-5L visual analogue scale, the Kansas City Cardiomyopathy Questionnaire (KCCQ) or the Minnesota Living with Heart Failure questionnaire (MLHFQ). The impact on of PAP monitoring technologies on HRQoL was mixed. Some CardioMEMS studies showed improvements, but findings were inconsistent and overall, the effect remains uncertain. For Cordella, data on HRQoL were limited and lacked direct comparisons, making it difficult to draw firm conclusions. Further details are reported in section 5.5.1.6 of the EAR.

## Secondary outcomes

There was no evidence that CardioMEMS reduced urgent care visits or cardiovascular mortality, and no comparative data were available for Cordella. CardioMEMS trials, showed more frequent medication changes and healthcare professional contact. Comparable data were not available for Cordella. All 3 RCTs on CardioMEMs reported either a similar or increased number of contacts with healthcare professionals in the intervention arm. compared to the control arm. All studies reported improvements in 6-minute walk test distance relative to baseline, though RCT evidence for CardioMEMS found no difference compared to control. Adherence to device use was high across both systems. All studies reported withdrawal of participants in both arms after implantation with proportion ranging from 0 to 39%. The most

common reasons were death followed by withdrawal of consent. Full details are reported in sections 5.5.2 and 5.5.3 of the EAR.

### Patient experience and satisfaction

Patient experience was generally positive. CardioMEMS users reported better understanding, reassurance, and ease of use. Cordella users also found the device easy to use and helpful, though fewer than half reported making lifestyle changes based on the data.

### Adverse events

3 studies reported on other adverse events, definitions and the level of AE reported varied across studies. Serious adverse events (SAE) were defined as an adverse event that led to death or deterioration in health. In GUIDE-HF over half of participants experienced SAEs with similar proportions across treatment groups (RR 1.06 (95% CI 0.95, 1.19). In SIRONA 2, 4 patients experienced AEs including skin irritation, haemoptysis, vessel trauma and haematoma. They also reported that one patient experienced a left ventricular lead revision, classified as an SAE. In the PROACTIVE-HF study, SAEs included death, life-threatening, hospitalisation (initial or prolonged), disability or permanent change, congenital anomaly/birth defect, required intervention to prevent permanent impairment or damage, other serious (important medical events). At 6 months follow-up, 196 participants were reported to have experienced a SAE.

### Data on subgroups

An overview of baseline characteristics of participants in included studies is provided in section **Error! Reference source not found.**. All studies reported age, sex and comorbidities at baseline, and all except MONITOR-HF reported on ethnicity. Most participants were older (mean age >60 years), with a higher proportion of men, and the majority of participants were white. Comorbidities ranged in prevalence and type across the six studies. No studies reported on cognitive impairment, problems with manual dexterity, and learning disabilities. Stratified results from single studies were available for NHYA

class, comorbidities and baseline PAP were for HFH, and baseline PAP for mortality.

### Quality assessment

Methodological quality was assessed for studies that reported the primary outcomes of hospitalisation for heart failure, all-cause mortality, health related quality of life and safety outcomes. The quality assessment strategy and summary of risk of bias assessment are reported in sections 4.3.3 and 5.4 of the EAR. GRADE (Grading of Recommendations Assessment, Development and Evaluation) was used to rate the certainty of the evidence for the primary outcomes. The approach to GRADE and summary of the assessment are described in sections 4.7 and 5.8 of the EAR.

## 5.3 Ongoing studies

An overview of ongoing studies can be found in table 29 of the EAR.

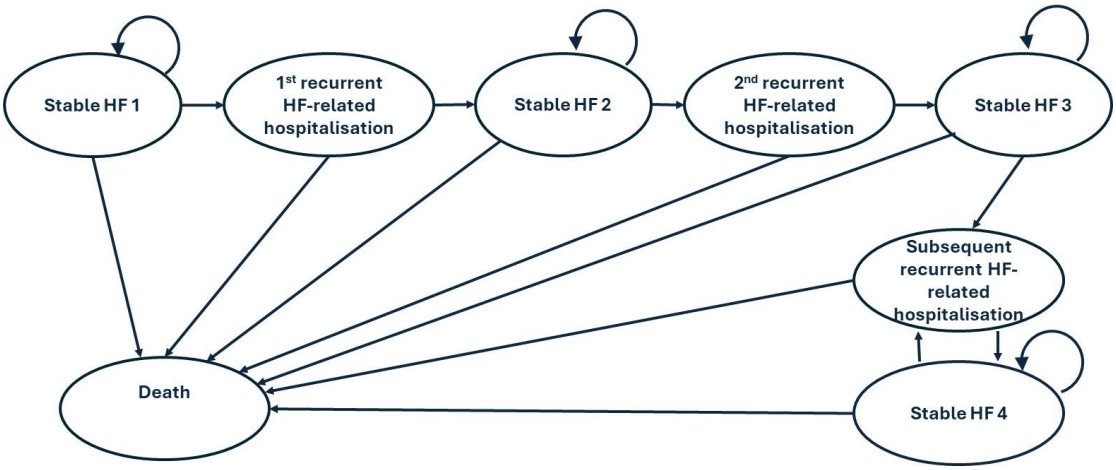
# 6. Health economic evidence

The external assessment group (EAG) conducted a review of existing health economic evidence including relevant health economic models. The EAG found 11 economic evaluations relevant to the decision problem for CardioMEMs. An overview of these 11 models is in table 11 of the external assessment report (EAR). No economic evaluations were identified for Cordella.

## 6.1 Health economic model

The EAG developed a decision analytic model that estimates the cost-effectiveness of remote PAP monitoring technologies compared with current monitoring practice (standard care). The model captures short and long term costs and benefits of the technologies. The model is run over a lifetime and a half cycle correction was implemented to reflect the timing of events within the cycle, and costs and QALYs (Quality-adjusted life year) were discounted at a rate of 3.5%.

**Figure 1 Markov model**




The Markov model (Figure 1) captures long-term health outcomes and comprises 8 mutually exclusive states (stable HF 1, 1st recurrent HFH, stable HF 2, 2nd recurrent HFH, stable HF 3, subsequent recurrent HFH, stable HF 4 and death) following the initial heart failure hospitalisation period. The recurrent HFH states are tunnel states for a single cycle from which people transition either into a stable state or death.

Further details of the economic modelling methods are in section 6.2 of the EAR.

## Population

The modelled population was NYHA Class III CHF patients who are eligible for remote PAP monitoring following an index HF-related hospitalisation (HFH). The population was 70% male with a mean age of 69 years based on the CardioMEMs post-market study (COAST).

## Key Assumptions

- Cordella has same cost as CardioMEMs (as a price for Cordella is not yet available) and both devices remain implanted for the lifetime of the patient.
- The HFH rate depends on the monitoring strategy, and the relative effect of each monitoring strategy is assumed to be the same regardless of the number of previous HFHs.

- The hazard ratio for mortality is 1(no direct effect) for both CardioMEMs and Cordella, because there was no statistical evidence for an effect on all-cause mortality.
- Routine monitoring is carried out by a band 5 nurse or band 5 cardiac physiologist for 10 minutes per patient per check, with three checks carried out per week (both based on clinical advice). Five minutes per month of a medical consultant was added for oversight, in line with the time used in the model from Health Technology Wales.
- All hospitalisations last for more than 2 days. The EAR states that clinical advice was that the average was around 9 days.
- Complication and comorbidity (CC) scores increase with the number of subsequent hospitalisations and no patients have CC scores of 1-3, as all had previously had a hospital admission.
- The disutility value for a single cycle for each HFH is 0.1, which is incurred in addition to the reduction in health-state utility for patients based on how many HFHs they have had.

## Model inputs

### HF-related hospitalisation (HFH) rates

The model allows the recurrent HFH rate to depend on the number of previous recurrent HFHs, where all patients in the model have had an index HFH.

**Table 6: Hazard ratio for HFH vs patients with 0 recurrent HFH after index event**

| Model State | Hazard ratio for HFH vs patients with 0 recurrent HFH after index event | Log-hazard ratio (95% CrI) and standard error (se) |
|---|---|---|
| Stable HF 1: standard care | 0.858 | -0.153 (annual)<br>se=0.0795 |
| Stable HF 2 | 1.70 | 0.532 (1.494, 1.944)<br>se= 0.0675 |
| Stable HF 3 | 1.86 | 0.619 (1.539, 2.222)<br>se= 0.0953 |

| | | |
|---|---|---|
| Stable HF 4 | 3.11 | 1.134 (2.263, 4.135)<br>se= 0.1613 |

The hazard-ratio for HFH for CardioMEMS relative to usual monitoring was based on a meta-analysis of the studies identified in the clinical effectiveness review for the NYHA class III subgroup data. The EAG notes that the control arm in PROACTIVE-HF involved telemonitoring of daily data on patients' vital signs (but not PAP measurements), which reflects more intensive monitoring than standard care. The hazard ratio for HFH from PROACTIVE-HF may therefore be unfavourable for Cordella compared with standard care.

**Table 7: Hazard ratio for HFH vs standard care**

| Technology | Hazard ratio for HFH vs standard care | Log-hazard ratio | Source |
|---|---|---|---|
| CardioMEMS | 0.66 95%CI (0.57, 0.76) | -0.415515444<br>se=0.0767 | Meta-analysis of studies for the NYHA class III subgroup data |
| Cordella | 0.61 95%CI (0.36, 1.04). | -0.494296322<br>se=0.2706 | PROACTIVE-HF trial estimate provided by company |

### Technology costs

Costs of the CardioMEMS device included the delivery system and sensor, a patient unit, ongoing access to the Merlin.net platform and training for physicians on both the implantation and the Merlin platform. A cost for the CardioMEMS reusable calibration unit for use in the hospital was assumed to be included within the HRG cost for implantation. Costs for Cordella are unknown as yet, but will include delivery system and sensor, patient reader

and reader dock, access to the Cordella Heart Failure System, and *ad hoc* training on implantation and the Cordella Heart Failure System.

**Table 8: Device-related costs**

| Technology | Cost | Source |
|---|---|---|
| Cordella device | £9,500 | Assumed equal to CardioMEMS |
| CardioMEMS device | £9,500 | Manufacturer |
| Implantation | £1,631 | National Cost Collection |
| Implantation failure (Cordella) | £2,771 | Assumed equal to CardioMEMS |
| Implantation failure (CardioMEMS) | £2,771 | National Cost Collection |
| Monitoring (per month) | £101 | PSSRU |
| Usual care (per month) | £91 | National Cost Collection, British National Formulary |

### Other treatment and follow-up costs

- Procedure costs to implant the device
- Device monitoring costs
- HFH costs
- Costs under standard care
- device or system related complications

### HFH Costs

Hospitalisation costs were derived from National Cost Collection data. The EAG calculated the cost of hospitalisation as the weighted average of complication and comorbidity (CC) score 0-14+ for the health resource groups (HRG) EB03 (heart failure or shock) using long-stay non-elective inpatient events. The first HFH post-insertion of the device was based on EB03C and EB03D (CC score of 4-10), the second post-insertion HFH was based on EB03B and EB03C (CC score of 8-13), and third and subsequent HFHs were based on EB03A and EB03B (CC score of 11-14+).

**Table 9: HFH costs**

| HF-related hospitalisations (HFH) | Cost |
|---|---|

| | |
|---|---|
| First post-insertion HFH | £3,242 |
| Second post-insertion HFH | £3,874 |
| Third and subsequent post-insertion HFH | £4,844 |

Further details on costs can be found in section 6.3.6 of the EAR.

## Health-related quality of life

The EAG used utility value of 0.66 95%CI (0.60, 0.70) for a patient in the Stable-HF state based on a meta-analysis of utilities for HF patients. For the Stable-HF2, Stable-HF3, and Stable-HF4 health states, the utility reductions estimated by Gohler et al, 2009 for patients with 1, 2, and 3+ re-hospitalisations respectively was applied. As patients progress through the Stable-HF states their utility will decline. The EAG did not include a further utility reduction over time as there is expected to be an average fall in utility. Details of the utility values at the different health states are in section 6.3.5.1 of the EAR.

## Mortality

Mortality rate depends on the number of previous HFHs, where all patients in the model will have had an index HFH at the start of the model. The hazard ratio for mortality rate by health states were derived from Lahoz et al. 2020, a large UK study using data from CPRD for patients with an index HFH recorded in HES, which was considered appropriate for the modelled population. For Stable HF 4, the value used corresponds to those with 3 recurrent HFHs (which was very similar to those with 4 recurrent HFHs).

**Table 10: Hazard ratios for mortality by number of recurrent HFH after the index HFH**

| Model State | Number of recurrent HFH after index event | Hazard ratio (95% CrI) for mortality vs patients with 0 recurrent HFH after index event | Log-hazard ratio (95% CrI) and standard error (se) |
|---|---|---|---|
| STABLE HF 1 | 0 | 1.00 | 0.000 |
| STABLE HF 2 | 1 | 1.98 (1.81, 2.17) | 0.683 (0.593, 0.775) se=0.0463 |

| Model State | Number of recurrent HFH after index event | Hazard ratio (95% CrI) for mortality vs patients with 0 recurrent HFH after index event | Log-hazard ratio (95% CrI) and standard error (se) |
|---|---|---|---|
| STABLE HF 3 | 2 | 2.39 (2.08, 2.74) | 0.871 (0.732, 1.008) se=0.0703 |
| STABLE HF 4 | 3 | 3.56 (2.92, 4.34) | 1.270 (1.072, 1.468) se=0.1011 |
| Subsequent stable HF | ≥4 | 3.47 (2.75, 4.38) | 1.244 (1.012, 1.477) se=0.1187 |

The mortality risks for standard care were derived from the Cowie models as this was validated against UK national audit data. The EAG's model is parameterised with age-specific mortality rates for Stable HF1, and hazard ratios for the other Stable HF states.

### Implant, device and sensor performance

The probability of implant failure and DSRC for CardioMEMS (0.017) was taken from the random effects model due to evidence of heterogeneity between studies. For Cordella the fixed effect model (0.007) was used due to insufficient evidence to estimate heterogeneity. Sensor failure for both CardioMEMS and Cordella was reportedly very rare, therefore, this was not included in the base-case.

## 6.2 Model results

### Base case

The total cost, QALYs and ICERs (incremental cost-effectiveness ratio) from the probabilistic base case are presented in Table 11 .

**Table 11: Base case results**

| Intervention | Total costs | Total QALYs | ICER vs standard care |
|---|---|---|---|
| CardioMEMS | £39,518 | 3.128 | £41,878 |
| Cordella | £39,013 | 3.193 | £31,541 |

| Intervention | Total costs | Total QALYs | ICER vs standard care |
|---|---|---|---|
| Standard care | £29,129 | 2.880 | - |

Both probabilistic and deterministic base case results show that CardioMEMs and Cordella are more effective and more expensive relative to standard care. The EAG cautioned about the interpretation of Cordella results, given the strong assumptions made for some of the clinical and costs parameters for this technology. Figure 2 and Figure 3 show the cost effectiveness plane with the probabilistic sensitivity analysis for CardioMEMs and Cordella. At a willingness-to-pay threshold of £20,000 or £30,000 per QALY, both technologies are not considered cost-effective with majority of the iterations falling in the north-east quadrant above the £30,000 willingness-to-pay threshold.

**Figure 2: Cost- effectiveness plane for CardioMEMS vs standard care at £20,000 and £30,000 willingness to pay threshold**

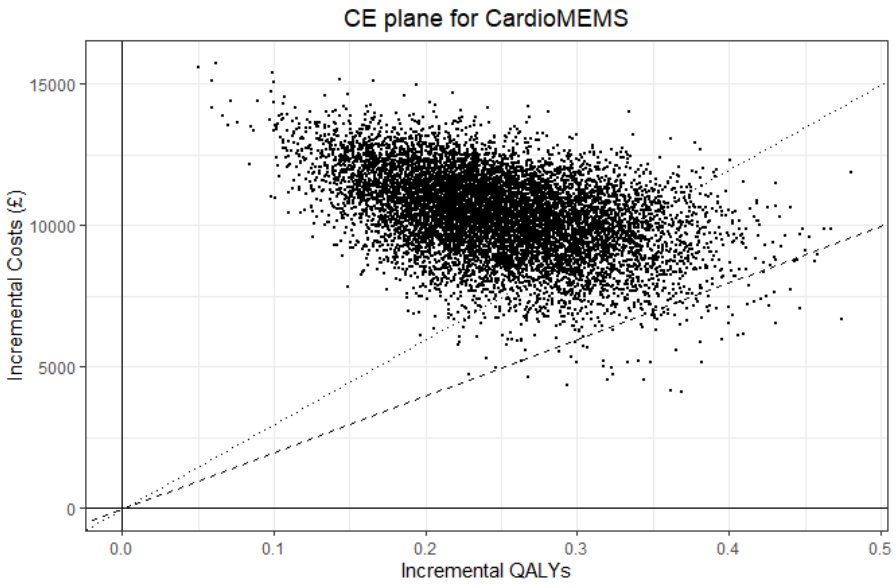
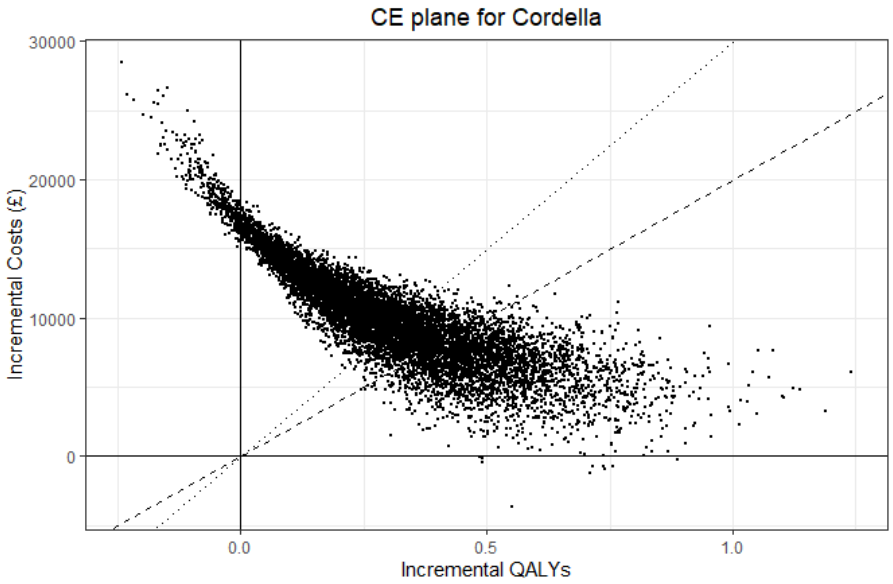


**Figure 3: Cost- effectiveness plane for Cordella vs Standard care at £20,000 and £30,000 willingness to pay thresholds**




When comparing all monitoring strategies, Cordella becomes more likely to be cost-effective than standard care at a willingness to pay threshold below £30,000, with CardioMEMS likely to become more cost-effective than standard care at just above £40,000 thresholds. With the assumed equivalence of device related costs for Cordella and CardioMEMS, Cordella had a lower ICER versus standard care and dominates CardioMEMs. These results were driven by the slightly more favorable hazard ratio for HFH for Cordella compared with CardioMEMS, which increased QALYs and reduced costs. However, the EAG states that these results are very uncertain, and no robust conclusions can be drawn for Cordella.

**Table 12: Fully incremental analysis of the probabilistic base case (10,000 iterations)**

| | Total costs | Total QALYs | ICER vs standard care | ICER vs Cordella |
|---|---|---|---|---|
| Standard care | £29,129 | 2.880 | - | - |

| | Total costs | Total QALYs | ICER vs standard care | ICER vs Cordella |
|---|---|---|---|---|
| Cordella | £39,013 | 3.193 | £31,541 | - |
| CardioMEMS | £39,518 | 3.128 | £41,878 | Strictly dominated by Cordella |

**Figure 4: CardioMEMS vs Standard care pairwise cost-effectiveness acceptability curve**

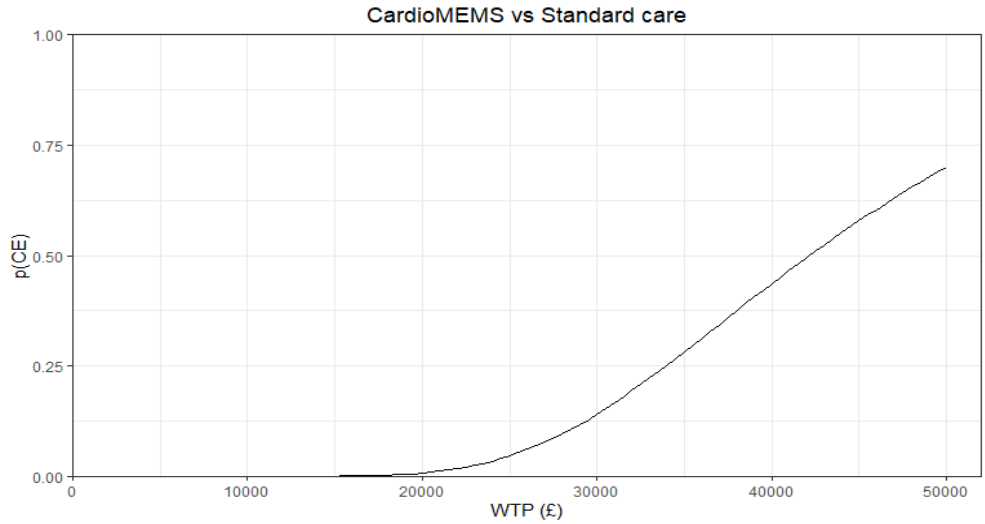
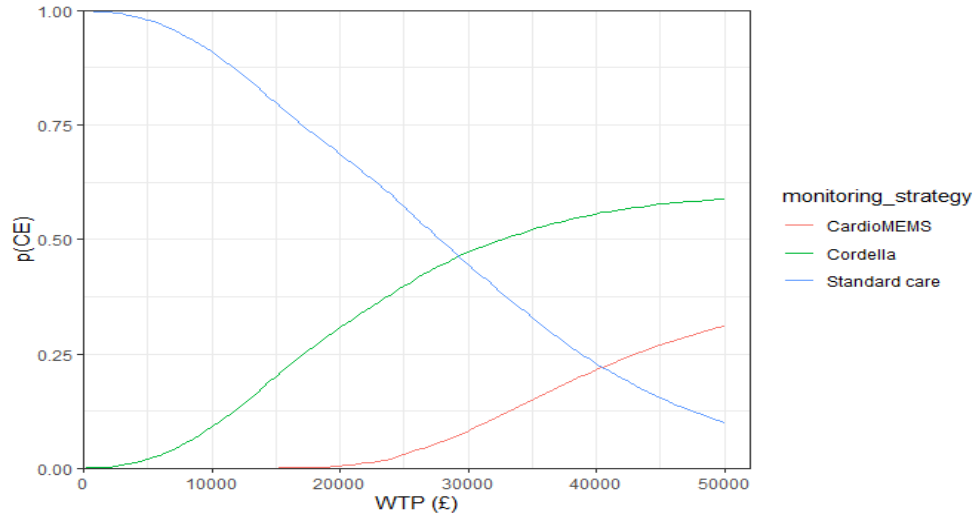



**Figure 5: Cost-effectiveness acceptability curve of all the monitoring strategies**




The probabilistic results are in table 24 and 25 in section 6.5.3 and the deterministic results in table 22 and 23 in section 6.5.1 of the EAR.

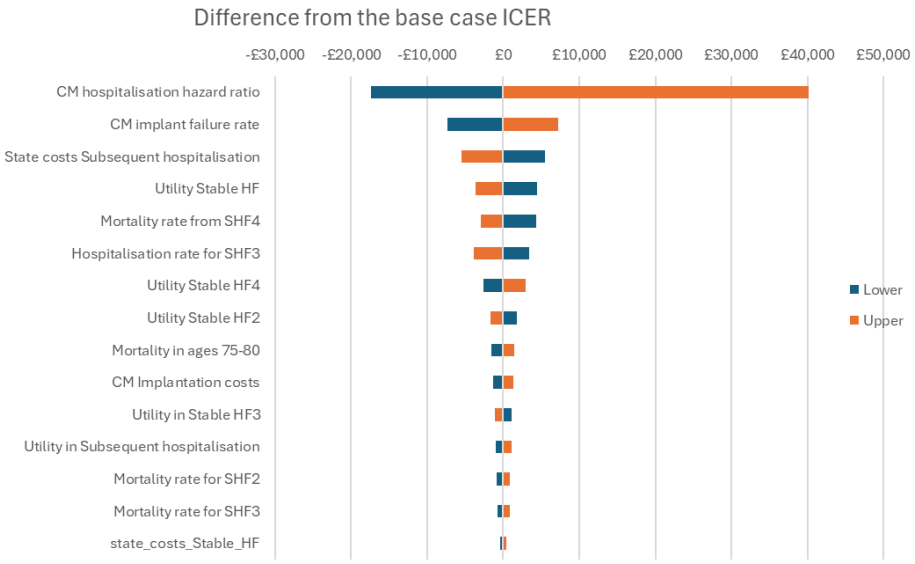
## Scenario and sensitivity analyses

The EAG performed a one-way sensitivity analysis and scenario analysis to explore which key structural and parameter assumptions have an impact on pairwise ICERs and the degree of uncertainty.

### One-way sensitivity analyses

One way sensitivity analyses for CardioMEMs vs standard care were conducted. Representative results are presented in a tornado plot (Figure 6), with parameters ranked by the level of impact on pairwise ICERs. Results were most sensitive to the clinical effectiveness on HFH with the CardioMEMS hazard ratio lower bound lowering the ICER by over £17,000 and the upper bound increasing it by over £40,000. All other variables had a less than £10,000 impact on the ICER, with implant failure rate having the biggest impact on the ICER, followed by the costs for 3 or more recurrent HFHs.

**Figure 6: Tornado plot for CardioMEMS vs standard care**




Abbreviations: CM, CardioMEMs; HF, heart failure; SHF, stable heart failure; ICER, incremental cost effectiveness ratio

Table 12 contains the results of the scenario analyses. The cost effectiveness results were largely insensitive to scenarios tested, with the exception the source of evidence for utilities, monthly device monitoring costs, the treatment effect on mortality, and adherence.

**Table 12: List of scenario analyses included**

| Scenario | Base-case Inputs | Scenario Inputs | Rationale for analysis | Key results |
|---|---|---|---|---|
| 1a Mean age from MEMS-HF<br>1b Mean age from SIRONA-2/SIRONA-2 | Mean age of 69 years for both studies<br>69 years | 67.2 years<br>71 years | Mean age varied across studies. This is the lowest mean age across studies | Lower cohort age resulting in slightly lower ICERs and<br>Higher cohort age resulting in higher icers for both monitoring interventions. |
| 2a Annual HFH rate for Stable HF1 under standard care based on Cowie 2023<br><br>2b Annual HFH rate for Stable HF1 under standard care based on upper limit from COAST UK 95%CI | Values from both studies:<br>Rate=0.8582<br>Log-rate= -0.153 | Rate=0.6165<br>Log-Rate= -0.484<br><br>Rate=0.9993<br>Log-rate= 0.001 | To explore the impact of a lower HFH rate the average value from Cowie 2023 model, with a correction factor described in section **Error! Reference source not found.** applied. Using the upper confidence limit (with a correction factor described in section **Error! Reference source not found.** applied) from the UK cohort of the COAST study as a proxy for a higher risk population | Similar ICERs to the deterministic base case |
| 3 Mortality HR from the meta-analysis for CardioMEMS is used | HR=1 | HR=0.91 | No direct effect of CardioMEMS or Cordella on mortality included in | Larger reduction in the ICERs as incremental QALYs increased for both |

| Scenario | Base-case Inputs | Scenario Inputs | Rationale for analysis | Key results |
|---|---|---|---|---|
| | | | base-case. This scenario tests the impact of the HR from the meta-analysis for CardioMEMS in addition to the indirect effect via number of HFH. | monitoring interventions. |
| 4 Including a probability of sensor failure at 12 months | 0 | 0.01 | Sensor failure was very rare. The impact of using the12 month probability of sensor failure from COAST-UK which had the highest annual sensor failure rate was examined. Those with sensor failure switch to routine monitoring in the model after 12 months. | Moderate increase in the ICERs of both monitoring interventions |
| 5a Adherence drop off at 1 year: 5%<br><br>5b Adherence drop off at 1 year: 10% | No drop off (100% adherence) | 95% adhere from 12 months onwards<br><br>90% adhere from 12 months onwards | This scenario was tested to explore the impact of patients stopping using the device to send readings over time. Those that do not adhere switch to routine monitoring in the model. | Moderate increase in the ICERs of both interventions. |

| Scenario | Base-case Inputs | Scenario Inputs | Rationale for analysis | Key results |
|---|---|---|---|---|
| 6a Using the utility assumptions from the Cowie model with inputs from CHAMPION used in first 12 months for CardioMEMS<br><br>6b Using the utility assumptions from the Cowie model with inputs from MONITOR-HF for CardioMEMS used in the first 12 months<br><br>6c Using utilities from MONITOR-HF for CardioMEMS in the first 12 months, then with base-case utilities after 12 months | Utilities based on number of HFHs | Utilities from CHAMPION and MONITOR-HF used in first 12months (with base-case utilities after 12 months for MONITOR-HF) | This scenario tests the sensitivity of results to the modelling approach used for utilities in CHAMPION-HF and MONITOR HF. | All 3 scenarios led to reduction in ICER with scenarios 6a and 6b leading to largest reductions |
| 7a Monthly monitoring costs using company suggested frequencies<br><br>7b Monitoring costs using band 6 healthcare professional<br><br>7c Monitoring costs using 15 minutes consultant time per month | CardioMEMS: £101<br>Cordella: £101 | CardioMEMS: £27<br>Cordella:<br>£69<br>£126<br>£112 | CardioMEMS: Company advice is at least twice per week during medication modification periods, then at least once per month<br>Cordella: Company advice is at least twice per week<br>Clinical opinion that more senior staff may deal with the ongoing monitoring | Significant effect on cost-effectiveness with scenario 7a which lowers the monthly monitoring costs lowering cost-effectiveness for both monitoring strategies and 7b and 7c which raise the monthly monitoring costs leading to higher ICERs. |

| Scenario | Base-case Inputs | Scenario Inputs | Rationale for analysis | Key results |
|---|---|---|---|---|
| | | | Clinical advice was that 5 mins per month may be an underestimate | |
| 8a Charging for wasted devices: None charged<br><br>8b Charging for wasted devices: All charged | £2,771 | £1,631<br>£3,911 | Charging for wasted devices is dealt with on a case-by-case basis: no charges is best case scenario and all charged is worst case scenario | The results are largely insensitive |
| 9a Additional cost of device or system related complications | £0 | £39 | Complications listed could not all be identified as HRG complications; use of HRGs can obscure differences between interventions that lead to additional complications. | The results are largely insensitive |
| 9b DSRC rate for Cordella based on meta-analysis with SIRONA removed | 0.001 | 0.007 | SIRONA is a small study with short follow-up, so a scenario analysis was run excluding it | Excluding SIRONA from the meta-analysis of DSRC for Cordella had no impact on the results due to the very low likelihood of DSRC. |

| Scenario | Base-case Inputs | Scenario Inputs | Rationale for analysis | Key results |
|---|---|---|---|---|
| 10 Disutility for HFH lasts for 2 months | 0.1 for 1 month | 0.1 for 2 months | There is no data on this disutility. This uncertainty is explored by assuming the disutility lasts for longer. | Extending the period of hospitalisation-related disutility to two months resulted in a slightly lower ICER for both monitoring strategies. |
| 11 Alternative cost of usual care, with 6 appointments over a year | £91 | £166 | Stakeholder comment suggests the usual care cost would be higher | Small increase in ICERs. |
| 12 Inclusion of the re-calibration unit costs | £0 | [redacted] | Cost was omitted in error in base case. Scenario including this cost added in response. | Negligible increase in the ICER. |

Sensitivity and scenario analyses results are in sections 6.5.2 and 6.5.4 of the EAR.

# 7. Equality considerations

The final scope and the scoping equality impact assessment describe equality considerations for this assessment. Key issues for discussion include:

- People with cognitive or physical impairments or learning disabilities may need additional support to use PAP monitoring technologies at home.
- Availability of remote PAP monitoring technologies may allow greater access to care for people who are less able to travel to in-person appointments.

The key studies in this assessment found no evidence of a difference in the hazard ratio for CardioMEMs or vs control. Therefore, the EAG did not conduct a subgroup analysis by age, baseline PAP or kidney function. The EAG did not identify additional equality issues.

# 8. Key points, limitations and considerations

## 8.1 Clinical effectiveness

### Key points

- High certainty evidence from the 3 RCTs suggests that CardioMEMS and Cordella are associated with reductions in HFH compared to standard heart failure management. Sensor failure and DSRC were rare for both devices.
- There was also a suggestion of reduced all-cause mortality and HRQoL by CardioMEMs, but results were less certain.
- There was a lack of comparative evidence for Cordella so the EAG could not robustly assess the clinical effectiveness of Cordella.
- Patient preference studies reported positive experiences on the use of CardioMEMs and Cordella.

### Limitations

- RCT evidence was only available for CardioMEMs.
- Studies for CardioMEMs were generally well conducted with low risk of bias for primary effectiveness outcomes in CHAMPION and GUIDE-HF, but there were some concerns for MONITOR-HF due to its open-label design.
- The single-arm evidence for Cordella is limited in proving cause and effect due to lack of comparison group or randomisation and small sample size.
- The available data for the comparative phase of the PROACTIVE-HF trial for Cordella are limited by the short follow-up and availability of data for only a proportion of the target population.
- There was not enough evidence to conduct a population-adjusted indirect comparison using multi-level network meta-regression.
- There was no evidence of effect modifying factors based on the subgroup analyses of RCT evidence for CardioMEMs.

- None of the RCTs reported data on frailty or number of co-morbidities and so it was not possible to adjust for these factors which are likely important prognostic factors
- There was a lack of evidence on population characteristics for the NYHA class III subgroup for GUIDE-HF to make an indirect comparison between CardioMEMs and Cordella using a regression model fitted to GUIDE HF and PROACTIVE HF.

### Considerations for committee:

- Is evidence from other settings generalisable to the UK NHS?
- What can the published studies tell us about the effectiveness of remote PAP monitoring technologies?
- What can the studies tell us about the likely impact of the technologies on downstream consequences such as hospitalisations and mortality patient outcomes or system impact?
- Are there specific patient populations where remote PAP monitoring technologies would be especially valuable or problematic?

## 8.2 Health economic evidence

### Key points:

- Economic modelling suggests CardioMEMS and Cordella (under the assumption of similar costs to CardioMEMS) are unlikely to be cost-effective.
- The results were sensitive to assumptions about the source of evidence for utilities, monthly device monitoring costs, the treatment effect on mortality, and adherence.
- There is not enough evidence to robustly assess the cost-effectiveness of Cordella.
- It is uncertain whether either technology is more cost-effective than the other.

### Limitations:

- The true cost of Cordella is unknown and the ICER for this technology is based on the cost of the CardioMEMS device.
- There is some uncertainty around the cost of CardioMEMS due to lack of information on the cost of the calibration unit for CardioMEMS.
- The fully incremental analysis results were driven by the slightly more favorable hazard ratio for HFH for Cordella compared with CardioMEMS, which is an area of uncertainty.
- There was not enough evidence to perform a subgroup analysis.
- There was no data on the disutility of a HFH event, and a value of 0.1 was used for a 1-month period. The model results were not sensitive to this assumption.
- Because of the lack of evidence comparing effectiveness between the remote PAP monitoring technologies and therefore uncertainty in the treatment effects from the NMA, there was considerable uncertainty in the model results.
- The costs of social care funded outside the NHS and informal care was not considered in the model, which are both important for HF patients.
- There was no evidence on carer HRQoL according to HFHs
- There was no evidence of the costs or benefits associated with use of remote PAP monitoring technologies in end-of-life care.
- The EAG's preferred method of estimating health utilities, which does not use the utilities measured in the RCTs, does not capture any additional utility benefit from using CardioMEMs beyond those resulting from HFHs. This may mean that the base case overestimates the ICER.

### Considerations for committee:

- Are the economic model structure, assumptions and clinical and cost parameters suitable to answer the decision question (see final scope) for this assessment?
- What can the model results suggest about the cost-effectiveness of the remote PAP monitoring technologies?
- Are the base case results plausible?

- Are the clinical and cost parameters appropriate to assess the potential cost-effectiveness of the technologies?
- Are there any other potential system benefits that are not captured by the economic model, and are these likely to generate improvements in QALYs in other areas of the NHS?

# Appendix

## Abbreviations

| | |
|---|---|
| CI | Confidence interval |
| CrI | Credible interval |
| EAG | External assessment group |
| EAR | External assessment report |
| HFH | Hospitalisation for heart failure |
| HR | Hazard ratio |
| HRQoL | Health-related quality of life |
| ICER | Incremental cost-effectiveness ratio |
| NT-pro-BNP | N-terminal pro-B-type natriuretic peptide |
| NYHA | New York Heart Association |
| PAP | Pulmonary artery pressure |
| QALY | Quality-adjusted life year |
| RCT | Randomised controlled trial |
| SE | Standard error |


# Pulmonary artery pressure technologies for remote monitoring of chronic heart failure [DG10087]
# A systematic review and economic model

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## Rider on responsibility for report

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Academic and commercial in confidence data provided by manufacturers, and specified as such, is redacted in this report

# Plain Language Summary: Remote monitoring of chronic heart failure using pulmonary artery pressure (PAP) sensors

## Key messages

- CardioMEMS and Cordella are pressure monitors (sensors) that are implanted into the artery in the lungs to help manage heart failure from home
- CardioMEMS lowers hospital admissions for heart failure; impact on deaths is less certain. Cordella may lower hospital admissions and deaths, but evidence is weaker.
- Both devices are safe and reliable with few problems and people found the sensors easy to use
- CardioMEMS is not likely to be a good use of NHS money. It is not known whether Cordella is a good use of NHS money.

## What is chronic heart failure?

Chronic heart failure (CHF) is a condition where your heart can't pump blood around your body as well as it should. Symptoms of CHF can include breathlessness, tiredness, swelling of legs, feeling light headed and fainting.

CHF is usually diagnosed by a doctor based on your signs and symptoms, physical examination and assessments. CHF needs to be monitored to check symptoms aren't getting worse and to make sure you get the best treatment.

One of the early signs of CHF getting worse is a change in pressure in the arteries that carry blood from the heart to the lungs. A small implanted device (sensor) can be used to detect changes in pressure in the lungs (called pulmonary artery pressure). These devices send information to an external monitor in the person's home that can then be seen by the CHF team from their clinic. This helps doctors check how a person's heart is doing while they're at home.

## What did we want to find out?

We wanted to know whether use of these pressure sensors will mean people get better treatment and have fewer visits to hospital. We also wanted to know whether introducing these sensors is a good use of NHS money. We were interested in two different sensors – CardioMEMS and Cordella.

## What did we do?

We looked at existing research and created models to study both the health benefits and costs of using the CardioMEMS and Cordella pressure sensors to see how well they work and if they are good value for money.

## What evidence did we find?

We found 11 studies (published across 60 reports) about implantable devices that monitor pulmonary artery pressure:

- Three studies looked at how well CardioMEMS works by comparing it to standard heart failure care.

- Three studies looked at Cordella. Everyone in theses studies received the device but there was no comparison group. One of these studies was first designed to compare Cordella with standard care, and it provided a small amount of data on this.
- We also included three more studies that looked at how well CardioMEMS worked as a device — for example, whether it could be successfully implanted and whether it kept working over time.
- Two studies gave information on what it was like for patients to use the devices.

## Main results

We found that:

- People with CardioMEMS had fewer admissions to hospital. There may also be fewer deaths, but the evidence is less certain.
- Cordella may also lower hospital admissions and deaths, but the evidence is weaker and less reliable.
- Some people using CardioMEMS reported better quality of life, but the results were mixed.
- Implanting the devices was usually successful and once implanted both devices worked well, with very few failures.
- Most people used the devices regularly, although this was measured differently across studies.
- People using CardioMEMS had more medication changes and contact with healthcare professionals, suggesting doctors were using the data to change care.
- CardioMEMS may not be good value for the NHS unless it can improve people's quality of life in the long-term as well as reducing hospital stays, or if the cost of monitoring it is lower.
- It is not clear whether Cordella is good value for the NHS or not.

## What are the limitations of the evidence

Overall we found very few studies that looked at CardioMEMS or Cordella. The studies which compared CardioMEMS against usual care were mostly well done and gave us more confidence in their results. However, some studies had issues, like being open-label (patients and doctors knew who was using the device) or not fully explaining how patients were chosen, and some were missing results for some participants, which could affect the results. The studies on Cordella mostly did not have comparison groups and were smaller, making it harder to be confident about their findings. Because there are no direct comparisons between the two devices, it's hard to say which one works better overall. There was also no cost data for Cordella.

There is little information about how the devices work in people from different ethnic backgrounds or with other health conditions. It's not clear whether CardioMEMS or Cordella help people live longer, or how much they improve quality of life over the long term.

# Scientific Abstract


## Background

Chronic heart failure (CHF) is a progressive condition where the heart's ability to pump blood is inadequate to meet the body's demands. Symptoms include breathlessness, fatigue and fluid retention. Often, patients experience episodes of decompensation during which symptoms worsen and typically require hospitalisation or changes in treatment. In the UK, CHF affects approximately 1.6% of the population. Incidence and prevalence increase significantly with age and prevalence is higher in men than in women. CHF is a leading cause of hospitalisation in people aged over 65 years and accounts for 1–2% of all NHS hospital admissions.

Monitoring for CHF aims to optimise treatment efficacy, promptly address any deterioration in the person's condition, and ultimately improve the quality and length of life for individuals living with CHF. Management of CHF involves a combination of pharmacological treatments, lifestyle modifications, and, in certain cases, device therapies.

Pulmonary artery pressure (PAP) sensors are used to collect data on PAP in people with CHF. They aim to detect decompensation at an early stage and may help optimise a patient’s treatment and reduce the risk of hospitalisation.

## Objectives

The overall aim was to appraise the clinical and cost effectiveness of remote pulmonary artery pressure monitoring systems, CardioMEMS and Cordella, in patients with CHF.

## Methods

### Clinical effectiveness review

We conducted a systematic review of studies that evaluated the CardioMEMS and Cordella sensors. We included randomised controlled trials (RCTs) that reported on eligible outcomes. Where randomised controlled trials were not available for one or more of the technologies of interest, then comparative non-randomised studies of interventions (NRSI) and single arm prospective studies were eligible. For outcomes related to the device where single arm data were most appropriate, we broadened inclusion criteria to include prospective single arm trials that reported on implant or sensor failure or device related consequences. Qualitative and survey studies that reported data on patient experience of using the technology were also eligible.

We searched MEDLINE, EMBASE and CINAHL from inception to 20 February 2025. We screened trial registries, reference lists of reviews and study reports, relevant websites and information submitted by device manufacturers.

Title and abstract screening and assessment of full text papers were conducted by two reviewers independently. Data extraction and risk of bias assessment were performed by one reviewer and checked by a second. Risk of bias was assessed with the RoB 2 (RCTs), and the JBI critical appraisal checklist for prevalence studies (single arm studies).

For each outcome, we provided a narrative summary of study details, risk of bias and results. Random and fixed effects meta-analysis was performed to generate summary effect estimates. Forest plots were produced to show individual and summary effect estimates with 95% confidence intervals (CIs). For outcomes with comparative evidence available for both devices (CardioMEMS and Cordella) against a common comparator (standard care), we conducted an indirect comparison using the Bucher method.

### Cost-effectiveness

We developed a decision-analytic model to evaluate the cost-effectiveness of remote PAP monitoring technologies compared with current monitoring practice (standard care) in patients with NYHA class III CHF. Model structure was informed by the findings of a review of cost-effectiveness studies and discussion with clinical advisors and committee members. We modelled patients moving between 8 health states: 1st recurrent heart failure hospitalisation (HFH), 2nd recurrent HFH, subsequent recurrent HFH, 4 stable HF states that depend on number of recurrent HFHs, and death.

Costs and quality adjusted life years (QALYs) were estimated using a 3.5% discount rate for both. Model inputs were derived from the clinical and cost-effectiveness reviews, supplemented by targeted literature searches. Where there was insufficient evidence, parameters were based on expert opinion. Uncertainty was explored using probabilistic analysis and a range of scenario analyses to test robustness of results to model assumptions.

## Results

### Clinical effectiveness review

We included 11 studies (60 reports). These comprised three RCTs of CardioMEMS and three prospective single-arm studies of Cordella. To further evaluate device-related outcomes for CardioMEMS, we included three additional prospective single-arm studies. We also identified two studies focused on patient experience with CardioMEMS — one used interviews and the other a survey. In addition, two of the Cordella single-arm studies included patient surveys that provided insights into user experience and satisfaction.

There was high certainty evidence from 3 RCTs that CardioMEMS was associated with reduced heart failure hospitalisations (HFH) compared to standard care. There was also a suggestion of reduced mortality, although the confidence interval crossed one, indicating uncertainty. For Cordella, lower-certainty evidence from the available studies also suggested a reduction in HFH, but the effect on mortality was unclear due to limited comparative data. An indirect comparison found no clear evidence of a difference between the two devices in reducing HFH or mortality.

The impact on health-related quality of life (HRQoL) was mixed. Some CardioMEMS studies showed improvements, but findings were inconsistent and overall the effect remains uncertain. For Cordella, data on HRQoL were limited and lacked direct comparisons, making it difficult to draw firm conclusions. Device-related outcomes were favourable for both systems, with implantation failure rates below 2% for CardioMEMS and approximately 5% for Cordella. Sensor failure and device- or procedure-related complications were rare across all studies.

There was no evidence that CardioMEMS reduced urgent care visits or cardiovascular mortality, and no comparative data were available for Cordella. CardioMEMS trials, showed more frequent medication changes and healthcare professional contact. Comparable data were not available for Cordella. All studies reported improvements in 6-minute walk test (6MWT) distance relative to baseline, though RCT evidence for CardioMEMS found no difference compared to control. Adherence to device use was high across both systems. Patient experience was generally positive. CardioMEMS users reported better understanding, reassurance, and ease of use. Cordella users also found the device easy to use and helpful, though fewer than half reported making lifestyle changes based on the data.

### Cost-effectiveness

We found that CardioMEMS was unlikely to be cost-effective compared with standard care in our base-case with incremental costs of £10,352, incremental QALYs of 0.25, and an ICER of £41,569 from the deterministic model. Results were similar from the probabilistic model with incremental costs of £10,389, incremental QALYs of 0.25, and an ICER of £41,878. The results were sensitive to assumptions about the source of evidence for utilities, monthly device monitoring costs, the treatment effect on mortality, and adherence.

Using the same approach to model utilities as the Cowie model reduced the deterministic ICER to £21,999 (using data from CHAMPION) and £25,666 (using data from MONITOR-HF). If the utilities from MONITOR-HF were used for 12months, with state-based utilities used after that, then the ICER was £35,596. Using the monitoring frequencies proposed by Abbott reduces the ICER to £22,777, due to lower costs of CardioMEMS resulting from less frequent monitoring. Using costs for a band 6 rather than a band 5 professional increases the ICER to £47,579. Including a direct mortality benefit based on a meta-analysis of the RCTs for CardioMEMS reduced the deterministic ICER to £29,986. However, this approach likely double-counts the mortality benefit already indirectly captured in the model due to reduced HFHs. If 10% of patients stop adhering to using the device after 12 months then the ICER increases to £47,934, however, we heard that adherence would likely be better than this.

We did not have the device cost for Cordella, and there was limited comparative evidence for Cordella. We therefore could not robustly assess the cost-effectiveness of Cordella.

## Conclusions

These findings suggest CardioMEMS is effective in reducing heart failure hospitalisations, with high certainty evidence from three RCTs, but that it may not be cost-effective. While Cordella may offer similar benefits and could be more cost-effective than CardioMEMS, the certainty of evidence is lower due to the reliance on non-comparative data on non-comparative data for some outcomes and comparative data for only a subset of the total trial population, with shorter duration of follow-up.

## Study registration

The review was registered at PROSPERO (CRD420251003375).

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# List of Tables

## List of Figures

# Definition of Terms and List of Abbreviations

| Term | Definition |
|---|---|
| AAHFN | American Association of Heart Failure Nurses |
| ACEI | Angiotensin-Converting Enzyme Inhibitor |
| AE | Adverse Event |
| AHF | Acute Heart Failure |
| ARB | Angiotensin Receptor Blocker |
| ARNI | Angiotensin Receptor-Neprilysin Inhibitor |
| BB | Beta Blockers |
| BL | Baseline |
| BMBF | German Federal Ministry of Education and Research |
| BNF | British National Formulary |
| CBA | Cost Benefit Analysis |
| CC | Complication and Comorbidity |
| CDSR | Cochrane Database of Systematic Reviews |
| CE | Cost-Effectiveness |
| CEA | Cost-Effectiveness Analysis |
| CHF | Chronic Heart Failure |
| CI | Confidence Interval |
| CIED | Cardiac Implantable Electronic Device |
| CKD | Chronic Kidney Disease |
| CM | CardioMEMS |
| CMA | Cost Minimisation Analysis |
| COPD | Chronic Obstructive Pulmonary Disease |
| CPRD | Clinical Practice Research Datalink |
| CRD | Centre for Reviews and Dissemination |
| CRT | Cardiac Resynchronisation Therapy |
| CTPA | Computed Tomography Pulmonary Angiogram |
| Ctrl | Control |
| CTRP | Clinical Trials Registry Platform |
| CUA | Cost-Utility Analysis |
| DM | Diabetes Mellitus |
| DSRC | Device/System-Related Complications |
| DAC | Diagnostic Appraisal Committee |
| EAG | Evidence Assessment Group |
| eGFR | Estimated Glomerular Filtration Rate |
| EQ-5D | EuroQol 5 dimensions |
| EQ-5D-5L | EuroQol 5 dimensions 5 Level |
| EQ-5D-5L-VAS | EuroQol 5 dimensions 5 Level Visual Analogue Scale |
| EQA | External Quality Assessment |
| ESC | European Society of Cardiology |
| FAMQoL | Family Caregiver-Specific Quality of Life |
| GBP | British pound sterling |
| GDMT | Guideline-Directed Medical Therapy |
| GRADE | Grading of Recommendations, Assessment, Development and Evaluation |

| Term | Definition |
|---|---|
| HAF | History of Atrial Fibrillation |
| HES | Hospital Episode Statistics |
| HF | Heart Failure |
| HFH | Heart Failure Hospitalization |
| HFR | Heart Failure Related |
| HFrEF | Heart Failure with Reduced Ejection Fraction |
| HFpEF | Heart Failure with Preserved Ejection Fraction |
| HFSA | Heart Failure Society of America |
| HR | Hazard Ratio |
| HRG | Healthcare Resource Group |
| HRQoL | Health Related Quality of Life |
| HT | Heart Transplant |
| HTA | Health Technology Assessment |
| HTW | Health Technology Wales |
| ICD | Implantable Cardioverter-Defibrillator |
| ICER | Incremental Cost-Effectiveness Ratio |
| IFU | Instructions for use |
| ITT | Intention to treat |
| JACC | Journal of the American College of Cardiology |
| JBI | Joanna Briggs Institute |
| KCCQ | Kansas City Cardiomyopathy Questionnaire |
| LVEF | Left Ventricular Ejection Fraction |
| LYs | Life years |
| MD | Mean Difference |
| MDT | Multi-Disciplinary Team |
| MLHFQ | Minnesota Living with Heart Failure Questionnaire |
| NA | Not Applicable |
| N/NI | No/No Information |
| NCC | National Cost Collection |
| NHS | National Health Service |
| NHS EED | National Health Service Economic Evaluations Database |
| NICE | National Institute for Health and Care Excellence |
| NICE DSU | National Institute for Health and Care Excellence Decision Support Unit |
| NIHR | National Institute for Health and Care Research |
| NR | Not Reported |
| NRSI | Non-Randomised Studies of Intervention |
| NT-proBNP | N-terminal prohormone of Brain Natriuretic Peptide |
| NYHA | New York Heart Association |
| ONS | Office for National Statistics |
| PAP | Pulmonary Artery Pressure |
| PN/PY | Probably No/Probably Yes |
| PPI | Patient and Public Involvement |
| PPY | Per Patient Year |
| ProHTA | Prospective Health Technology Assessment |
| PS | Private Sector |

| Term | Definition |
|---|---|
| PSS | Personal Social Services |
| PSSRU | Personal Social Services Research Unit |
| Pts | Patients |
| QALY | Quality Adjusted Life Year |
| QoL | Quality of Life |
| RCT | Randomized Controlled Trial |
| RHC | Right Heart Catheterisation |
| RoB | Risk of Bias |
| SAE | Serious Adverse Event |
| SD | Standard Deviation |
| SE | Standard Error |
| SGLT-2 | Sodium-Glucose Co-Transporter 2 |
| SoC | Standard of Care |
| SS | Social Security |
| Tx | Treatment |
| UK | United Kingdom |
| USA | United States of America |
| WHO | World Health Organisation |
| Y/PY | Yes/Probably Yes |

# 1 Background

## 1.1 Population

### 1.1.1 Definition and classification of chronic heart failure

Chronic heart failure (CHF) is a progressive condition where the heart's ability to pump blood is inadequate to meet the body's demands, leading to symptoms including breathlessness, fatigue, and fluid retention.[1] This condition can result from structural or functional cardiac disorders that impair ventricular filling or ejection of blood. Symptoms and signs of CHF could be due to pulmonary and systemic congestion, or the structural abnormalities either causing or caused by CHF. A recent international consensus document on the "Universal definition and classification of CHF"[2] proposed the following definition of CHF: *"a clinical syndrome with symptoms and or signs caused by a structural and/or functional cardiac abnormality and corroborated by elevated natriuretic peptide levels and or objective evidence of pulmonary or systemic congestion"*.

This consensus document also includes a system to classify heart failure based on the measurement of left ventricular ejection fraction (LVEF), which assesses the percentage of blood the left ventricle ejects with each contraction.[2] This classification is summarised in Table 1.

**Table 1 Overview of universal classification of heart failure**

| Subtype | Definition | Pathophysiology |
|---|---|---|
| Heart Failure with Reduced Ejection Fraction (HFrEF) | LVEF ≤40% | Characterised by systolic dysfunction, where the heart's ability to contract is diminished, leading to decreased cardiac output. Common causes include ischemic heart disease and dilated cardiomyopathy. |
| Heart Failure with Preserved Ejection Fraction (HFpEF) | LVEF ≥50% | Characterised by diastolic dysfunction, where the left ventricle is stiff and has impaired relaxation, resulting in inadequate filling during diastole. Hypertension and aging are common contributing factors. |
| Heart Failure with Mildly Reduced Ejection Fraction (HFmrEF) | LVEF between 41-49% | Represents an intermediate group with features of both systolic and diastolic dysfunction. This is more like HFrEF in response to treatment. |
| Heart Failure with Improved Ejection Fraction (HFimpEF) | Patients previously diagnosed with HFrEF who now have an improvement in LVEF to >40%, accompanied by a ≥10-point increase from baseline | Reflects a subset where medical therapy or interventions have led to significant recovery in ventricular function. Continuous management is essential as the underlying myocardial pathology may persist. |

As well as the universal criteria summarised above, there are a number of functional classifications. One commonly used classification is the New York Heart Association (NYHA) Functional Classification which classifies CHF based on impact of symptoms as follows:[3]

- **Class I:** No limitation of physical activity; ordinary activities do not cause symptoms.

- **Class II:** Slight limitation of physical activity; comfortable at rest, but ordinary activity results in symptoms.
- **Class III:** Marked limitation of physical activity; comfortable at rest, but less than ordinary activity causes symptoms.
- **Class IV:** Unable to carry out any physical activity without discomfort; symptoms may be present at rest.

There is some subjectivity involved in this classification so that different clinicians may classify the same patient as having different NYHA stages.[4] The majority of CHF patients will be in class II or III.

## 1.2 Epidemiology and burden of CHF

CHF affects approximately 1–2% of the adult population in developed countries,[5] with an analysis of over 4 million primary care records reporting a UK prevalence of 1.6% in 2014.[6] The European Society of Cardiology long-term outpatient registry reports that 55% of patients have HFrEF, 21% have HFmrEF, and 24% have HFpEF.[7] Incidence and prevalence increase significantly with age – the average age of diagnosis is 77 and incidence peaks at 1.5% in men aged over 85 years.[6] Prevalence is higher in men than in women, particularly in younger age groups, likely due to the earlier onset of coronary artery disease in men.[6] Factors associated with a greater risk of developing CHF include: smoking, being overweight or obese, socio-economic status, and co-morbidities including ischaemic heart disease, hypertension, chronic kidney disease, osteoarthritis, cancer, and diabetes.[6] The overall prevalence of CHF is increasing as a result of an ageing population and increasing rates of obesity.

CHF is a progressive and clinically fluctuating condition. Often, patients experience episodes of decompensation during which symptoms worsen and typically require hospitalisation or changes in treatment, including uptitration.[5] CHF is a leading cause of hospitalisation in people aged over 65 years and accounts for 1–2% of all NHS hospital admissions.[5] On average, a General Practitioner (GP) will look after 30 people with CHF and will suspect a new diagnosis in about 10 people annually. When CHF patients are admitted to hospital, admissions are often long (average 8 days)[8] and it has been estimated that CHF accounts for 2% of all NHS hospitalised bed-days and 5% of all NHS medical emergency admissions.[1]

CHF is also associated with significant mortality. One-year mortality rates after diagnosis vary with recent reviews reporting average mortality rates of 23-33%, underscoring the importance of early detection and comprehensive management strategies.[9, 10] Five year survival rates are around 50%.[10] Survival for people with end-stage heart failure is poor. Despite optimal medical management, only 65% of patients in New York Heart Association (NYHA) class IV are alive at an average follow up of 17 months.[11]

## 1.3 Diagnostic and Care pathway

### 1.3.1 Diagnosis of CHF

CHF is diagnosed through a combination of clinical assessment, imaging, and biomarker analysis. Patients often consult their GP with multiple non-specific symptoms such as breathlessness and fatigue, and many have other long-term co-morbidities. The National Institute for Health and Care Excellence (NICE) guideline NG106 provides comprehensive

guidelines for diagnosing and managing CHF in adults.[12] These recommend that a core specialist heart failure multidisciplinary team (MDT) should work in collaboration with the primary care team to diagnose CHF.[12] The diagnostic process should start with a detailed history and physical examination to identify symptoms such as breathlessness, fatigue, and ankle swelling. They also recommend measurement of natriuretic peptides, particularly NT-proBNP. Elevated NT-proBNP levels indicate myocardial stress and volume overload.[13] Patients with NT-pro-BNP levels above 2,000 ng/L should be referred for urgent transthoracic echocardiography and specialist assessment within two weeks, while those with levels between 400 and 2,000 ng/L should be assessed within six weeks. [12]

Echocardiography should be performed in patients with suspected CHF and raised NTproBNP to evaluate cardiac structure and function, including left ventricular ejection fraction (LVEF), to distinguish between CHF with reduced ejection fraction (HFrEF) and preserved ejection fraction (HFpEF), as this has implications for optimal treatment. Objective evidence of cardiac abnormalities is necessary for the diagnosis of CHF to be made.[2]

Once a diagnosis of CHF has been made, NICE guidance recommends that severity, aetiology, precipitating factors, type of cardiac dysfunction and correctable causes should be assessed. [12] Additional tests, such as electrocardiography, chest X-rays, or cardiac MRI, may be used to identify underlying causes like ischaemic heart disease or valvular abnormalities. Other tests including blood tests (renal, thyroid, liver, lipids, HbA1c, and full blood count), urinalysis and peak flow or spirometry, may be used to evaluate possible aggravating factors or differential diagnoses, such as chronic obstructive pulmonary disease (COPD) or renal dysfunction. [12] Invasive haemodynamic assessment via right heart catheterisation is occasionally used in complex cases.[14]

### 1.3.2 Monitoring of CHF

Monitoring for CHF aims to optimise treatment efficacy, promptly address any deterioration in the person's condition, and ultimately improve the quality and length of life for individuals living with CHF. NICE guidelines[12] recommend regular (6-monthly) reviews to manage the condition effectively and prevent exacerbations, although monitoring for CHF is currently highly variable across the NHS. Quality and Outcomes Framework (QOF) for GPs only require reviews every 12 months.[15] At a minimum, case reviews should include a clinical assessment of functional capacity, fluid status, cardiac rhythm (at a minimum, examining the pulse), cognitive status, nutritional status, and assessment of renal function. Additionally, a thorough review of the person's medication regimen is conducted to ensure optimal therapy and to monitor for potential side effects. More detailed monitoring may be needed if people have co-morbidities or have deteriorated since their previous review. Where there is a change in the person's clinical condition or medication, more frequent monitoring (days to two weeks) is recommended to closely observe the person's response to treatment adjustments. [12] Monitoring of patients with CHF is often done by specialist nurses and pharmacists.[16, 17]

In individuals with CHF who have cardiac implantable electronic devices (CIEDs) such as pacemakers and/or defibrillators, NICE have recently issued guidance recommending that HeartLogic and TriageHF be considered for algorithm-based remote monitoring .[18] These algorithms analyse and collate different clinical data recorded by the device to detect gradual worsening of CHF, potentially allowing for earlier intervention. These systems should be

integrated into a specialist multidisciplinary heart failure service, with alerts monitored and managed by specialist healthcare professionals.[18]

### 1.3.3 Treatment of CHF

NICE and the European Society of Cardiology (ESC) guidelines recommend that management of CHF involves a combination of pharmacological treatments, lifestyle modifications, and, in certain cases, device therapies.[12, 13] These treatment strategies aim to alleviate symptoms, enhance quality of life, and reduce mortality in patients with CHF.

NICE guidelines on diagnosis and management of CHF recommend that patients with reduced ejection fraction be offered treatments from each of the four evidence-based drug classes as early as possible[12]:

- **Sodium-Glucose Co-Transporter 2 (SGLT2) inhibitors:** Considered for patients intolerant to ACEIs
- **Angiotensin-Converting Enzyme Inhibitors (ACEIs), Angiotensin II Receptor Blockers (ARBs) or angiotensin receptor-neprilysin inhibitor (ARNI):** To improve symptoms and reduce mortality.
- **Beta-blockers (BB):** To improve symptoms and reduce mortality.
- **Mineralocorticoid Receptor Antagonists (MRAs):** Added for patients who remain symptomatic despite optimal ACEI and beta-blocker therapy.

Where an ACE inhibitor, ARB or ARNI is not tolerated, the other three treatment classes should still be used alongside an SGLT2 inhibitor.

If symptoms persist despite first-line treatment, then the following options can be considered:

- **Angiotensin receptor–neprilysin inhibitor (ARNI) (Sacubitril or Valsartan):** To replace ACEI or ARB in those with ejection fraction <35%.[19]
- **Ivadribine:** Added to other interventions to control sinus rhythm in those with heart rate >75 and ejection fraction <35%.[20]
- **Hydralazine and nitrate:** These can be added to other interventions, particularly in those of African-Caribbean descent.
- **Digoxin:** For heart failure with sinus rhythm to improve symptoms.
- **SGLT2 inhibitors:** Dapagliflozin or empagliflozin have been recommended by NICE for treating CHF if symptom persist despite first line treatment.[21]

Specialists can also consider recommending the following device-based interventions:

- **Implantable Cardioverter-Defibrillators (ICDs):** Considered for patients at risk of life-threatening arrhythmias.
- **Cardiac Resynchronisation Therapy (CRT):** Recommended for patients with significant ventricular dyssynchrony to improve cardiac function, evidenced by prolonged QRS duration on ECG.

In patients with preserved ejection fraction NICE recommends that comorbidities (diabetes, hypertension, atrial fibrillation) are managed in line with NICE guidance and that all patients with stable disease are offered a personalised exercise based cardiac rehabilitation

programme. This is also offered to those with reduced ejection fraction. In addition, a SGLT2 inhibitor and an MRA should be considered in those with preserved ejection fraction.
All patients with CHF should be offered diuretics to relieve congestive symptoms and fluid retention. NICE guidelines also recommend intravenous iron therapy should be considered in patients with reduced ejection fraction and iron deficiency, defined as transferrin saturation <20%, or ferritin <100 ng/mL, and haemoglobin <150 g/L.

ESC guidelines also recommend that intravenous iron supplementation with ferric carboxymaltose should be considered in symptomatic people with CHF who have recently been hospitalised for CHF, who have left ventricular ejection fraction below 50% and an iron deficiency to reduce the risk of CHF hospitalisation. ESC guidance is currently being updated.

# 2 Decision Problem

The decision question for this assessment is: "does remote pulmonary artery pressure monitoring for CHF represent a clinically and cost-effective use of NHS resources?".

## 2.1 Technologies of interest

Pulmonary artery pressure (PAP) sensors are used to collect data on PAP in people with CHF. They aim to detect decompensation – worsening of symptoms due to the heart's inability to maintain adequate circulatory function – at an early stage so that patient's treatment can be optimised to reduce the risk of hospitalisation. The sensor is implanted into an appropriate branch of the pulmonary artery via a large vein, typically the femoral vein. It collects PAP data, including pressure trends and waveforms, and transmits it to an external monitor in the patient's home. The monitor securely forwards this information to a remote database accessible by the CHF care team. Patients usually transmit data daily, or more frequently if required. This process provides data to guide the management of CHF, with the goal of reducing hospitalisations related to the condition.

There are two main PAP technologies. **CardioMEMS HF System** (Abbott)[22] and **Cordella Pulmonary Artery Sensor System and Cordella Heart Failure System** (Endotronix/Edwards Lifesciences).[23] These are referred to as "CardioMEMS" and "Cordella" PAP monitoring technologies from here.

CardioMEMS is indicated for wirelessly measuring and monitoring PAP and heart rate in patients with NYHA Class II or III and who have been either hospitalised for heart failure and or/have elevated natriuretic peptides.[22, 24] CardioMEMS includes a small pressure sensor that is permanently implanted in the distal pulmonary artery during a minimally invasive right heart catheterisation procedure. The sensor, secured with nitinol wire loops, measures PA pressure changes, which reflect fluid congestion in the lungs due to worsening CHF. At home, patients use a portable electronics unit and a pillow with an embedded antenna. By lying down and placing the pillow under their back and activating the device, patients initiate daily pressure readings by pressing a button, these are wirelessly transmitted to a secure website for clinicians to review. This allows healthcare providers to observe trends and adjust medications or treatments as needed, often before symptoms appear, reducing the risk of decompensation and hospitalisation. The system, which holds a Class III CE mark, enables proactive heart failure management without requiring frequent outpatient visits or home interventions.[25]

Cordella is designed to measure, record, and transmit pulmonary artery pressure (PAP) data in patients with NYHA Class III heart failure. The sensor is implanted in the pulmonary artery, and readings can be taken at home by holding a wireless handheld device against the right pectoral region for 20 seconds. In addition to PAP data, the Cordella Heart Failure System measures, records and transmits vital signs such as blood pressure, heart rate, weight, and oxygen saturation. Additional peripheral devices that connect to the Cordella "myCordellaHub" are required to provide these measurements. Collected data is sent to the myCordella Hub, which guides patients in using the system's peripherals, asks health-related questions, and transmits information to the myCordella Patient Management Portal for clinician access.[15] This system aims to assist healthcare providers in assessing and managing heart failure, potentially reducing hospitalisations.

NICE has issued interventional procedures guidance on PAP sensors for monitoring CHF and covers both the CardioMEMS and Cordella systems. It recommends these technologies under standard arrangements, meaning they can be used within the NHS provided there are measures in place to ensure clinical governance, patient consent, and data auditing.[26]

## 2.2 Comparator

The comparator for this appraisal is current monitoring practice as outlined in section 1.3.2. This is currently highly variable across the NHS.

## 2.3 Population

The population of interest for this appraisal is NYHA class III patients. Both PAP monitoring technologies are indicated for this population in the UK. CardioMEMS further specifies that patients should have had a prior CHF hospitalisation within the last 12-months regardless of ejection fraction whereas Cordella specifies that it is for patients who are at home on diuretics and guideline-directed medical therapy (GDMT), and have been stable for 30 days on GDMT. Both technologies are contraindicated in those who are unable to take dual antiplatelet or anticoagulants for one month post implant.

## 2.4 Place of the technology in the diagnostic and care pathway

PAP monitoring technologies would be used as an add-on test in the care pathway to supplement standard clinical management for NYHA class III patients. PAP monitoring technologies should be integrated into a specialist multidisciplinary heart failure service, with alerts and trend data monitored and managed by specialist healthcare professionals.

# 3 Aim and Objectives

The overall aim of this appraisal is to determine whether remote pulmonary artery pressure monitoring for chronic heart failure is clinically and cost-effective to the NHS. We have identified the following objectives to address this aim:

1. What is the clinical effectiveness of remote pulmonary artery pressure monitoring for chronic heart failure?
2. What is the cost-effectiveness of remote pulmonary artery pressure monitoring for chronic heart failure?

# 4 Assessment of clinical effectiveness

Sections of this Chapter have been reproduced from the protocol document, available on the NICE website.[27]

We conducted a systematic review to summarise the evidence on the clinical effectiveness of remote PAP monitoring technologies for CHF. The systematic review followed the principles outlined in the Centre for Reviews and Dissemination (CRD) guidance for undertaking reviews in health care and the NICE Health Technology Evaluations Manual.[28, 29] The protocol was registered on PROSPERO (CRD420251003375).

## 4.1 Inclusion and exclusion criteria

We included studies that met the criteria outlined in Table 2:

**Table 2 Systematic review inclusion criteria**

| Component | Criteria |
|---|---|
| Participants | People with CHF. Studies in all NYHA class sub-populations were included. |
| Technology | Remote PAP monitoring technologies:<br>• **CardioMEMS HF System** (Abbott)[22]<br>• **Cordella Pulmonary Artery Sensor System and Cordella Heart Failure System** (Endotronix/Edwards Lifesciences)[23] |
| Comparator | Any comparator intervention, including standard care, no monitoring or no comparator |
| Outcome | Studies were required to report at least one of the following outcomes:<br>• Changes to clinical management (including medication changes)<br>• Failure of sensor implantation or sensor<br>• Hospitalisation for heart failure<br>• Urgent care for heart failure (hospital attendance for i.v. diuretics)<br>• Worsening of heart failure (e.g., decompensation, change of NYHA symptom class)<br>• Functional capacity<br>• Improvement in co-morbidities<br>• Mortality due to heart failure<br>• All-cause mortality<br>• Adverse events<br>• Complications associated with sensor implantation<br>• Patients lost to follow-up<br>• Health-related quality of life<br>• Adherence to using the device<br>• Adherence to treatment<br>• Qualitative data of patient experience of using the technology |
| Study design | Randomised controlled trials (RCTs); where randomised controlled trials were not available for one or more of the technologies of interest, then comparative non-randomised studies of interventions (NRSI) were eligible. Where NRSI were not available, single arm prospective studies were eligible. Qualitative studies that reported data on patient experience of using the technology were also included. |

| Component | Criteria |
|---|---|
| | For outcomes that can only occur in the presence of the device, we broadened inclusion criteria to include prospective multi-centre single arm trials that reported device-related outcomes (implant or sensor failure or device related complications). |

## 4.2 Study identification

Studies were identified using bibliographic and non-bibliographic search methods following guidance in the NICE technology appraisal manual and recent guidance specific to technologies.[29, 30]

### 4.2.1 Bibliographic searching

The following databases were searched:

- MEDLINE (Ovid SP) 1946 to February 20, 2025;
- EMBASE (Ovid SP) 1974 to 2025 February 20; and
- CINAHL (Cumulative Index to Nursing and Allied Health Literature) (EBSCOhost) 1981-current.

We used a sensitive search strategy based on terms for each of the technologies eligible for inclusion. The search strategies are reported in Appendix 0.

### 4.2.2 Non-bibliographic search methods

Completed and ongoing trials were identified through searches of the following trial registries:

- ClinicalTrials.gov via www.clinicaltrials.gov/www.
- World Health Organisation (WHO) International Clinical Trials Registry Platform (ICTRP) via www.who.int/clinical-trials-registry-platform

Additional relevant studies were identified by:

- Screening reference lists of any reviews (systematic or non-systematic) identified by our searches;
- Reviewing the reference lists of any study report included at full-text;
- Hand searching the websites of the manufacturer/or licence holders for each test; and
- Information submitted by test manufacturers

### 4.2.3 Managing the searches

Search results were exported to EndNote 20 for deduplication using the default deduplication settings followed by a manual review of records.

## 4.3 Review strategy

All stages of the review process, except the meta-analysis, were conducted using the online systematic review software Nested Knowledge (www.nested-knowledge.com).

### 4.3.1 Study selection

Two reviewers independently screened titles and abstracts identified by the searches. Full copies of all reports considered potentially relevant were obtained and two reviewers

independently assessed these for inclusion. Any disagreements were resolved by consensus or discussion with a third reviewer.

### 4.3.2 Data extraction

Data were extracted using standardised data extraction forms. Data extraction forms were piloted on a small sample of papers and adapted as necessary. Data were extracted by one reviewer and checked in detail by a second reviewer. Any disagreements were resolved by consensus or discussion with a third reviewer.

Data were extracted on the following:

- Study design (RCT, NRSI, single arm trial)
- Funding sources (public, industry, mixed)
- Study location
- Inclusion criteria
- Population
  - Age
  - Sex
  - Ethnicity
  - BMI
  - Left ventricular ejection fraction
  - Kidney function
  - NT-proBNP
  - NYHA functional class
  - Comorbidities
  - Treatment history
- PAP monitoring device (CardioMEMS or Cordella) and details of monitoring with device and response to elevation of pulmonary artery pressure
- Comparator monitoring details
- Primary outcomes (outcomes that informed the model)
  - Heart failure hospitalisation (HFH)
  - All cause mortality
  - Failure of sensor implantation
  - Sensor failure
  - Device/system or procedure related complications
  - Health related quality of life (HRQoL)
- Secondary outcomes
  - Urgent care visits for heart failure
  - Cadiovascular mortality
  - Changes to clinical management
    - Changes to medication
    - Changes to the frequency of contact with healthcare professionals
  - Functional capacity: 6 minute walk test
  - Change in NYHA classification
  - Improvement in co-morbidities
  - Adherence to using the device
  - Adherence to adjusted medication triggered by change in PAP data

- Withdrawals
- Other adverse events
- Patient experience and satisfaction of using the technology (qualitative data only)

We considered the PROGRESS-Plus population factors, where reported.[31] PROGRESS-Plus is an acronym that describes factors that contribute to health inequity. PROGRESS stands for: place of residence, race/ethnicity/culture/language, occupation, gender/sex, religion, education, socioeconomic status, and social capital. "Plus" stands for any additional factors considered important for the specific topic under review. We extracted the following PROGRESS-Plus factors:

- Personal characteristics associated with discrimination: characteristics of relevance to the current review include age, sex, ethnicity
- Comorbidities, including renal dysfunction
- Baseline PAP
- Cognitive impairment, problems with manual dexterity, and learning disabilities (*this group may need additional support to initiate PAP measurement at home*)

We extracted whether each PROGRESS-Plus factor was reported at baseline (y/n), the baseline data concerning the factor as reported by the authors, and whether the study reported results data stratified by the factor. Where stratified data were reported, these were extracted.

Dichotomous data were extracted as number of patients with events and/or number of events and total number of patients in each treatment arm. Time to event data were extracted as the proportion of participants with events in each treatment arm, and as hazard ratios (HR) and 95% confidence intervals. For continuous data, where available, we extracted means/medians together with ranges, standard deviations (SD), standard errors (SE) and/or confidence intervals (CIs) for the outcome at baseline, follow-up and for change from baseline in each treatment group. For all types of data, we extracted summary effect estimates together with 95% CIs and p-values for comparisons between groups.

Study findings were extracted from qualitative studies. Where appropriate we extracted direct quotes to support the qualitative findings.

### 4.3.3 Quality assessment strategy

We assessed the methodological quality of included studies that reported the primary outcomes of HFH, all-cause mortality, HRQoL and safety outcomes. The methodological quality of included RCTs was assessed using the updated Cochrane Risk of Bias Tool (ROB 2.0).[32] Risk of bias assessment was done at the outcome level for the primary outcomes specified above.

Single-arm studies were assessed using the JBI critical appraisal checklist for prevalence studies.[33] Where single arm data from RCTs were included (e.g. for device related outcomes), these were also assessed using this tool. Assessments were done at the study level. The tool includes nine questions, however the item "Were study participants sampled in an appropriate way?" was deemed not applicable, as participants in the single-arm trials were screened based on predefined eligibility criteria. This question was therefore excluded from our assessments.

We produced an overall indication of the risk of bias for each study based on the responses to the 8 questions on which each study was assessed. If studies were answered as "no" for any of these questions and this was considered likely to have impacted on the reliability of the study findings, studies were judged as high risk of bias. If insufficient information was reported, studies were judged at some concerns for risk of bias. If all questions were answered as yes, or if issues flagged by the questions were not considered likely to have impacted on the reliability of the study findings, the study was judged at some concerns for risk of bias due to the non-comparative nature of the evidence. For outcomes for which comparative data were not expected, for example for device related outcomes such as device failure or complications, we considered single arm data to be appropriate and so studies could be judged as low risk of bias for these outcomes if no other concerns were identified by the assessment.

Detailed guidance for reviewers on how to complete the assessments for studies included in the review were produced prior to starting the quality assessment. Quality assessment was undertaken by one reviewer and checked by a second reviewer. Any disagreements were resolved by consensus or discussion with a third reviewer.

## 4.4 Synthesis methods

We present a narrative summary of all the included studies, supported by tabulation of key study characteristics and results. This includes a summary of the study characteristics, outcomes reported and study quality. We also included quantitative meta-analysis to summarise effect estimates across studies, where appropriate data were available. The synthesis is stratified by technology evaluated.

### 4.4.1 Data manipulation

#### 4.4.1.1 Time to event data: HFH, mortality, urgent care visits

Where hazard ratios were not reported, these were estimated from events for person years (EPPY) by dividing the EPPY in the intervention group by the EPPY in the control group. This gave a rate ratio which we assumed to approximate to an HR. This assumed that the hazard was approximately constant over time. To estimate confidence intervals (CIs) for the relative effects, we first calculated the standard error (SE) of the log rate ratio and then derived the 95% CI on the log scale. These were then exponentiated to obtain the CI for the rate ratio on the original scale. Where event-per-patient-year (EPPY) rates were not reported, these were calculated by dividing the number of events by the total patient-years of follow-up.

#### 4.4.1.2 Continuous outcome data

For the continuous outcomes HRQoL and the 6-minute walk test, we required the mean difference in change from baseline between intervention and control groups along with the standard error of the difference for the meta-analysis. Where mean difference in change from baseline between groups was not provided, we derived this by subtracting the mean change in scores in the control group from that in the intervention group. SEs were calculated using the following formula, where group-specific sample sizes and standard deviations were available:

$$SE = \sqrt{[(SD_1^2 / n_1) + (SD_2^2 / n_2)]}$$

When only 95% confidence intervals were available, SEs were derived using the formula:

$$SE = [(\text{Upper CI} - \text{Lower CI})/2] \times 1.96$$

#### 4.4.1.3 Proportions

Device related outcomes were analysed as the proportion of participants who experienced an event. Outcomes considered were device implant failure, device failure, and device and system related complications. Where devices were implanted in both intervention and control arms but information was only acted on for the intervention arm, data were used for the two arms combined. Data for these outcomes were effectively single arm, non-comparative data. To ensure consistency in how outcomes were calculated across studies we selected the following denominators:

- Device implant failure: participants in whom device implant was attempted
- Device failure: participants in whom device was implanted
- Device and system related complications: participants in whom device implant was attempted

### 4.4.2 Meta-analysis

Meta-analyses were carried out to summarise effect estimates using data for the NYHA class III population, where available. Both fixed- and random-effects models were considered. Fixed-effects models, using the inverse variance method,[34] were used when statistical heterogeneity was low, visual examination of the forest plots suggested little evidence of heterogeneity and study populations and outcome definitions were deemed sufficiently similar. When substantial heterogeneity was considered present, a Der Simonian and Laird random-effects model was applied.

For meta-analyses of time to event and dichotomous outcomes we entered data as the summary effect estimate (HR or rate ratio) and 95% confidence intervals for each study. These were transformed to a log-scale and then pooled using the *metan* command.[35] Summary estimates were then changed back to the original scale using the *eform* command. Continuous outcomes were entered as the mean difference in change from baseline together with the standard error of the estimate or as mean, standard deviation and number of participants in each intervention group.

For meta-analyses of proportions, pooled estimates were obtained as a weighted average using the *metaprop_one* command.[36] For each study, the number of events and denominator were entered. Studies with zero events were included in the analysis without applying a continuity correction. Proportions were stabilized using the Freeman–Tukey double arcsine transformation,[37] and confidence intervals were calculated using the score method.[38]

Heterogeneity and inconsistency across studies were quantified using the tau and $I^2$ statistics and assessed visually using forest plots.[34] Analyses were conducted in Stata 19.[39]

Where sufficient data was available, we stratified analyses based on:

- Kidney Function
    - eGFR ≥60 mL/min/1.73m$^2$
    - eGFR 30 - 60 mL/min/1.73m$^2$
    - eGFR < 30 mL/min/1.73m$^2$
- Age

    - Age <75 years
    - ≥75 years
- Baseline PAP
- NYHA function class
    - Class III vs all classes combined

Where data were not available for the thresholds reported above, we explored subgroups for these variables for which data were available. We had intended to conduct meta-regression to investigate the impact of subgroups but there were insufficient data for this.

## 4.5 Indirect comparison

For outcomes with comparative evidence available for both devices (CardioMEMS and Cordella) against a common comparator (standard care), we conducted an indirect comparison using the Bucher method.[40] This approach estimates the relative effect between two interventions by comparing their effect estimates relative to a shared comparator. The log hazard ratio (HR) for CardioMEMS compared to Cordella was calculated as the difference between the log HRs of each device versus the common comparator. The standard error of the indirect comparison was derived by taking the square root of the sum of the variances of the two log HRs, and used to calculate a 95% confidence interval.[40]

## 4.6 Assessment of publication bias

We had intended to assess publication bias through visual examination of a funnel plot and statistically using the Egger test.[41] However, there were insufficient studies for formal assessment of publication bias. We also searched clinical trial registries to identify any trials that had been registered but where data were not available.

## 4.7 GRADE and Summary of findings

GRADE (Grading of Recommendations Assessment, Development and Evaluation) was used to rate the certainty of the evidence for the primary outcomes.[42] Assessments were performed independently by one reviewer and checked by a second. Any disagreements were resolved by consensus or discussion with a third reviewer.

GRADE assessments consider five domains:

1. Risk of bias (identification of a systematic error in the results);
2. Imprecision (uncertainty around the effect estimate);
3. Inconsistency (variability of the result);
4. Indirectness (relevance to the review question);and
5. Publication bias (potential for selective publication of studies).

The GRADE ratings of very low, low, moderate, or high-quality evidence reflect the extent to which we are confident that the effect estimates are reliable.[42] Evidence from randomised controlled trials (RCTs) was initially rated as high certainty. Evidence from single arm studies were treated as observational, with outcomes initially rated as low certainty, but could be downgraded or upgraded. For outcomes which can only occur in the presence of the device, where single arm data were appropriate, we started with a provisional grade of high certainty evidence and then downgraded as for RCTs.

We downgraded by one level per domain, if serious concerns were identified. We downgraded for risk of bias where the majority of studies were judged as high or some concerns for any specific outcome; for inconsistency where there was substantial evidence of heterogeneity, either statistical or clinical, for an outcome; for indirectness when the majority of the data did not relate specifically to the NYHA class III population; for imprecision where confidence intervals were wide and included one; and for publication bias where evidence of publication bias was found for any of the specific outcomes.

For each of the primary outcomes we produced a simplified summary of findings table displaying the summary effect estimates or a summary of results, number of studies, and GRADE certainty of evidence with a plain language summary of findings.

## 4.8 Protocol changes

The following changes were made to the systematic review methods compared to what was specified in the review protocol:[27]

For outcomes which can only occur in the presence of the device, where single arm data were appropriate, we broadened inclusion criteria to include prospective multi-centre single arm trials that reported device related outcomes (implant or sensor failure or device related complications).

We grouped outcomes into primary and secondary outcomes – this distinction was not pre-specified in the protocol. Primary outcomes were those that were used to inform the economic model. These were subjected to an in-depth risk of bias and GRADE assessment and were included in the summary of findings tables. Results are presented for secondary outcomes but these were not assessed for risk of bias or included in GRADE assessments.

Only one study reported specifically on heart failure mortality. Other studies reported the related outcome of cardiovascular mortality so we broadened this outcome to include cardiovascular mortality; we also report results for the specific outcome of heart failure mortality.

There were insufficient data to complete a Bayesian network meta-analysis or to synthesise RCT and single-arm evidence to produce indirect comparisons, adjusting for potential confounders. Instead, we present a simple indirect comparison for outcomes for which comparative evidence was available for both devices.

We added a GRADE assessment to our review. This was omitted from the protocol but we considered that this would be a helpful addition to summarise the results and reliability of the available evidence.

# 5 Results of clinical effectiveness review

## 5.1 Results of the searches

The searches identified a total of 740 records, of which 169 records were considered potentially relevant after initial screening of titles and abstracts. Eleven studies (60 reports) were included in the review. Three RCTs (1898 participants) evaluated CardioMEMS: CHAMPION[43], MONITOR-HF[44] and GUIDE-HF.[45] Three single-arm studies (587 participants) evaluated Cordella: SIRONA,[46] SIRONA 2[47] and PROACTIVE-HF.[48] PROACTIVE-HF was originally designed as an RCT but was changed to a single arm design early in the study and some data were available for the comparative phase. We included an additional three prospective multi-centre single arm trials (1659 participants) of CardioMEMS for the device related outcomes only: MEMS-HF,[49] COAST,[50] and CardioMEMS-PAS.[51] An additional two studies[52, 53] assessed patients' experience of using the CardioMEMS device but did not provide quantitative outcome data. The process of study identification and selection is summarised in Figure 1.

Table 35 (Appendix 3) summarises the included studies and linked reports. Studies excluded at full text screening are summarised in Table 32 (Appendix 2), together with reasons for exclusion. We identified a further six studies (in seven reports) that fulfilled our inclusion criteria but are currently ongoing. These are summarised in 29 (Appendix 2). Of these six studies, five are evaluating CardioMEMS and one study is evaluating Cordella. The study of Cordella is an RCT, but is not due to complete until September 2028. Of the five CardioMEMS studies, one is a single arm study and the others are RCTs.

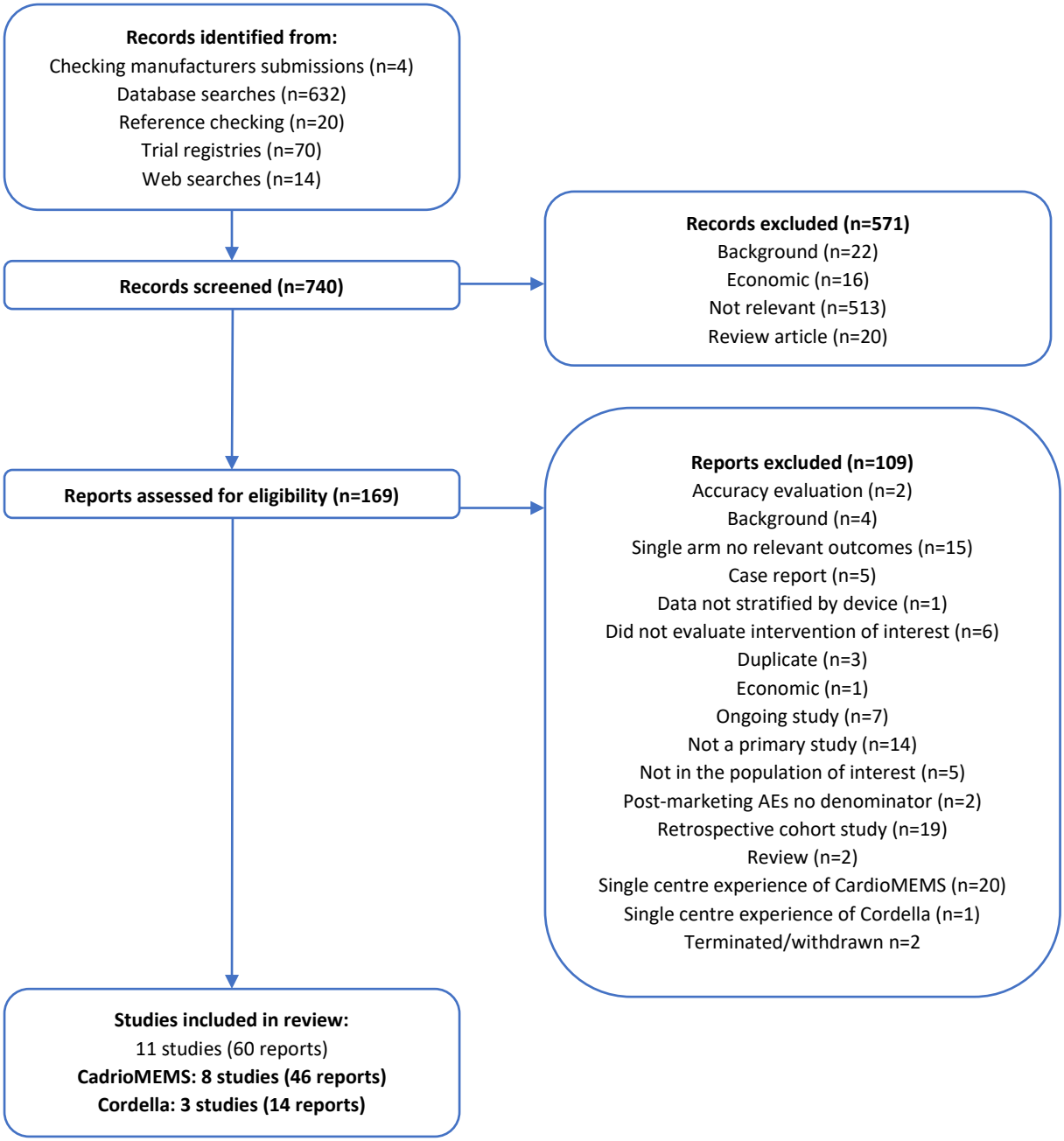
## 5.2 Additional information provided by the device manufacturers

Both device manufacturers provided a submission which included a list of evidence for the Evidence Assessment Group (EAG) to consider. Four relevant study reports not identified by our searches were included in these submissions, 3 of which were associated with studies already identified in our review and 1 was a review. Table 30 and Table 31 set out where study reports from submissions had already been included in our review or the reason why the report was excluded.

In addition to the information provided in the manufacturers' submissions, each company provided additional information following requests for specific information from the EAG. From Endotronix/Edwards Life Sciences (Cordella), the EAG requested any comparative data available from the start of the PROACTIVE-HF trial; Kaplan-Meier plots for the heart failure hospitalisation outcome from the PROACTIVE-HF study; clarification around patient compliance in the SIRONA trial and sufficient data to conduct a population adjusted indirect comparison of Cordella vs CardioMEMs for heart failure hospitalisation rate. Endotronix/Edwards Life Sciences (Cordella) provided event rates for the primary endpoint for the PROACTIVE-HF study, including data for the previously enrolled control and treatment arms. They also supplied additional analyses and hazard ratios for HFH and all-cause mortality separately for the former control groups and former treatment group sample in the PROACTIVE-HF study. Kaplan-Meier curves for time to first heart failure hospitalisation over the first 12 months of the study were also submitted, along with regression coefficients and a covariance matrix for log-hazards from a Cox proportional hazards model. These data were requested to allow us to conduct population adjusted indirect comparisons of the two devices, however, as the full data required for this were not available these data did not inform this appraisal.

The EAG requested the following additional information from Abbott (CardioMEMS): results for the components of the composite outcome (i.e. mortality and HFH) separately for the Class III NYHA subgroup from GUIDE-HF and regression coefficients and covariance matrix from a Cox-Proportional hazards model for HFH adjusted for supplied prognostic covariates at baseline. Abbott (CardioMEMS) provided disaggregated results for the individual components of the composite outcome – mortality and HFHs - for the NYHA Class III subgroup from the GUIDE-HF trial. Additionally, they submitted regression coefficients and covariance matrices for both the GUIDE-HF and CHAMPION studies, however not all covariates requested were included based on data availability and interdependence. They were also unable to provide regression coefficients and covariance matrices for the MONITOR-HF trial as they did not have access to patient-level data from the trial. The EAG also requested a Kaplan-Meier data and/or curve for time to first HFH outcome in the subset of patients with NYHA class III and baseline characteristics of the subset of patients with NYHA class III, for covariates provided. However Abbott were unable to provide this information due to confidential data, therefore the EAG were unable to do complete a population adjusted indirect comparison.

**Figure 1 PRISMA flow diagram for the clinical effectiveness review**



## 5.3 Overview of included studies

Table 3 and Table 34 (Appendix 3) provide an overview of baseline characteristics for all included studies. A more detailed summary of baseline characteristics is provided in Table 36 (Appendix 3) for studies that provided quantitative outcome data. Table 37 and Table 38 (Appendix 3) provide additional detail on baseline medical, surgical and medication history for the studies that provided full quantitative outcome data.

### 5.3.1 Studies that provided full quantitative outcome data

Participants in the intervention arms of the three studies that evaluated CardioMEMS (CHAMPION, MONITOR-HF and GUIDE-HF) received standard of care heart failure management with additional guidance from the haemodynamic information from the implanted sensors. All three trials used standard care, defined as guideline-directed medical therapy (GDMT) or standard heart failure management, as the comparator intervention. In both CHAMPION and GUIDE-HF, randomisation occurred after device implantation. Patients in both intervention arms were required to take daily measurements using the devices, but data from the devices was only available to clinicians in the intervention groups.

Three single-arm studies (587 participants) evaluated Cordella: SIRONA,[46] SIRONA 2[47] and PROACTIVE-HF.[48] All participants in the three studies that evaluated Cordella (SIRONA, SIRONA 2 and PROACTIVE-HF) had daily PAP measurement and vital sign monitoring, which was used to guide HF management. PROACTIVE-HF was originally designed as an RCT, with randomisation occurring after device implantation. The control arm in PROACTIVE-HF involved standard heart failure management with additional telemonitoring of daily data on patients vital signs (but not PAP measurements), which reflects more intensive monitoring than current monitoring. After 72 participants had been randomised to the control arm and 88 participants to the intervention arm, PROACTIVE-HF was changed to a single arm design. This change was prompted by emerging evidence supporting PAP-guided HF management in NYHA class III patients, increased access to reimbursed PAP technology, and disruptions from the COVID-19 pandemic.[54] Additionally, the availability of the CardioMEMS system reduced willingness to participate in a blinded trial. Following this change, those originally assigned to the intervention group (former treatment arm) continued under the same protocol, whilst those originally assigned to the control group (former control arm) switched to the same protocol as the intervention group. The control group participants did not contribute to the primary safety and effectiveness outcomes. Participants in the former treatment arm, along with newly enrolled single arm patients, comprised the primary cohort of the PROACTIVE-HF trial. The manufacturer has shared some results data for the randomised period; most data for this study relate to the single arm component of the study.

Duration of follow-up for the RCTs that evaluated CardioMEMS ranged from 12 to 48 months. The CHAMPION study included an open label extension with an average follow-up of an additional 13 months; data for this period are not included in this review as no device related outcomes were reported. For the single arm studies of Cordella, duration of follow-up ranged from 3 to 12 months. Follow-up for the randomised phase of PROACTIVE-HF was up to 12 months in the intervention arm and a median of 167 days in the control arm. All studies received funding from the test manufacturers - Abbott for the CardioMEMS studies and Endotronix/Edwards Lifesciences for the Cordella studies. The MONITOR-HF trial was also

funded by the Dutch Ministry of Health and National Health Care Institute. Studies were conducted in the USA, Canada, the Netherlands, Belgium, Ireland and Germany.

All studies except GUIDE-HF were restricted to patients with NYHA Class III heart failure, GUIDE-HF included patients with NYHA Class II (30%), III (65%) or IV (5%) heart failure. Where data were available, analyses were restricted to the Class III subgroup to ensure comparison with the other included studies and for closest alignment to the population of interest for this appraisal. Mean or median age ranged from 61 to 71 years across studies. Mean/median age was lower in the CHAMPION and PROACTIVE-HF studies at 62 and 64 years than in other studies where mean/median age was close to 70 years. All studies included more men than women (range 66 to 78% across treatment arms in included studies). Baseline mean pulmonary artery (PA) pressure was reported for all CardioMEMS RCTs but only for the PROACTIVE-HF Cordella study and was similar across studies (range 28 to 33). Where reported, the majority of participants were white; MONITOR-HF did not report ethnicity. Baseline kidney function was higher in the CHAMPION trial than in other studies, although this was not reported for the two SIRONA studies. The mean baseline LVEF ranged from 30 to 40%, where reported and the proportion of participants with LVEF ≥40% ranged from 20 to 54% - this was highest in the PROACTIVE-HF study (54%) and GUIDE-HF (45-49% across groups) and lowest in CHAMPION.

### 5.3.2 Studies included for device related outcomes only

All three additional studies included for device related outcomes were prospective single-arm, multicentre, open-label study evaluations of the CardioMEMS device. The COAST study aimed to enrol 800 patients from 85 sites across the UK, Europe and Australia.[55] Results are currently available for the UK[50] and French cohorts[56] – these are included separately. MEMS-HF was conducted in Germany, the Netherlands and Ireland, and CardioMEMS-PAS in the USA. [50, 56]

All participants received standard of care heart failure management guided by the haemodynamic information from the implanted CardioMEMS sensors and all were restricted to patients with NYHA class III heart failure. Duration of follow-up was 24 months for the French cohort of the COAST study and CardioMEMS-PAS, and 12 months in MEMS-HF and the UK cohort of the COAST study. All were funded by Abbott. Baseline characteristics were in line with those from studies that contributed to the full clinical effectiveness review. Mean age ranged from 67 to 70 years, and the proportion of men ranged from 62 to 78%. The proportion of participants with LVEF ≥40% ranged from 28-29% in the two studies that reported on this (MEMS-HF and COAST French cohort).

### 5.3.3 Studies that reported on patient experience and satisfaction

Four studies provided data on patient experience and satisfaction. Two evaluated the CardioMEMS device.[52, 53] One of these involved semi-structured interviews with 12 patients[53] and the other involved a web-based survey to 37 patients.[52] Both studies were conducted in the USA. Only the interview study reported baseline characteristics of participants: mean age 70.5 (SD 13.1), 66.7% male, and 66.7% white. Neither study received specific grants from any funding agency in the public, commercial, or not-for-profit sectors. They did not provide other quantitative outcome data.

Two studies evaluated patient experience of the Cordella device via survey within the SIRONA 2[47] and PROACTIVE-HF[57] studies. These studies also provided other quantitative data and are

discussed in section 5.3.1. SIRONA 2 was conducted in Belgium, Germany, and Ireland. The survey was optional and administered to patients at 90 days – 37 participants completed the survey and no baseline details were provided. PROACTIVE-HF was conducted in the USA, Belgium, and Ireland. Participants from the former control group were sent a survey – 63 completed it. Again, no baseline details for these participants were provided.

## Table 3 Overview of study details and baseline characteristics

| Study name | Design | Treatment arm/comparator arm | Number with device implanted | Duration | Study location | Age Mean (SD) | % Male | PA mean pressure mmHg Mean (SD) | eGFR mL/min/1.73 m2 Mean (SD) |
|---|---|---|---|---|---|---|---|---|---|
| **Studies that provided full quantitative outcome data** | | | | | | | | | |
| CHAMPION[43] | RCT | CardioMEMS: HF management guided by PAP obtained remotely via an implanted sensor | 270 | 18 months (mean 15 months, SD 7) | USA | 61 (13) | 72 | 29 (10) | 60 (23) |
| | | Standard care: GDMT | 280 | | | 62 (13) | 73 | 30 (10) | 62 (23) |
| GUIDE-HF[45] | RCT | CardioMEMS: HF management guided by PAP obtained remotely via an implanted sensor | 497 | 12 months | USA, Canada | 71 (64, 76)* | 62 | 28 (22, 35)* | 51 (39, 65)* |
| | | Standard care: GDMT | 503 | | | 70 (64, 77)* | 63 | 29 (22, 35)* | 48.9 (38, 65)* |
| MONITOR-HF[44] | RCT | CardioMEMS: HF management guided by PAP obtained remotely via an implanted sensor | 176 | 48 months (mean: 1.8 years, SD 0.9) | Netherlands | 69 (61, 75)* | 78 | 33 (11) | 48 (35, 60)* |
| | | Standard care: GDMT and diuretics | 172[$] | | | 70 (61, 75)* | 73 | NR | 48 (38, 63)* |
| SIRONA[46] | Prospective single-arm | Cordella: Daily PAP readings performed while seating | 15 | 3 months | Belgium & Ireland | 71 | 67 | NR | NR |
| SIRONA 2[47] | Prospective single-arm + survey | Cordella: Daily PAP readings measured by the handheld patient reader for 18 seconds | 70 | 12 months | Belgium, Germany, Ireland | 71 (10) | 71 | NR | NR |
| PROACTIVE-HF[48] | RCT phase | Cordella: HF management guided by PAP obtained remotely via an implanted sensor | 88 | Up to 12 months | USA, Ireland, Belgium | NR | NR | NR | NR |
| | | Standard care: GDMT | 72 | Median 167 days | | 66 (11) | 58 | 27 (9) | 50 (20) |
| | Single arm phase + survey | Cordella: Daily PAP measurements | 456 | 12 months | USA, Ireland, Belgium | 64 (13) | 61 | 28 (10) | 55 (19) |

| Study name | Design | Treatment arm/comparator arm | Number with device implanted | Duration | Study location | Age Mean (SD) | % Male | PA mean pressure mmHg Mean (SD) | eGFR mL/min/1.73 m2 Mean (SD) |
|---|---|---|---|---|---|---|---|---|---|
| **Studies included for device related outcomes only** | | | | | | | | | |
| MEMS-HF[49] | Prospective single-arm | CardioMEMS: HF management guided by PAP obtained remotely via an implanted sensor | 234 | 12 months | Germany, Netherlands, Ireland | 68(11) | 78 | 30(11) | NR |
| COAST-UK[50] | Prospective single-arm | CardioMEMS: HF management guided by PAP obtained remotely via an implanted sensor | 100 | 12 months | UK | 69(12) | 70 | 34(11) | 51(17) |
| COAST-FRANCE[56] | Prospective single-arm | CardioMEMS: HF management guided by PAP obtained remotely via an implanted sensor | 103 | 24 months | France | 67(12) | 78 | 36(11) | 53(22) |
| CardioMEMS-PAS[51] | Prospective single-arm | CardioMEMS: HF management guided by PAP obtained remotely via an implanted sensor | 1214 | 24 months | USA | 70(12) | 62 | NR | 53(21) |
| **Studies that reported on patient experience and satisfaction** | | | | | | | | | |
| Assaad et al.[58] | Survey | CardioMEMS: HF management guided by PAP obtained remotely via an implanted sensor | 30 | NA | USA | NR | NR | NR | NR |
| Haynes et al.[53] | Interview study | CardioMEMS: HF management guided by PAP obtained remotely via an implanted sensor | 12 | 106-1522 days with device | USA | 71 (13) | 67 | NR | NR |

AE - adverse event, Ctrl – Control, DSRC – device/system related complication, eGFR – estimated glomerular filtration rate, GDMT - guideline-recommended medical therapy, HF – heart failure, HFH – heart failure hospitalisations, HFR – heart failure related, NA – not applicable, NR – not reported, PAP - pulmonary artery pressure, QoL – quality of life. Tx – treatment

*median and lower and upper ranges reported $ Device not implanted in control group

## 5.4 Risk of bias

Table 4 provides a summary of the risk of bias assessments using the RoB 2 tool for each of the primary outcomes for which comparative data were available, stratified according to outcome. Assessments are for the three RCTs that evaluated CardioMEMS and the randomised phase of the PROACTIVE-HF study that evaluated Cordella.

None of the studies were judged as low risk of bias for all outcomes. The CHAMPION trial was judged as high risk of bias for the HRQoL outcome and low risk of bias for all other outcomes. GUIDE-HF and MONITOR-HF were judged as some concerns for the HRQoL outcomes but as low risk of bias for other outcomes. PROACTIVE-HF was judged at some concerns overall for both heart failure hospitalisation and all-cause mortality.

The three RCTs that evaluated CardioMEMS were judged at low risk of bias for domain 1 (risk of bias arising from the randomisation process). The PROACTIVE-HF trial was judged at some concerns as no information was available on allocation concealment. Most trials were double blinded as devices were implanted prior to randomisation and conducted an intention-to-treat analysis, and so were considered at low risk of bias for domain 2 (risk of bias due to deviations from the intended interventions). The exception to this was the MONITOR-HF study where participants were aware of their treatment allocation. There was no information on whether there were any deviations from the intended intervention that arose because of the trial context and so this RCT was rated as some concerns for this domain for all outcomes. Although PROACTIVE-HF implanted devices prior to randomisation, it was single blinded and did not provide any information on whether an intention-to-treat analysis was conducted and so was also judged at some concerns for this domain.

There were very little missing outcome data and so most trials were judged as low risk of bias for domain 3 (risk of bias due to missing outcome data) for most outcomes. The PROACTIVE-HF trial was judged as some concerns for domain 3 for the HFH and all-cause mortality outcome. The availability of data for these outcomes among participants was unclear as there was no information on patient withdrawals. The CHAMPION trial was judged as high risk of bias for the HRQoL outcome for domain 3. The availability of data for this outcome among participants was unclear, and the absence of sensitivity analyses to explore the effect of missing data means that missing data could plausibly be related to the outcome, introducing potential bias. The GUIDE-HF and MONITOR-HF studies were judged as some concerns for domain 3 for the HRQoL outcomes. In both studies there was a notable proportion of missing data and this was considered potentially related to the outcome. However, responder analysis was confirmed and consistent in all sensitivity analyses for missing data in the MONITOR-HF study and missing data was relatively balanced and reasons for withdrawal similar across the two treatment groups in the GUIDE-HF study.

All RCTs except MONITOR-HF were judged at low risk of bias for all outcomes for domain 4 (measurement of the outcome). MONITOR-HF was judged as some concerns for this domain for the HRQoL outcomes. As the HRQoL outcomes were self-reported and the MONITOR-HF study was an open-label trial, outcome assessors (in this case the participants themselves) were unblinded. For all other outcomes, this RCT was judged at low risk of bias as assessments were administered by independent research personnel, predominantly on paper, and were

intensively monitored on adherence to study protocol and completeness during the study. All RCTs were judged at low risk of bias for domain 5 across all outcomes.

Quality assessment of the three single arm Cordella studies was done at the study level using the JBI critical appraisal checklist for prevalence studies. There were concerns regarding the small sample size of the SIRONA study and it was unclear whether the statistical analysis for this study was appropriate, this study was therefore judged at high risk of bias overall. No other concerns were raised; however, the remaining studies were judged to have some concerns regarding risk of bias for outcomes requiring comparative evidence to provide an unbiased estimate of device effectiveness, due to their single-arm designs. (Table 4).

For device-related outcomes (failure of sensor implantation, sensor failure, and device/system-related complications), we considered single-arm data to be the most appropriate source of evidence. The SIRONA-2 and PROACTIVE-HF studies were therefore judged to have low concerns for these outcomes. Although the three RCTs evaluating CardioMEMS were comparative in design, they only contributed single-arm data for these outcomes and so were assessed accordingly using the JBI checklist. The same checklist was also applied to the three additional studies included specifically for the device-related outcomes. All six CardioMEMS studies were judged as low risk of bias for these outcomes.

## Table 4 Risk of bias for RCT

| Study | Outcome | Domain | | | | | Overall | Rationale |
|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 | | |
| CHAMPION[43] | HFH | Low | Low | Low | Low | Low | **Low** | Although no statistical analysis plan available and protocol published after completion of the study, considered unlikely that outcome selected from multiple eligible outcome measurements or analyses of data as this is a standard outcome reported and analysed in the expected way. |
| | All-cause mortality | Low | Low | Low | Low | Low | **Low** | |
| | HRQoL - MLHFQ | Low | Low | High | Low | Some concerns | **High** | No information on how many patients had outcome data. No sensitivity analyses were carried out. Missing data potentially related to outcome. |
| GUIDE-HF[45] | HFH | Low | Low | Low | Low | Low | **Low** | No concerns for any domains |
| | All cause mortality | Low | Low | Low | Low | Low | **Low** | No concerns for any domains |
| | HRQoL - KCCQ | Low | Low | Some concerns | Low | Low | **Some concerns** | Notable proportion of missing data at 12-month follow-up. No sensitivity analyses carried out and missingness could depend on true value. |
| | HRQoL – EQ-5D-5L | Low | Low | Some concerns | Low | Low | **Some concerns** | |
| MONITOR-HF[44] | HFH | Low | Some concerns | Low | Low | Low | **Some concerns** | Trial was open-label and no information provided on deviations from the intended intervention. |
| | All cause mortality | Low | Some concerns | Low | Low | Low | **Some concerns** | |
| | HRQoL - KCCQ | Low | Some concerns | Some concerns | Some concerns | Low | **Some concerns** | Trial was open-label and no information provided on deviations from the intended intervention. Higher rates of missing data among certain subgroups. Missingness could depend on true value. Responder analysis confirmed and consistent in all sensitivity analyses. Outcome assessors were unblinded as it was an open-label trial. |
| | HRQoL - EQ-5D-5L | Low | Some concerns | Some concerns | Some concerns | Low | **Some concerns** | |
| PROACTIVE-HF randomised phase[48] | HFH | Some concerns | Some concerns | Some concerns | Low | Low | **Some concerns** | No information on allocation sequence concealment, whether an appropriate analysis (e.g. ITT) used and no information whether outcome data was available for all patients. |
| | All-cause mortality | Some concerns | Some concerns | Some concerns | Low | Low | **Some concerns** | |

Domain 1: Risk of bias arising from the randomization process; Domain 2: Risk of bias due to deviations from the intended interventions; Domain 3: Risk of bias due to missing outcome data; Domain 4: Risk of bias in measurement of the outcome; Domain 5: Risk of bias in selection of the reported result

EQ-5D-5L – EuroQol five-dimensional five-level questionnaire, HFH – heart failure hospitalisation, HRQoL – health related quality of life, ITT – intention-to-treat, KCCQ – Kansas City Cardiomyopathy Questionnaire

## Table 5 Risk of bias for single-arm studies

| Study | Outcome | Domain | | | | | | | | Overall | Rationale |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Q1 | Q2 | Q3 | Q4 | Q5 | Q6 | Q7 | Q8 | | |
| SIRONA[46] | HFH; HRQoL; device related outcomes | Y | N | Y | Y | Y | Y | ? | Y | **High** | Sample size was small (N=15), unclear what statistical analysis was implemented for some of the outcomes. |
| SIRONA 2[47] | HFH; HRQoL | Y | ? | Y | Y | Y | Y | Y | Y | **Some concerns** | No sample size calculation provided and non-comparative evidence. |
| | Device related outcomes | Y | ? | Y | Y | Y | Y | Y | Y | **Low** | Outcome for which comparative data not expected |
| PROACTIVE-HF single-arm[48] | HFH; HRQoL | Y | Y | Y | Y | Y | Y | Y | Y | **Some concerns** | Non-comparative nature of the evidence |
| | Device related outcomes | Y | Y | Y | Y | Y | Y | Y | Y | **Low** | Outcome for which comparative data not expected |
| CHAMPION[43] | Device related outcomes | Y | Y | Y | Y | Y | Y | Y | Y | **Low** | Outcome for which comparative data not expected |
| GUIDE-HF[45] | Device related outcomes | Y | Y | Y | Y | Y | Y | Y | Y | **Low** | Outcome for which comparative data not expected |
| MONITOR-HF[44] | Device related outcomes | Y | Y | Y | Y | Y | Y | Y | Y | **Low** | Outcome for which comparative data not expected |
| MEMS-HF[49] | Device related outcomes | Y | Y | Y | Y | Y | Y | Y | Y | **Low** | Outcome for which comparative data not expected |
| COAST[50] | Device related outcomes | Y | Y | Y | Y | Y | Y | Y | Y | **Low** | Outcome for which comparative data not expected |
| CardioMEMS-PAS[51] | Device related outcomes | Y | Y | Y | Y | Y | Y | Y | Y | **Low** | Outcome for which comparative data not expected |

HFH – heart failure hospitalisation, HRQoL – health related quality of life; Y – yes; N – no; ? - Unclear

Q1: Was the sample frame appropriate to address the target population?

Q2: Was the sample size adequate?

Q3: Were the study subjects and the setting described in detail?

Q4: Was the data analysis conducted with sufficient coverage of the identified sample?

Q5: Were valid methods used for the identification of the condition?

Q6: Was the condition measured in a standard, reliable way for all participants?

Q7: Was there appropriate statistical analysis?

Q8: Was the response rate adequate, and if not, was the low response rate managed appropriately?

## 5.5 Outcomes

Table 6 provides a summary of which studies contributed data to the synthesis for each of the outcomes of interest. Risk of bias assessment for the primary outcomes is indicated by shading of the cells: green for low risk of bias; yellow for some concerns; and red for high risk of bias. Full results data for each study are reported in Appendix 4 (Table 39 to Table 44). None of the studies reported data on adherence to adjusted medication triggered by change in PAP or improvement in co-morbidities.

**Table 6 Overview of outcomes reported in each of the included studies**

| Outcome | CHAMPION[43] | GUIDE-HF[45] | MONITOR-HF[44] | SIRONA[46] | SIRONA 2[47] | PROACTIVE-HF RCT[48] | PROACTIVE-HF Single -arm[48] | Assaad, 2019[52] | Haynes, 2020[53] | MEMS-HF[49] | COAST[50] | CardioMEMS-PAS[51] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **PRIMARY OUTCOMES** | | | | | | | | | | | | |
| Heart failure hospitalisation | x | x | x | x | x | x | x | | | | | |
| All-cause mortality | x | x | x | | | x | | | | | | |
| Failure of sensor implantation | x | x | x | x | x | | x | | | x | x | x |
| Sensor failure | x | | x | x | x | | x | | | x | x | x |
| Device/system/procedure related complications | x | x | x | x | x | | x | | | x | x | x |
| HRQoL | x | x | x | x | x | | x | | | | | |
| **SECONDARY OUTCOMES** | | | | | | | | | | | | |
| Urgent care visits for heart failure | | x | x | | | | x | | | | | |
| Cadiovascular mortality | x | x | x | | | | x | | | | | |
| Changes to clinical management: medication | x | x | x | | x | | x | | | | | |
| Changes to clinical management: contact with healthcare professional | x | x | x | | | | | | | | | |
| Functional capacity: 6 minute walk test | | x | x | | x | | x | | | | | |
| Change in NYHA classification | | | | x | x | | x | | | | | |
| Improvement in co-morbidities | | | | | | | | | | | | |
| Other adverse events | x | x | | x | x | | x | | | | | |
| Adherence to using the device | | x | x | x | x | | x | | | | | |
| Adherence to adjusted medication triggered by change in PAP data | | | | | | | | | | | | |
| Patients lost to follow-up | x | x | x | x | x | | x | x | x | x | x | x |
| Patient experience and satisfaction | | | | | x | x | | x | x | | | |

### 5.5.1 Primary outcomes

#### 5.5.1.1 Heart failure hospitalisations (HFH)

All studies that reported on HFH suggested beneficial effects of the PAP monitoring devices in reducing hospitalisation at between 3 and 48 month follow-up (Table 39 in Appendix 4 and Figure 2). Definitions of HFH were broadly similar across studies and were defined as a hospitalisation due to heart failure longer than 6 hours and the need for additional HF therapy. For GUIDE-HF we used data from the NYHA class III subgroup provided by the device manufacturer in our meta-analysis. Across the three RCTs that evaluated CardioMEMS, the summary HR was 0.66 (95% CI 0.57, 0.76), with little evidence of heterogeneity ($I^2$=0.0%). Data supplied by the manufacturer of Cordella for the randomised phase of the PROACTIVE-HF trial

suggested a similar improvement associated with Cordella (HR 0.61, 95 CI 0.36, 1.04), although confidence intervals were wide due to the reduced sample size and power from the shorter enrolment and follow-up periods. Indirect comparison of Cordella with CardioMEMS suggested no difference in HFH between the two devices [redacted].

The CHAMPION RCT reported additional data for the subgroups with COPD, CKD, baseline PAP and those with a history of atrial fibrillation (Table 39; Appendix 4). All subgroups showed a reduction in HFH in the intervention group compared to control. Data from GUIDE-HF for the combined population irrespective of NYHA class also suggested a reduction in HFH but the effect was smaller than in the NYHA class III population (HR 0.83, 95% CI 0.68, 1.01). GUIDE-HF also reported stratified data based on the period of the trial that took place during the COVID pandemic compared to the period prior to the pandemic. These data are for the full trial population that was not restricted to those with NYHA class III CHF. There was no difference between intervention and control group during the pandemic, but there was evidence for reduced hospitalisation prior to the pandemic (HR 0.72 (95% CI: 0.57, 0.92). MONITOR-HF reported subgroup analyses based on age, sex, eGFR and diabetes. There was no evidence for a difference in effect across any of these subgroups.

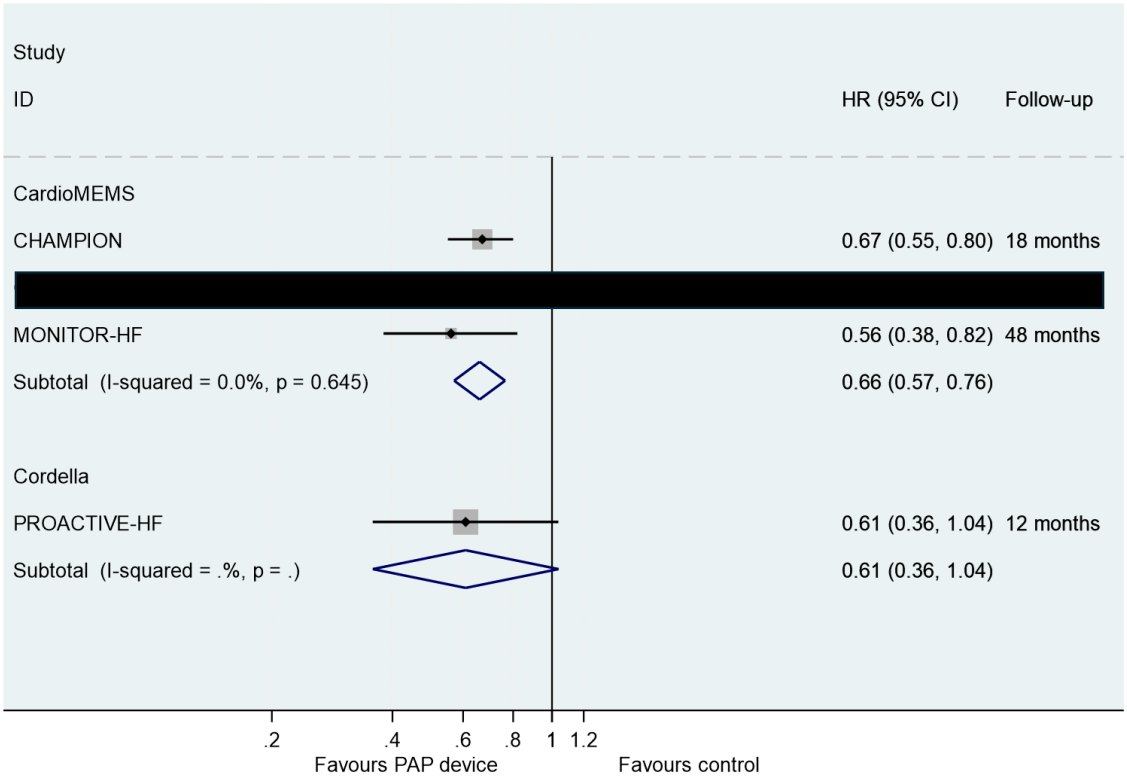



**Figure 2 Forest plot showing hazard ratios (HRs) and 95% confidence intervals for heart failure hospitalisation for individual studies, stratified by device type. Summary estimates from fixed-effect meta-analyses are also shown for each device. [GUIDE-HF data for NYHA III subgroup AiC]**

Two of the three single arm studies that evaluated Cordella reported a reduction in HFH following device implantation. PROACTIVE-HF reported that the average HFHs per patient in the 6 months before implant was 0.6 (SD= 0.7) compared to 0.1 (SD=0.4) in the 6 months after

implant in the single-arm phase of the study (p< 0.0001). In the SIRONA 2 study, the event rate decreased from 1.26 events per patient-year (EPPY), in the 12 months prior to device implantation to 0.27 EPPY in the 12 months post-implantation (p< 0.0001). The SIRONA Cordella study was very small (15 patients) with a very short follow-up of 3 months. This study reported 1 HFH event and so it was not possible to determine the impact of the Cordella device in this study.

#### 5.5.1.2 All Cause Mortality

All-cause mortality was reported across all three RCTs that evaluated CardioMEMS and for the comparative and single arm phases of the PROACTIVE-HF Cordella study and the SIRONA 2 study (Table 39; Figure 3). In the CHAMPION trial, over an 18 month follow-up, there were 50 deaths in the intervention group compared to 64 in the standard care group. For GUIDE-HF we used data from the NYHA class III subgroup provided by the device manufacturer in our meta-analysis. Event rates were similar across arms in the GUIDE-HF trial at 12 months [redacted] and the MONITOR-HF trial at 48 months (42 deaths in the intervention group and 45 deaths in the standard care group). Overall, there was a suggestion for a small decrease in mortality across the three CardioMEMS RCTs and from data provided by the manufacturer of Cordella for the comparative phase of the PROACTIVE HF trial, but confidence intervals were wide and consistent with both an increased and decreased risk of death (HR 0.91, 95% CI 0.70, 1.17 for CardioMEMS and HR 0.51, 95% CI 0.20, 1.32 for Cordella). Indirect comparison of Cordella with CardioMEMS suggested no evidence of a difference in all cause mortality between the two devices [redacted], although the estimate is very imprecise.

Data from GUIDE-HF for the combined population irrespective of NYHA class were similar to data for the NYHA class III subgroup. GUIDE-HF also provided mortality data separately for the pre-COVID and COVID period of the trial; there was no evidence for an impact on mortality in either trial period. The CHAMPION study provided mortality data stratified on baseline PAP. This suggested that only those with low baseline PAP had a mortality benefit from the CardioMEMS device. In those with baseline PAP ≤0.583, the intervention group had a reduction in mortality compared to control (HR 0.54, 95% CI 0.31, 0.92), however there was no difference in mortality in those with baseline PAP of >0.583 (HR 1.18, 95% CI 0.70, 1.99).

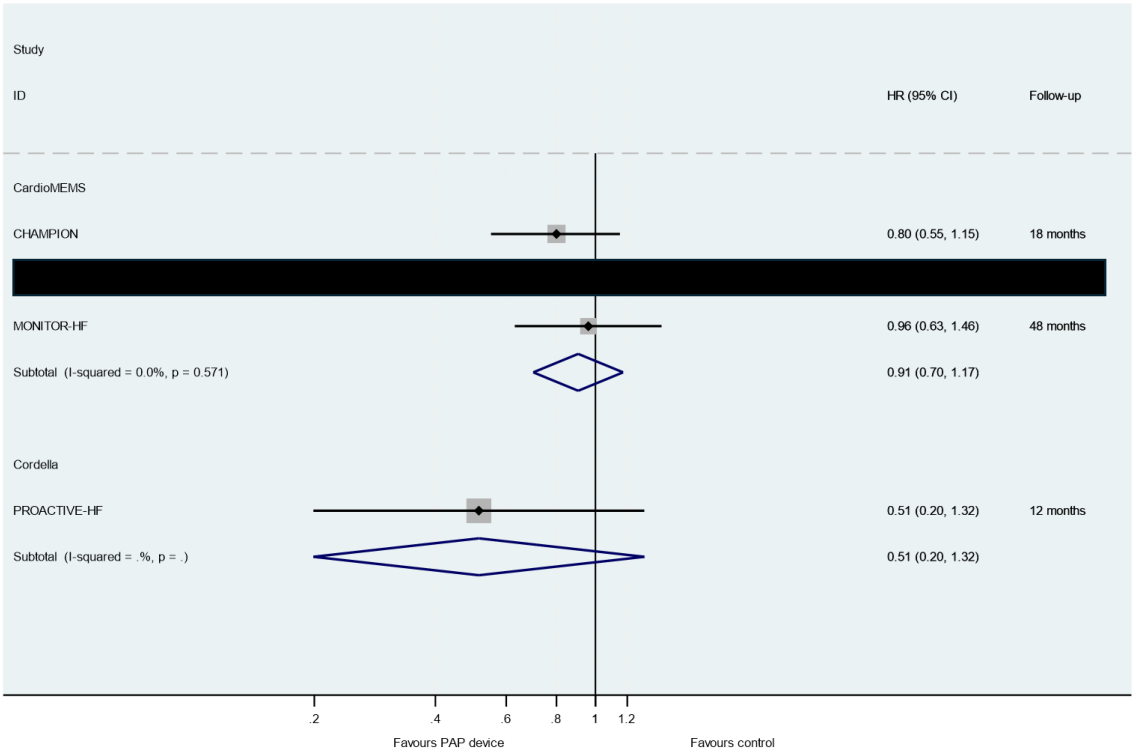



**Figure 3 Forest plot showing hazard ratios (HRs) and 95% confidence intervals for all cause mortality for individual studies, stratified by device type. Summary estimates from fixed-effect meta-analyses are also shown for each device. [GUIDE-HF data for NYHA III subgroup AiC]**

#### *5.5.1.3 Failure of sensor implantation*

All studies provided data on failure of sensor implantation (Table 40; Figure 4). Where participants in both intervention and control arms were implanted with the device, results are considered for the full trial population (i.e. combined across both arms); data are also reported for the three prospective multi-centre single arm trials that evaluated CardioMEMS. The proportion of participants in whom the device failed to implant ranged from 0 to 7.5% across studies, with a summary estimate of 1.7% (95% CI 0.8%, 2.9%) in the CardioMEMS studies and 4.9% (95% CI 3.1%, 7.0%) in the Cordella studies. There was substantial heterogeneity for the CardioMEMS studies ($I^2$ = 81%) and so results are presented for the random effects model. For Cordella, results are presented for the fixed effects model. We considered this more appropriate due to the small number of studies, difficulties in estimating heterogeneity, and the disproportionate weight given to the small SIRONA study by the random effects model.

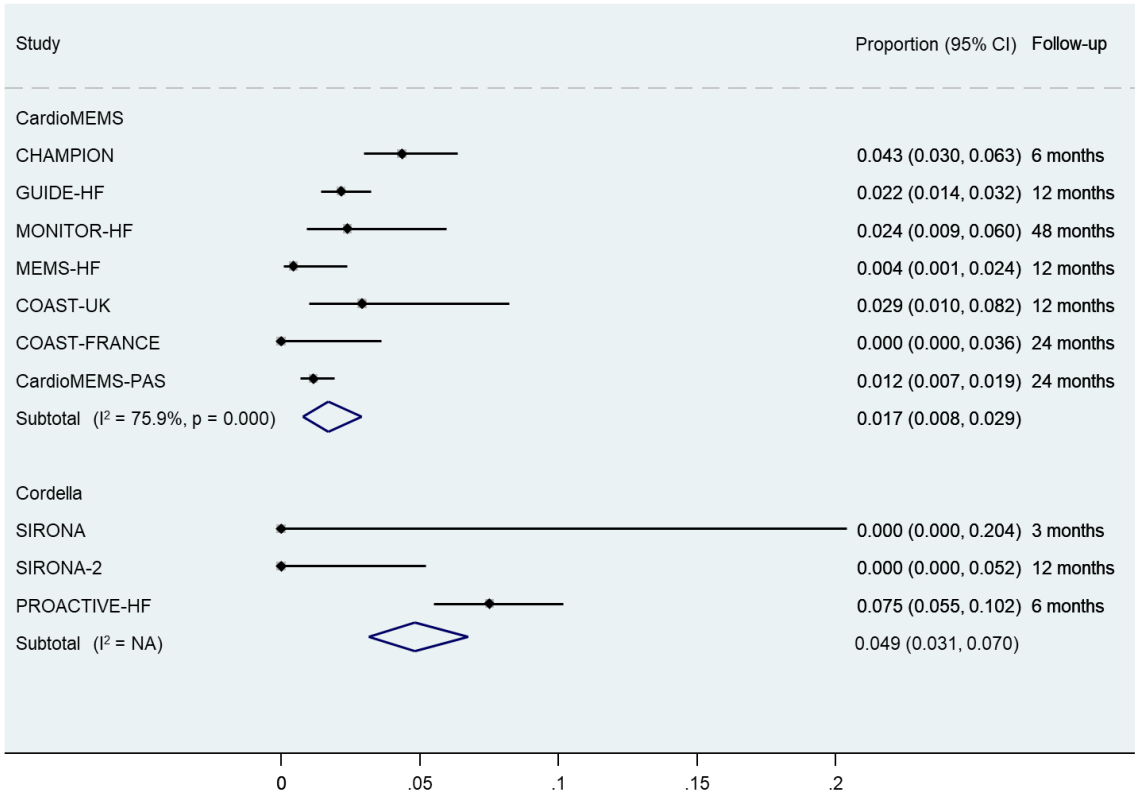



**Figure 4 Forest plot showing hazard ratios (HRs) and 95% confidence intervals for proportion of participants in whom sensor implantation failed, stratified by device type. Summary estimates from random effects meta-analysis for CardioMEMS and fixed-effect meta-analysis for Cordella.**

In both the CHAMPION and GUIDE-HF studies, the CardioMEMS devices were implanted prior to randomisation. In the CHAMPION study, out of 575 participants enrolled, 25 (4.3%) were not implanted due to: 19 devices not opened; 2 sensors did not release and were successfully removed; 1 transient ventricular tachycardia; 1 difficulty maintaining guide-wire position due to severe chronic cough; 1 transient left bundle branch block; 1 discovery of pre-existing deep vein thrombosis or pulmonary embolism during pulmonary angiogram. In the GUIDE-HF study, of the 1022 participants enrolled, there were 22 (2.2%) failures to implant, however reasons were not reported. In the MONITOR-HF study, implantation of the CardioMEMS device occurred after randomisation in the intervention group alone. Of the 168 participants who received the device there were 4 failures to implant on the first attempt: 1 unexpected abnormal anatomy, 3 operator or (technical) facility related, however all implants were successful on the second attempt. The French cohort of the COAST study reported that there were no failures to implant. Sensor implant was unsuccessful in three out of 103 patients in the UK cohort of the COAST study due to haemoptysis, anatomical constraints, or inability to gain venous access. There was one failure to implant in the MEMS-HF study due to haemoptysis during the implantation. In the CardioMEMS-PAS study, 14 out of 1214 devices failed to implant, reasons for failure were not reported.

The two SIRONA studies that evaluated Cordella reported that there were no failures to implant in the 15 (SIRONA) and 70 (SIRONA 2) participants in which implantation was attempted. In the

larger PROACTIVE-HF study, of the 493 participants enrolled, 37 devices failed to implant. This was due to a combination of adherence to instructions for use (IFU), prior undiagnosed comorbidities or procedural skills and challenges.

#### 5.5.1.4 Sensor failure

All studies, except GUIDE-HF, reported on sensor failure at between 3 and 48 months follow-up (Table 40, Appendix 4). Where participants in both intervention and control arms were implanted with device, results are considered for the full trial population (i.e. combined across both arms); data are also reported for the three prospective multi-centre single arm trials that evaluated CardioMEMS. The proportion of participants with a device implanted in whom the sensor subsequently failed was low (0 to 1.2%). The proportion of sensor failures was highest in the MONITOR-HF study which had the longest duration of follow-up (48 months). However, other studies with longer follow-up (24 months) showed very low proportions of sensor failures. The summary estimate for the proportion of sensor failures of 0.1% (95% CI 0.0, 0.6%; Figure 5 Forest plot showing hazard ratios (HRs) and 95% confidence intervals for proportion of participants in whom sensors failed, stratified by device type. Summary estimates from random effects meta-analysis for CardioMEMS and fixed-effect meta-analysis for Cordella.) for CardioMEMS and 0% (95% CI 0, 0.1%) for Cordella. There was moderate heterogeneity for the CardioMEMS studies ($I^2$ = 44%) and so results are presented for the random effects model. For Cordella, results are presented for the fixed effects model. We considered this more appropriate due to the small number of studies, difficulties in estimating heterogeneity, and the disproportionate weight given to the small SIRONA study by the random effects model.

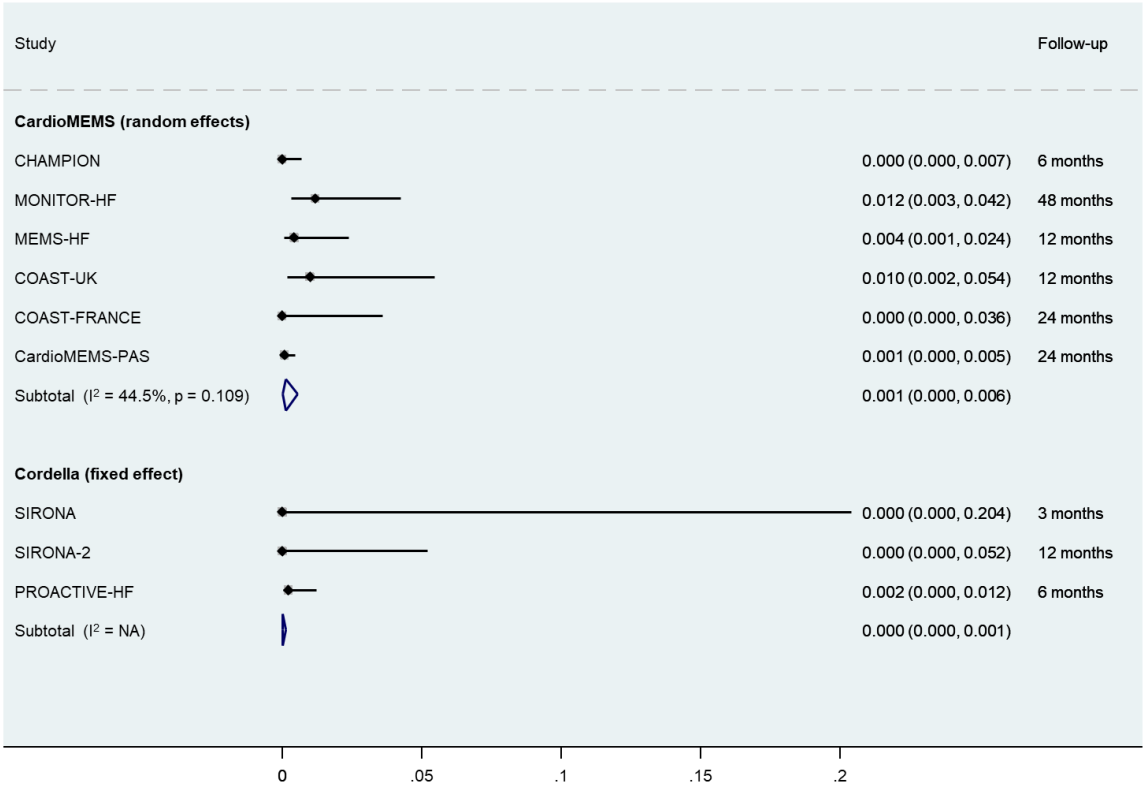


**Figure 5 Forest plot showing hazard ratios (HRs) and 95% confidence intervals for proportion of participants in whom sensors failed, stratified by device type. Summary estimates from random effects meta-analysis for CardioMEMS and fixed-effect meta-analysis for Cordella.**

In the CHAMPION study, there were no failures of the CardioMEMS device, defined as an inability to obtain readings at 6 months follow-up. MONITOR-HF defined failure of the CardioMEMS device as any longstanding inability to obtain readings due to malfunction of the sensor (resulting in signal loss/no readings). At 48 months, in the 168 participants who had the CardioMEMS device implanted, there were 2 sensor failures (1.2%). One participant lost signal due to complex posture and no re-implant was attempted; one patient lost signal due to displacement and was reimplanted to continue monitoring. No events required removal of the sensor. MEMS-HF, COAST-UK and the CardioMEMS-PAS study each reported single instances of sensor failure, but reasons for these were not reported. There were no reports of failure of the Cordella device in either the SIRONA or SIRONA 2 studies or for the COAST-FRANCE study of CardioMEMS. In the PROACTIVE-HF study, there was 1 sensor failure (0.2%).

#### 5.5.1.5 Device/system or procedure related complications and procedure related complications

All studies provided data on device or system related complications (DSRC) at between 3 and 48 months follow-up (Table 7 and Table 39, Appendix 4). Where participants in both intervention and control arms were implanted with device, DSRC are considered for the full trial population (i.e. combined across both arms); data are also reported for the three prospective multi-centre single arm trials that evaluated CardioMEMS. Definitions of a DSRC were broadly similar across studies and were defined as an adverse event that was definitely or potentially related to the PAP monitoring device treated by invasive means other than intramuscular administration of drugs or a right-heart catheterisation. GUIDE-HF, MONITOR-HF, MEMS-HF, COAST, SIRONA and PROACTIVE-HF also included events that resulted in the death of the participant or the explant of the device in their definitions. SIRONA-2 did not provide a definition. Table 7 provides an overview of the DSRC across included studies.

The proportion of DSRC were very low across studies for both CardioMEMS and Cordella (range 0.8 to 2.4%). The summary proportion of DSRC across trials was 0.7% (95% CI 0.3, 1.3%) for CardioMEMS and 0.1% (0.0, 0.09%) for Cordella. There was moderate heterogeneity for the CardioMEMS studies ($I^2$ = 44%) and so results are presented for the random effects model. For Cordella, results are presented for the fixed effects model. We considered this more appropriate due to the small number of studies, difficulties in estimating heterogeneity, and the disproportionate weight given to the small SIRONA study by the random effects model. We conducted a sensitivity analysis by removing the SIRONA study from the analysis for the Cordella studies due to its very small sample size and short follow-up time. The proportion of DSRC for this analysis increased slightly to 0.7% (95% CI 0.1, 1.70%).

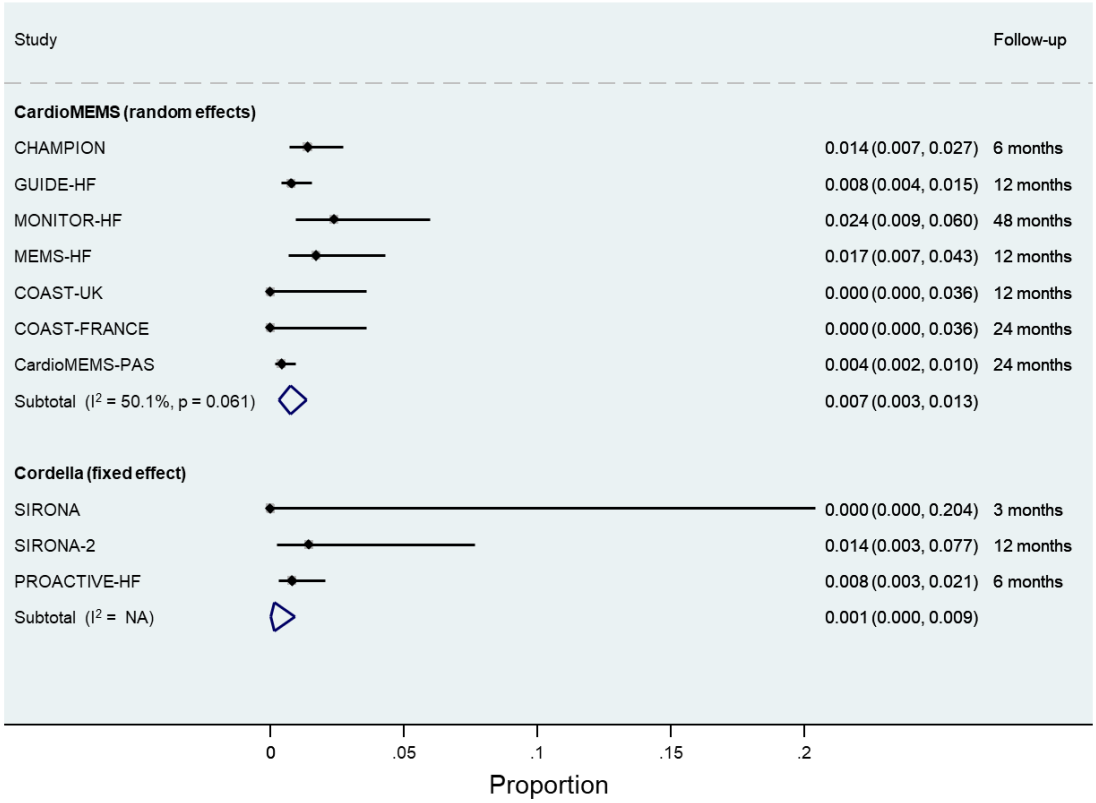



**Figure 6 Forest plot showing hazard ratios (HRs) and 95% confidence intervals for proportion of participants with DSRC, stratified by device type. Summary estimates from random effects meta-analysis for CardioMEMS and fixed-effect meta-analysis for Cordella.**

Three studies, CHAMPION, MEMS-HF, and PROACTIVE-HF, also reported on procedure related AEs in addition to DSRC, and SIRONA also reported on AEs related to the device (Table 7). CHAMPION reported that 7/575 participants (1.2%) experienced a procedure related AE, details of the events were reported overall combined with DSRC (Table 7). PROACTIVE-HF reported that 4/493 (5%) participants experienced a procedure related adverse event but did not provide details of these. MEMS-HF reported that 21/234 (9%) of participants experienced a procedure related adverse event but also provided no further details. SIRONA reported that 4/15 (27%) of participants experienced an AE related to the device, details of these are summarised in Table 7.

**Table 7 Overview of DSRC, procedure related complications and sensor failure reported in included studies**

| Study | Outcome | Device | Number of DSRC (%) | Details |
|---|---|---|---|---|
| CHAMPION[43] | DSRC | CardioMEMS | 8/575 (1.4) | *Details reported for DSRC and procedure related complications combined:*<br>4 bleeding events<br>3 hospitalisations related to anticoagulation treatment<br>2 exacerbations of pre-existing atrial dysrhythmias during right heart catheterisation |
| | Procedure related AEs | | 7/575 (1.2) | |

| Study | Outcome | Device | Number of DSRC (%) | Details |
|---|---|---|---|---|
| | | | | 2 febrile illnesses<br>1 pulmonary in situ thrombus during right-heart catheterisation<br>1 cardiogenic shock<br>1 atypical chest pain<br>1 delivery-system failure that required a snare to remove the delivery system |
| GUIDE-HF[45] | DSRC | CardioMEMS | 8/1022 (0.8) | Details not provided |
| MONITOR-HF[44] | DSRC | CardioMEMS | 4/168 (2.4) | 2 haemoptysis with invasive measures<br>2 arrythmias |
| MEMS-HF[49] | DSRC | CardioMEMS | 4/234 (1.7) | Not reported |
| | Procedure related AEs | | 21/234 (9) | |
| COAST-UK[50] | DSRC | CardioMEMS | 0/103 | NA |
| COAST-FRANCE[56] | DSRC | CardioMEMS | 0/103 | NA |
| CardioMEMS -PAS[51] | DSRC | CardioMEMS | 5/1214 (0.4) | Not reported |
| SIRONA[46] | DSRC | Cordella | 0/15 | NA |
| | AEs related to the device | | 4/15 (27) | 1 sensor dislodged from the target location of deployment into the main pulmonary artery during withdrawal of the delivery system<br>1 transient complete heart block as the sensor passed through the right heart<br>2 post-procedure minor haemoptysis<br><br>All events resolved without clinical sequelae or impairment of device function. |
| SIRONA 2[47] | DSRC | Cordella | 1/70 (1.3) | LV lead dislodgement |
| PROACTIVE-HF[48] | DSRC | Cordella | 4/493 (0.8) | 1 further migration of the Cordella sensor/device dislocation<br>1 right internal jugular blood vessel complications secondary to device insertion attempt/ procedure complication<br>1 implant device complication/ complication associated with device<br>1 Device breakage/ pressure sensor fracture |
| | Procedure related AE | | 26/493 (5.3%) | Details not provided |

#### 5.5.1.6 Quality of life

All studies provided data on health related quality of life (HRQoL) measured using the EQ-5D-5L visual analogue scale (VAS), the Kansas City Cardiomyopathy Questionnaire (KCCQ) and the Minnesota Living with Heart Failure questionnaire (MLHFQ) (Table 39). There was some suggestion that CardioMEMS was associated with improved HRQoL compared to control groups, but results were not consistent across studies.

### EQ-5D-5L

GUIDE-HF and MONITOR-HF reported data on change in EQ-5D-5L scores from baseline to 12 month follow-up in intervention and control groups. There was no difference in change in EQ-5D-5L VAS scores between intervention and control groups in the GUIDE-HF study. However, data were only available for the full trial population which includes those with NYHA class II who are likely to be a less ill population. The MONITOR-HF study reported a greater improvement from baseline in EQ-5D-5L VAS scores in the CardioMEMS group compared to standard care (MD 6.0, 9%% CI 1.1, 10.9). The summary estimate for the mean difference in change from baseline between groups for EQ-5D at 12 month follow-up was 1.75 (95% CI -6.03, 9.53;Figure 7).

### KCCQ

All studies except the CHAMPION study reported data on the KCCQ HRQoL scores, with higher scores indicating better health status. GUIDE-HF reported improvements in scores in both intervention and control groups, but found no difference between groups in change from baseline at 12 months follow-up (p=0.48). However, data were only available for the full trial population which includes those with NYHA class II who are likely to be a less ill population. MONITOR-HF reported a greater improvement in scores in the CardioMEMS group compared to standard care at 12 months follow-up (MD 7.13, 95% CI 1.51, 12.75). The summary estimate for the mean difference in change between groups for KCCQ was 3.62 (95% CI: -2.24, 9.47; Figure 7). PROACTIVE-HF reported an improvement in KCCQ scores at 12 months follow-up (p<0.0001), but data were available only for the single arm phase of the trial. SIRONA and SIRONA 2 did not find any difference between baseline and KCCQ scores at 3 month and 12 months follow-up respectively.

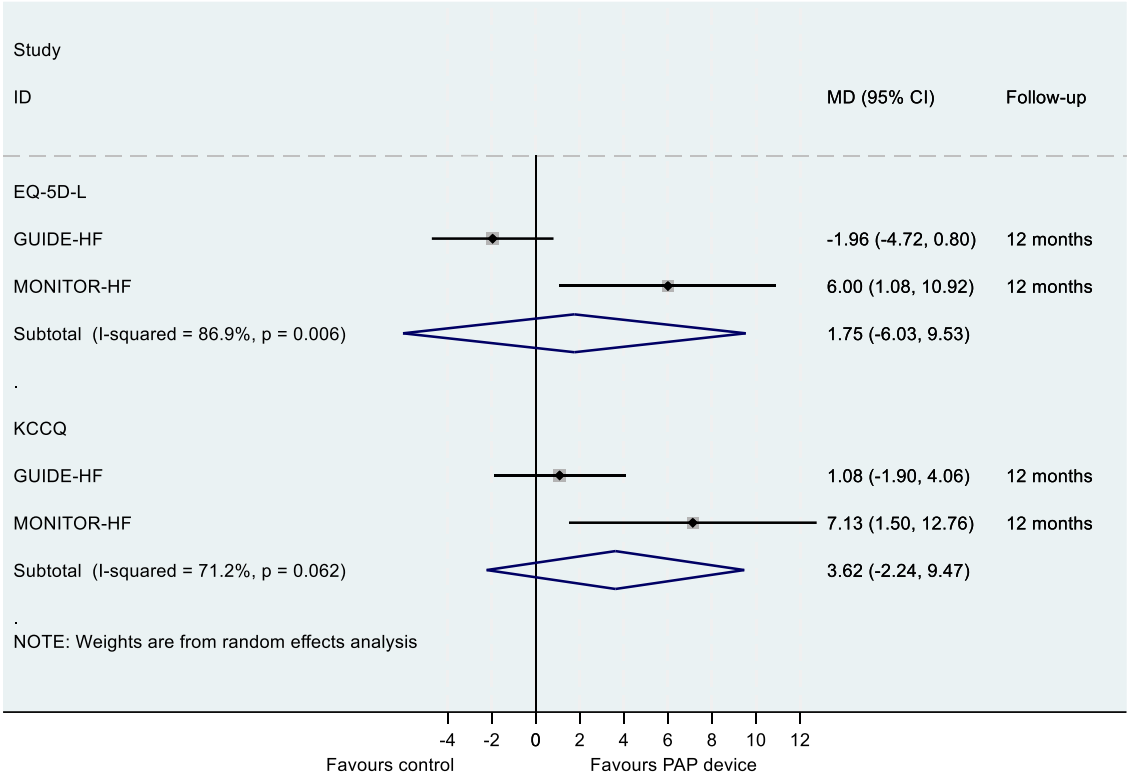



**Figure 7 Forest plot showing mean difference (MD) in change from baseline and 95% confidence intervals for HRQoL, stratified by HRQoL scale. Summary estimates from random effects meta-analysis are also shown.**

### MLHFQ

Only the CHAMPION study provided data on HRQoL assessed using the MLHFQ scale. This study reported a lower score (suggesting better health status) in the intervention group (47.0) compared to control (56.5) at 12 month follow-up (p=0.0267).

## 5.5.2 Secondary outcomes

### 5.5.2.1 Urgent care visits for heart failure

Three studies reported on urgent care visits for heart failure at 6 and 48 months follow-up – GUIDE-HF, MONITOR-HF and the single arm phase of PROACTIVE-HF (Table 42 in Appendix 4). Where reported, urgent care visits for heart failure were defined as unplanned admission to hospital shorter than 6 hours and the use of intravenous diuretics. For GUIDE-HF we used data from the NYHA class III subgroup provided by the device manufacturer in our meta-analysis. There was no evidence for a difference in urgent care for heart failure between the two intervention groups across GUIDE-HF and MONITOR-HF (HR 1.05, 95% CI 0.56, 1.96; Figure 8).

PROACTIVE-HF reported that at 6 months follow-up, 14 patients had 17 emergency department/outpatient IV diuretic visits but there were no comparative data available for this outcome.

#### 5.5.2.2 Cardiovascular mortality

Only GUIDE-HF reported data on death due to heart failure (Table 42 in Appendix 4). This outcome can be difficult to adjudicate and so may be why not reported in other studies. There was no evidence for a difference in heart failure deaths over the 12 month follow-up period between intervention arms (HR 1.13, 95% CI 0.57, 2.27, ) with 17 events in the intervention group compared to 15 in the standard care group.

Cardiovascular mortality was reported in all three RCTs that evaluated CardioMEMS at 12 to 48 months follow-up but in none of the Cordella studies (Table 42 in Appendix 4). CHAMPION and GUIDE-HF did not report data as HRs so these were calculated from number of events, number of participants and follow-up time as outlines in the methods. There was no evidence for a difference in cardiovascular mortality between the intervention groups across the two trials (HR 0.98, 95% CI 0.74, 1.29; Figure 8). For GUIDE-HF we used data for all NYHA classes in our meta-analysis as data were not available for the subgroup with NYHA class III CHF.

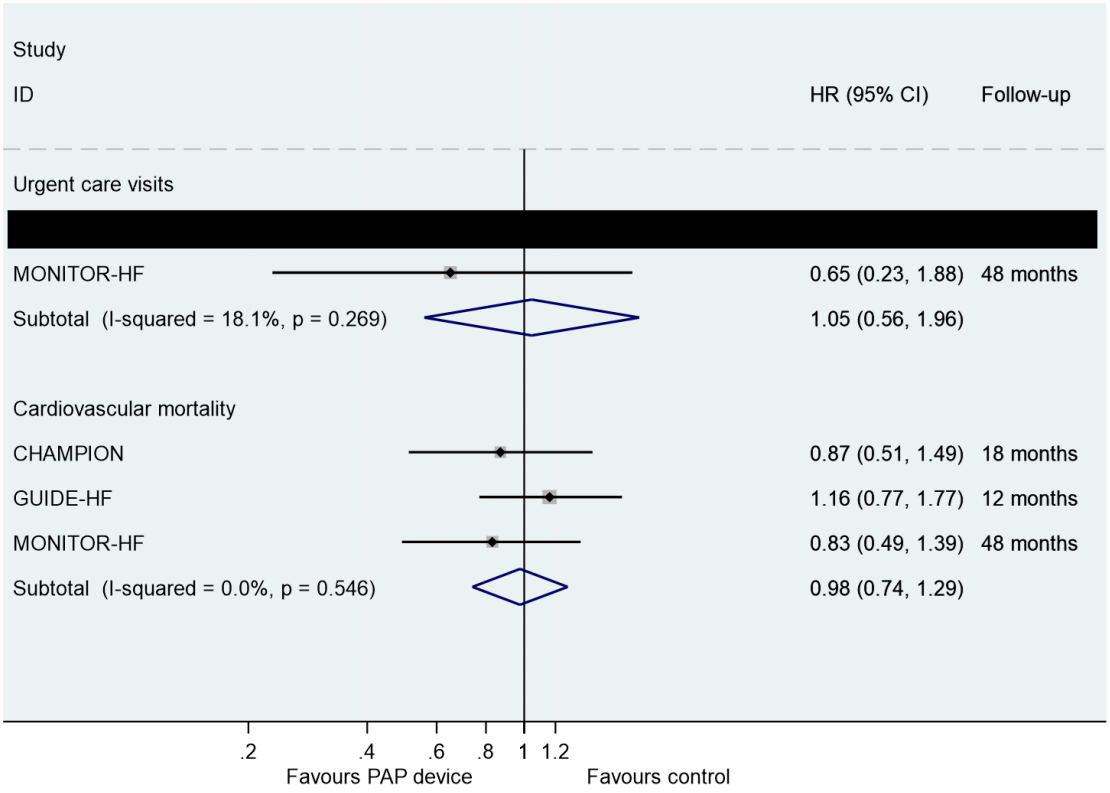



**Figure 8 Forest plot showing hazard ratios (HRs) and 95% confidence intervals for urgent care visits and cardiovascular mortality with summary estimate from random effects meta-analysis**

#### 5.5.2.3 Changes to clinical management

**Changes to medication**

All three RCTs that evaluated CardioMEMS reported on changes to medication. Two of the single arm studies of Cordella, PROACTIVE-HF and Sirona 2, also reported on this outcome

(Table 42 in Appendix 4). Data were not available for the comparative phase of the PROACTIVE-HF study.

All three studies of CardioMEMS reported increased medication changes in the intervention group compared to control at between 6 and 48 months follow-up.

The CHAMPION study reported increased overall medication changes in the intervention group compared to control (2,468 vs 1061, $p<0.0001$), increased changes in diuretics (1547 vs 585, $p<0.0001$) and greater frequency of decreases in medication doses in the intervention group ($p<0.05$). The GUIDE-HF RCT reported a greater number of medication changes (1.03 changes per month per patient in the intervention group compared to 0.61 changes per month per patient in the control group). Diuretic use remained similar in both the intervention and standard care groups compared to baseline at around 95% at 12 months follow-up. MONITOR-HF reported that the cumulative number of changes, intensifications, and downgrades in diuretics and guideline-directed medical therapy at 12 months were higher in the intervention group compared to the control group. At 48 months follow-up, medication changes remained higher in the intervention group compared to control group (0.73 changes per patient month vs 0.47 changes per patient month). It was not possible to calculate a summary estimate for medication changes as MONITOR-HF and GUIDE-HF did not report a measure of variation. Neither of the single arm Cordella studies compared changes in medication to the pre-intervention period and so it was not possible to determine the impact of the Cordella device in these studies.

### Frequency of contact with healthcare professionals

All three RCTs that evaluated CardioMEMS reported on changes to the frequency of contact with healthcare professionals (Table 42 in Appendix 4). None of the studies evaluating Cordella reported frequency of contact. The CHAMPION study reported similar numbers of contacts in the intervention groups compared to control (mean contacts per patient: 6.5 vs 6.4). No measure of variance was reported and so results from this trial could not be included in the synthesis. Across the MONITOR-HF and the GUIDE-HF study there were greater numbers of contacts per patient per month in the CardioMEMS groups compared to control (MD = 0.43, 95% CI 0.23, 0.63; Figure 9 ).

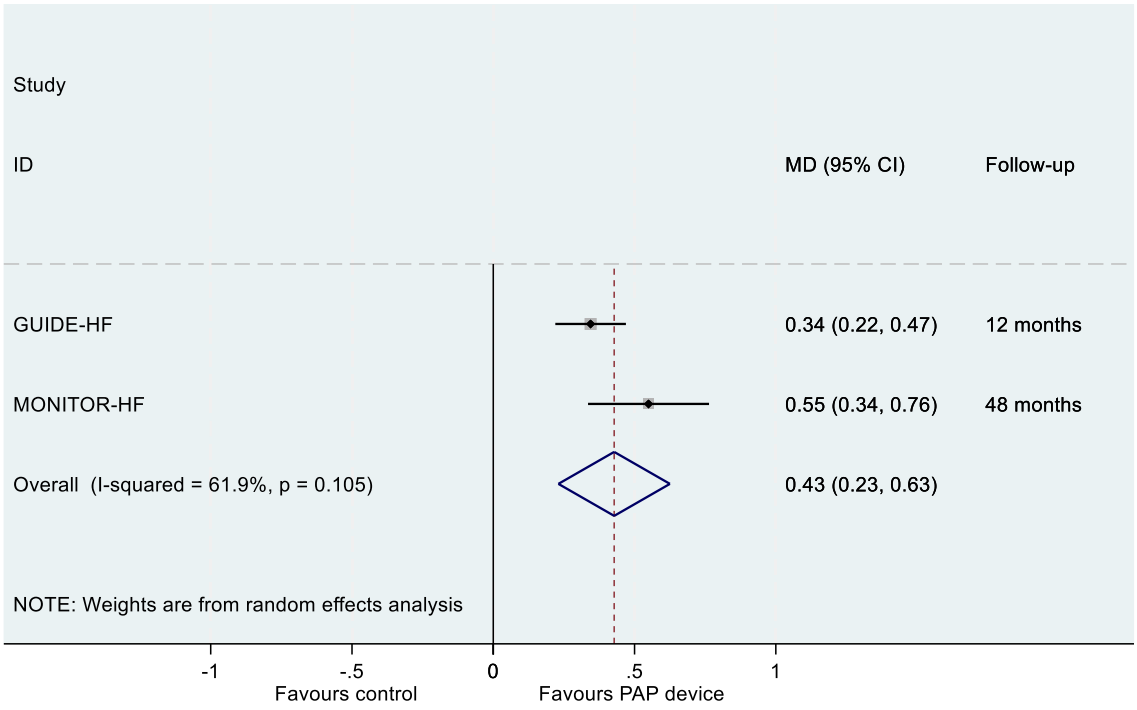



**Figure 9 Forest plot showing mean difference (MD) in HCP contact at follow-up. The summary estimate from random effects meta-analysis is also shown.**

#### 5.5.2.4 Functional capacity: 6 minute walk test

Four studies, two of CardioMEMS (Guide-HF and MONITOR-HF) and two single arm Cordella studies (SIRONA 2 and PROACTIVE-HF) reported on functional capacity as measured by change in the 6 minute walk test (Table 42 in Appendix 4). All four studies reported an increase in the distance walked from baseline to follow-up among those in the PAP monitoring groups. However, a meta-analysis of the two comparative studies reported no difference in change from baseline compared to the control groups (MD = 4.12, 95% CI -20.8, 29.0; Figure 10).

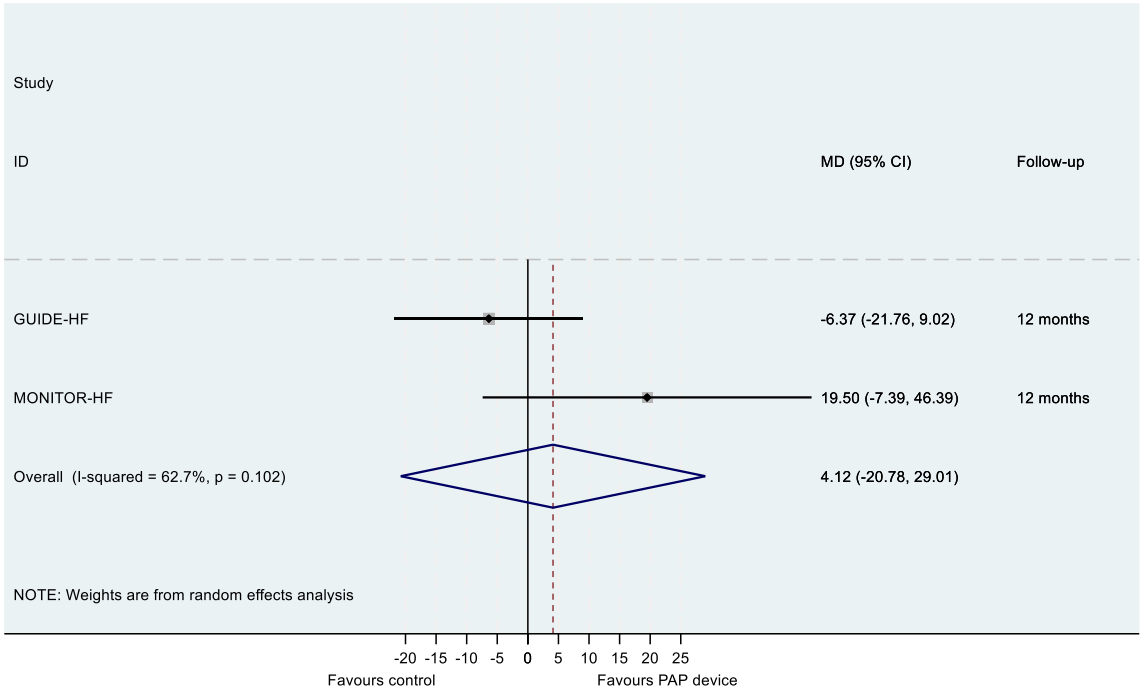



**Figure 10 Forest plot showing mean difference (MD) in change from baseline in 6 minute walk test. The summary estimate from random effects meta-analysis is also shown.**

#### 5.5.2.5 Change in NYHA class

All three single arm studies of Cordella (SIRONA, SIRONA 2 and PROACTIVE-HF) provided data on improvement in NYHA class, SIRONA 2 also reported on worsening of NYHA class (Table 42 in Appendix 4). None of the CardioMEMS studies provided data for this outcome. All studies reported an improvement in NYHA class, but comparative data were not available and so it was not possible to determine the impact of Cordella for this outcome.

#### 5.5.2.6 Adherence to using the device

Five studies provided data on adherence to daily measurement and transmission – GUIDE-HF, MONITOR-HF, SIRONA, SIRONA 2 and PROACTIVE-HF (Table 42). Adherence was generally high, although appeared slightly higher for the Cordella studies. For CardioMEMS, MONITOR-HF reported that patient adherence was 84% at 48 months and GUIDE-HF study reported that patient adherence was between 80 and 90% in both groups. For the Cordella device, adherence to daily measurements ranged from 88 to 99%, although the very high adherence estimate was from the SIRONA study that included only 15 participants.

#### 5.5.2.7 Withdrawals prior to sensor implantation

None of the CardioMEMS studies reported withdrawals prior to sensor implantation. All three studies of Cordella reported that some participants withdrew from the study prior to implantation of sensors (Table 43 in Appendix 4)): 4 (27%) in SIRONA, 11 (16%) in SIRONA 2, and 48 (9%) in PROACTIVE-HF. Reasons for not receiving the implant included: withdrawal of consent, death, adverse events, anatomical reasons, exclusion criteria, withdrawn by physician, surgery, hospitalisation, insurance denial and loss to follow-up.

#### 5.5.2.8 Withdrawals post sensor implantation

All studies provided data on withdrawals post sensor implantation (Table 43 in Appendix 4). The proportion of withdrawals ranged from 0 to 39% across studies. Withdrawal rates were similar across treatment arms in the CardioMEMS RCTs and were highest in CHAMPION and MONITOR-HF, these studies also had the longest duration of follow-up (18 and 48 months respectively). There were 110 withdrawals (39%) in the control arm and 93 (34%) in the CardioMEMS arm in the CHAMPION trial. In MONITOR-HF there were 50 withdrawals in the control arm (29%) and 49 (28%) in the CardioMEMS arm. The most common reasons for withdrawals in both trials were death followed by withdrawal of consent. There were fewer withdrawals in the GUIDE-HF RCT: 25 (5%) in the CardioMEMS arm and 33 (9%) in the control arm. There were fewer deaths in this trial with most withdrawals due to withdrawal of consent.

Withdrawal rates were lower in the Cordella studies, but these had a shorter duration of follow-up. There we no withdrawals in the very small SIRONA study which only had a follow-up duration of 3 months. SIRONA 2, with 6 month follow-up, reported that two participants (3%) withdrew but details were not available on these. PROACTIVE-HF also had a low proportion of withdrawals (3.5%) but this also had a short duration of follow-up of 6 months. Reasons for loss to follow-up included death (10 participants), withdrawal of consent (2 participants), adverse events (2 participants), physician decision (1 participant) and loss to follow-up (1 participant).

#### 5.5.2.9 Other Adverse events

Three studies provided data on adverse events other than DSRC or other procedure related AEs. Definitions of AEs and the level of AE reported varied across studies (Table 8 and Table 44 in Appendix 4). In GUIDE-HF over half of participants experienced a serious adverse event (SAEs), defined as an AE that led to death or deterioration in health, with similar proportions across treatment groups (RR 1.06 (95% CI 0.95, 1.19). SIRONA 2 provided data on AEs with four patients experiencing AEs including skin irritation, haemoptysis, vessel trauma and haematoma. They also reported that one patient experienced a left ventricular lead revision, classified as an SAE. In the PROACTIVE-HF study, AEs were considered SAEs when the patient outcome was: death, life-threatening, hospitalisation (initial or prolonged), disability or permanent change, congenital anomaly/birth defect, required intervention to prevent permanent impairment or damage, other serious (important medical events). At 6 months follow-up, 196 participants were reported to have experienced a SAE.

**Table 8 Overview of AEs reported across studies**

| Study | Type of AE | Group | Number of patients with AE (%) | Details |
|---|---|---|---|---|
| GUIDE-HF[45] | SAE – AE that led to death or deterioration in health not including DSRC | CardioMEMS | 282/497 (57%) | Details not provided |
| | | Control | 268/503 (53%) | |
| SIRONA 2[47] | AEs | Cordella | 4/75 (5%) | Skin irritation, haemoptysis, vessel trauma and haematoma. All observed complications recovered without lasting effects |
| | SAE | Cordella | 1/75 (1%) | 1 LV lead revision |
| PROACTIVE-HF[48] | SAE | Cordella | 196/493 (40%) | Details not provided |

### 5.5.3 Patient experience and satisfaction

#### 5.5.3.1 CardioMEMS

One study involved semi-structured qualitative interviews with 12 patients to explore their experience of having an implanted CardioMEMS device.[53] We organised themes emerging from the data in this study into three broad conceptual categories: engagement, management, and underlying motivation for sustained use of the device (Appendix 4). These categories and associated themes are outlined below, illustrated by quotes from the study.

Only one other study provided patient experience data for CardioMEMS, via a seven-question, web-based survey of 37 patients who had undergone implantation of the device.[58] Findings from this survey are incorporated into the below synthesis, where relevant, and other data from the survey are presented in Appendix 4.

**Engagement**

*Health literacy*

Qualitative interviews revealed that before using CardioMEMS, patients had feelings of low health literacy and uncertainty surrounding how to handle their condition.

*"I was becoming quite frustrated with not really knowing necessarily what I should do…it was a constant up and down not really knowing if I was doing the right thing."*

The introduction of the CardioMEMS device appeared to help patients to better understand their condition by linking symptoms with real-time pressure readings, fostering a sense of connection with their health.

*"Once I got the CardioMEMS I was able to manage a little better knowing that when I felt bad I could tell my readings were high and I'd get a phone call. So I started being able to judge based on my physical condition and abilities what my CardioMEMS was going to report."*

*"The CardioMEMS keeps me more connected with what's going on in my body on a daily basis."*

The survey study did not contribute findings to this theme.

*Seeing the value of the device*

In qualitative interviews, patients appeared to see the value of the device. They noted that they had experienced a time when their pressure readings were high even though they didn't have any symptoms; this served to reinforce patients' belief that CardioMEMS had helped them to stay out of the hospital.

*"I had one situation where my pressures were up and I didn't even realize…and had I not had that reading I would have been in the hospital."*

The survey study suggested that patients felt that the equipment was easy to use. Patients were asked about the ease of use of the CardioMEMS device to transmit the numbers as requested and 70% (21/30) found the equipment easy to use to transmit data.

*Being engaged in healthcare*

Patients noted in interviews that the readings on the CardioMEMS device helped them to be more proactive and most patients indicated that they liked to track their health and record measurements using the device.

*"Having the readings would help me a lot. It would allow me to be more proactive than reactive."*

Findings from the survey study initially suggested that patients were not acting so proactively, as when asked if patients had made any changes to their lifestyle since receiving the device, only 33% (10/30) answered yes. However, 70% (21/30) then said they had made improvements to their diet and 43% (13/30) had increased their physical activity.

### Management

*Self-concept*

Qualitative interviews revealed that patients appeared to view themselves differently regarding how they follow medical advice. Some patients noted in qualitative interviews that they viewed themselves as disciplined and compliant, strictly following medical advice.

*"I'm a person who commits. I've always been religious about doing [the readings]…I committed to do it so I'm gonna do it."*

Other patients, described as "integrators", adapted device use to suit their lifestyle, using readings to guide selective behaviour changes.

*"My wife doesn't put any added salt into her cooking. She uses low-salt products. So that's as best we can do. But meat's got what meat's got…And then when you go out …It's like my nurse says, [Patient]'s gonna do what [Patient]'s gonna do."*

*"It would be nice to know the numbers because I would know ahead of time, if its high, let me lesser my salt, lesser my drinks."*

The survey study did not contribute findings to this theme.

### Underlying motivation for sustained use of the device

*Avoiding hospitalisation*

Patients in qualitative interviews suggested that their sustained use of CardioMEMS was largely motivated by a desire to avoid hospital stays, which were associated with a diminished quality of life.

*"I use [the CardioMEMS] because I want to have the best quality of life and to me that means not living in the hospital. I don't want to be in the hospital. I want to be as far away as I can. That's no life being in that hospital. It's no life whatsoever."*

*Peace of mind*

Patients reported that another motivation to continue using the device was the increased peace of mind it brings. They reported that CardioMEMS reduced anxiety surrounding the management of their condition and they liked the feeling that their condition was being regularly monitored.

*"My mind is a little bit more relaxed. Knowing that they are keeping track of my heart makes me more relaxed, knowing that at least I'm getting checked somehow instead of ending up in the emergency room or the hospital."*

The survey study did not contribute findings to this theme.

#### 5.5.3.2 Cordella

Patient experience of using the Cordella device was evaluated by two survey studies. As noted, one was conducted as part of the SIRONA 2 study,[47] and the other as part of the PROACTIVE-HF study.[57] The SIRONA 2 survey consisted of 11 multiple choice questions administered to participants at the 90-day study point, with responses from 34-37 participants depending on the question. The PROACTIVE-HF study included a four-question survey to 63 participants from the former control group of the PROACTIVE-HF study concerning patient engagement with daily PA pressure readings. Full results are reported in Appendix 4.

Overall, patients who completed the survey in the SIRONA 2 study were positive about the Cordella device: 75% of respondents found the device very easy to use, 97% would recommend it to others, and 67% reported they take notice and monitor their daily measurement. Just under half of the participants (46%) indicated that they made lifestyle changes based on the readings, while the rest of the participants (54%) were neutral.

Similarly, findings from the PROACTIVE-HF survey revealed that 45% of respondents noted regularly making changes to their lifestyle based on PAP trends, 33% said they sometimes do and 23% answered that they do not make lifestyle changes. In contrast to SIRONA 2, participants in PROACTIVE-HF were not asked about whether the Cordella device is easy to use, but they were asked about the importance of the device, whether they monitor trends, and its impact on health. Among respondents, 88% reported understanding the importance of PAP, but only 55% stated they regularly monitored PAP trends. Overall, 73% rated the impact of PAP monitoring and clinician intervention on their health as very good or excellent.

## 5.6 Progress Plus

An overview of baseline characteristics of participants in included studies is provided in section 5.3. All studies reported age, sex and comorbidities at baseline, and all except MONITOR-HF reported on ethnicity. Most participants were older (mean age >60 years), with a higher proportion of men, and the majority of participants were white. Comorbidities ranged in prevalence and type across the six studies. No studies reported on cognitive impairment, problems with manual dexterity, and learning disabilities

Very few studies provided stratified results data; where available these are included in the main summary of results (section 5.5). Stratified results from single studies were available for NHYA class, comorbidities and baseline PAP were for HFH, and baseline PAP for mortality.

## 5.7 Assessment of publication bias

There were insufficient studies for formal assessment of publication bias. There was no suggestion of a difference in effect from small and larger studies and our comprehensive approach to study identification, including a review of studies included in manufacturer submissions and searches of trials registers, reduced the risk of publication bias. Comparison of trial registry entries and published reports did not identify any studies that had been registered and for which results were not available.

## 5.8 GRADE and Summary of findings

A tabular summary of our GRADE assessments is reported in Table 41 (Appendix 4) and the overall GRADE rating is included in the Summary of Findings table (Table 9).

There was high certainty evidence that CardioMEMS is associated with a reduced risk of HFH. Findings were uncertain for all cause mortality where the evidence was judged as moderate due to the wide confidence interval that included one. The evidence suggested that Cordella may lead to fewer hospitalisations and reduced all cause mortality, but the certainty of the evidence was low for both outcomes due to concerns regarding risk of bias and the wide confidence interval from the comparative phase of the PROACTIVE-HF trial.

It was unclear whether CardioMEMS and Cordella impact quality of life, measured using the EQ-5D and KCCQ scores. The evidence was rated as low certainty evidence for both HRQoL scales for CardioMEMS due to inconsistency in estimates across the two RCTs in which these were reported and imprecision of the summary estimate. For Cordella, the evidence was considered as very low certainty due to differences in findings across studies and the single arm nature of the evidence.

Estimates of device related outcomes (failure of sensor implantation, sensor failure and DSRC) were low for both devices. Whilst observational/single arm studies are usually awarded a provisional GRADE rating of low, for outcomes related to the device where single arm data were most appropriate, we started with a provisional grade of high certainty evidence. There was some inconsistency in the estimates for all outcomes and so the certainty of the evidence was downgraded to moderate for all device related outcomes for both devices.

**Table 9 Summary of findings table for primary outcomes evaluated in the review**

| Outcomes | Device | Results | Number of studies | Certainty of the evidence (GRADE)† | Plain language summary |
|---|---|---|---|---|---|
| Heart failure hospitalisation | CardioMEMS | HR 0.66 (95% CI 0.57 to 0.76) | 3 RCTs | ⨁⨁⨁⨁ High | CardioMEMS leads to fewer hospitalisations for heart failure based on the evidence from three RCTs. |
| | Cordella | HR 0.61 (95% CI 0.36, 1.04) | 1 RCT | ⨁⨁⨀⨀ Low | Cordella may lead to slightly fewer hospitalisations for heart failure based on the evidence from the randomised phase of PROACTIVE-HF. |
| | | Reduction in HFH after Cordella implantation | 3 single arm studies | ⨁⨁⨀⨀ Low | |
| All-Cause Mortality | CardioMEMs | HR 0.91 (95% CI 0.70 to 1.17) | 3 RCTs | ⨁⨁⨁⨀ Moderate | It is uncertain whether CardioMEMS reduces all-cause mortality based on evidence from the randomised phase of PROACTIVE-HF. |
| | Cordella | HR 0.51 (95% CI 0.20, 1.32) | 1 RCTs | ⨁⨀⨀⨀ Low | It is uncertain whether Cordella reduces all-cause mortality based on the evidence from the randomised phase of PROACTIVE-HF. |
| HRQoL: EQ-5D | CardioMEMs | MD –0.05 (95% CI –2.46 to 2.36) | 2 RCTs | ⨁⨁⨀⨀ Low | It is uncertain whether CardioMEMS improves quality of life based on the evidence from two RCTs. |
| | Cordella | No studies | NA | NA | There were no studies for this outcome. |
| HRQoL: KCCQ | CardioMEMs | MD 2.41 (95% CI –0.23 to 5.04) | 2 RCTs | ⨁⨁⨀⨀ Low | It is uncertain whether CardioMEMS improves quality of life based on the evidence from two RCTs. |
| | Cordella | PROACTIVE HF reported an improvement in KCCQ scores at 12 months follow-up (p<0.0001). SIRONA and SIRONA 2 did not find any difference between baseline and follow-up KCCQ scores. | 3 single arm studies | ⨁⨀⨀⨀ Very low | It is uncertain whether Cordella improves quality of life based on results from three single arm studies. |
| Failure of sensor implantation | CardioMEMS | Summary proportion of sensors that failed to implant: 1.7% (95% CI: 0.8% to 2.9%). | 7 single arm studies | ⨁⨁⨁⨁ High | The proportion of people in whom sensor implantation fails is less than 2% |
| | Cordella | Summary proportion of sensors that failed to implant: 4.9% (95% CI 3.1%, 7.0%) | 3 single arm studies | ⨁⨁⨁⨁ High | The proportion of people in which sensor implantation fails is around 5%. |

| Outcomes | Device | Results | Number of studies | Certainty of the evidence (GRADE)† | Plain language summary |
|---|---|---|---|---|---|
| Sensor failure | CardioMEMS | Summary proportion of sensors that failed 0.1% (95% CI 0.0, 0.6%; | 7 single arm studies | ⨁⨁⨁⨁ High | The proportion of people in whom sensors fail is very low. |
| | Cordella | Summary proportion of sensors that failed 0% (95% CI 0, 0.1%) | 3 single arm studies | ⨁⨁⨁⨁ High | The proportion of people in whom sensors fail is very low. |
| DRSC | CardioMEMS | Summary proportion of DSRC 0.7% (95% CI 0.3, 1.3%) | 7 single arm studies | ⨁⨁⨁⨁ High | The proportion of people with DSRC is very low |
| | Cordella | Summary proportion of DSRC 0.1% (0.0, 0.9%) | 3 single arm studies | ⨁⨁⨁⨁ High | The proportion of people with DSRC is very low |

# 6 Assessment of cost effectiveness

Sections of this Chapter have been adapted from the project's Protocol document, available at the NICE website.[27] We made one post-protocol amendment. We applied the Philips checklist only to the three UK models (Cowie 2017/2023 and the HTW model), rather than all the models identified and included in the systematic review of economic evaluations. This was to situate our review of models specifically to the UK context.

## 6.1 Review of economic evaluations of remote PAP monitoring technologies and previous model structures

### 6.1.1 Review methods

We conducted a systematic review of economic evaluations comparing remote PAP monitoring technologies to usual care. The systematic review followed the principles outlined in the Centre for Reviews and Dissemination (CRD) guidance for undertaking reviews in health care and the NICE Health Technology Evaluations Manual.[28, 29]

The objectives of the review were:

1. To obtain an overview of modelling approaches used in remote PAP monitoring, including summarising the types of model used in this condition and data sources/inputs
2. To summarise the findings of previous cost–utility, cost-effectiveness, and cost–benefit studies conducted in, or generalisable to, the UK
3. To summarise the key drivers of cost-effectiveness in remote PAP monitoring

We also reviewed the model structures used in economic models for a CHF population, to inform the structure of our model. Given the large number of models published for heart failure, and the existence of systematic reviews reporting models for CHF, we undertook a review of systematic reviews (umbrella review) of economic models in CHF published within the last ten years. The objectives of this review were to summarise the main model structures and health states used in economic models of heart failure.

#### 6.1.1.1 Inclusion and exclusion criteria

Studies were included where they met the criteria set out in Table 10.

**Table 10 Inclusion criteria for the cost-effectiveness reviews**

| | Review of cost-effectiveness studies of remote PAP monitoring | Review of systematic reviews of heart failure economic models |
|---|---|---|
| **Population** | CHF | CHF |
| **Intervention** | Remote PAP monitoring technologies | Any |
| **Comparator(s)** | Usual care or remote PAP monitoring device | Any |
| **Outcomes** | Any cost-effectiveness outcomes | Any cost-effectiveness outcomes |
| **Study type** | Published economic evaluations (including economic models) | Systematic review of published economic models |

| | Review of cost-effectiveness studies of remote PAP monitoring | Review of systematic reviews of heart failure economic models |
|---|---|---|
| | Cost and resource studies reporting UK data. | |
| **Limits** | None | Reported in English and published since 2015. |

#### 6.1.1.2 Study identification

Studies were identified using bibliographic and non-bibliographic search methods following the NICE technology appraisal manual and recent guidance.[29, 30]

#### 6.1.1.3 Bibliographic searching

The MEDLINE search strategies are detailed in Appendix 1 using a search narrative.[59]

For the review of remote PAP monitoring, we searched the following resources from inception to date of search:

- MEDLINE (MEDALL, Ovid) 1946 to February 27, 2025;
- Embase (Ovid) 1974 to 2025 February 27;
- EconLit (EBSCO) 1981-2025;
- NHS Economic Evaluations Database (NHS EED) via: www.crd.york.ac.uk/CRDWeb/ (the archive was searched as the database is no longer supported and has not been updated since 2015)
- INAHTA database via: www.inahta.org/hta-database/
- Tufts CEA Registry via: https://cear.tuftsmedicalcenter.org/

For the systematic review of reviews, we searched the following resources with a date limit 2015-current:

- MEDLINE (MEDALL, Ovid) 1946 to February 26, 2025; and
- Embase (Ovid) 1974 to 2025 February 26.

We did not search the Cochrane Database of Systematic Reviews (CDSR) as Cochrane reviews seldom incorporate specific economic research objectives.

#### 6.1.1.4 Non-bibliographic searching

- Eligible studies or systematic reviews identified in the systematic review of clinical effectiveness were reviewed for inclusion.
- The references of studies included at full-text were reviewed for any studies eligible for inclusion in this review. At the same time, studies were checked for any post-publication amendment (e.g., Errata/Corrections, Retractions, Expressions of concern, Editorial notes).
- Websites of the manufacturer/or licence holders were hand-searched for each test; and
- Information submitted by the manufacturers was checked to identify any eligible studies or systematic reviews

#### 6.1.1.5 Managing the searches

Search results were exported to EndNote 20 for de-duplication using the default de-duplication settings followed by a manual review of records.

#### 6.1.1.6 Review strategy

Two reviewers independently screened titles and abstracts identified by the searches against the criteria set out in Table 10. Full copies of all reports considered potentially relevant were obtained and two reviewers independently assessed these for inclusion. Disagreements were resolved by consensus or discussion with a third reviewer.

Data extraction forms were piloted on a small sample of reports (10%). Data were extracted by one reviewer and checked in detail by a second reviewer. Disagreements were resolved by consensus or discussion with a third reviewer. The following data were extracted:

For the review of remote PAP monitoring:

- Contextual study data: research aim, patient group, device evaluated and any comparison, and funding;
- Evaluation specific data: type of economic evaluation, study perspective, time horizon, discount rate, price year, model structure, health states included, any assumptions reported by the authors, source of data/ model inputs;
- Findings: results, any limitations reported by the authors, and where reported any discussion on the key drivers of the analyses/model. Costs in overseas currencies were converted to GBP based on the year average conversion rate for the cost year of the study (or two years prior to publication where cost year was not reported). Bank of England historical exchange rate data[60] were used for euros and US dollars, and exchange-rates.org for Argentine peso.[61]

For the systematic review of reviews of heart failure models:

- Contextual study data: research question, patient group;
- Evaluation specific data: type of economic evaluation, type of model used and structure.

#### 6.1.1.7 Quality assessment strategy

The methodological quality of included economic evaluations for the remote PAP review were assessed using the Drummond checklist,[62] and the key relevant economic models identified were appraised using the Philips checklist.[63] We did not appraise the quality of the systematic reviews included in the systematic review of reviews, as these reviews were used only to inform our choice of model structure. Quality assessment was undertaken by one reviewer and checked by a second reviewer. Disagreements were resolved by consensus or discussion with a third reviewer.

#### 6.1.1.8 Synthesis methods

A narrative summary of included economic evaluation studies comparing remote PAP monitoring technologies is presented below.

### 6.1.2 Results of study identification: review of cost-effectiveness studies of remote PAP Monitoring

The process of identification and selection of economic evaluations is reported in the PRISMA flow diagram (Figure 11).

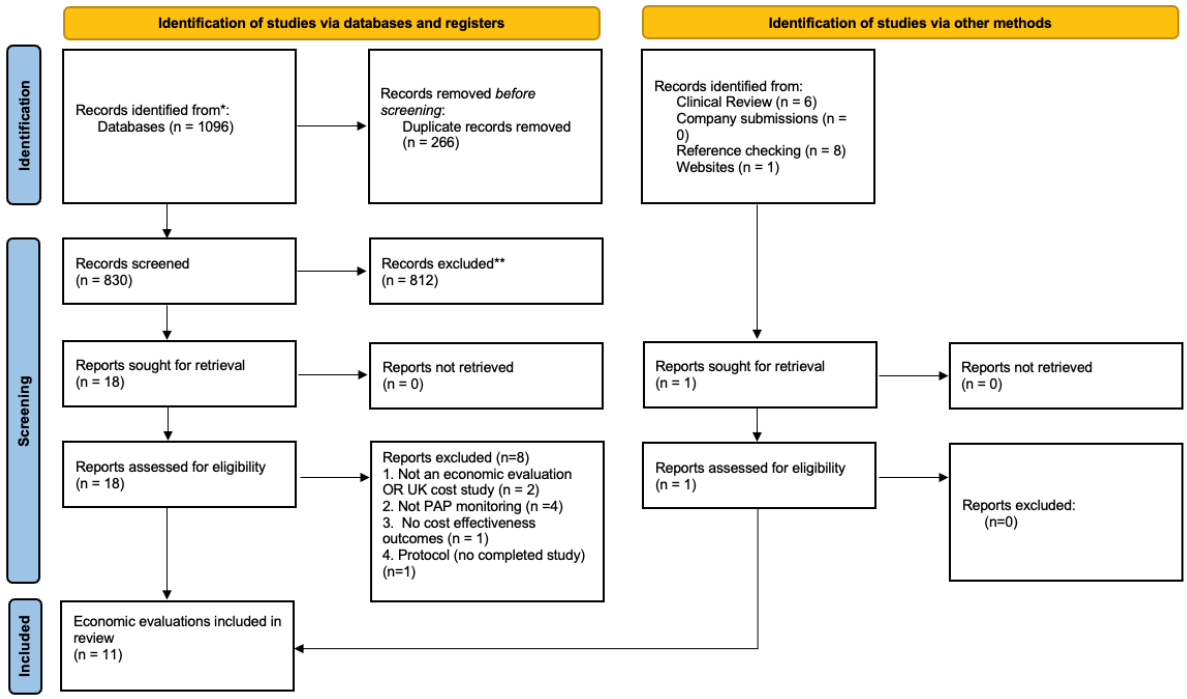
Eleven evaluations were included (although one (Cowie 2023) was an update of an earlier study (Cowie 2017)).[64-74] Eight evaluations were excluded at full-text (Table 33 in Appendix 2). We identified the REM-HF study which reported that an economic evaluation was planned[75] but the final study report[76] did not report this evaluation. We contacted the study author but received no reply, so this study was excluded. We did not identify any economic evaluations of Cordella, including from a review of the manufacturer materials.

#### 6.1.2.1 Quality assessment of cost-effectiveness studies of remote PAP monitoring

Study quality was deemed overall good for the economic evaluations included in the review using the Drummond Checklist.

The full version of the Philip's checklist was used to evaluate the three models which focused specifically on the UK: Cowie 2017, Cowie 2023, and Health Technology Wales (HTW).[65, 68, 73] A tabular report Philip's checklist is reported in Appendix 5, Table 49 and the findings are summarised below.

**Figure 11 PRISMA flow diagram for the review of economic evaluations**




### 6.1.3 Results of the review of cost-effectiveness studies of remote PAP Monitoring

Below we report the results of the review of economic evaluations. We align reporting with the Objectives of the review.

#### 6.1.3.1 Objective 1 – to obtain an overview of the economic modelling approaches used in remote PAP monitoring

Table 11 provides a tabular overview of the economic evaluations. All economic evaluations focused on a comparison of CardioMEMS to usual care. Evaluations were published between 2016 and 2024, focusing on seven countries (Argentina, Germany, Italy, Netherlands, Spain, UK, and USA). Two models with three evaluations were specific to the UK, the Cowie 2017 model which was updated in Cowie 2023 (we collectively refer to these two evaluations as "the Cowie model"), and the Health Technology Wales (HTW) model.

Eight evaluations reported Markov models, Messori reported a budget impact model, Codina reported a cost-utility analysis, and Kolominsky-Rabas reported Prospective Health Technology Assessment (ProHTA), which they described as 'a "hybrid simulation" model, with system dynamics models for macrosimulation and discrete event models for microsimulation'.[72]

The simplest model structure was developed by Cowie et al. (2017) and updated in 2023.[65, 68] This includes two long-term health states (stable heart failure and death) in which patients can move from stable heart failure to death with additional health events which take the form of health state modifiers with more short-term impacts. This UK-based model was influential in the development of several other models of remote PAP monitoring, including the HTW model, which employs the same structure.[73] Adaptations of this model have been developed to include a distinction between stable HF pre- and post- HF-related hospitalisation (HFH), [64] and to distinguish between HFHs and hospitalisations for other reasons, [66, 70, 71] to allow for more refined modelling of subgroups in the heterogeneous heart failure population to separate HF and non-HF related effects.

## Table 11 Descriptive overview of the economic evaluations of remote PAP monitoring

| Study, Funding, Setting | Population | Comparisons | Model type, structure, health states, and assumptions. | Outcomes, Cost year, time horizon, discount, and currency |
|---|---|---|---|---|
| **Study:** Alcaraz 2021[64]<br><br>**Study funding:** Abbott Argentina<br><br>**Setting:** Argentina | NYHA Class III HF patients, with one or more hospitalisations for HF in previous 12 months. Patient characteristics similar to CHAMPION trial. | CardioMEMS vs usual medical care | **Type:** Markov (MS Excel)<br><br>**Health states (n=4)**<br>1. Heart failure functional class III (stable)<br>2. HF hospital admission<br>3. Post HF hospital admission<br>4. Death<br><br>**Assumptions:**<br>• Initial cost relating to implantation of device/complications.<br>• After a cycle, patients who entered the HF hospital admission state and are still alive, enter the post HF hospital admission cycle, and then return to an outpatient/stable cycle or require another hospital admission.<br>• Patients hospitalized and in the post HF hospital admission cycle have higher odds to die and accrue lower QALYs in comparison to patients who remain outpatient/stable.<br>• non-HF hospital admission and no AE for pharmacological treatments were assumed equal for both cohorts. | **Outcomes:** ICER, Costs, QALY<br>**Cost year:** 2020<br>**Time horizon:** lifetime<br>**Perspective:** Third-party payer perspective -Social Security (SS) and Private Sector (PS)<br>**Discount: 5%**<br>**Currency:** Peso |
| **Study:** Codina 2024[74]<br><br>**Study funding:** None<br><br>**Setting:** Spain | 43 CardioMEMS patients. 14 NYHA II (32.6%) and 29 NYHA III (67.4) | CardioMEMS vs usual medical care | **Type:** cost-utility analysis based on pre/post implant data from a HF clinic<br><br>**Health states:** N/A<br><br>**Assumptions:**<br>• QALY valued at €25,000 with 0.3 QALY taken as reference per CHAMPION.[43]<br>• No confounding the in before/after nature of this study. | **Outcomes:** Costs, QALYs, Net-Benefit<br>**Cost year:** 2022<br>**Time horizon:** 5 yr.<br>**Perspective:** Hospital centre<br>**Discount:** 3%<br>**Currency:** Euro € |
| **Study:** Cowie 2017[65]<br><br>**Study funding:** NR<br><br>**Setting:** UK | Hypothetical population of 20 000 patients with HF based on CHAMPION.[43] | CardioMEMS vs usual medical care | **Type:** Markov (TreeAge)<br><br>**Health states (n=2)**<br>1. Stable heart failure<br>2. Dead<br><br>**Assumptions:** | **Outcomes:** ICER, Costs, QALY<br><br>**Cost year:** NR<br>**Time horizon:** 10 yr.<br>**Perspective:** Healthcare payer perspective in Europe. |

| Study, Funding, Setting | Population | Comparisons | Model type, structure, health states, and assumptions. | Outcomes, Cost year, time horizon, discount, and currency |
|---|---|---|---|---|
| | | | • HF hospitalisation modelled as a transient event with costs rather than as a health state.<br>• Patients assumed to revert to stable HF or die after HFH.<br>• Mortality rate depends on age and monitoring strategy<br>• Mortality effect not modelled beyond 5 yrs as risk assumed identical between cohorts. | **Discount:** 3.5%.<br>**Currency:** GBP £ |
| **Study:** Cowie 2023[68] – update of Cowie 2017.<br><br>As Cowie 2017 above | As Cowie 2017 above | As Cowie 2017 above | As Cowie 2017 above | As Cowie 2017 above<br>**Cost year:** 2020 |
| **Study:** Kolominsky-Rabas 2016[72]<br><br>**Study funding:** German Federal Ministry of Education and Research (BMBF)& St Jude Medical GmbH, Eschborn (no industry funding)<br><br>**Setting:** Germany | NYHA Class III HF<br>Age >45 | PA pressure guided medical management (CHAMPION scenario) versus standard treatment (reference scenario). | **Type:** Prospective Health Technology Assessment (ProHTA) described as 'a "hybrid simulation" model, with system dynamics models for macrosimulation and discrete event models for microsimulation.'<br><br>**Health states:** Unclear.<br><br>**Assumptions:**<br>• Configuration parameters to account for differences between US and German healthcare systems and hospitalisation frequencies. | **Outcomes:** Costs (culminative), Reduction in hospitalisations, QoL (MLHFQ)<br>**Cost year:** 2010-2021<br>**Time horizon:** 12.5 yr<br>**Perspective:** German payer's perspective (German statutory health insurance).<br>**Discount:** NR<br>**Currency:** Euro € |
| **Study:** Martinson 2017[66]<br><br>**Study funding:** NR<br><br>**Setting:** US | NYHA Class III HF. | CardioMEMS vs control (unspecified) | **Type:** Markov (software NR)<br><br>**Health states (n=4)**<br>1. Stable HF<br>2. Hospitalised for HF<br>3. Hospitalised for another cause)<br>4. Death<br><br>**Assumptions:**<br>• Patients in intervention group started with an implant-related hospitalisation and control group started in stable HF. | **Outcomes:** ICER, Costs, QALYs<br>**Cost year:** 2014<br>**Time horizon:** 5 yr.<br>**Perspective:** Medicare and private insurance<br>**Discount:** 3%.<br>**Currency:** US $ |

| Study, Funding, Setting | Population | Comparisons | Model type, structure, health states, and assumptions. | Outcomes, Cost year, time horizon, discount, and currency |
|---|---|---|---|---|
| | | | • patients less than 65 years old at implant were assumed to be paid through private insurance and those 65 years or older at implant were assumed to be paid by Medicare. | |
| **Study:** Messori 2024[69]<br><br>**Study funding:** Unfunded<br><br>**Setting:** Italy (Tuscany) | 166 cases of NYHA class III with >1 hospital admission. | CardioMEMS (no comparison) | **Type:** Budget impact (application NR)<br><br>**Health states** NA<br><br>**Assumptions:**<br>• CardioMEMS would be used in all 166 cases | **Outcomes:** Cost per year<br>**Cost year:** NR<br>**Time horizon:** 4 yr.<br>**Perspective:** Italian public healthcare setting<br>**Discount:** 3%.<br>**Currency:** Euro € |
| **Study:** Mokri 2024[67]<br><br>**Study funding:** Unfunded<br><br>**Setting:** Netherlands | CHF NYHA class III with >1 hospital admission. | CardioMEMS vs. SoC | **Type:** Markov (R Studio 4.2.1)<br><br>**Health states (n=3)**<br>1. Stable heart failure<br>2. Heart failure hospitalisation<br>3. Death<br><br>**Assumptions:**<br>• Costs of device and implant allocated to 1st cycle.<br>• Patients can move from stable HF to HF hospitalisations<br>• Patients spend a max. of 1 cycle in HFH before transition to stable HF or Death.<br>• Monthly costs of stable HF included all costs not related to HFH | **Outcomes:** ICER, Costs, QALYs<br>**Cost year:** 2022<br>**Time horizon:** Lifetime (max. 30 yrs)<br>**Perspective:**<br>i) healthcare perspective (all costs)<br>ii) Dutch societal perspective<br>**Discount:** 4% costs and 1.5% for effects<br>**Currency:** Euro €[77, 78] |
| **Study:** Sandhu 2016[70]<br><br>**Study funding:** Various academic sources.<br><br>**Setting:** US | NYHA class III HF (mean age 62) hospitalised within 1 yr. | CardioMEMS vs. usual care | **Type:** Decision tree followed by a Markov (software not specified)<br><br>**Health states (n=5)**<br>1. HF hospitalisation<br>2. Non-HF hospitalisation<br>3. Both HF and non-HF hospitalisation<br>4. No hospitalisation<br>5. Dead<br><br>**Assumptions:**<br>• CardioMEMS placement from outset, which could involve procedural complication or device failure. | **Outcomes:** Hospitalisations, survival, Costs, QALY, ICER<br>**Cost year:** 2014<br>**Time horizon:** Lifetime<br>**Perspective:** Societal<br>**Discount:** 3% annually.<br>**Currency:** US $ |

| Study, Funding, Setting | Population | Comparisons | Model type, structure, health states, and assumptions. | Outcomes, Cost year, time horizon, discount, and currency |
|---|---|---|---|---|
| | | | • Patients could experience device complication each month<br>• Patients had increased mortality risk during hospitalisation for HF and for 2 months post-hospitalisation. | |
| **Study:** Schmier 2017[71]<br><br>**Study funding:** St. Jude Medical<br><br>**Setting:** US | Not explicitly stated, but based on CHAMPION | CardioMEMS vs. SoC | **Type:** Markov (Excel)<br><br>**Health states (n=4)**<br>1. HF entry to the model<br>2. Outpatient Stable<br>3. Hospital admission (HF or Non-HF)<br>4. Dead<br><br>**Assumptions:**<br>• Patients in treatment or SoC remain stable or may require hospitalisation<br>• After each cycle, patients can enter stable outpatient or require hospitalisation<br>• Patients who have a hospitalisation have a different rate of accrual of utilities in the immediate posthospitalisation cycle.<br>• All patients are insured (75% of the population is covered by Medicare and 25% are covered by commercial insurers). | **Outcomes:** ICER<br>**Cost year:** 2016<br>**Time horizon:** 5 yr<br>**Perspective:** NR<br>**Discount:** 3% annually.<br>**Currency:** US $ |
| **Study:** Health Technology Wales (HTW)[73]<br><br>**Study funding:**<br><br>**Setting:** Wales (UK) | People with Chronic HF (CHF) | PAPS in addition to guideline-directed monitoring vs guideline-directed monitoring | **Type:** Markov (Excel)<br><br>**Health states** (n=2)<br>1. CHF<br>2. Dead<br><br>**Assumptions:**<br>• HF hospitalisation modelled as a transient event with costs rather than as a health state<br>• Most assumptions based on the "Cowie model", but mortality based on meta-analysis rather than life-tables | **Cost year:** 2023<br>**Time horizon:** Lifetime<br>**Perspective:** UK NHS and personal social services (PSS)<br>**Discount:** 3.5%<br>**Currency:** GBP £ |

Key: **BL** = base line, **CHF** = Chronic Heart Failure, **HFH** = Heart Failure Hospital Admission, **HR** = hazard ratio, **ICER =** Incremental Cost-Effectiveness Ratio**, KCCQ** = Kansas City Cardiomyopathy Questionnaire, **MLHFQ** = Minnesota Living with HF Questionnaire, **PPY** = per patient year, **SoC** = Standard of Care.

Table 12 provides a summary of data inputs used in the models. Whilst the models varied in structure and methodology, the conceptualisation of data inputs, were broadly consistent between the models. Here we summarise the main inputs for the two models specific to the UK, the two versions of the Cowie model[65, 68], and the HTW model [73].

### Hospitalisation rates

The Cowie 2017 model used a hazard ratio for hospitalisation from the CHAMPION trial.[43] The HTW model applied a hazard ratio for total HF hospitalisation from a meta-analysis of the CHAMPION, GUIDE-HF and MONITOR-HF studies.[43-45] This hazard ratio also included other urgent hospital visits. As a scenario analysis they also applied a higher hazard ratio from the GUIDE-HF study alone.

The updated Cowie 2023 model explored different heart failure-related hospitalisations in scenario analyses including: heart failure hospitalisation HRs from the COAST trial; heart failure hospitalisation HRs from the MEMS-HF trial;[49] hospitalisation HRs and baseline hospitalisation rates from the CHAMPION trial; and baseline heart-failure hospitalisations from the COAST trial.[50]

### Mortality rates

The Cowie model used age stratified baseline risks of mortality for routine monitoring from Griffiths,[79] and then applied the hazard ratio from CHAMPION to obtain the mortality rate for CardioMEMS. Griffiths et al. estimated mortality rates based on the CARE HF trial, which was a RCT conducted on NYHA III and IV HF patients who had had a prior hospitalisation event. Griffiths and co-authors then adjusted the rates from the trial for UK age groups in 5 year intervals. The updated Cowie 2023 model assumed that there was no relative effect of CardioMEMS on mortality (ie a hazard ratio of 1), but ran scenario analyses using a mortality HR from the CHAMPION trial and from the GUIDE HF trial.

The HTW model used a meta-analysis to inform baseline mortality in their base-case. They ran scenario analyses using the same baseline mortality assumptions as the Cowie model, and a Weibull curve extrapolated using overall survival data from MONITOR-HF. They applied a hazard ratio for CardioMEMS based on a meta-analysis of CHAMPION, MONITOR-HF, and GUIDE-HF, and used a hazard ratio of 1 in a scenario.

### Utilities

The Cowie model used utility values based on the EQ-5D-3L data from the CHAMPION trial. This included four different utility scores taken at 1 month, 3 months, 6 months and 12 months from randomisation. After 12 months the patients were assumed to decline in utility by 0.008 per year. After 5 years utility scores were taken from a 2015 study by Matza et al.[80] which aims to calculate the acute and chronic impact of cardiovascular events on health state utilities. A further 0.008 decrement was applied to the Matza utility each year after that. A disutility of 0.1 lasting 1 month was applied for each hospitalisation after 5 years, which was reported to be based on a model built by Klersy et al. (2011),[81] but appears to be based on an assumption made by Yao et al (2008) that a hospitalisation would have a similar impact on (Health Related Quality of Life (HRQoL) as moving to the next NYHA class (class III to class IV).[82]

The HTW model used the utility value from Matza et al.[80] for the chronic HF state, and applied the same disutility of 0.1 as in the Cowie model, lasting 1 month for each hospitalisation. They ran a scenario analysis using an alternative hospitalisation disutility of -0.059 from Sandhu et al (2016), [70] and another scenario analysis using the sample utility assumptions as in the Cowie model.

### Costs

The updated Cowie 2023 model used a cost of £9500 for the device. In addition, they included a cost of the implantation procedure which was assumed to be £1215, based on the cost of a standard cardiac catheterisation procedure from NHS reference costs. Cowie et al. applied a fixed monthly cost of £39 for treatment of patients undergoing usual care. Cowie et al. modelled the cost of a complication (£1175 in the updated model) by using a weighted average of the 8 device-related complications that were reported in the CHAMPION trial and assigning NHS reference costs to them. The HTW model used the same inputs as the updated Cowie model for device, procedure costs, treatment and complications costs.

One aspect that differed between the Cowie model and the HTW model was the different hospitalisation inputs applied. The most recent Cowie model applied a higher cost of hospitalisation than the HTW model. Cowie et al. used NHS reference costs for 'non-elective long stays' using a weighted average of reference codes. The hospitalisation cost of £4093 is significantly higher than the HTW base case input of £2583, which includes both non-elective short stay and non-elective long stay costs. They calculate the cost of hospitalisation as the weighted average of CC score 0-14+ for the HRG EB03 (heart failure or shock) in the non-elective short stay and non-elective long stay settings.

### Adverse events

The Cowie model includes a risk of implant complications of 0.0272 based on the CHAMPION study. The HTW model included a risk of device/system complications of 0.011, and a risk of sensor failure of 0.003, both based on a meta-analysis.[83] HTW ran a scenario where these were assumed to be 0.

## Table 12 Model inputs and sources used in economic evaluations of remote PAP monitoring

| Study | Epidemiological data | Treatment effect | Adverse events | Utilities | Costs & Resource use (values given for UK studies) |
|---|---|---|---|---|---|
| Alcaraz 2021[64] | **Mean age:** 66 (range 61-69)<br>**% female:** NR<br><br>**Baseline HFH rate**: 1.13 ppy (based on CHAMPION,[43] CardioMEMS post approval study,[51, 84] MEMS-HF.<br><br>**Baseline mortality risk:** 0.16 at 12m (CardioMEMS post approval study)[84]<br><br>**HR of mortality in hospitalisation and post-hospitalisation vs stable HF:** 3.32 (based on Solomon 2007[85] (which was based on CHARM[86])) | **HR HFH CardioMEMS vs Standard:** 0.48 (meta-analysis of CHAMPION,[43] CardioMEMS post approval study,[51, 84]<br><br>**HR Mortality CardioMEMS vs Standard:** 1 | **Complications:** 0.03 (months 1-7) based on Vaduganathan 2017)[87]<br><br>**Mortality due to implant:** 0.004 (months 1-7) based on Vaduganathan 2017)[87] | **Baseline utility:** 0.71 from CHAMPION[43]<br><br>**Monthly change in utility:** Based on CHAMPION[43]<br>Control:<br>1-6m: -0.005<br>7-60: -0.003<br><br>CardioMEMS:<br>1-6m: 0.001<br>7-60m: 0.003<br><br>**Disutility of HFH**: 0.045 (Schmier 2017)[71] | **Device acquisition:** from Abbott<br>**Device implant, device monitoring, device complication and unit costs:** based on IECS Healthcare Cost Database[88]<br><br>**HFH cost:** based on IECS Healthcare Cost Database, Waisman 2018, and Pichon-Riviere 2015 [88-90] |
| Codina 2024[74] | **Mean age:** 75.5<br>**% female:** 48.8%<br><br>**Baseline rate of HFH:** 1.10 ppy<br>**Baseline mean length of hospitalisation:** 12.53 days | **HFH hazard ratio CardioMEMS vs Standard:** 0.22<br><br>**Mean difference in length of hospitalisation (CardioMEMS vs Standard:** 17.97 days | Complications: 1/43 complication implanting CardioMEMS resulting in 29day hospital stay | QALYs based on study data | **Device acquisition and implant costs:** based on study data<br>**Device monitoring:** based on local regional data<br>• Monitoring by a nurse 30 min. daily 5 days/week<br>• nurse visits once every 4 months<br>• cardiologist visit every 6 months<br><br>**Device complications:**<br>• Chest computed tomography<br>• Thoracic computed tomography angiography<br><br>**HFH cost:** from local regional data |

| Study | Epidemiological data | Treatment effect | Adverse events | Utilities | Costs & Resource use (values given for UK studies) |
|---|---|---|---|---|---|
| Cowie 2017[65] (UK) | **Mean age:** 70<br>**% female:** NR<br><br>**Baseline monthly risk of HFH:** 0.035 based on Klersy 2016 meta-analysis[81]<br><br>**Baseline monthly mortality risk by age-group:** based on Griffiths 2014[79], adjusted using UK life-tables | **HR for HFH (CardioMEMS vs. control):** 0.67 from CHAMPION[91]<br><br>**HR for mortality (CardioMEMS vs. control):** 0.8 from CHAMPION[91] | **Risk of implant complication:** 0.0272 (CHAMPION)[91] | **Utilities during first 12 months by monitoring strategy:** based on CHAMPION[43]<br>**Utilities after 12m:** 0.008 annual decrease based on Swedish cohort[92]<br><br>**Utilities after 5 years:** 0.57 for both monitoring strategies based on UK data from Matza 2015)[80]<br><br>**Disutility for each HRH:** 0.1 for 1 month [81] (Klersy 2016) | **Device acquisition:** Uknown at time of study<br><br>**Device implant:** £12,000 (estimate – bundled cost of device, and implant)<br><br>**Device monitoring costs:** None. In scenario analysis monitoring by band 5 nurse with hourly rate £36 (PSSRU)<br><br>**Device complication costs:** implant complication £1090 (UK reference costs)<br><br>**HFH costs:** £2038 (UK reference costs)<br><br>**Other costs:**<br>• Monthly cost of medical care: £36.31[79] (Griffiths 2014) |
| Cowie 2023[68] (UK) | **Mean age: 70**[81])<br>**% female:** NR<br><br>**Baseline monthly HFH hospitalization risk:** 0.087 (average of CHAMPION, COAST, MEMS-HF: [43, 49, 50])<br><br>**Baseline monthly mortality risk:** As for Cowie 2017. The estimates were in line with 0.016 from the National HF audit 2019-20. [93] | **HR for hospitalization:** As for Cowie 2017.<br><br>**HR for mortality:** 1 (assumption) | As for Cowie 2017 | As for Cowie 2017. | **Device acquisition cost:** £9500 (Abbott)<br><br>**Device implant cost:** £1215 **(**NHS reference costs[94])<br><br>**Device monitoring cost:** £38 (NHS reference costs[94])<br><br>**Device complication cost:** £1175 (CHAMPION, as used in Cowie 2017[65])<br><br>**HFH cost:** £4093 based on NICE TA679 and NHS reference costs[94, 95] |

| Study | Epidemiological data | Treatment effect | Adverse events | Utilities | Costs & Resource use (values given for UK studies) |
|---|---|---|---|---|---|
| | | | | | **Monthly cost usual care HF:** £39 as used in Cowie 2017[65] |
| Kolominsky-Rabas 2016[72] (DE) | **Mean age:** NR<br>**% female:** NR<br><br>**HF incidence:** Based on Johansson 2001[96]<br><br>**Baseline HFH:** Rates from CHAMPION used with a configuration adjustment to reflect hospitalisations in Germany | **HFH HR**: based on CHAMPION study | NR | CHAMPION scenario assumed gain of points in MLHFQ of 10.6 compared to a 7.4 gain of points in the reference scenario. | Based on data taken from German Institute for the Hospital Remuneration System (InEK)[97] |
| Martinson 201[66] (US) | Mean age: 80 (medicare), 57 (private insurance)<br>% female: 50% (medicare), 40% (private insurance)<br><br>**Baseline monthly probabilities:**<br>All based on from CHAMPION[91]<br>• Proportion of patients implanted in the inpatient vs. out patient setting: 0.20<br>• Probability of HFH in SoC arm: 0.0567<br>• Probability of non-HFH in SoC arm: .0800 (mean)<br>• Probability of mortality in SoC arm: .0140 | All based on from CHAMPION[91]<br><br>**HFH HR (CardioMEMS vs Standard:** 0.67<br><br>**Non-HFH HR (CardioMEMS vs Standard):** 0.97<br><br>**Mortality HR (CardioMEMS vs Standard):** 0.80 | **Device and system related complications:** taken from CHAMPION [91] | **Utilities during first 12 months by monitoring strategy:** based on CHAMPION [91]<br><br>**Utilities after 12 months:** assumed equal to the value at 12 months | **Device acquisition:** NR<br><br>**Device implant:** $17,827 (Medicare) $17,827 (insurance) including complications<br><br>**Device monitoring costs:** based on Medicare fee schedule (medical) and assumption (insurance)<br><br>**Device complications costs:** based on CHAMPION and assumption<br><br>**HFH costs:** based on MARKETSCAN data<br><br>**Other costs:** based on MARKETSCAN data<br>• Annual out-patients healthcare utilization<br>• Non-HF hospitalisation<br>• Monthly out-patient care of a HF patient |

| Study | Epidemiological data | Treatment effect | Adverse events | Utilities | Costs & Resource use (values given for UK studies) |
|---|---|---|---|---|---|
| Messori 2024[69] (IT) | **Mean age:** 69<br>**% female:** NR<br><br>**Prevalence of CHF:** 2.04%<br>**CHF patients with >1 HFH in last 12m:** 17.7%<br>**NYHA Class III:** 12.4% | **Budget Impact Analysis:** using data from MONITOR-HF, CHAMPION, and Cowie 2017 and Cowie 2023. | NR | **Budget Impact Analysis:** using data from MONITOR-HF, CHAMPION, and Cowie 2017 and Cowie 2023. | **Device costs:** presented for budget-neutral price and current device price<br><br>**HFH costs :** based on local costs[98] |
| Mokri 2024[67] | All based on MONITOR-HF. [44]<br><br>**Mean age:** 70<br>**% female:** NR<br><br>**Baseline monthly risk of HFH:** 0.055<br><br>**Baseline mortality:** Weibull Shape parameter: 1.131 and Scale parameter: 2206.28 | **HR reduction in HFH:** 0.56 based on MONITOR-HF[44]<br><br>**HR in mortality:** 0.92 based on meta-analysis.[83] | **Implant complications:** Displacement: 2%<br><br>Unsuccessful 1st attempt (reimplant): 4%<br><br>haemoptysis (2%)and arrhythmia (1 A1F and 1 AV block) | **Utilities during first 12 months by monitoring strategy:** based on MONITOR-HF[44]<br><br>**Utilities after 12 months:** Annual reduction of 0.004 based on Heijink 2011[99]<br><br>Disutility for HF hospitalisation days: 0.10 based on Klersy[81] | **Device implant and acquisition cost:** based on MONITOR-HF and Abbott<br><br>**Device monitoring, Stable HF (*1st and subsequent years), and HFH costs:** based on MONITOR-HF. Mean length of stay for HFH 12.9 days (CardioMEMS) and 10.4 days (SoC)<br><br>**Implant complication costs:** From Dutch costing manual |
| Sandhu 2016[70] (US) | **Mean age:** 62<br>**% female:** NR<br>**%pEF:** 21.7%<br><br>**Monthly baseline risks:** All based on CHAMPION [43]<br>**Mortality:** 0.0099<br>**HFH:** 0.0876<br>**Non-HFH:** 0.0830<br><br>**Inpatient HFH monthly mortality risk:** 0.0390[100, 101]<br><br>**Risk Ratio of death after HFH:** 3.32 | **Risk Ratio for HFH (CardioMEMS vs usual care):** 0.63 based on CHAMPION[43]<br><br>**Risk Ratio for mortality (CardioMEMS vs usual care):** 1 (assumption) | **Placement failure risk:** 0.0435 from CHAMPION [43] | **Utilities during first 12 months:** Based on CHAMPION [43] converted into EQ-5D.[102]<br>Baseline: 0.55<br>CardioMEMS increased utility: 0.01<br><br>**Utilities after 12 months:** Baseline: 0.55<br>CardioMEMS increased utility: 0.004 | **Device acquisition costs:** based on local costs[104]<br><br>**Device implant costs:** based on local costs [104, 105]<br><br>**Device monitoring:** based on a physician compensation survey and occupational employment statistics [106, 107]<br><br>**Device complication costs:**<br>• r/sided catheterisation and angiography (Medicare costs, 2014) |

| Study | Epidemiological data | Treatment effect | Adverse events | Utilities | Costs & Resource use (values given for UK studies) |
|---|---|---|---|---|---|
| | **Includes Risk Ratios for pEF vs rEF patients** | | | **Disutility of HFH** 0.059 based on Jaagosild 1998[103] | • device placement: assumption<br><br>**HFH costs:** based on [108] |
| Schmier 2017[71] | **Mean age:** NR<br>**% female:** NR<br><br>**Baseline hospitalisation and mortality rate/risks:** taken from CHAMPION [43] Reported separately for each arm (see Treatment effect column) | Data from CHAMPION [43]<br><br>**Hospitalisation**<br>*Randomised period*<br>CardioMEMS: 1.38 events ppy<br>SoC: 1.65 events ppy<br>*Open access period*<br>CardioMEMS: 1.31 events ppy<br>SoC: 1.65 events ppy<br><br>**% hospitalisations due to HF**<br>*Randomised period*<br>CardioMEMS: 33%<br>SoC: 42%<br>*Open access period*<br>CardioMEMS: 36%<br>SoC: 42%<br><br>**% mortality**<br>*Randomised period*<br>CardioMEMS: 18.5%<br>SoC: 22.9%<br>*Open access period*<br>CardioMEMS: 14.7% SoC: 22.9% | **Implant Complications: Based on** CHAMPION [43]<br>CardioMEMS: 1.4%<br>SoC: 0% | **Utilities:** Based on CHAMPION [43]<br>**Baseline:** 0.711<br>**Change 1-6m:** CardioMEMS 0.001 SoC -0.005<br>**Change 7-60m:** CardioMEMS 0.003 SoC -0.003<br><br>**Utility decrement for hospitalisation:**<br>A based on Gohler 2009[109])<br>**Hospitalisation cycle:**<br>CardioMEMS 0.045<br>SoC 0.045<br>**Following cycle:**<br>CardioMEMS 0.0225<br>SoC 0.0225 | **Device acquisition:** Average sales prices<br><br>**Device implant:** based on Medicare Fee Schedule<br><br>**Device monitoring, HFH, device complications, outpatient costs:** Based on Martinson inflated to 2016 price year.[66] |
| Health Technology | **Mean age:** 67.7<br>**% female:** NR<br><br>**Baseline monthly risks:** | **Hazard ratios:** based on a meta-analysis of CHAMPION,[43] GUIDE- | **Freedom from device or system complication:** | **Utilities for Stable HF state:** 0.570 based on Cowie(2017)[65] | Costs based on Cowie 2023[68]<br>**Device acquisition:** £9,500<br>**Device monitoring:** £38 |

| Study | Epidemiological data | Treatment effect | Adverse events | Utilities | Costs & Resource use (values given for UK studies) |
|---|---|---|---|---|---|
| Wales 2023[73] | based on a meta-analysis of CHAMPION,[43] GUIDE-HF[45] and MONITOR-HF[45]<br>• **HFH:** 0.0857<br>• **Mortality:** 0.00112 | HF[45] and MONITOR-HF[45]<br>• **HR for HFH:** 0.71<br>• **HR for Mortality:** 0.92 | 98.9% based on meta-analysis[83]<br>**Freedom from sensor failure:** 99.7% based on meta-analysis[83] | **Disutility for HFH:** 0.1 for one month based on Cowie(2017)[65] | **Device implant:** £1,487 from NHS reference costs[110]<br>**Complication costs:** £1,175<br>**Monthly CHF costs excluding complications:** £39<br>**HFH cost:** £2,582 NHS reference costs[110]<br>**Sensor failure:** incurs implantation cost above |

Key: **CHF** = Chronic Heart Failure, **HFH** = Heart Failure Hospital Admission, **HR** = hazard ratio, **KCCQ** = Kansas City Cardiomyopathy Questionnaire, **MLHFQ** = Minnesota Living with HF Questionnaire, **ppy** = per patient year, **SoC** = Standard of Care.

#### 6.1.3.2 Objective 2 – to summarise the findings of previous cost–utility, cost-effectiveness, and cost–benefit studies conducted in, or generalisable to, the UK

Table 13 provides a summary of the findings in the evaluations. We focus here on the two models specific to the UK.

**Cowie 2017 and 2023[65, 68]**

Cowie reported one model in 2017 and updated this model in 2023. In their 2017 model, using CardioMEMS increased costs by £10,916 over a ten-year horizon compared to usual care. The 2017 model estimated an increase in mean survival of 0.38 years in favour of CardioMEMS (4.79 usual care and 5.17 CardioMEMS) reflecting a QALY gain of 0.57 (2.57 QALYs for usual care compared to 3.14 for CardioMEMS). The ICER was £19,274/QALY.[65]

In their (updated) 2023 model, PAP monitoring using CardioMEMS increased costs by £6,337 over a ten-year horizon compared to usual care. The 2023 model estimated an increase in mean survival of 4.79 years for CardioMEMS compared with usual care, reflecting a QALY gain of 0.32 for CardioMEMS. The ICER was £19,674/QALY.[68]

The subtle difference in ICERs between the 2017 and 2023 models is due to the 2023 model assuming no mortality benefit and incorporating monitoring costs, which were offset by higher baseline hospitalisation rates and higher costs per heart failure hospitalisation.

**Health Technology Wales (HTW) model[73]**

The HTW base case model increased costs for PAP in addition to usual care by £10,375 over a lifetime horizon compared to usual care alone. This reflected a QALY gain of 0.36 for PAP treatment in addition to usual care and an ICER of £28,523. Mean survival was not explored in the model.

#### 6.1.3.3 Objective 3 - To summarise the key drivers of cost-effectiveness in remote PAP monitoring

Table 13 provides a brief summary of drivers of cost-effectiveness in the models. We summarise here the key drivers, as reported by study authors, for the two UK specific models.

**Cowie 2017 and 2023[65, 68]**

Cowie considered that staff costs, in particular monitoring costs, were a key driver in their models. In their 2017 report, a scenario analysis explores the impact of staff costs by increasing monitoring time to 70 minutes per month. This increased the ICER from £19,274/QALY to £25,464/QALY.

In the 2023 model, Cowie do not include an effect of CardioMEMS on mortality, but report scenarios examining the effect of varying the hazard ratio for mortality. When the hazard ratio from CHAMPION was used (0.8), the results indicate an ICER of £14,234/QALY (compared to the Cowie 2023 base case of £19,762/QALY). Using the hazard ratio from GUIDE-HF (1.81), CardioMEMS was dominated by usual care. This demonstrates the sensitivity of the results to the impact on mortality, which is uncertain. Longer term data are needed on long-term mortality.

### Health Technology Wales (HTW) model[73]

The HTW model considered baseline rate of hospitalisation, cost of a PAP device, costs of hospitalisation, and monthly risk of heart failure hospitalisation (HFHA), as key drivers of the cost-effectiveness results.[73] The effect of these potential drivers were explored in deterministic sensitivity analyses.

With all other assumptions matching their base case, the authors found the following (although it wasn't clear if these statements were based a threshold of £20,000 or £30,000 per QALY):

- A baseline rate of hospitalisation at 12.97% was the threshold for cost-effectiveness.
- The PAP device would need to reduce from £9,500 to £6,400 (GBP) for the PAP device to become cost-effective.[73]
- That hospitalisation costs (especially non-elective long-stay) impacted the ICER.[73] The authors found that using the baseline rate of hospitalisation from the COAST study (11.8%), combined with lower monitoring costs, reduced the ICER to £20,418/QALY (from £28,523/QALY).
- That the use of a hazard ratio for HFHA aligned to the UK (from Cowie 2023), compared to the hazard ratio from the CHAMPION study, reduced the ICER to £18,084/QALY.
- Further reductions in the ICER were examined by testing increased costs of hospitalisation (similar to Cowie 2023) which reduced the ICER to £10,443/QALY.[56]

**Table 13 Findings, drivers and limitations of models included in the review of economic evaluations of remote PAP monitoring**

| Study (Country)<br><br>Funding | Findings | Drivers | Limitations |
|---|---|---|---|
| **Study:** Alcaraz 2021 (Argentina)[64]<br><br>**Currency:** Peso | **ICER:** ARS 2,937,756 (£32,812) per QALY for Social Security and ARS 2,496,015 (£27,878) per QALY Private Sector | • Hazard ratio of HF hospital admission<br>• Acquisition price of CardioMEMS. | • lack of long-term efficacy data beyond 1 year |
| **Study:** Codina 2024[74]<br><br>**Currency:** Euro € | **Incremental Net Monetary Benefit (CardioMEMS vs SoC):** €3,002 (£2,559) after 1 year, and €346 (£295) after 2 years, based on €25,000 (£21,300) willingness to pay per QALY | • Hospitalisation costs are lower in Spain than the UK<br>• Hospitalisation post implant were considerably longer then pre implant.<br>• The fact that CardioMEMS requires no batteries or replacement, makes invasive monitoring amid-long term cost-effective strategy. | • Small sample of patients<br>• Single centre analysis.<br>• Short f-up (1 yr) |
| **Study:** Cowie 2017 (UK)[65]<br><br>**Currency:** GBP £ | **ICER:** £19,274 | • Staff cost scenario with nurses monitoring for 23 mins per month, and doctors 7 mins per month, ICER increased to £22, 342.<br>• If nurse was needed for 70 min p/m then ICER £25, 464 | • Uncertain estimate of effect of mortality. CHAMPION not powered for this outcome. |
| **Study:** Cowie 2023 (UK)[68]<br><br>**Currency:** GBP £ | **ICER:** £19,671 | • Time spent monitoring pts (staff costs) | • Pressure sensor failure not considered in model (as assumed rare) |
| **Study:** Kolominsky-Rabas 2016[72] (Germany) | **Annual cost savings (CardioMEMS vs reference):** ranged from €4,000,000 (£3,400,000) in 2010 to | • Hospitalization reductions<br>• Life quality gains with and without PA pressure<br>• Monitoring | • Uncertainty due to low sample in CHAMPION.<br>• Restricted to a 12.5 year time period. |

| Study (Country)<br><br>Funding | Findings | Drivers | Limitations |
|---|---|---|---|
| **Currency:** Euro € | €106,000,000 (£91,000,000) in 2021.<br><br>**Quality of life (MLHFQ) point gain (CardioMEMS vs reference):** ranged from 20,000 in 2010 to 4,964,546 in 2021 | • Annual percentage increases of costs | • Complexity of the ProHTA simulation model |
| **Study:** Martinson 2017[66](US)<br><br>**Currency:** US $ | **ICER:** US $12,262 (£7,442) | • Time horizon<br>• Hospitalisation rates<br>• Hospitalisation costs<br>• Mortality rates<br>• Implant cost | • Both the control and treatment groups started the trial with high prevalence of guideline-directed medical therapies at baseline at target doses. |
| **Study:** Messori 2024[69] (IT)<br><br>**Currency:** Euro € | **ICER:** €38,435 (£32,761)<br>If used in 166 cases, the total investment in Tuscany would be €0.77 million (£0.66 million) at the budget-neutral price of €4,332 (£3,692) per device or €1.99 million (£1.70 million) at the current price of the device or €2.76 million (£2.35 million) at the price of €16,662 (£14,202). | • Device cost | • Organisational impact – quantification of staff resources for monitoring is unclear.<br>• Population size (166) likely an underestimate.<br>• Cost of device – early drop-out or death shortly after implementation would not capture benefits. |
| **Mokri 2024**[67] (Netherlands)<br><br>**Currency:** Euro € | **ICER:** €20,753 (£17,689) per QALY (base case). €10,406 (£8,870) per QALY for Dutch healthcare perspective (excluding costs of informal care and travel). | • Device and implant costs<br>• Long-term mortality effect<br>• Time horizon | • Trials underpowered to estimate of mortality effects |
| **Sandhu 2016**[70] (US) | **ICER:** $71,462 (£43,371) | • Device durability | • Use of a single trial for study data.<br>• Lack of long-term safety data. |

| Study (Country)<br><br>Funding | Findings | Drivers | Limitations |
|---|---|---|---|
| **Currency:** US $ | | • Cost effect if trial effectiveness sustained over long periods. | • Data lacking on the average national cost of monitoring patients. |
| **Schmier 2017**[71] (US)<br><br>**Currency:** US $ | **ICER:** $44,832 (£33,106) | • Device cost | • Short-term data from CHAMPION<br>• Assumed linear increase/decrease for utilities which could lead to double-counting. |
| **Health Technology Wales (HTW)**[73]<br><br>**Currency:** GBP £ | **ICER:** £28,523 | • Monitoring cost<br>• Baseline rate of HF hospitalisation<br>• Cost of hospitalisation<br>• Using assumptions from Cowie 2023 reduces the ICER | • Duration of HFH disutility (one month) could overestimate the impact on utility.<br>• Insufficient data to model hospitalisations and urgent visits requiring IV diuretics separately<br>• Hospitalisations may result in other resource use in practice.<br>• Impact of monitoring strategy in management of drugs, GP visits or outpatient attendances not captured<br>• Monitoring costs based on assumptions from previous models |

Key: **BL** = base line, **CHF** = Chronic Heart Failure, **HFH** = Heart Failure Hospital Admission, **HR** = hazard ratio, **KCCQ** = Kansas City Cardiomyopathy Questionnaire, **MLHFQ** = Minnesota Living with HF Questionnaire, **PPY** = per patient year, **pts** = patients, **SoC** = Standard of Care.

### 6.1.4 Results of the review of systematic reviews of heart failure

The process of identification and selection of systematic reviews is reported in Figure 12. Fifteen reports of 14 systematic reviews fulfilled inclusion (Avzar 2025 reported the same review as Besse 2024).[111-124] Reviews were published between 2016-2024.

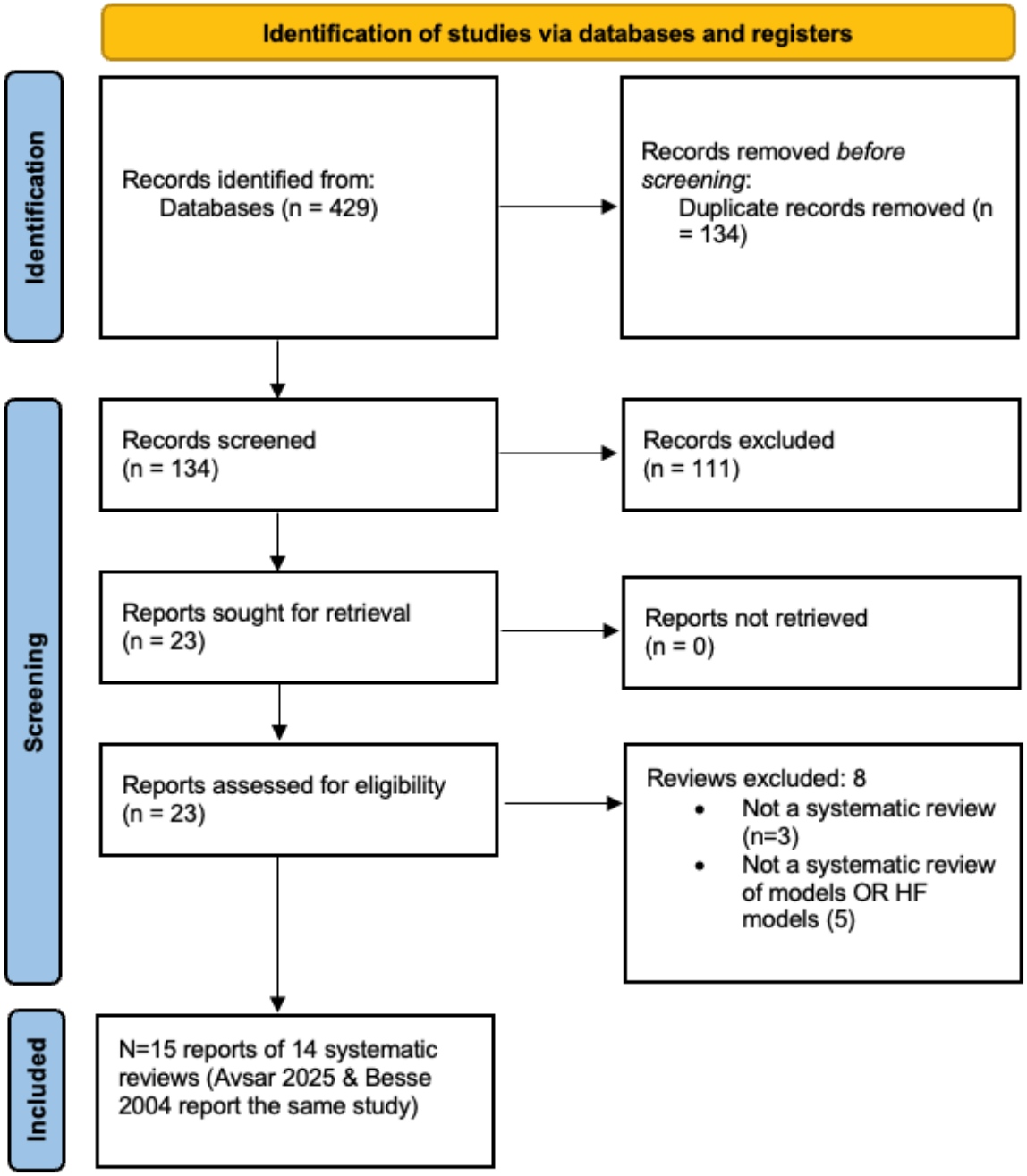
In Appendix 5 Table 50 we summarise the reviews identified, including their research questions, inclusion criteria (where reported), the number of studies fulfilling inclusion, and types of models by type included (where reported).

The review identified 3 types of model structures used to assess the cost-effectiveness of interventions for chronic heart failure patients:

1. Markov models;
2. Partitioned survival models; and
3. Discrete event simulation models.

Markov models were the most common model structure used to evaluate remote PAP monitoring, and were also for models for HF more generally where the model states were often based on New York Heart Association (NYHA) stages. Partitioned survival models which use NYHA stage classifications to determine a patient's modelled disease burden and outcomes, making the assumption that disease severity progresses over time, have also been used in HF models. A systematic review by Di Tanna et al. (2019) finds 5 such models, most of which are assessing the cost-effectiveness of pharmaceutical interventions on patients with heart failure.[125] Discrete event simulation models have also been employed to model the cost-effectiveness of monitoring for HF patients, for example by Albuquerque de Almeida et al. (2021),[126] which used a sample of simulated patients to capture long-term outcomes for 8 heart failure-related health events in a cost-effectiveness model of early warning systems.

**Figure 12 PRISMA flow diagram for the systematic review of systematic reviews of economic models of interventions for heart failure**




### 6.1.5 Summary of relevance of existing evidence to this economic evaluation

Of the models identified in our reviews the most appropriate were those designed specifically to assess the cost-effectiveness of remote PAP monitoring because these captured the impact of monitoring on hospitalisation which our clinical advisors agreed would be a key benefit of effective monitoring, and aligns with the available clinical trial endpoints. The most relevant previous model in a UK context was the Markov model structure developed by Cowie et al. 2017, updated in 2023, and adapted in the HTW model (Health Technologies Wales, 2024).[65, 68, 73] However, the model structure is very simple, with just two health states with patients

available to transition to (stable heart failure and dead), with the possibility of a transitory heart failure hospitalisation event. There have been various alternatives to the Cowie model, including states to distinguish between HF-related and non-HF related hospitalisations,[66, 70] states to distinguish between in- and out-patient hospitalisations, [71] and including a post-hospitalisation state.[64] We heard from our clinical advisors that HF patients may have repeated hospitalisations, and quality of life, resource use, future hospitalisation, and mortality would depend on number of previous hospitalisations. Furthermore, there exists evidence on re-hospitalisation rates for patients with PAP monitoring implants, and so we considered it appropriate to include subsequent hospitalisations in our model.

We considered which model structure would be most appropriate. Markov models are cohort models, and do not account for the impact of patient heterogeneity on outcomes. However they are simple to construct and may be adequate when there are no non-linear effects between patient characteristics and model outcomes, and the states can be defined so that transitions only depend on past history via the patients current state.[127] Discrete event simulation models are useful in modelling heterogeneous populations who may experience disparate health outcomes and to capture the impact of patient history. We heard from our clinical advisors that number of previous hospitalisations is an important factor future events, but felt that this could be captured using a Markov model with states defined by numbers of previous HFHs. Whilst HFHs vary with patient characteristics, there was no evidence of subgroup effects for the relative treatment effects of PAP monitoring, and so there was not a strong rationale for fitting a discrete event simulation model. Partitioned survival models, which have been used in the context of models of pharmacological interventions for HF focus on NYHA staging progression because the goal of these treatments is to delay disease progression. This modelling approach was considered less relevant in the context of PAP monitoring where the goal of monitoring is to improve medical management and reduce HFHs.

On the basis of these considerations a de novo Markov model (described in section 6.2.3) which captured the impact of HFHs with health states that depend on number of previous HFHs was developed as the most appropriate structure that could be estimated with the available evidence.

## 6.2 Model structure and methods of economic evaluation

A decision-analytic model was developed to estimate the incremental costs and quality-adjusted life years (QALYs) of remote PAP monitoring technologies compared with current monitoring practice (as described in section 1.3.2). For brevity, we refer to “current monitoring practice” as “standard care” throughout.

### 6.2.1 Population

We consider a population of CHF patients who are to be monitored following an index HF-related hospitalisation (HFH). We assume all patients are classified as NYHA class III at the time that the monitoring strategy decision is made, regardless of whether they subsequently change class afterwards.

### 6.2.2 Strategies for monitoring CHF patients

We compared the following different monitoring strategies for CHF patients:

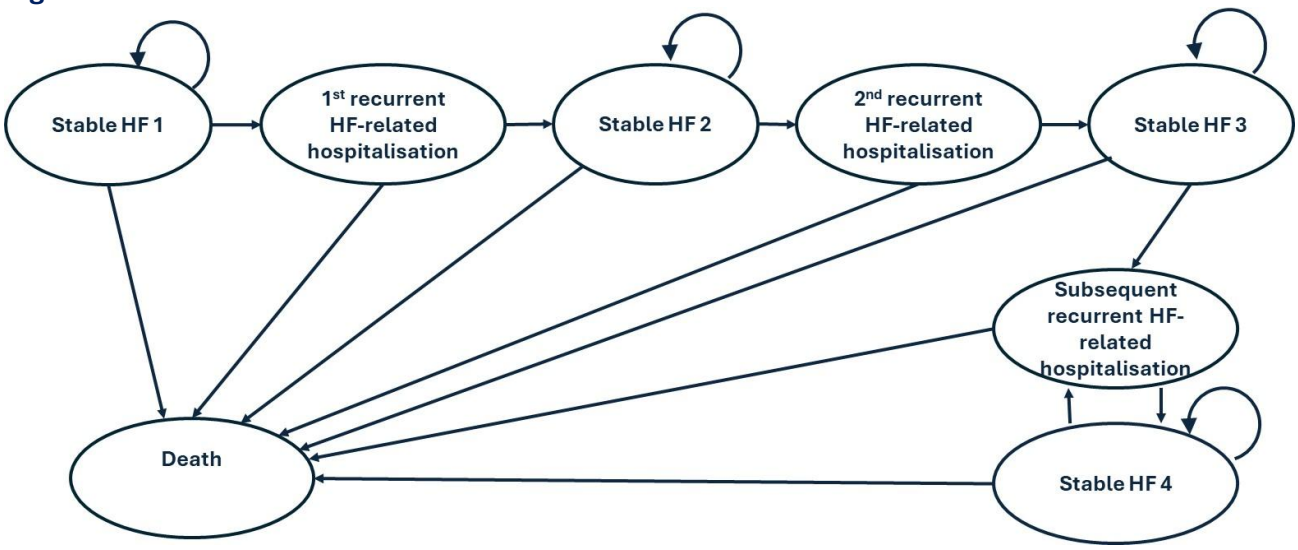
- CardioMEMS plus standard care
- Cordella plus standard care
- Standard care.

However, there was limited comparative data available for Cordella and furthermore, the price of Cordella was not available at the time of writing this report. For illustration only we report results for Cordella assuming the same cost as CardioMEMS.

### 6.2.3 Model structure

The model structure (Figure 13) was developed to capture the short- and long-term costs and benefits of remote PAP monitoring technologies, and was informed by the findings of our review of cost-effectiveness studies and discussions with our clinical advisors and specialist committee members.

**Figure 13 Markov model structure**




Patients who are being monitored following an index HFH begin in the stable HF 1 state, which reflects the health state for patients who have stabilised after an index HF hospitalisation. If they have a HFH, then they move to the 1st recurrent HFH state and incur the average costs and health-related quality of life impact of a 1st HFH event for a single cycle. Patients only stay in the 1st recurrent HFH state for a single cycle after which they either die or move to the Stable HF 2 state. This allows costs, health-related quality of life, and rates of future HFH and mortality to differ for those who have had one HFH event (Stable HF 2), compared to those who have not had a HFH event (Stable HF1). If patients have a 2nd recurrent HFH, they move from the Stable HF 2 state to the 2nd recurrent HFH state and incur the average costs and health-related quality of life impact of a 2nd HFH event for a single cycle. Patients only stay in the 2nd recurrent HFH state for a single cycle after which they either die or move to the Stable HF 3 state. This allows costs, health-related quality of life, and rates of future HFH and mortality to differ for those who have had two recurrent HFH events (Stable HF 3), compared to those who have had just one

(Stable HF 2) or no HFH events (Stable HF1). If patients have a further HFH, they move to the subsequent HFH state and incur the average costs and health-related quality of life impact of a 3rd or subsequent HFH event for a single cycle. Patients only stay in the 2nd recurrent HFH state for a single cycle after which they either die or move to the Stable HF 4 state. This allows costs, health-related quality of life, and rates of future HFH and mortality to differ for those who have had three or more recurrent HFH events (Stable HF 4), compared to those who have had just two (Stable HF 3), one (Stable HF 2) or no HFH events (Stable HF1). Patients may continue to have further HFH moving between the Stable HF 4 and the Subsequent HFH state, where patients spend just a single cycle in the Subsequent HFH state. The HFH rate is assumed to depend on the monitoring strategy, and the relative effect of each monitoring strategy is assumed to be the same regardless of the number of previous HFHs. Non-HF hospitalisations were not modelled as our clinical advisors did not expect these to differ between monitoring strategies, and it was not an outcome reported in the clinical trials of monitoring strategies. The impact of non-HF hospitalisations may still differ between treatments if there is a difference in mortality across treatments, so this is a potential limitation of the model, however there was no evidence of a mortality benefit of remote PAP monitoring (Figure 3). Mortality can occur from any state, with state-specific rates.

### 6.2.4 Perspective and time-horizon

An NHS and personal social services (PSS) perspective was taken with a life time horizon where costs and QALYs were discounted at an annual rate of 3.5%. The model included the impact on health related quality of life on patients, however due to a lack of evidence the impact on HRQoL of carers was not included (see section 6.3.5.3).

### 6.2.5 Uncertainty

Parameter uncertainty was captured using a probabilistic analysis where parameters were simulated from probability distributions to estimate mean costs, mean QALYs, incremental cost-effectiveness ratios and expected net benefits at commonly used NICE willingness to pay thresholds. Uncertainty is presented using cost-effectiveness planes and cost-effectiveness acceptability curves. One-way deterministic sensitivity analyses were performed for all key model parameters and tornado diagrams are presented.

### 6.2.6 Model Implementation and Validation

The model is implemented in the R programming language and the model was developed using the R studio IDE.[128] All files to run the model are provided, including a guide to running the model and code is provided to install the necessary packages upon running the model. The model underwent internal validation a member of the team not involved in the building of the model, following Büyükkaramikli et al..[129] The validation included face validity tests, checks of model calculations, examination of the model outputs, and comparison with the results from the HTW model.

The model code was checked during development. When the final model was completed a more thorough review of the model code was completed and at this stage no model bugs were identified. The TECH-VER checklist was completed with all applicable tests producing results as expected by the checklist.

We further validated our model against the HTW model, by setting our model inputs to match their model assumptions. There was a large difference in results due to the way in which the HFH disutility was applied. In the HTW report it states that the same approach is taken to the disutilities as in the Cowie model, also the same approach taken in our model, which is to use an annualised disutility of 0.1 for a 1 month cycle, ie a monthly disutility of 0.1/12=0.0083. However, elsewhere in the HTW report this is described as a 0.1 disutility applied for the month where the HFH occurs, and this is what is applied in their model. When we ran our model with inputs matching the HTW assumptions using the HFH disutility as in Cowie and our base-case then the ICER was £51,346 which is much higher than that reported in the HTH report. However, when we use 0.1 disutility applied for the month of the HFH then we get an ICER of £31,464 which is much closer to the £28,523 reported in the HTW report. The remaining differences are due to differences in the discounting calculations and half-cycle corrections. There were slight differences in the way we calculated discounting, as we used annual discount rates whilst the HTW applied monthly discount rates (after the first year). In addition, there was a difference in the way we calculated the final cycle in the half cycle correction, with our final half-cycle-corrected cycle state trace set equal to the non-corrected final cycle, whereas the HTW applied a mean between the last non-corrected cycle and 0 for the state occupancy of living patients. The differences in discounting and half cycle corrections approaches to led to only minor differences in results but the disutility differences had a significant impact on total and incremental QALYs, and thus the ICERs (see section 7.5.2).

## 6.3 Model inputs

Model inputs were derived from the clinical and cost-effectiveness reviews where possible, supplemented by targeted literature searches. Where there was insufficient evidence available we based parameters on expert opinion and conducted scenario analyses to explore the impact of these assumptions on the results. The model input values used in the base-case with distributions assumed and source of evidence are summarised in Table 20, and described in detail below.

### 6.3.1 Population characteristics

The relevant population are NYHA class III patients in England and Wales who have had a previous HFH, to be eligible for a remote PAP monitoring device. The only study we identified providing population characteristics in this specific population was the UK-specific results from the CardioMEMS Post-Market Study (COAST) study reported by Cowie et al. 2022.[50] This was a small cohort of n=100 with mean age 69 years and 70% male, however these values were in line with previous economic models (Table 12) and studies in other European countries (Table 15), and so we used these values in our model.

### 6.3.2 HF-related hospitalisation (HFH) rates

#### 6.3.2.1 HFH rate based on number of previous HFHs

The model (Figure 13) allows the recurrent HFH rate to depend on the number of previous recurrent HFHs, where all patients in the model have had an index HFH We searched for appropriate UK and European data sources providing information on recurrent HFH rates based on number of previous recurrent HFHs. Lindmark et al. 2021[130] reports cumulative incidence curves for time to next HFH based on number of recurrent HFHs for 3878 patients with an index HFH in Sweden, using linked national health registers and electronic medical records. The

same information is reported by Huusko et al. 2020,[131] but also broken down by ejection fraction status for 2888 patients with at least one HFH in Finland. Lahoz et al. 2020[132] reports the median time and inter-quartile range between recurrent HFHs (Table 14) in 8,603 HF patients identified in the UK Clinical Practice Research Datalink (CPRD) with an index HFH recorded in the Hospital Episode Statistics (HES). All studies showed that time to subsequent recurrent HFH decreased with each re-hospitalisation. It is possible to estimate a hazard ratio from the ratio of the reciprocal of medians under either an Exponential distribution or a Weibull distribution with the same shape across groups. This assumption seemed plausible from visual inspection of the Kaplan-Meier curves in the Lindmark and Huusko studies. This meant that we were able to estimate hazard ratios from the median times reported in Lahoz et al. 2020 (Table 14). Uncertainty was estimated by assuming a log-Normal distribution for time to next recurrent HFH, and using the approximation that the standard error for the median on the log-scale can be approximated by a constant times the standard error for the mean on the log-scale (where the constant is 1.2533). Lahoz et al. 2020 was the largest study and the only study based on UK data, and so it was considered the most appropriate source of evidence for the hazard ratios for time to next HFH based on number of previous recurrent HFHs. We therefore used the hazard ratios in Table 14 in our model.

**Table 14 Median number of days to next HFH by number of recurrent HFH after the index HFH from Lahoz et al. 2020[132]. Estimated hazard ratio, log-hazard ratio (with 95%CrI and standard error)**

| Model State | Number of recurrent HFH after index event | Median days to next HFH (IQR) | Hazard ratio for HFH vs patients with 0 recurrent HFH after index event | Log-hazard ratio (95% CrI) and standard error (se) |
|---|---|---|---|---|
| Stable HF 1 | 0 | 143 (35 – 464) | 1.00 | 0.000 |
| Stable HF 2 | 1 | 84 (21 – 272) | 1.70 | 0.532 (1.494, 1.944)<br>se= 0.0675 |
| Stable HF 3 | 2 | 77 (26 – 237) | 1.86 | 0.619 (1.539, 2.222)<br>se= 0.0953 |
| Stable HF 4 | 3 | 46 (11 – 127) | 3.11 | 1.134 (2.263, 4.135)<br>se= 0.1613 |

#### 6.3.2.2 HFH rate in the Stable HF1 state under standard care

Previous UK models used different evidence sources for recurrent HFH after an index HFH (Table 12). Cowie 2017[65] used a meta-analysis of 17 studies of HF telemonitoring,[81] Cowie 2023[68] used an average of the CHAMPION[43] control arm, COAST (UK cohort)[49] and MEMS-HF (German and Netherlands cohorts), [44, 49] and the Welsh HTA model used a meta-analysis of the control arms from CHAMPION, GUIDE-HF, and MONITOR-HF. These all combined estimates from different countries which may differ in HFH rates. For our model we preferred to use evidence from a UK cohort (or European if no relevant UK data found) that represented the population eligible for a remote PAP monitoring device (ie NYHA class III patients with an index HFH).

Table 15 shows annualised HFH rates under standard monitoring practice for the UK and European studies that were conducted on a population eligible for a remote PAP monitoring

device: COAST (UK and French cohorts), MEMS-HF, and MONITOR-HF cohorts. The HFH rates are very similar for COAST (UK and French cohorts) and MEMS-HF (in the 12 months prior to having a device inserted), but differ to the control arm of the MONITOR-HF RCT. MONITOR-HF was affected by the covid-19 pandemic, and the HFH rate was higher in the pre-covid follow-up period than in the post-covid follow-up period, and more in line with the findings from the other studies (Table 15). We preferred the UK-specific COAST estimate of 1.52 annual rate as most relevant to inform the HFH rate in our model. However, it is important to note that this represents an *average* of the HFH rate for patients in the Stable HF1, Stable HF2, Stable HF3, and Stable HF4 states, whereas our model is parameterised with a HFH rate for Stable HF1, and hazard ratios for the other Stable HF states (see section 6.3.2.1). Lahoz et al. 2020[132] reports that the percentage of patients with 0, 1, 2, ≥3 recurrent HFHs are 71.58%, 18.2%, 6.02%, and 4.2% respectively. We estimated the recurrent HFH rate in the Stable HF1 state required to give a weighted average rate of 1.52, by calculating a correction factor of the weighted HR for Stable HF1 divided by the average weighted HRs across the states: 0.7158/(0.7158*1 + 0.182*1.7 + 0.602*1.86 + 0.042*3.11) = 0.5646. This gives an estimated HFH rate for Stable HF1 of 0.8582 95%CI (0.7317, 0.9993).

In a scenario analysis we explored the sensitivity of results to using a lower *average* baseline HFH annual rate of 1.092 used in the Cowie 2023 model, which corresponds to a corrected HFH rate for Stable HF1 of 0.6165. In another scenario analysis we use an average baseline HFH rate of 1.77 which was the upper confidence limit from the UK cohort of the COAST study to reflect a high-risk population, which corresponds to a corrected HFH rate for Stable HF1 of 0.9993.

**Table 15 Demographics and HFH rate under standard care for studies in UK or European populations eligible for remote PAP monitoring**

| Study | Cohort | N | Mean age | % female | Control annualised HFH rate (per patient year) (95%CI) |
|---|---|---|---|---|---|
| COAST-UK[50] | UK: 15 centres | 100 | 69 | 30% | 1.52<br>(1.296, 1.770) |
| COAST-France[56] | France | 103 | 67.9 | 21.8% | 1.59<br>(1.365, 1.840) |
| MEMS-HF[49] | Germany: 26 centres<br>Netherlands: 4 centres<br>Ireland:1 centre | 234 | 67.2 | 22.3% | 1.55<br>(1.396, 1.719) |
| MONITOR-HF[44] | Netherlands: 25 centres | 176 (CardioMEMS)<br>172 (Control) | 69.5 | 24.4% | 0.678<br>(0.590, 0.776)<br><br>Pre-covid subgroup:<br>1.4<br>(0.867, 2.140) |
| SIRONA-2[47, 133] | “Europe” | 70 | 71 | 28.6% | N/A |

#### 6.3.2.3 Relative effects for routine PAP monitoring on HFH

The hazard-ratio for HFH for CardioMEMS relative to usual monitoring was based on a meta-analysis of the studies identified in the clinical effectiveness review for the NYHA class III subgroup data, which gave a hazard ratio of 0.66 95%CI (0.57, 0.76) (see section 5.5.1.1, Figure 2**).**

For Cordella, the only comparative evidence was from the initial stage of the PROACTIVE-HF trial[48] before it changed to a single-arm design. Endotronix provided the estimated hazard ratio for HFH in the randomised stage of the trial, which was 0.61 95%CI (0.36, 1.04). This gives an indirect comparison of Cordella vs CardioMEMS of [redacted] (see section 5.5.1.1). We note however that the control arm in PROACTIVE-HF involved telemonitoring of daily data on patients' vital signs (but not PAP measurements), which reflects more intensive monitoring than standard care. The hazard ratio for HFH from PROACTIVE-HF may therefore be unfavourable for Cordella compared with standard care. We explored the possibility of using an alternative approach based on a population-adjusted indirect comparison,[134, 135] which would enable the complete data for Cordella from PROACTIVE-HF to be used and avoids assuming that the control arm is the same as standard care. However, we had insufficient evidence to use this alternative approach (see section 7.4.2), and so used the hazard ratio from the randomised stage of PROACTIVE-HF in our model. As previously noted, the model results for Cordella are illustrative only due to the limitations with the available evidence.

### 6.3.3 Mortality

#### 6.3.3.1 Mortality based on number of previous HFHs

The model (Figure 13) allows for mortality rate to depend on the number of previous HFHs, where all patients in the model will have had an index HFH at the start of the model. We searched for appropriate data sources providing hazard ratios for mortality based on number of previous HFHs, and identified a recent review by Ketabi et al(2024).[136] Of the studies identified by Ketabi et al, the only UK study that is relevant to our population is Lahoz et al. 2020.[132] As noted in section 6.3.2.1, Lahoz 2020 is a large UK study using data from CPRD for patients with an index HFH recorded in HES, which we considered appropriate for our modelled population. We therefore used the hazard ratios for mortality by health state in Table 16 in our model, where for Stable HF 4 we use the value corresponding to those with 3 recurrent HFHs (which was very similar to those with 4 recurrent HFHs).

**Table 16 Hazard ratios for mortality by number of recurrent HFH after the index HFH from Lahoz et al. 2020[132].**

| Model State | Number of recurrent HFH after index event | Hazard ratio (95% CrI) for mortality vs patients with 0 recurrent HFH after index event | Log-hazard ratio (95% CrI) and standard error (se) |
|---|---|---|---|
| STABLE HF 1 | 0 | 1.00 | 0.000 |
| STABLE HF 2 | 1 | 1.98 (1.81, 2.17) | 0.683 (0.593, 0.775) se=0.0463 |
| STABLE HF 3 | 2 | 2.39 (2.08, 2.74) | 0.871 (0.732, 1.008) se=0.0703 |
| STABLE HF 4 | 3 | 3.56 (2.92, 4.34) | 1.270 (1.072, 1.468) se=0.1011 |

| Model State | Number of recurrent HFH after index event | Hazard ratio (95% CrI) for mortality vs patients with 0 recurrent HFH after index event | Log-hazard ratio (95% CrI) and standard error (se) |
|---|---|---|---|
| | ≥4 | 3.47 (2.75, 4.38) | 1.244 (1.012, 1.477) se=0.1187 |

#### 6.3.3.2 Mortality rates under standard care

The Cowie models[65, 68] used monthly mortality risks (Table 17) based on a previous model by Griffiths et al. 2014,[79] adjusted for age using national life-tables. Cowie 2023 also estimate a monthly mortality risk from the National HF Audit of 0.016,[93] which was in line with the Griffiths estimate for the 75–80 age-group. The Welsh HTA model instead used a meta-analysis of the control arms from CHAMPION, GUIDE-HF,[45] and MONITOR-HF,[45] in their model base case. However, these studies were conducted in the US, US and Canada, and Netherlands respectively. In our model, we preferred to use the mortality risks from the Cowie models (Table 17), as this was validated against UK national audit data. However, as noted for the HFH outcome these risks represent an *average* of the mortality risks for patients in the Stable HF1, Stable HF2, Stable HF3, and Stable HF4 states, whereas our model is parameterised with age-specific mortality rates for Stable HF1, and hazard ratios for the other Stable HF states (see section 6.3.3). Lahoz et al. 2020[132] reports that the percentage of patients with 0, 1, 2, ≥3 recurrent HFHs are 71.58%, 18.2%, 6.02%, and 4.2% respectively. We estimated the age-specific monthly mortality rate in the Stable HF1 state required to give a weighted average rate to match that used in the Cowie models, by calculating a correction factor of the weighted HR for Stable HF1 divided by the average weighted HRs across the states: 0.7158/(0.7158*1 + 0.182*1.98 + 0.602*2.39 + 0.042*3.56) = 0.5227. This was then applied to the monthly rates from Cowie which were then transformed to give monthly probabilities of mortality, as set out in Table 17.

**Table 17 Monthly mortality risk used in the Cowie models, based on Griffiths et al. 2014, the corresponding monthly mortality rates, and with a correction factor applied to represent the monthly mortality rates and probabilities in the Stable HF1 state**

| Age-range | Monthly mortality probability | Monthly mortality rate | Corrected monthly mortality rate | Corrected monthly mortality probability |
|---|---|---|---|---|
| 60-65 | 0.0046 | 0.004611 | 0.00241 | 0.002407 |
| 65-70 | 0.00698 | 0.007004 | 0.003661 | 0.003654 |
| 70-75 | 0.01044 | 0.010495 | 0.005485 | 0.00547 |
| 75-80 | 0.01566 | 0.015784 | 0.008249 | 0.008216 |
| 80-85 | 0.02136 | 0.021591 | 0.011285 | 0.011221 |
| 85-90 | 0.02301 | 0.023279 | 0.012167 | 0.012093 |
| 90+ | 0.01864 | 0.018816 | 0.009834 | 0.009786 |

#### 6.3.3.3 Relative effects of routine PAP monitoring on all-cause mortality

The meta-analysis of all-cause mortality for CardioMEMS relative to usual monitoring for the NYHA class III subgroup data gave a hazard ratio of 0.91 95%CI (0.70, 1.17) (Section 5.5.1.2,

Figure 3). The direction of the estimated hazard ratios varied across studies, but in [redacted]. The model already indirectly accounts for a treatment effect on mortality because CardioMEMS reduces HFHs, and hence reduces the number of patients with more recurrent HFHs who have a higher mortality rate (Table 16). Due to there being no statistical evidence for an effect of CardioMEMS on all-cause mortality, and clinical advice that the main benefit of remote PAP monitoring is a reduction in HFHs, we follow the approach taken in the Cowie 2023 model by assuming the hazard ratio for mortality is 1. Whilst this assumes there is no *direct* effect of CardioMEMS on mortality, there is still an *indirect* effect as noted above. This approach has also been taken previously by Alcaraz 2021[64]. We run a scenario using the pooled hazard ratio for all-cause mortality from the meta-analysis reported in Section 5.5.1.2.

For Cordella, the only comparative evidence was from the initial stage of the PROACTIVE-HF trial[48] before it changed to a single-arm design. Endotronix provided the estimated hazard ratio for all-cause mortality in the randomised stage of the trial, which was 0.51 95%CI (0.20, 1.32). The very wide confidence interval which includes 1 (no effect) indicates the high level of uncertainty due to lack of robust comparative data on mortality for Cordella. Rather than use this very uncertain estimate we assumed that the hazard ratio was 1 for Cordella to match the assumption for CardioMEMS, since there was no reason to suppose that there would be a direct impact of Cordella on all-cause mortality when no such effect has been demonstrated for CardioMEMS. We use the CardioMEMS estimate of 0.91 in a scenario analysis.

### 6.3.4 Implant, device and sensor performance

#### 6.3.4.1 Implant failure

The proportion of procedures where the implant failed were based on the meta-analyses reported in section 5.5.1.3. The probability of implant failure for CardioMEMS was taken from the random effects model due to evidence of heterogeneity between studies giving an estimate of 0.017 (95% CI 0.008, 0.029). For Cordella the fixed effect model was used due to insufficient evidence to estimate heterogeneity, giving an estimate of 0.049 (95% CI 0.031, 0.070) for Cordella.

#### 6.3.4.2 Sensor failure

The clinical review found that sensor failure for both CardioMEMS and Cordella was very rare (section 5.5.1.4). We therefore did not include sensor failure in our base-case model. We ran a scenario where there was a small probability of sensor failure after which patients switch to the hospitalisation rates of routine monitoring. We use a probability of sensor failure of 0.01 at 1 year in the scenario based on the COAST-UK study, which had the highest annual sensor failure rate.

#### 6.3.4.3 Device or system related complications (DSRC)

The probabilities of DSRC were based on the meta-analyses reported in section 5.5.1.5. For CardioMEMS a random effects model was fitted due to evidence of heterogeneity, giving an estimate of 0.007 (95% CI 0.003, 0.013). For Cordella the fixed effect model was used due to insufficient evidence to estimate heterogeneity, giving an estimate of 0.001 (95%CI 0.000, 0.009). In a scenario we use a value of 0.007 for Cordella based on the meta-analysis excluding SIRONA.

#### 6.3.4.4 Adherence

Adherence to using both devices was generally good (section 5.5.2.6). Because the outcomes from the clinical studies correspond to the adherence rates observed in those clinical studies, the impact of adherence is already accounted for over the duration of the study follow-ups. We therefore did not include adherence in our base-case. However, we ran scenario analyses where a proportion of patients do not continue to use the sensor after 1 year in the model.

### 6.3.5 Utilities

#### 6.3.5.1 Health-state utilities

The Cowie model used EQ-5D data directly from the CHAMPION study for each arm for the first 12 months of the model, then applied a 0.08 reduction per year. This has the advantage of reflecting the HRQoL for CardioMEMS and standard care for the patient trajectories that were observed in CHAMPION, however, it does require extrapolation. Furthermore, the utilities from CHAMPION are specific to CardioMEMS and so cannot be applied for Cordella, and our model has health states that depend on number of previous HFHs, which are expected to differ in utilities. We therefore took a different approach to modelling utilities based on the number of previous HFHs.

In our base-case we assume that the utility for a patient in the Stable-HF state is 0.66 95%CI (0.60, 0.70) based on a meta-analysis of utilities for HF patients.[137] This figure is also in line with the baseline utilities observed in the MONITOR-HF study (mean EQ-5D 0.665 with an adjustment to the Dutch value set to obtain UK relevant values), which was considered the most relevant RCT to a European population. For the Stable-HF2, Stable-HF3, and Stable-HF4 health states we apply the utility reductions estimated by Gohler et al 2009 for patients with 1, 2, and 3+ re-hospitalisations respectively (Table 18).[109] We use these values in our base-case. As patients progress through the Stable-HF states their utility will decline, and so there will be an average fall in utility over time in our model. We therefore do not include a further utility reduction over time.

**Table 18 Impact of re-hospitalisations on EQ-5D utilities from Gohler et al.**

| State | Utility reduction Mean (se) | Health-state utility (se) | 95% CI |
|---|---|---|---|
| STABLE-HF | Reference | 0.660 (0.026) | (0.600, 0.700) |
| STABLE-HF2 | -0.024 (0.007) | 0.636 (0.026) | (0.584, 0.688) |
| STABLE-HF3 | -0.031 (0.009) | 0.629 (0.027) | (0.576, 0.682) |
| STABLE-HF4 | -0.055 (0.001) | 0.605 (0.026) | (0.555, 0.655) |

In a scenario analysis we use the approach to utilities from the Cowie model for the first 12 months (Table 19), followed by a 0.08 reduction per year until 5-years, after which the utilities are set equal at 0.57 across arms with a 0.08 reduction per year. However, since the MONITOR-HF study also provides EQ-5D data, collected at baseline, 3, 6 and 12 months, in the Netherlands, which may be more representative of a European population, we also ran a scenario analysis using the MONITOR-HF utilities with the same extrapolation assumptions as used by the Cowie model. Because the MONITOR-HF utilities were valued with the Dutch value set, a correction to account for a UK population was applied (Table 19).[138] In a further scenario we used the utilities from MONITOR-HF for the first 12 months (Table 19), and then the health-state utilities in Table 18 thereafter.

**Table 19 Utilities for first 12 months from the Cowie model and from MONITOR-HF based on UK correction to the Dutch value set used in scenario analyses**

| Model parameter | Utilities based on Cowie 2023 | Utilities based on MONITOR-HF |
|---|---|---|
| Baseline (remote PAP monitoring) | | 0.665 |
| 1mo | 0.688 | |
| 3mo (remote PAP monitoring) | 0.646 | 0.676 |
| 6mo (remote PAP monitoring) | 0.617 | 0.677 |
| 12mo (remote PAP monitoring) | 0.653 | 0.688 |
| Baseline (standard of care) | 0.645 | 0.665 |
| 3mo (standard of care) | 0.569 | 0.622 |
| 6mo (standard of care) | 0.566 | 0.608 |
| 12mo (standard of care) | 0.547 | 0.607 |

#### 6.3.5.2 Disutility for HFH

Previous models have used a disutility for HFH of 0.1 for a 1-month period based on an assumption that a hospitalisation would have a similar impact on HRQoL as moving to the next NYHA class (class III to class IV).[82] The Cowie model applied the impact of hospitalisation from 5 years onwards only, because the impact of hospitalisations is already captured in their trial data. The HTW model instead used a fixed utility for the HF-STABLE state and applied the disutility for HF-hospitalisation throughout the duration of their model in their base-case. We also include a disutility for a single cycle for each HFH, which is incurred in addition to the reduction in health-state utility for patients based on how many HFHs they have had. We did not identify any relevant evidence on which to base this disutility, and so assume a value of 0.1 for 1 month, in line with previous models. We run a scenario analyses with the value of 0.1 for a 2 month period.

#### 6.3.5.3 Carer disutilities

We identified two studies that reported HRQoL for carers of patients with HF. Iqbal et al. 2010[139] collected data from 131 carers of HF patients (41% NYHA class ≥III) in Scotland. They found that HRQoL measure for correlated with the HRQoL of the patient, with a mean EQ-5D-3L score of 0.72 (se=0.01) for carers of patients with poor HRQoL (below median) compared with 0.83 (se=0.01) for carers of patients with higher HRQoL (above median). However, note that it would be expected that patients and their carers HRQoL would be correlated due to common confounders, and so this does not represent an effect of the impact of change in patient HRQoL on carer HRQoL. Iqbal also reported that carer quality of life depended on the patient's NYHA class, although did not provide any estimates of effect. Lahoz et al 2021[140] collected HRQoL data from 361 carers (30% NYHA class ≥ III) in 5 European countries (including UK) but found there was no impact of NYHA class on carer EQ-5D, although there was an effect on the Family Caregiver-Specific Quality of Life Scale (FAMQOL).

Whilst caring for a patient with HF clearly impacts carer HRQoL, the only relevant effects to include in our model are those that differ by monitoring strategy, i.e. HFH rate. Neither of the studies that we identified presented results for carer HRQoL according to HFHs, and so we were not able to include this in our model. We acknowledge this as a possible limitation of the

model, but note carer disutility has also not been included in any of the previous models of remote PAP monitoring.

### 6.3.6 Resource use and costs

Resource use and costs were obtained from routine NHS sources (NHS National Cost Collection, Personal Social Services Research Unit (PSSRU), British National Formulary (BNF)), our reviews of previous cost-effectiveness models, targeted literature searches, and through discussions with the manufacturers and clinical advisors. We did not include costs that are incurred regardless of monitoring strategy. Costs are based on the year 2023/24.

#### 6.3.6.1 Device-related costs

**Device and equipment costs**

Costs of the CardioMEMS device included the delivery system and sensor, a patient unit, ongoing access to the Merlin.net platform and training for physicians on both the implantation and the Merlin platform. A cost for the CardioMEMS reusable calibration unit for use in the hospital was supplied by the manufacturer. In our base-case we assumed this cost to be included within the HRG cost for implantation. In a scenario analysis we include a rough estimate of the cost of the calibration unit per patient. To obtain this we estimated the annual number of eligible patients per hospital per year as 233,320*0.323/(4*335) = 56.24, based on patients who survived an index heart failure admission across 335 NHS hospitals between Jan 1, 2019, and Dec 31, 2022NHS data (Fletcher et al 2024).[187] If the calibration unit lasts for 10 years, then this would give a per patient cost of [redacted](56.24*10) which is approximately [redacted]. This is only indicative, based on some strong assumptions, and doesn't account for the proportion of eligible patients who decline the implantation or annuitizing the cost.

Costs for Cordella are unknown as yet, but will include delivery system and sensor, patient reader and reader dock, access to the Cordella Heart Failure System, and *ad hoc* training on implantation and the Cordella Heart Failure System. For illustration we assume that the cost of Cordella is the same as for CardioMEMS. Both devices are assumed to remain implanted for the lifetime of the patient.

**Procedure costs to implant the device**

Costs for insertion of the device were calculated as a weighted average of the Standard Cardiac Catheterisation costs (HRGs EY43A to EY43F) carried out as a day case procedure (from National Cost Collection Admitted Patient Care data) for both Cordella and CardioMEMS. Consumables for implantation (*e.g.* guidewires) were assumed to be included within the HRG cost.

Implantation failure was costed on the basis of a repeat day case insertion, plus an additional cost to account for wasted devices. Of those cases with implantation failure, devices were assumed to be opened but unusable in 6/25 (24%) of cases (based on CHAMPION data), with recharges (the full device cost) applied in half of these cases. Clinical input suggested that most of the reasons given in CHAMPION were device-related or complications that were unpredictable in advance; we therefore run scenario analyses with all or none of the devices recharged.

**Device monitoring costs**

Ongoing monitoring of the device output was derived based on the routine monitoring being carried out by a band 5 nurse or band 5 cardiac physiologist (in equal proportions, costed using data from the Unit Costs of Health and Social Care 2024, without the inclusion of qualification costs). The length of time required was assumed to be 10 minutes per patient per check, with three checks carried out per week (both based on clinical advice). Five minutes per month of a medical consultant was added for oversight, in line with the time used in the Welsh model. We conducted scenario analyses based on the frequency of monitoring recommended by the manufacturers (a minimum of twice weekly for Cordella; twice weekly during modification periods, with each patient assumed to have 3 months of modification periods in a year, then at least once a month during stable periods for CardioMEMS). Based on clinical opinion that the consultant oversight time might be an underestimate, we also conducted a scenario analysis with 15 minutes per month of a medical consultant.

**Costs under standard care**

Standard care during stable periods was assumed to include outpatient follow-up and ongoing medications. Each patient was assumed to have had one outpatient follow-up appointment per year (clinician advice), which was costed using National Cost Collection data for a consultant-led cardiology attendance (non-admitted, face-to-face, £180). Patients were assumed to be taking medications in the proportions at baseline observed in the PROACTIVE-HF trial (the most recently available data, reflecting contemporary medication approaches). Medications were mapped to British National Formulary entries and costed using the online drug tariff prices in July 2025 and converted to 2024 prices using Office for National Statistics (ONS) data for pharmaceutical products;[141] mapping accuracy was checked with a clinician (monthly medication costs of £76). The average monthly cost for usual care is therefore £180/12 + £76 = £91. In a scenario analysis patients were assumed to have 6 outpatient appointments per year, giving an average monthly cost of £180*6/12 + £76 = £166.

Clinical advice was that the main medication change resulting from remote PAP monitoring would be diuretics. Owing to the low cost of these medications we did not include a cost of medication changes resulting from monitoring, which is in line with previous economic models of remote PAP monitoring.

#### 6.3.6.2 HFH costs

Hospitalisation costs were derived from National Cost Collection data. All hospitalisations were assumed to last for more than 2 days (clinical advice was that the average was around 9 days),[8] and a weighted average of HRGs for Heart Failure or Shock (EB03) was taken using long-stay non-elective inpatient events. Complication and comorbidity (CC) scores were assumed to increase with the number of subsequent hospitalisations. No patients were assumed to have CC scores of 1-3, as all had previously had a hospital admission. The first HFH post-insertion of the device was based on EB03C and EB03D (CC score of 4-10), the second post-insertion HFH was based on EB03B and EB03C (CC score of 8-13), and third and subsequent HFHs were based on EB03A and EB03B (CC score of 11-14+).

#### 6.3.6.3 Device or system-related complications

As HF complications are accounted for in the HRGs from which the hospitalisation costs are derived, they were not costed separately. In the base case, we also assumed that device or system-related complications (DSRCs) were captured in the hospitalisation HRGs. We mapped

the DSRCs reported in MONITOR-HF, PROACTIVE-HF and MEMS-HF to complications listed in the HRG4+ National Costs Groupers casemix listing (EB_CC)[142] where possible to find the score that contributed to the HRG split. We assumed that unmapped DSRCs (6/11) had CC scores of 1 (4/5 of the mapped CCs and nearly 90% of all CC scores for EB_CC were 1, with 1/5 of the matched CCs having a score of 2). We assumed that each additional score of 1 contributed £39 to the HRG based on the difference between EY43C and EY43D day case insertion, where an additional CC score of 3 led to an increase in costs of £118. In scenario analysis, we applied a cost of £39 to each DHRC, to take account of the fact that we could not be sure that all the complications listed were captured in the HRGs.

**Table 20 Summary of model inputs, values and distribution assumed in base-case analysis, and source of evidence. Each parameter was estimated separately, and so model parameters assumed to be independent in the PSA.**

| Model parameter | Value in base-case | Distribution for PSA | Evidence source |
|---|---|---|---|
| **Population and natural history parameters** | | | |
| Mean age<br>% female | 69 years<br>30% | N/A<br>N/A | COAST UK cohort[50] |
| HFH annualised rate in Stable HF1: standard care | 0.858 | 95% CI (0.7317, 0.9993)<br>Normal distribution for log-rate with mean= -0.153 and se=0.0795 | Estimated to give an average HFH rate over number of recurrent HFHs to match the rate in the COAST UK cohort[50], using HRs and weights from Lahoz et al. 2020[132] (section 6.3.2.2) |
| Hazard ratio for HFH: patients with 1 vs 0 recurrent HFH (stable HF2 vs stable HF1) | 1.70 | Normal distribution for log-hazard ratio with mean 0.532 and se= 0.0675 | Lahoz et al. 2020[132] |
| Hazard ratio for HFH: patients with 2 vs 0 recurrent HFH ((stable HF3 vs stable HF1) | 1.86 | Normal distribution for log-hazard ratio with mean 0.619 and se= 0.0953 | Lahoz et al. 2020[132] |
| Hazard ratio for HFH: patients with 3 vs 0 recurrent HFH (stable HF4 vs stable HF1) | 3.11 | Normal distribution for log-hazard ratio with mean 1.134 and se= 0.1613 | Lahoz et al. 2020[132] |
| Monthly mortality risk in Stable HF1: standard care | | | |
| 65-70 years | 0.003654 | Normal distribution with mean equal to the probability and the se equal to 10% of the mean | Estimated to give an average age-specific mortality rate over number of recurrent HFHs to match the rates Griffiths et al. 2014[79], using HRs and weights from Lahoz et al. 2020[132] (section 6.3.3.2) |
| 70-75 years | 0.00547 | | |
| 75-80 years | 0.008216 | | |
| 80-85 years | 0.011221 | | |
| 85-90 years | 0.012093 | | |
| 90+ years | 0.009786 | | |
| Hazard ratio for mortality: patients with 1 vs 0 recurrent HFH (stable HF2 vs stable HF1) | 1.98 | 95% CI for HR (1.81, 2.17)<br>Normal distribution for log-hazard ratio with mean= 0.683 and se=0.0463 | Lahoz et al. 2020[132] |
| Hazard ratio for mortality: patients with 2 vs 0 recurrent HFH ((stable HF3 vs stable HF1) | 2.39 | 95% CI for HR (2.08, 2.74)<br>Normal distribution for log-hazard ratio with mean=0.871 and se=0.0703 | Lahoz et al. 2020[132] |

| Model parameter | Value in base-case | Distribution for PSA | Evidence source |
|---|---|---|---|
| Hazard ratio for mortality: patients with 3 vs 0 recurrent HFH (stable HF4 vs stable HF1) | 3.56 | 95% CI for HR (2.92, 4.34)<br>Normal distribution for log-hazard ratio with mean=1.270 and se=0.1011 | |
| **Relative effects** | | | |
| Hazard ratio for hospitalisation CardioMEMS vs standard care | 0.66 | 95% CI for HR (0.57, 0.76)<br>Normal distribution for log-hazard ratio with mean= -0.4155 and se=0.0734 | Meta-analysis of CHAMPION, GUIDE-HF, and MONITOR-HF (section 5.5) |
| Hazard ratio for hospitalisation Cordella vs standard care | 0.61 | 95%CI (0.36, 1.04)<br>Normal distribution for log-hazard ratio with mean= -0.4943 and se=0.2706 | Hazard ratio from comparative phase of PROACTIVE-HF [48] , provided by Endotronix |
| Hazard ratio for mortality CardioMEMS vs standard care | 1 | N/A | Assumption in line with Cowie 2023[68] |
| Hazard ratio for mortality Cordella vs standard care | 1 | N/A | Assumption |
| **Device and procedure performance** | | | |
| Probability of sensor failure | 0 | N/A | Meta-analysis (see section |
| Probability of implant failure: CardioMEMS | 0.017 | 95% CI (0.008, 0.029)<br>Normal distribution for log-odds of implant failure with mean=-4.0574<br>and se=0.3340 | Meta-analysis (see section 5.5.1.36.3.4.1 ) |
| Probability of implant failure: Cordella | 0.049 | 95% CI (0.031, 0.070)<br>Normal distribution for log-odds of implant failure with mean=-2.9657 and se=0.21826 | Meta-analysis (see section 5.5.1.3) |
| Probability of device or system related complication: CardioMEMS | 0.007 | 95%CrI (0.003, 0.013)<br>Normal distribution for log-odds of DSRC with<br>Mean= -4.9548<br>and se=0.37664 | Meta-analysis (see section 5.5.1.5) |

| Model parameter | Value in base-case | Distribution for PSA | Evidence source |
|---|---|---|---|
| Probability of device or system related complication: Cordella | 0.001 | 95%CrI (0.000, 0.009)<br>Normal distribution for log-odds of DSRC with<br>mean= -6.90675 and se=1.15019 | Meta-analysis (see section 5.5.1.5) |
| **Resource use and costs** | | | |
| Cordella device | £9500 | Assumed to be fixed in the PSA | Assumed equal to CardioMEMS |
| CardioMEMS device | £9500 | Assumed to be fixed in the PSA | Manufacturer |
| Implantation | £1631 | Gamma distribution α = 1631 , β =1 | National Cost Collection |
| Implantation failure (Cordella) | £2771 | Gamma distribution α = 2771 , β =1 | Assumed equal to CardioMEMS |
| Implantation failure (CardioMEMS) | £2771 | Gamma distribution α = 2771 , β =1 | National Cost Collection |
| Monitoring (per month) | £101 | Gamma distribution α = 101 , β =1 | PSSRU |
| Usual care (per month) | £91 | Gamma distribution α = 91 , β =1 | National Cost Collection, British National Formulary |
| HF-related hospitalisations (HFH) | | | |
| First post-insertion HFH | £3242 | Gamma distribution α = 3242 , β =1 | National Cost Collection |
| Second post-insertion HFH | £3874 | Gamma distribution α = 3874 , β =1 | |
| Third and subsequent post-insertion HFH | £4844 | Gamma distribution α = 4844 , β =1 | |
| Utilities | | | |
| STABLE-HF | 0.660 | 95%CI (0.600, 0.700)<br>Normal distribution with se=0.026 | Santos et al |
| STABLE-HF2 | 0.636 | 95%CI (0.584, 0.688)<br>Normal distribution with se=0.026 | Gohler et al |
| STABLE-HF3 | 0.629 | 95%CI (0.576, 0.682)<br>Normal distribution with se=0.027 | Gohler et al |
| STABLE-HF4 | 0.605 | 95%CI (0.555, 0.655)<br>Normal distribution with se=0.026 | Gohler et al |
| Disutility for HFH | 0.1 | | Yao et al |

## 6.4 Subgroup and scenario analyses

### 6.4.1 Subgroup analyses

We explored the value of conducting subgroup analyses by age, baseline PAP, and kidney function.

#### 6.4.1.1 Age

MONITOR-HF was the only study to provide a subgroup analysis for HFH by age, and found no evidence of a difference in the hazard ratio for CardioMEMS vs control in those <69.4 years (HR 0.49 (0.28, 0.87)) compared with those >=69.4 years (HR 0.64 (0.38, 1.08)). [143] We felt it would be misleading to conduct a subgroup analysis by age, due to the overlapping confidence intervals. Instead, we ran a scenario analysis varying the mean age of the modelled population.

#### 6.4.1.2 Baseline PAP

CHAMPION was the only study to provide a subgroup analysis for HFH by baseline PAP measurement, and found no evidence of a difference in the hazard ratio for CardioMEMS vs control in those with baseline PAP<= 0.583 (HR 0.73 (0.57, 0.94)) compared with those with baseline PAP>0.583 (HR 0.57 (0.42, 0.76)).[144] Again, due to the overlapping confidence intervals, we did not feel it appropriate to conduct a subgroup analysis by baseline PAP. However, baseline PAP is a prognostic factor for HFH. We explored the impact of this using a scenario analysis varying the baseline HFH rate.

#### 6.4.1.3 Kidney function

The only kidney function variable explored in subgroup analyses for HFH was eGFR in MONITOR-HF, which found no evidence of a difference in the hazard ratio for CardioMEMS vs control in those with eGFR >= 60 ml/min (HR 0.40 (0.16, 0.99)) compared with those with eGFR< 60 ml/min (HR 0.61 (0.39, 0.95)). [143] We felt it would be misleading to conduct a subgroup analysis by eGFR, due to the wide and overlapping confidence intervals. However, eGFR may be a prognostic factor for HFH. We explored the impact of this using a scenario analysis varying the baseline HFH rate.

### 6.4.2 Scenario analyses

Scenario analyses were conducted to explore the sensitivity of results to key model assumptions, summarised in Table 21 together with a rationale for each scenario. All scenarios were conducted using deterministic analyses, and compared with the deterministic base-case.

**Table 21 List of scenario analyses included**

| Scenario | Description | Base-case | Scenario Analysis | Rationale for analysis |
|---|---|---|---|---|
| 1a | Mean age from MEMS-HF[49] | 69 years | 67.2 years | Mean age varied across studies. This is the lowest mean age across studies (Table 15) |
| 1b | Mean age from SIRONA-2/SIRONA-2[47, 133] | 69 years | 71 years | Mean age varied across studies. This is the highest mean age across studies (Table 15) |
| 2a | Annual HFH rate for Stable HF1 under standard care based on Cowie 2023 | Rate=0.8582<br>Log-rate= -0.153 | Rate=0.6165<br>Log-Rate= -0.484 | To explore the impact of a lower HFH rate the average value from Cowie 2023 model, with a correction factor described in section 6.3.2.2 applied. |
| 2b | Annual HFH rate for Stable HF1 under standard care based on upper limit from COAST UK 95%CI | Rate=0.8582<br>Log-rate= -0.153 | Rate=0.9993<br>Log-rate= 0.001 | Using the upper confidence limit (with a correction factor described in section 6.3.2.2 applied) from the UK cohort of the COAST study as a proxy for a higher risk population |
| 3 | Mortality HR from the meta-analysis for CardioMEMS is used | HR=1 | HR=0.91 | No direct effect of CardioMEMS or Cordella on mortality included in base-case as the results from the meta-analysis have a confidence interval which crosses 1, and indirect mortality benefit included through number of HFH. In the scenario the HR from the meta-analysis for CardioMEMS is used. Note this will be in addition to the indirect effect via number of HFH. |
| 4 | Including a probability of sensor failure at 12 months | 0 | 0.01 | Sensor failure was very rare. We use the 12 month probability of sensor failure from COAST-UK in this scenario, which had the highest annual sensor failure rate. Those with sensor failure switch to routine monitoring in the model after 12 months. |
| 5a | Adherence drop off at 1 year: 5% | No drop off (100% adherence) | 95% adhere from 12 months onwards | To explore the impact of patients stopping using the device to send readings over time. Those that do not adhere switch to routine monitoring in the model. |
| 5b | Adherence drop off at 1 year: 10% | No drop off (100% adherence) | 90% adhere from 12 months onwards | To explore the impact of patients stopping using the device to send readings over time. Those that do not adhere switch to routine monitoring in the model. |
| 6a | Using the utility assumptions from the Cowie model with inputs from CHAMPION for CardioMEMS | Utilities based on number of HFHs | Utilities from CHAMPION used in first 12months (Table | To explore the sensitivity of results to the modelling approach used for utilities. |

| Scenario | Description | Base-case | Scenario Analysis | Rationale for analysis |
|---|---|---|---|---|
| | | | 19), with extrapolation from Cowie model | |
| 6b | Using the utility assumptions from the Cowie model with inputs from MONITOR-HF for CardioMEMS | Utilities based on number of HFHs | Utilities from MONITOR-HF used in first 12months (Table 19), with extrapolation from Cowie model | To explore the sensitivity of results to the modelling approach used for utilities. |
| 6c | Using utilities from MONITOR-HF for CardioMEMS in the first 12 months, then state based utilities after 12 months | Utilities based on number of HFHs | Utilities from MONITOR-HF used in first 12months (Table 23), with base-case utilities after 12 months | To explore the sensitivity of results to the modelling approach used for utilities. |
| 7a | Monthly monitoring costs using company suggested frequencies | CardioMEMS: £101<br>Cordella: £101 | CardioMEMS: £27<br>Cordella: £69 | CardioMEMS: Company advice is at least twice per week during medication modification periods, then at least once per month<br>Cordella: Company advice is at least twice per week |
| 7b | Monitoring costs using band 6 healthcare professional | £101 | £126 | Clinical opinion that more senior staff may deal with the ongoing monitoring |
| 7c | Monitoring costs using 15 minutes consultant time per month | £101 | £112 | Clinical advice was that 5 mins per month may be an underestimate |
| 8a | Charging for wasted devices: None charged | £2771 | £1631 | Charging for wasted devices is dealt with on a case-by-case basis: no charges is best case scenario |
| 8b | Charging for wasted devices: All charged | £2771 | £3911 | Charging for wasted devices is dealt with on a case-by-case basis: all charged is worst case scenario |
| 9a | Additional cost of device or system related complications | £0 | £39 | Complications listed could not all be identified as HRG complications; use of HRGs can obscure differences between interventions that lead to additional complications. |

| Scenario | Description | Base-case | Scenario Analysis | Rationale for analysis |
|---|---|---|---|---|
| 9b | DSRC rate for Codella based on meta-analysis with SIRONA removed | 0.001 | 0.007 | SIRONA is a small study with short follow-up, so we ran a scenario analysis excluding it. |
| 10 | Disutility for HFH lasts for 2 months | 0.1 for 1 month | 0.1 for 2 months | There is no data on this disutility. This uncertainty is explored by assuming the disutility lasts for longer. |
| 11 | Alternative cost of usual care, with 6 appointments over a year | £91 | £166 | Stakeholder comment #8 suggests the usual care cost would be higher. |
| 12 | Inclusion of the re-calibration unit costs | £0 | [redacted] | Cost was omitted in error in base-case. Scenario including this costs added in response to stakeholder comments. |

## 6.5 Model Results

### 6.5.1 Deterministic base-case analyses

The deterministic base case results are shown in Table 22, and the fully incremental analysis is shown in Table 23. All the results for Cordella are presented assuming equivalence of device related costs with CardioMEMS as described in section 6.3.6.1, but this is a strong assumption and so interpretation of the cost-effectiveness results should focus on CardioMEMS and Standard case, with results for Cordella as illustrative only. The results show that in the base case CardioMEMS produced an ICER of £41,569 vs standard care. The analysis for Cordella resulted in a ICER of £31,257 vs standard care. The fully incremental analysis first compared Cordella with standard care and produced an ICER of £31,257. CardioMEMS was then compared with Cordella and found to be strictly dominated with positive incremental costs and negative incremental QALYs – however this finding relies on strong assumptions for Cordella.

**Table 22 Results from the deterministic base case**

| Monitoring strategy | Total costs | Total LYs | Total QALYs | Incremental costs vs standard care | Incremental QALYs vs standard care | ICER vs standard care |
|---|---|---|---|---|---|---|
| CardioMEMS | £39,293 | 4.99 | 3.12 | £10,352 | 0.25 | £41,569 |
| Cordella | £38,408 | 5.06 | 3.17 | £9,468 | 0.30 | £31,257 |
| Standard Care | £28,940 | 4.65 | 2.87 | - | - | - |

**Table 23 Fully incremental analysis of the deterministic base case**

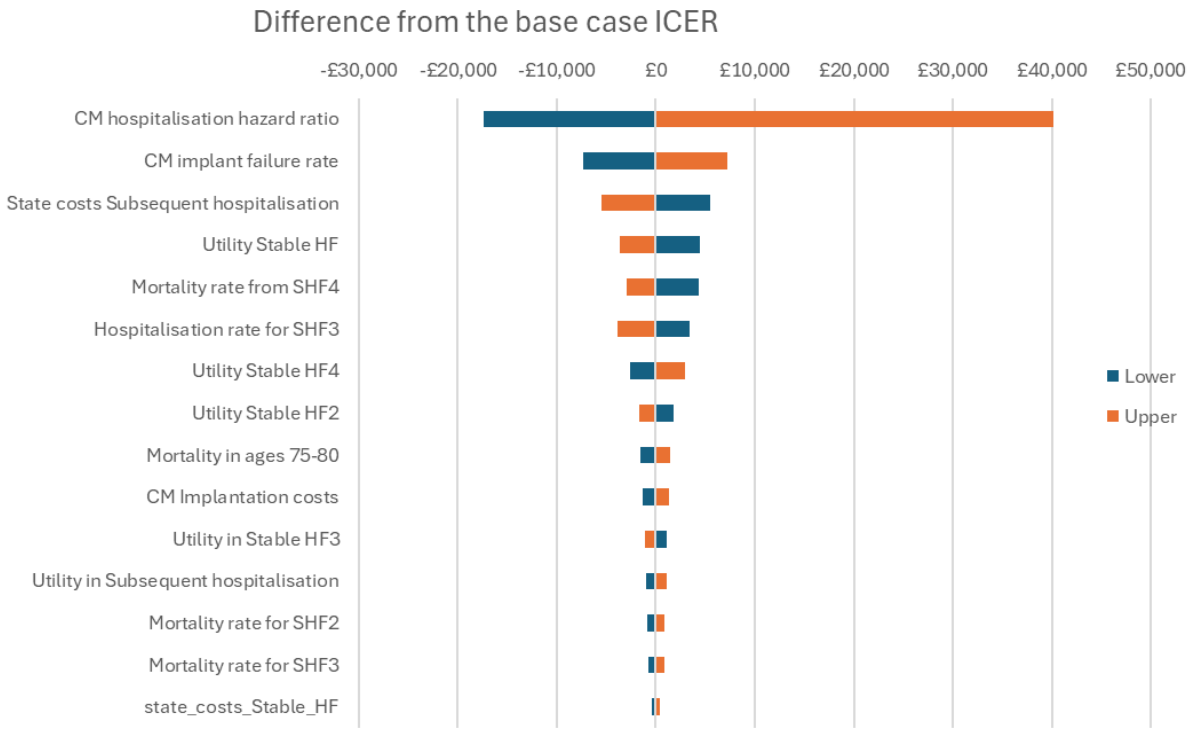
| Monitoring strategy | Total costs | Total LYs | Total QALYs | ICER vs standard care | ICER vs Cordella |
|---|---|---|---|---|---|
| Standard Care | £28,940 | 4.65 | 2.87 | - | - |
| Cordella | £38,408 | 5.06 | 3.17 | £31,257 | - |
| CardioMEMS | £39,293 | 4.99 | 3.12 | £41,569 | Strictly dominated by Cordella |

### 6.5.2 Deterministic sensitivity analyses

The results from the deterministic sensitivity analysis are displayed in a tornado plot (Figure 14) for CardioMEMS versus Standard Care, for the 15 parameters that had the largest impact on the ICER. The clinical effectiveness on HFH had the largest impact on the ICER with the CardioMEMS hazard ratio lower bound lowering the ICER by over £17,000 and the upper bound increasing it by over £40,000.

All other variables included in the deterministic sensitivity analysis had a less than £10,000 impact on the ICER, with implant failure rate having the biggest impact on the ICER, followed by the costs for 3rd or more recurrent HFHs.

**Figure 14 Tornado plots for CardioMEMS vs Standard care**




### 6.5.3 Probabilistic analysis

The probabilistic base case results are shown in Table 24, and the fully incremental analysis is shown in Table 25. The results show that similar cost-effectiveness results to the deterministic base case, with CardioMEMS producing an ICER of £41,878 versus standard care. With the assumed equivalence of  device related costs for Cordella with CardioMEMS, Cordella had a lower ICER versus standard care of £31,541, but this is based on strong assumptions for Cordella. Both the CardioMEMS and Cordella ICERs had probabilistic ICERs within £500 of their deterministic ICERs.  Total costs and QALYs are also similar in the probabilistic results compared with the deterministic base case after running the probabilistic analysis for 10,000 iterations.

The fully incremental analyses largely mirror the results of the deterministic incremental analysis, with Cordella being first compared with standard care. CardioMEMS is strictly dominated when compared with Cordella with positive incremental costs and lower incremental QALYs, however this finding relies on strong assumptions for Cordella.

Figure 15 and Figure 16 show the cost-effectiveness planes for CardioMEMS and Cordella respectively. The cost-effectiveness plane for CardioMEMS shows a wide spread of iterations that lie above and below the £30,000 and £20,000 willingness-to-pay thresholds, with a central clustering above the £30,000 threshold line. All iterations lay in the north-east quadrant of the cost-effectiveness plane. The figure for Cordella produced a larger spread of results with some iterations falling within the north-west and south-east quadrants of the cost-effectiveness plane, reflecting greater uncertainty in the Cordella treatment effect. However, the majority of iterations fell in the north-east quadrant with a central clustering just above the £30,000 willingness to pay threshold.

The cost-effectiveness acceptability curves are shown for CardioMEMS and Standard Care in Figure 17, and for all monitoring strategies in Figure 18. The CardioMEMS pairwise comparison shows a steady increase in the likelihood of cost-effectiveness when the willingness to pay threshold is increased between £25,000 and £50,000. At willingness to pay thresholds of £45,000 there is a high probability of being cost-effective.

When comparing all monitoring strategies, Cordella becomes more likely to be cost-effective than standard care at a willingness to pay threshold below £30,000, with CardioMEMS likely to become more cost-effective than standard care at just above £40,000 thresholds, however this finding is based on strong assumptions for Cordella.

**Table 24 Results from the probabilistic base case, based on strong assumptions for Cordella (10,000 iterations)**

| | Total costs | Total LYs | Total QALYs | Incremental costs | Incremental QALYs | ICER vs standard care |
|---|---|---|---|---|---|---|
| CardioMEMS | £39,518 | 5.003 | 3.128 | £10,389 | 0.248 | £41,878 |
| Cordella | £39,013 | 5.094 | 3.193 | £9,884 | 0.313 | £31,541 |
| Standard care | £29,129 | 4.667 | 2.880 | - | - | - |

**Table 25 Fully incremental analysis of the probabilistic base case, based on strong assumptions for Cordella (10,000 iterations)**

| | Total costs | Total LYs | Total QALYs | ICER vs standard care | ICER vs Cordella |
|---|---|---|---|---|---|
| Standard care | £29,129 | 4.667 | 2.880 | - | - |
| Cordella | £39,013 | 5.094 | 3.193 | £31,541 | - |
| CardioMEMS | £39,518 | 5.003 | 3.128 | £41,878 | Strictly dominated by Cordella |

**Figure 15 Cost- effectiveness plane for CardioMEMS vs Standard care (10,000 iterations) – with £20,000 and £30,000 willingness to pay threshold**

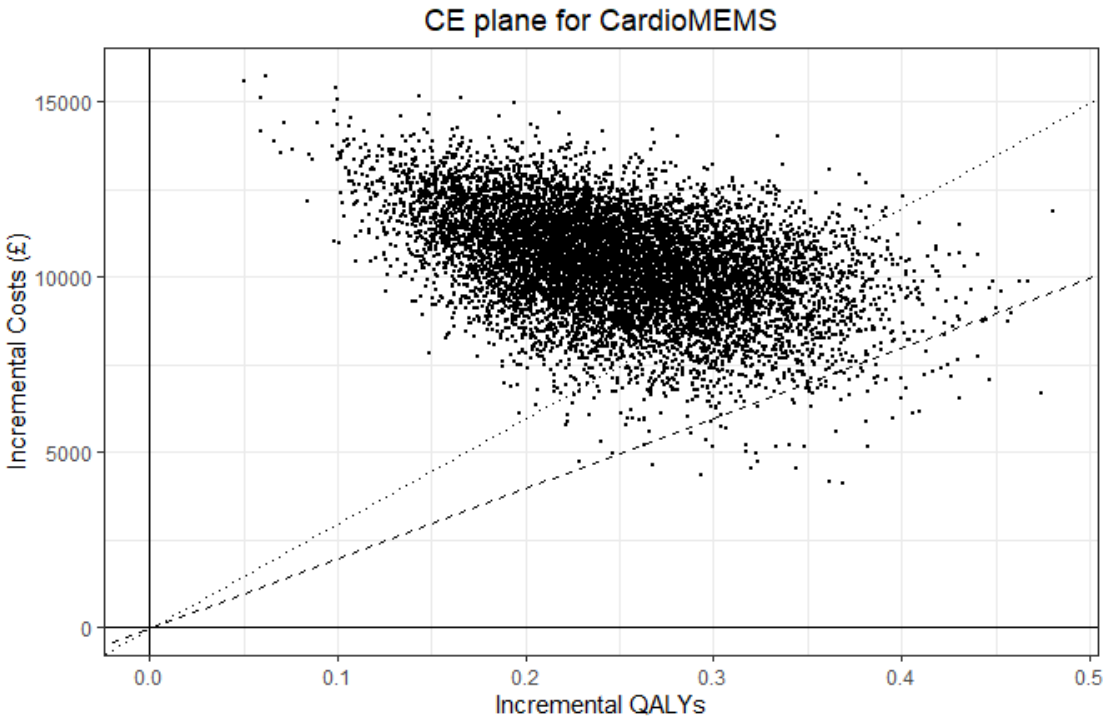



**Figure 16 Cost- effectiveness plane for Cordella vs Standard care (10,000 iterations) – with £20,000 and £30,000 willingness to pay thresholds**

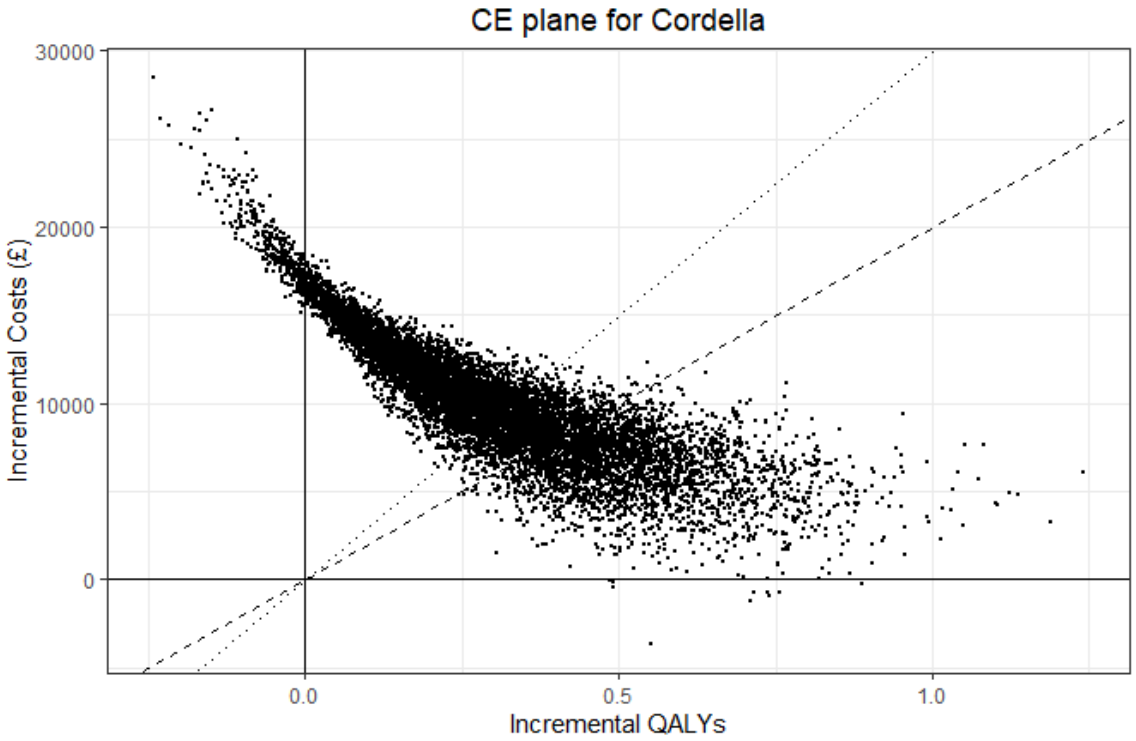


**Figure 17 CardioMEMS vs Standard care pairwise cost-effectiveness acceptability curve**

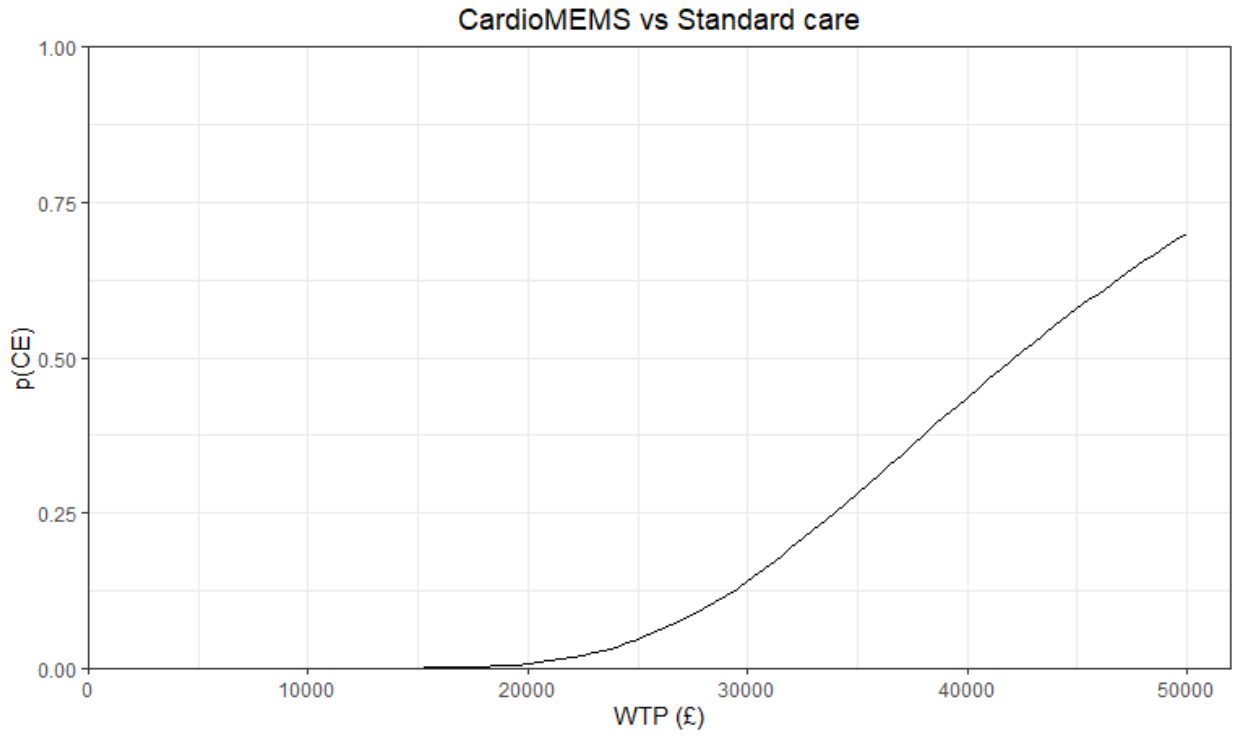
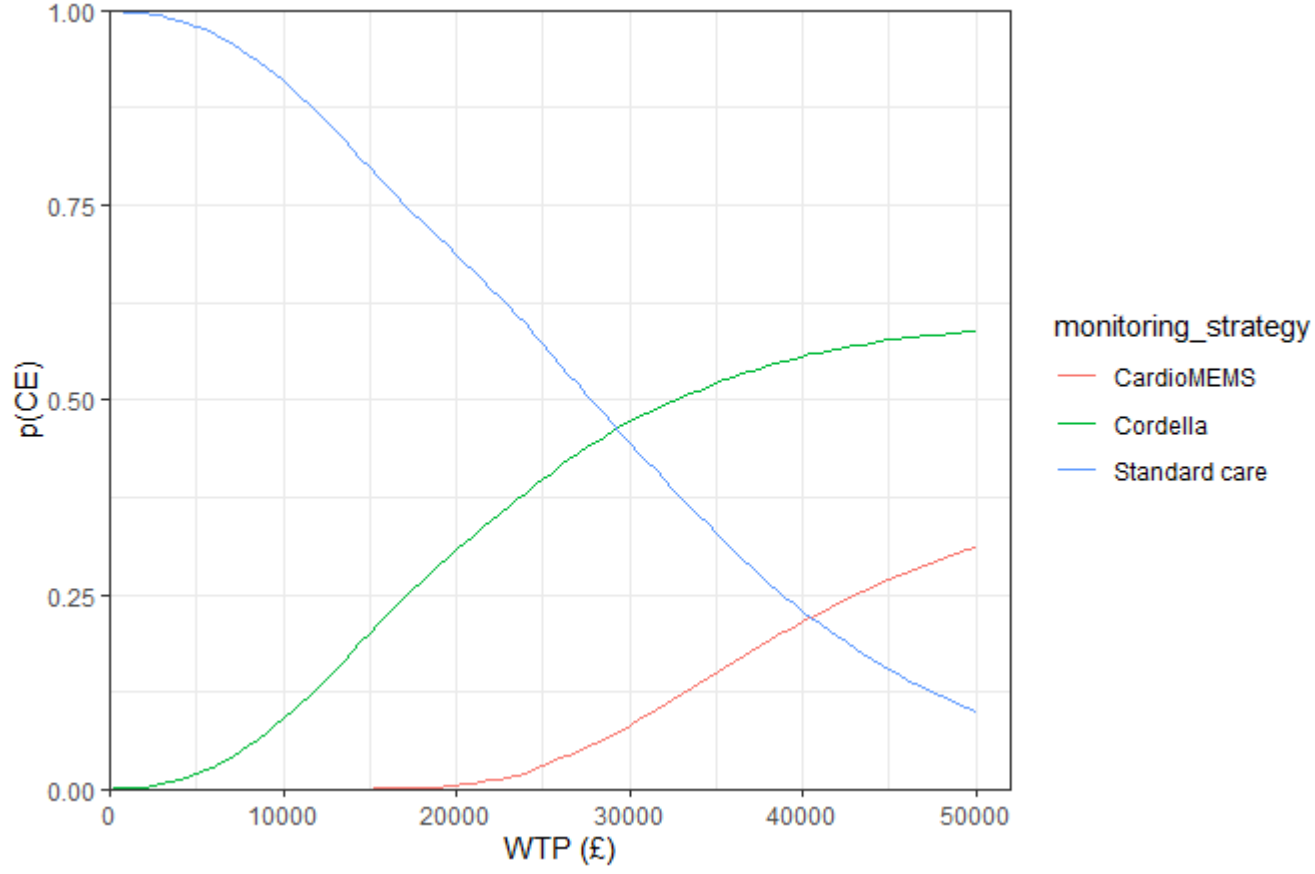



**Figure 18 Cost-effectiveness acceptability curve of all the monitoring strategies, based on strong assumptions for Cordella**



### 6.5.4 Scenario analyses

Table 26 reports the results of the scenario analyses with the results of the deterministic base case provided for reference. Mean age had a modest effect on the results, with a lower cohort age resulting in slightly lower ICERs and a higher cohort age resulting in higher ICERs for both monitoring interventions. Scenario 2 which explored the use of alternative HFH rates resulted in similar ICERs to the deterministic base case. Scenario 3 which uses a direct mortality benefit for both CardioMEMS and Cordella based on the meta-analysis for CardioMEMS, in addition to the indirect mortality benefit via number of recurrent HFHs, resulted in a large reduction in the ICERs as incremental QALYs increased for both monitoring interventions. Including sensor failure resulted in a moderate increase in the ICERs of both monitoring interventions. Scenario 5, which includes a monitoring adherence drop off after 1 year resulted in a moderate increase in the ICERs of both interventions. Scenario 6 explored the impact of using utilities collected in trials, and had the greatest impact on cost-effectiveness of the scenarios explored. Scenarios 6a and 6b used the approach to extrapolating utilities from the Cowie model with utilities for the first 12months from CHAMPION (Scenario 6a) and MONITOR-HF (Scenario 6b), which lead to a large reduction in the ICER, which was greatest when CHAMPION was used (Scenario 6a). In scenario 6c we used the MONITOR-HF utilities for the first 12 months, but used health-state based utilities for extrapolation, which led to a reduction in the ICER, but not as great a reduction as when the Cowie approach to extrapolation was used (scenarios 6a and 6b). Scenario 7 which explored the impact of monitoring costs also had a significant effect on cost-effectiveness with scenario 7a which lowers the monthly monitoring costs lowering cost-effectiveness for both monitoring strategies and 7b and 7c which raise the monthly monitoring costs leading to higher ICERs. Device-related costs (scenarios 8 and 9a) led to a small impact on the ICER. Excluding SIRONA from the meta-analysis of DSRC for Cordella had no impact on the results due to the very low likelihood of device or system related complications (scenario 9b. Extending the period of hospitalisation-related disutility to two months resulted in a slightly lower ICER for both monitoring strategies (scenario 10). Scenario 11 which explored the impact of alternative costs for usual care resulted in a small increase in ICERs and scenario 12 which included the cost of the recalibration unit for CardioMEMS resulted in a negligible increase in the ICER.

**Table 26 Scenario analyses with CardioMEMS and Cordella compared against standard care**

| | CardioMEMS | | | | | Cordella | | | | | Standard care | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Scenario** | **Total Costs (£)** | **Total QALYs** | **Incremental costs (vs SC) (£)** | **Incremental QALYs (vs SC) (£)** | **ICER vs SC (£)** | **Total Costs (£)** | **Total QALYs** | **Incremental costs (vs SC)(£)** | **Incremental QALYs (vs SC) (£)** | **ICER vs SC (£)** | **Total costs (£)** | **Total QALYS** |
| Base case | £39,293 | 4.99 | £10,352 | 0.25 | £41,569 | £38,408 | 5.06 | £9,468 | 0.30 | £31,257 | 29,129 | 2.880 |
| 1a - Mean age 67.2 | 41,856 | 3.360 | 9,976 | 0.245 | 40,686 | 40,844 | 3.414 | 8,964 | 0.299 | 29,958 | 31,880 | 3.115 |
| 1b – Mean age 71 | 36,880 | 2.891 | 10,535 | 0.239 | 44,045 | 36,096 | 2.943 | 9,752 | 0.291 | 33,505 | 26,344 | 2.651 |
| 2a - Cowie 2023 HFH rate | 35,688 | 3.361 | 12,400 | 0.295 | 41,991 | 35,096 | 3.423 | 11,807 | 0.357 | 33,046 | 23,289 | 3.065 |
| 2b – COAST HFH rate | 41,395 | 3.023 | 9,364 | 0.228 | 41,109 | 40,359 | 3.072 | 8,328 | 0.278 | 30,006 | 32,031 | 2.795 |
| 3 – Mortality HR from meta-analysis for CM | 40,897 | 3.270 | 11,956 | 0.399 | 29,986 | 39,939 | 3.325 | 10,998 | 0.453 | 24,267 | 28,940 | 2.872 |
| 4 – Including sensor failure | 39,362 | 3.118 | 10,422 | 0.246 | 42,289 | 38,488 | 3.171 | 9,547 | 0.299 | 31,881 | 28,940 | 2.872 |
| 5a – Adherence drop off 5% | 39,582 | 3.110 | 10,642 | 0.238 | 44,647 | 38,740 | 3.160 | 9,800 | 0.289 | 33,929 | 28,940 | 2.872 |
| 5b – Adherence drop off 10% | 39,871 | 3.100 | 10,931 | 0.228 | 47,934 | 39,073 | 3.147 | 10,133 | 0.275 | 36,795 | 28,940 | 2.872 |
| 6a – Trial utilities CHAMPION | 39,293 | 2.729 | 10,352 | 0.471 | 21,999 | 38,408 | 2.759 | 9,468 | 0.500 | 18,943 | 28,940 | 2.259 |
| 6b – Trial utilities | 39,293 | 2.855 | 10,352 | 0.403 | 25,667 | 38,408 | 2.885 | 9,468 | 0.433 | 21,845 | 28,940 | 2.452 |

| | CardioMEMS | | | | | Cordella | | | | | Standard care | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Scenario** | **Total Costs (£)** | **Total QALYs** | **Incremental costs (vs SC) (£)** | **Incremental QALYs (vs SC) (£)** | **ICER vs SC (£)** | **Total Costs (£)** | **Total QALYs** | **Incremental costs (vs SC)(£)** | **Incremental QALYs (vs SC) (£)** | **ICER vs SC (£)** | **Total costs (£)** | **Total QALYS** |
| MONITOR HF | | | | | | | | | | | | |
| 6c – Trial utilities ≤12 months, state utilities > 12 months | 39,293 | 3.144 | 10,352 | 0.291 | 35,596 | 38,408 | 3.197 | 9,468 | 0.344 | 27,522 | 28,940 | 2.853 |
| 7a – Company monthly monitoring costs | 34,862 | 3.121 | 5,921 | 0.249 | 23,777 | 36,463 | 3.175 | 7,523 | 0.303 | 24,837 | 28,940 | 2.872 |
| 7b – Monitoring costs band 6 professional | 40,789 | 3.121 | 11,849 | 0.249 | 47,579 | 39,927 | 3.175 | 10,987 | 0.303 | 36,272 | 28,940 | 2.872 |
| 7c – Monitoring costs 15min consultation p/m | 39,951 | 3.121 | 11,011 | 0.249 | 44,213 | 39,076 | 3.175 | 10,136 | 0.303 | 33,463 | 28,940 | 2.872 |
| 8a – No wasted device costs | 39,273 | 3.121 | 10,333 | 0.249 | 41,491 | 38,352 | 3.175 | 9,412 | 0.303 | 31,072 | 28,940 | 2.872 |
| 8b – All wasted device costs included | 39,312 | 3.121 | 10,372 | 0.249 | 41,646 | 38,464 | 3.175 | 9,523 | 0.303 | 31,441 | 28,940 | 2.872 |
| 9a – System complication costs included | 39,293 | 3.121 | 10,353 | 0.249 | 41,570 | 38,408 | 3.175 | 9,468 | 0.303 | 31,257 | 28,940 | 2.872 |

| | CardioMEMS | | | | | Cordella | | | | | Standard care | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Scenario** | **Total Costs (£)** | **Total QALYs** | **Incremental costs (vs SC) (£)** | **Incremental QALYs (vs SC) (£)** | **ICER vs SC (£)** | **Total Costs (£)** | **Total QALYs** | **Incremental costs (vs SC)(£)** | **Incremental QALYs (vs SC) (£)** | **ICER vs SC (£)** | **Total costs (£)** | **Total QALYS** |
| 9b – SIRONA excluded from DSRC for Cordella | N/A | N/A | N/A | N/A | N/A | £38,408 | 3.17 | £9,468 | 0.30 | £31,257 | £28,940 | 2.87 |
| 10 – 2 month disutility effect | £39,293 | 3.09 | £10,352 | 0.26 | £39,512 | £38,408 | 3.14 | £9,468 | 0.32 | £29,779 | £28,940 | 2.83 |
| 11 – Increased cost of usual care | £43,488 | 3.12 | £10,773 | 0.25 | £43,257 | £42,688 | 3.17 | £9,973 | 0.30 | £32,925 | £32,715 | 2.87 |
| 12 – Inclusion of the re-calibration unit costs | £39,311 | 3.12 | £10,370 | 0.25 | £41,641 | N/A | N/A | N/A | N/A | N/A | £28,940 | 2.87 |

# 7 DISCUSSION

## 7.1 Statement of principal findings

High certainty evidence from the 3 RCTs suggests that CardioMEMS is associated with a reduction in HFH compared to standard heart failure management. There was also a suggestion of reduced all-cause mortality, but results were less certain. We found that CardioMEMS was unlikely to be cost-effective in our base-case. The results were sensitive to assumptions about the source of evidence for utilities, monthly device monitoring costs, the treatment effect on mortality, and adherence.

We did not have the device cost for Cordella, and there was limited comparative evidence for Cordella. We therefore could not robustly assess the clinical- or cost-effectiveness of Cordella.

## 7.2 Overview of findings from the assessment of clinical effectiveness

We identified 11 studies (60 reports) evaluating the use of implantable pulmonary artery pressure monitoring devices in people with chronic heart failure, focusing on the CardioMEMS and Cordella systems. Three RCTs evaluated CardioMEMS and three prospective single-arm studies evaluated Cordella – one of these was originally designed as an RCT and some comparative data were available for the initial randomised phase. We included three additional prospective single-arm studies of CardioMEMS for device-related outcomes. We also identified two additional studies addressing patient experience of using the CardioMEMS device, one interview study and one survey study. Two of the single arm trials of Cordella included patient surveys that also contributed data on patient experience and satisfaction.

For the primary outcome of heart failure hospitalisation (HFH), high certainty evidence suggests that CardioMEMS is associated with a reduction in HFH compared to standard heart failure management. There was also a suggestion of reduced all-cause mortality, although the confidence interval crossed one, indicating uncertainty. For Cordella, low certainty evidence from the comparative phase of the PROACTIVE-HF study and the three single-arm studies also suggests reduction in HFH, but the impact on all-cause mortality remains unclear. An indirect comparison using the Bucher method found no evidence of a difference between the two devices in terms of HFH or all-cause mortality.

CardioMEMS appeared to be associated with improvements in HRQoL in some studies, but findings were inconsistent, and the overall effect remains uncertain. The impact on HRQoL was all uncertain for Cordella due to the lack of comparative evidence. For device-related outcomes, there was high-certainty evidence that sensor implantation failure was uncommon, occurring in less than 2% of people in whom implantation was attempted for CardioMEMS and approximately 5% for Cordella. Sensor failure and DSRC were rare for both devices.

Among the secondary outcomes, there was no evidence of a difference in urgent care visits or cardiovascular mortality for CardioMEMS, and no comparative or cardiovascular mortality data were available for Cordella. In the CardioMEMS RCTs, there was a higher frequency of medication changes and increased contact with healthcare professionals (HCPs), suggesting greater clinical responsiveness to physiological data; however, this could not be evaluated for Cordella due to the absence of comparable data. Improvements in 6-minute walk test distance

were reported in all studies relative to baseline, but RCT evidence for CardioMEMS showed no difference compared to control. Change in New York Heart Association (NYHA) class was not reported for CardioMEMS but was assessed in all Cordella studies, which showed improvement; again, without a comparator, the clinical significance is uncertain. Adherence to device use was generally high for both systems, though ways in which this was assessed varied.

Findings concerning patient experience suggested that patients were mostly positive about the use of CardioMEMS (two studies) and Cordella (two studies). Qualitative interviews in one study revealed that patients felt that CardioMEMS had improved their understanding and proactive management of their condition, helped them to stay out of hospital (which was highly valued by patients), and enhanced their peace of mind. A brief survey in another study highlighted that patients thought that CardioMEMS was easy to use. Likewise, Cordella was reported by patients to be very easy to use and patients also noted that they use it to monitor their condition and would recommend it to others. Although, two surveys found that less than half of respondents made lifestyle changes based on Cordella readings.

## 7.3 Overview of findings from the assessment of cost-effectiveness

The model developed by Cowie et al. 2017, updated in 2023, and adapted in the HTW model (Health Technology Wales, 2024)[65, 68, 73] was the most relevant previous economic model in a UK context that we identified. The Cowie model has just two health states (stable heart failure and dead) and HFH events, however HF patients may have repeated hospitalisations, and quality of life, resource use, future hospitalisation, and mortality depends on number of previous hospitalisations. We therefore developed a de novo Markov model with health states that depend on number of previous HFHs to capture the impact of repeated HFHs.

We found that CardioMEMS was unlikely to be cost-effective in our base-case with £10,352 incremental costs, 0.25 incremental QALYs, and ICER of £41,569 from the deterministic model, and £10,389 incremental costs, 0.25 incremental QALYs, and ICER of £41,878 from the probabilistic model. The results were sensitive to assumptions about the source of evidence for utilities, monthly device monitoring costs, the treatment effect on mortality, and adherence.

Using the Cowie approach to model utilities reduced the deterministic ICER to £21,999 (using data from CHAMPION) and £25,666 (using data from MONITOR-HF). In the Cowie model the utilities from CHAMPION were used for the first 12 months, and then they were extrapolated assuming a linear decline over time but keeping the utility difference between CardioMEMS and standard care constant for 5 years. This approach has the advantage that actual utility benefits observed in CHAMPION are directly reflected in the model, and these may include benefits over and above those resulting from HFHs. However, the utility benefits at 12 months are then extrapolated for a further 4 years, which may not reflect how the utility benefit changes as patients deteriorate, which would mean the ICER is underestimated using the Cowie model utilities. In our base-case we do not use the utilities measured in the RCTs, but instead use utilities associated with number of recurrent HFHs to more accurately reflect the impact of repeated hospitalisations as patients' condition deteriorates. We acknowledge however that this does not capture any additional utility benefit from using CardioMEMS over and above those resulting from HFHs, and so our base-case may overestimate the ICER.

Using the minimum monitoring frequencies proposed by Abbott reduces the ICER to £22,777, due to lower costs of CardioMEMS arising from less frequent monitoring than we used in our base-case (which was based on clinical opinion). Using costs for a band 6 professional rather than a band 5 professional increases the ICER to £47,579. We heard that more senior staff may be required for monitoring or to oversee more junior staff.

Including a direct mortality benefit based on a meta-analysis of the RCTs for CardioMEMS in addition to the indirect mortality benefit already captured in the model due to reduced HFHs, reduced the deterministic ICER to £29,986. None of the RCTs were powered to detect a mortality benefit, all of the confidence intervals contained 1 (no effect), and only the CHAMPION study gave an estimate indicative of a benefit (Figure 3). Furthermore, the 0.34 difference in life years from our base-case model that results from the indirect mortality benefit captured in the model due to reduced HFHs, is similar in magnitude to the additional 0.22 life years benefit when the direct mortality benefit is included. This suggests that our model already captures the mortality benefit observed in the RCTs, and including an additional direct effect would double-count that effect.

In our scenario where 10% of patients stop adhering to using the device after 12 months then the ICER increases to £47,934. However, we heard from our clinical advisors that adherence would likely be better than this. The clinical review found that adherence may be better with Cordella due to ease of use, but more evidence is required to assess this.

We did not have the device cost for Cordella, and there was limited comparative evidence for Cordella. We therefore could not robustly assess the cost-effectiveness of Cordella. For illustrative purposes only we conducted an analysis where we assumed the device cost for Cordella was the same as for CardioMEMS. Under this assumption the base-case analysis estimated a deterministic ICER for Cordella of £31,257, a probabilistic ICER of £31,541, and Cordella strictly dominated CardioMEMS. These results were driven by the slightly more favorable hazard ratio for HFH for Cordella compared with CardioMEMS, which increased QALYs and reduced costs. We stress, however, that these results are very uncertain and no robust conclusions can be drawn for Cordella.

## 7.4 Strengths and limitations of the assessment

### 7.4.1 Strengths and limitations of the clinical effectiveness review

Our review followed established methodological guidance for the conduct of systematic reviews and was reported in accordance with the PRISMA 2020 statement.[145] The protocol was pre-registered on the PROSPERO database (PROSPERO CRD420251003375) and published on the NICE website.[27] Clearly defined, objective inclusion criteria were pre-specified; any deviations from the protocol are highlighted and justified within the report. Comprehensive literature searches were conducted across multiple databases without restrictions on language, date, or publication status, to maximise retrieval of relevant studies. Although we explored the potential for publication bias, a formal assessment was limited by the small number of included studies. All publications relating to each included study are listed in Appendix 3, with clear documentation of whether data were extracted from each source.

Risk of bias was formally assessed for all included studies. For randomised controlled trials (RCTs), we used the RoB 2 tool, performing assessments at the outcome level as recommended. These focused on outcomes that informed the economic model, identified as primary outcome for this assessment. Risk of bias judgements are reported in the results tables, enabling readers to qualitatively assess whether bias may have influenced study findings. For single-arm studies, we used the Joanna Briggs Institute (JBI) critical appraisal checklist for prevalence studies. This tool was chosen because many of the single-arm studies provided only descriptive data on device-related outcomes or event rates without a comparator group. While widely used, the JBI checklist has limitations in this context: it is not designed to assess key sources of bias relevant to intervention studies lacking comparators, such as confounding or selection bias; some checklist items are open to subjective interpretation; and it provides no standard method for deriving an overall judgement. To address this, we applied a structured approach to synthesise item-level responses into overall study-level risk-of-bias assessments, as described in the methods.

Meta-analyses were conducted to summary pooled effect estimates. Where hazard ratios (HRs) were calculated from events per person year, we assumed constant HRs over time. We acknowledge this assumption may not always hold; however, insufficient data were available to support alternative time-varying methods. We also conducted a simple indirect comparison. This assumes that control arms in trials of the two devices are equivalent. However, the control arm for the PROACTIVE-HF trial that evaluated Cordella includes enhanced monitoring in the control arm, and so this assumption does not fully hold. The results of this comparison should therefore be treated with some caution. The strength of the evidence was assessed using the GRADE approach, which provides a transparent and structured method for rating the certainty of evidence across key domains including risk of bias, inconsistency, indirectness, imprecision, and publication bias. The use of GRADE added rigour to the interpretation of the findings and helped identify areas where the evidence base remains uncertain or incomplete.

### 7.4.2 Limitations of the evidence base

We identified a small number of RCTs that evaluated the CardioMEMS device. Studies were generally well conducted with risk of bias judged as low for the primary effectiveness outcomes in CHAMPION and GUIDE-HF, but there were some concerns for MONITOR-HF due to its open-label design.

There was a lack of comparative evidence for Cordella. The PROACTIVE-HF trial was originally designed as an open-label study, but switched to a single arm design after 12 months of patient enrolment. This change was prompted by emerging evidence supporting PAP-guided HF management in NYHA class III patients, increased access to reimbursed PAP technology, and disruptions from the COVID-19 pandemic. The device manufacturer shared data for the comparative phase of the trial for the primary outcomes of HFH and all-cause mortality, but these data are limited by the short follow-up and availability of data for only a proportion of the target population. We identified one ongoing RCT that is evaluating Cordella in patients with class II-III NYHA heart failure (PROACTIVE-HF-2 (NCT05934487));[146] this study is due to complete in September 2028 and so will provide comparative data for Cordella. The other studies included for Cordella were single arm trials, one of which (SIRONA) was very small with only 15 participants and only had 3-months follow-up. The SIRONA study was at high risk of bias due to its very small sample size, while the SIRONA 2 and single arm phase of the

PROACTIVE-HF trial were judged as some concerns for the effectiveness outcomes and HRQoL due to the non-comparative natures of the evidence. For device-related outcomes, risk of bias was generally low, except again for SIRONA.

We explored the possibility of conducting a population-adjusted indirect comparison using multi-level network meta-regression,[134 135, 147] which aims to reduce confounding effects in indirect comparisons by adjusting for potential prognostic covariates (factors that affect the overall outcome) and effect modifying covariates (factors that affect the relative intervention effect). This would enable the complete data for Cordella from PROACTIVE-HF to be used and avoids assuming that the control arm is the same as routine monitoring. We had insufficient evidence to use this approach, but outline it here for consideration in future analyses. We aimed to compare the Cordella arm from PROACTIVE-HF with an arm from one of the CardioMEMS RCTs. To do this we planned to use a development version of the multinma R package[148] allows the models to be fitted using reported regression coefficients and covariance matrices that are sufficient statistics for having the IPD, and so we made a data request to Endotronix and Abbott.

We inspected subgroup analyses in all the RCT and single arm studies for CardioMEMS and Cordella to identify the key prognostic covariates and effect modifiers for HFH. We did not identify evidence of effect modifying factors based on the subgroup analyses of the RCT evidence for CardioMEMS, and so focussed on prognostic factors. We found that the following factors were potentially prognostic:

- elevated NTproBNP
- HF hospitalisation in past year
- mean pulmonary artery pressure
- reduced ejection fraction
- CRT use

Our clinical advisor agreed that these factors would be expected to be prognostic for HFH, but also noted that frailty, age, and number of co-morbidities were also likely to be important prognostic factors. None of the PROACTIVE, CHAMPION or GUIDE-HF studies reported data on frailty or number of co-morbidities and so it would not be possible to adjust for these factors, which would be a limitation of the analysis.

Following data requests Endotronix provided regression coefficients from fitting a model including the covariates listed above (excluding frailty and number of comorbidities) as prognostic factors for PROACTIVE-HF (from a Cox proportional hazards model for time to first HFH), and Abbott provided this for CHAMPION and the NYHA Class III subgroup for GUIDE-HF (from Andersen-Gill models for HFH, accounting for recurrent events). The Andersen-Gill model[149] assumes independence between repeated HFH, and so the estimates should correspond to the estimates from a Cox model for time to first HFH. The CHAMPION study [redacted] which is an important prognostic factor, and for this reason we preferred the GUIDE-HF study to make the indirect comparison with Cordella. We planned to run two scenario analysis, the first using the regression model fitted to GUIDE-HF and the second using the regression model fitted to PROACTIVE-HF. However, we did not have population characteristics for the NYHA class III subgroup for GUIDE-HF, nor the survival curve for first HFH from GUIDE-HF, which we needed to run the analysis. We were therefore

unable to complete these analyses, but it would be helpful for further work if the information were made available in the future.

### 7.4.3 Economic model strengths and limitations

A de novo model structure was used to capture the impact of repeated HFHs on quality of life, resource use, future hospitalisation, and mortality. This has the advantage of being able to model the benefits of PAP monitoring devices via their impact on reducing HFHs, which is the key outcome that has demonstrated efficacy in the clinical trials. We populated the model using evidence identified in our clinical effectiveness review, our review of cost-effectiveness studies and models of remote PAP monitoring, clinical advice and using targeted searches for specific inputs required in the economic model. This is also the first economic modelling study to examine the cost-effectiveness of Cordella.

We restricted to NYHA class III HF patients, and did not model the transitions between NYHA classes. The majority of the evidence for remote PAP monitoring was for NYHA class III, and we heard that this is the group where remote PAP monitoring would be used in practice. We did not find any evidence for differential effectiveness of PAP monitoring by subgroup, and so did not run subgroup analyses. Different subgroups (by baseline PAP, kidney function, and age) would be expected to differ in HFH rate, however results were robust to scenarios varying the HFH rate on standard care. Varying mean age from 69 to 71 gave a small increase in the ICER from £41,569 to £44,045.

As discussed in section 7.1 we took a different approach to modelling HRQoL than the Cowie model. Using utilities associated with number of recurrent HFHs has the advantage of capturing the long-term utility benefits of routine PAP monitoring due to the impact on HFHs. This avoids the strong extrapolation assumptions made in the Cowie model, but does not capture any additional utility benefit from using CardioMEMS over and above those resulting from HFHs. Our base-case may therefore overestimate the ICER, however the Cowie model likely gives an underestimate because it assumes that the 12 month difference in utility is maintained for a further 4 years. We therefore ran a further scenario where we used utilities from MONITOR-HF for the first 12 months (reflecting the follow-up period of the trial) and our state-based approach to the utilities beyond 12 months. This gave an ICER of £35,596 for CardioMEMS vs standard care that reflects a compromise between the two approaches, although we note this is still higher than a £30,000 willingness-to-pay threshold.

We did not find any data on the disutility of a HFH event, and so we followed previous models by using a value of 0.1 for a 1-month period. The model results were not sensitive to this assumption however.

We took an NHS and personal social services (PSS) perspective as defined in the NICE reference case.[150] That meant that we only included NHS costs and did not include the costs of social care funded outside the NHS and or the costs of informal care, which are both important for HF patients. We also did not include carer HRQoL in our model because we did not find evidence on carer HRQoL according to HFHs. We acknowledge this as a possible limitation of the model, but note carer disutility has also not been included in any of the previous models of remote PAP monitoring.

Owing to delays with the CE certification process and the lack of clarity on the approved indications for Cordella, a price was not available for inclusion in the model. The ICER derived for the Cordella device was therefore based on the cost of the CardioMEMS device, representing a significant limitation to the results for Cordella. There was also no information supplied by Abbot about the cost of the calibration unit for CardioMEMS, so there is also some uncertainty around the cost of CardioMEMS.

We did not include medication changes arising from the use of the PAP monitoring device, based on clinical advice that the medications most likely to be changed were low-cost diuretics. This is supported by Dauw et al,[151] who found that there were very few changes in medications prescribed for HF other than diuretics in a study involving both Cordella and CardioMEMS. Guichard *et al* found in the PROACTIVE-HF trial that medication changes were common in the first 6 months following implantation, the majority of which (69%) were oral diuretics.[48] Dose increases were slightly more common than decreases; however, there was no significant difference in the numbers of patients taking any type of HF medication between baseline and 6 months. The model, however, was not sensitive to the cost of ongoing care, to which medication was the prime contributor, and so we would not expect inclusion of medication changes to have a big impact on the ICER.

The cost associated with monitoring the device on an ongoing basis was driven mostly by the time taken by nursing staff to look regularly at the data supplied remotely by patients. Clinical advice suggested that this activity took 10 minutes per patient per monitoring event. However, it is possible that there could be an economy of scale when monitoring multiple patients in a single login session, as logging in to the system was noted to be slow, which might mean that this activity is slightly over-costed. The unit cost for an hour of a medical consultant's time used in the derivation of the cost of ongoing device monitoring appeared to be an outlier, changing from £109 in 2023 to £67 in 2024. Consultant monitoring may, therefore, be under-costed. However, the consultant contribution to the overall cost of monitoring (which is driven mainly by the more regular monitoring by nursing staff) is small. Our scenario analysis costing the nursing staff at band 6 rather than band 5 resulted in a larger change to the overall cost of monitoring than the impact of the consultant unit cost. The model results were sensitive to assumptions around monitoring costs, with lower costs leading to a lower ICER. Data on the time and resources required for monitoring in NHS practice would be valuable to reduce this uncertainty.

In common with previous UK-based models, we used HRGs to cost hospital events. Our model was more granular than previous models with multiple hospitalisation states, which allowed us to differentiate the costs by number of hospitalisations, utilising the complication and comorbidity contributions to the HRG split. However, HRGs provide a blunt tool with which to compare similar procedures, and it is possible that important differences between the devices were obscured in terms of the implantation procedure and both the rate and nature of complications arising from the use of the devices. The approach taken in the Cowie model to cost complications arising from the device or implantation was to separately map the complications observed in the CHAMPION trial to NHS reference costs (now called NHS Cost Collection) and to derive a weighted average. However, many of the observed complications are already accounted for within the HRG costs for implantation and we note that additional comorbidities and complications contribute a relatively small additional cost within the HRGs. Cowie's approach is therefore likely to over-emphasise the impact of device-related complications.

The cost of HFH may change in the future with a trend in the NHS towards hospital at home (HaH), ambulatory care, and same day emergency care. Also, while NICE guidelines are that all HF patients should be monitored twice a year, clinician advice was that they would only be seen annually in secondary care if relatively stable. In future, we heard from clinicians that there will be two care pathways based on whether the patient is above or below 50% ejection fraction.

Our model did not account for the costs associated with end of life care, which our clinical advisors note is important in this patient group. As the device typically remains implanted for life, it is possible that information from the remote monitoring could impact on care given within the end of life period, which could result in a quality of life benefit due to improved medication management. However, the lack of clarity around the definition of end of life care, the myriad providers (some NHS, but also many charitable organisations) and the lack of data on when patients enter end of life care meant that it was not possible to meaningfully capture the effects in our model. Previous models have also omitted end of life care.

## 7.5 Comparison with previous studies

### 7.5.1 Comparison with previous SRs

We are aware of two other recent, relevant reviews that have assessed remote PAP monitoring devices: the Health Technology Wales (HTW)[73] and Clephas et al. (2023)[83] systematic reviews. Some results from the Clephas review were also included in the HTW review. Both reviews restricted inclusion to only the CardioMEMS device, whereas our review also includes assessment of the Cordella device. Findings from the two reviews were consistent with our findings for CardioMEMS. Both reported reduced HFH associated with the CardioMEMS device, but no clear evidence of a difference between intervention and control groups for overall mortality, cardiovascular mortality or urgent care visits. Both reviews also found implantation of the PA sensor was safe and durable with a low number of device-related complications and sensor failures.

Compared with the HTW and Clephas reviews, our review applied a more rigorous and transparent methodology and had broader inclusion criteria. Clephas et al. was restricted to the three RCTs that evaluated CardioMEMS; the HTW review also included these 3 RCTs with some additional data from the single arm MEMS-HF and CardioMEMS-PAS trials. However, whilst we only included data from single arm trials for device related outcomes where comparative data would not be appropriate, the HTW review included these data for effectiveness outcome for outcomes (change in NYHA functional class) and subgroups (HFH stratified by baseline PAP) for which they stated data were not available from comparative studies. However, we were able to include HFH stratified on baseline PAP from the CHAMPION trial and found that without comparative data, information on change in NYHA class was not informative. They stated that no data on patient satisfaction were available. We identified additional survey and qualitative to provide insights into patient experience and satisfaction with using the devices, and also included additional data from single arm studies to evaluate device related outcomes which can only be assessed in single arm data, providing more precise summary estimates for these outcomes. Both reviews pooled data for all patients in the GUIDE-HF trial, whereas we focused on the NYHA class III subgroup where data were available. This decision ensured better comparability with the CHAMPION and MONITOR-HF trials, both of which exclusively enrolled NYHA class III patients, and aligned more closely with our research

question. The HTW review did not include a formal risk of bias (ROB) assessment or GRADE rating for the quality of evidence, although it did provide some narrative discussion of study limitations. The Clephas review assessed risk of bias using the RoB 2 tool, the same tool used in our review but did not incorporate their findings into their synthesis or apply a GRADE assessment. Notably, the Wales report lacks a detailed description of its methods, which limits replicability and transparency.

### 7.5.2 Comparison with previous modelling studies

All seven of the studies that interpreted cost-effectiveness outcomes in our systematic review of economic evaluations of PAP monitoring devices reported that the ICER indicated that PAP monitoring was cost-effective, or plausibly cost-effective, in the relevant jurisdiction. Of particular relevance are the UK-based studies.

Cowie et al reported ICERs of below £20,000 (£19,274 per QALY gained in 2017, and £19,761 per QALY in the updated 2023 model). Our base-case model gives a higher ICER than the Cowie model which is largely due to the different way that HRQoL is modelled and different monthly monitoring costs. The HTW model used state-based utilities in their model, and also found this was the reason that their ICER was higher than for the Cowie model. For our model, clinical advice was that PAP data would be reviewed three times per week for each patient with each check taking 10 minutes. This is somewhat higher than the 40 minutes per month used in both the HTW and Cowie models, and is a reason why our ICER is higher.

The Welsh HTW model reported an ICER of £28,523. Their scenario analyses, including the plausibly underestimated rate of hospitalisation at baseline, led to a recommendation in Wales that the device could be cost-effective but that further real-world evidence data were required. When we ran our model with inputs to match the HTW model assumptions but where the disutility of a HFH was modelled in the same way as the Cowie model (and our model), we obtained a much higher ICER of £51,346 (section 6.2.6), which is higher than our base-case ICER. Other difference that drive the difference between the results from the HTW model and our base-case are that we include the impact of repeated HFHs on health-state utilities and costs, and differences in monthly monitoring costs.

## 7.6 Patient and Public Involvement

We involved two patient representatives with lived experience of heart failure in this project. They attended team meetings (one at the beginning of the project and one closer to the end of the project), gave feedback on the protocol and plain language summary, and wrote the section below about the impact that these interventions may have on people with heart failure.

## 7.7 Impact on patients

Heart failure patients in general are aware that with good care from the health service and common sense from themselves, their lives need be only partially limited by their condition. They nevertheless understand that they have entered a “one-way street”: their condition is chronic, is unlikely to improve noticeably and may develop periods that are more critical. Patients whose condition is less stable may suffer an unexpected worsening of symptoms that not infrequently leads to hospitalisation.

This background of ever-present uncertainty can have a detrimental effect on quality of life. The constant monitoring provided by an implanted device would remove much uncertainty, giving a reassurance akin to that of 24-hour care and an expectation of treatment that, in some cases at least, should avoid hospitalisation with all the disruption of normal life that brings.

## 7.8 Equality, Diversity and Inclusion

Our research was based on existing literature and so we had no control over the participants enrolled. We were broad in our inclusion criteria such that studies from any country and in any language of publication were eligible. The majority of participants across the included studies were white, which limits the generalisability of the findings to more ethnically diverse populations. This is particularly relevant in the context of heart failure, where the burden of disease and response to treatment may vary by ethnicity.

People with heart failure are a diverse population, and many are older with multiple comorbidities. The average age at diagnosis is 77 years, and both the incidence and prevalence of heart failure increase steeply with age. Participants in included studies were generally younger than this, with most reporting mean age close to 70 years, while CHAMPION and PROACTIVE-HF enrolled younger populations with a mean age of 62 to 64 years. Heart failure with reduced ejection fraction is more common in men due to higher rates of coronary artery disease, whereas heart failure with preserved ejection fraction is more common in women. Included studies included a greater proportion of men than women (61 to 78%). This is a considerably higher proportion of men than the UK distribution of heart failure cases based on CPRD data which reported that 55% of those with a first hospitalisation due to heart failure were men.[132]

People living with heart failure may be covered under the Equality Act 2010, as the condition can have a substantial and long-term impact on daily living. Certain groups, such as people with cognitive impairment, learning disabilities, or problems with manual dexterity, may require additional support to initiate pulmonary artery pressure monitoring at home. While the devices used are pre-programmed with several languages, provision of additional language support may be necessary for some users. No potential equality concerns were identified in relation to pregnancy, ethnicity, religion, sexual orientation, or gender reassignment. Nevertheless, future implementation should consider how best to support accessibility and usability of these technologies for people with diverse needs, including those with limited health literacy or digital capability.

# 8 CONCLUSIONS

## 8.1 Implications for practice

These findings suggest CardioMEMS is effective in reducing heart failure hospitalisations, with high certainty evidence from three RCTs, but that it may not be cost-effective. While Cordella may offer similar benefits and could be more cost-effective than CardioMEMS, the certainty of evidence is lower due to the reliance on non-comparative data for some outcomes and comparative data for only a subset of the total trial population, with shorter duration of follow-up. If the devices were to be recommended for clinical practice, the choice between devices should take into account factors such as availability, patient preferences, and practical considerations around monitoring and adherence. However, the limited comparative evidence for Cordella restricts firm conclusions about its relative effectiveness, and lack of cost information means its cost-effectiveness is unknown.

There are additional potential benefits for remote monitoring systems in terms of sustainability. The use of remote monitoring systems could reduce the number of unnecessary hospital appointments, reducing travel for people with heart failure and reducing carbon emissions. Training and appropriate staffing is required to facilitate sensor implantation and PAP monitoring. Patients and/or their carers would need training on how to initiate the measurement. Training on PAP trends and escalation processes should be provided to the healthcare professional who access patient PAP data. Heart failure specialist nurses are well placed to access and monitor the data, as a heart failure specialist nurse would be able to read and interpret PAP trend data and prescribe medications if required.

## 8.2 Research recommendations

There is a need for comparative evidence on the Cordella device with sufficient power to detect differences between monitoring strategies and adequate follow-up. We identified one ongoing RCT evaluating Cordella that is due to report in September 2028, this should help to address the lack of comparative data for this device. Future research should prioritise the inclusion of underrepresented groups, particularly in terms of ethnicity and socioeconomic background, to ensure that evidence on the effectiveness and acceptability of implantable monitoring devices is applicable to all populations affected by heart failure. Studies should consider reporting stratified results for relevant patient subgroups to improve generalisability. There is also a need for longer-term outcome data.

Data on the long-term impact of remote PAP monitoring devices on HRQoL would be useful, as the cost-effectiveness results are sensitive to assumptions about this. Similarly, the cost-effectiveness results are sensitive to the device monitoring costs and so data on the resources in terms of time and staff required to monitor the device would help resolve that uncertainty.

# 9 Additional information

## 9.1 Declaration of competing interests

None

## 9.2 Contributions of authors

**Rachel James** - Conceptualisation; data extraction and risk of bias assessment; meta-analyses; project administration; writing – original draft; writing – reviewing and editing
**Joe Carroll** - Conceptualisation; health economic modelling; project administration; visualisation; writing – original draft; writing – reviewing and editing
**Joanna Thorn** - Conceptualisation; health economic modelling; project administration; visualisation; writing – original draft; writing – reviewing and editing
**Chris Cooper** – Conceptualisation; Literature searches; data extraction and risk of bias assessment; Systematic reviews Health Economics; writing – original draft; writing – reviewing and editing
**Eve Tomlinson** – Data extraction; writing – reviewing and editing
**Angus Nightingale** - Writing – reviewing and editing; other – clinical advice
**John Walsh** - Writing – reviewing and editing; other – PPI contributions
**Francesco Palma** - Writing – reviewing and editing; other – PPI contributions
**Mary Ward** – Model validation; writing – original draft
**David Phillippo** – statistical advice; methodology
**Nicky Welton** – Conceptualisation; formal analysis; funding acquisition; methodology; investigation; project administration; supervision of economic modelling; visualisation; writing – original draft; writing – reviewing and editing
**Penny Whiting** – Conceptualisation; formal analysis; funding acquisition; methodology; investigation; project administration; supervision of systematic review; visualisation; writing – original draft; writing – reviewing and editing

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## 9.4 Data-sharing statement

All data extracted for the systematic review and the results of the risk of bias assessments are provided in full in the appendices to this report. The economic model can be obtained from the

corresponding author and will be shared upon reasonable request for academic collaboration.

## 9.5 Ethics Statement

The research included in this report is secondary research and as such did not require ethical approval.

## 9.6 Information Governance Statement

There were no personal data involved in the production of this report.

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# Appendix 1

## Literature search strategies

### a. Clinical effectiveness searches

| Resource | N |
|---|---|
| MEDLINE | 507 |
| Embase | 461 |
| CINAHL | 70 |
| Total | 1059 |
| - Duplicates | -426 |
| To screen | 632 |

**Database: MEDLINE (MEDALL)**
Host: Ovid
Data parameters: 1946 to February 20, 2025
Date of search: 24 Feb 2025

| # | Search strategy | Hits | Search narrative |
|---|---|---|---|
| 1 | (CardioMEMS* or (cardi* and ("Micro-Electro-Mechanical System" or MEMS))).ti,ab,kw,kf. | 301 | The search focuses on the named technologies under review, CardioMEMS and the Cordella device.<br><br>Line 1 to 3 focus on CardioMEMS. We have the recognised brand name, followed by a search for the mechanism of device action. This limited to cardiac in case MEMS is used in other non-relevant conditions.<br><br>Line 2 targets the known studies evaluating the MEMS device, namely: CHAMPION, GUIDE, TEAM, and PASSPORT. These studies were identified by scoping searches in the development of the protocol. The combination of free-text terms in Line 1 for any report on the technologies alongside study specific reports ensures the sensitivity of the approach to study identification. |
| 2 | (NCT00531661 or NCT03387813 or NCT02279888 or NCT06526195 or NCT04398654).ti,ab,kw,kf. or ((CHAMPION or "GUIDE-HF" or "TEAM HF" or "PASSPORT HF") adj3 (trial or study or random*)).ti,ab. | 146 | |
| 3 | 1 or 2 | 420 | |
| 4 | (Cordella* or myCordella* or CorPASS or (CHFS and heart fail*)).ti,ab,kw,kf. | 39 | Lines 4 to 6 focus on the Cordella device. The logic of splitting the search for brand names and known studies is followed again. |
| 5 | (NCT03375710 or NCT04012944 or NCT05934487 or NCT04089059 or NCT03623165).ti,ab,kw,kf. or ((SIRONA or "SIRONA 2" or "PROACTIVE-HF" or | 60 | |

| # | Search strategy | Hits | Search narrative |
|---|---|---|---|
| | "PROACTIVE-HF 2" or PRODIGY) adj3 (trial* or study or random* or accura*)).ti,ab. | | |
| 6 | 4 or 5 | 93 | |
| 7 | 3 or 6 | 507 | Line 7 completes the search of MEDLINE by combining the search for CardioMEMS (Line 3) OR the search for Cordella (Line 6). The search is not limited by language, date of publication, or study design. |

### Database: Embase

Host: Ovid

Data parameters: 1974 to 2025 February 20

Date of search: 24 Feb 2025

| # | Search strategy | Results |
|---|---|---|
| 1 | (CardioMEMS* or (cardi* and ("Micro-Electro-Mechanical System" or MEMS))).ti,ab,kw,kf. | 617 |
| 2 | (NCT00531661 or NCT03387813 or NCT02279888 or NCT06526195 or NCT04398654).ti,ab,kw,kf. or ((CHAMPION or "GUIDE-HF" or "TEAM HF" or "PASSPORT HF") adj3 (trial or study or random*)).ti,ab. | 354 |
| 3 | 1 or 2 | 901 |
| 4 | (Cordella* or myCordella* or CorPASS or (CHFS and heart fail*)).ti,ab,kw,kf. | 67 |
| 5 | (NCT03375710 or NCT04012944 or NCT05934487 or NCT04089059 or NCT03623165).ti,ab,kw,kf. or ((SIRONA or "SIRONA 2" or "PROACTIVE-HF" or "PROACTIVE-HF 2" or PRODIGY) adj3 (trial* or study or random* or accura*)).ti,ab. | 114 |
| 6 | 4 or 5 | 174 |
| 7 | 3 or 6 | 1069 |
| 8 | limit 7 to embase | 461 |

### Database: CINAHL

Host: Ovid

Data parameters: 1981 to present

Date of search:

| # | Search strategy | Results |
|---|---|---|
| S1 | TI ((CardioMEMS* OR Cordella* or myCordella* or CorPASS)) OR AB ((CardioMEMS* OR Cordella* or myCordella* or CorPASS)) | 120 |
| S2 | TI ((CardioMEMS* OR Cordella* or myCordella* or CorPASS)) OR AB ((CardioMEMS* OR Cordella* or myCordella* or CorPASS)) | 90 |
| S3 | S1 or S2 | 70 |

### Trials registers resources

| | |
|---|---|
| ClinicalTrials.gov | 63 |
| ITCRP | 44 |
| Total | 107 |
| -duplicates | -37 |
| To screen | 70 |

### Database: Clinical Trials.gov

Host: https://clinicaltrials.gov/expert-search
Date of search: 24 Feb 2025
Searcher location: London, UK.

Viewing 1-55 out of 55 studies
Showing results for: Other terms: ((CardioMEMS) OR (("Micro-Electro-Mechanical System" OR MEMS) AND (heart failure)))
Viewing 1-8 out of 8 studies
Showing results for: Other terms: ((Cordella OR myCordella OR CorPASS) OR (CHFS AND heart failure))

### Database: WHO International Clinical Trials Registry Platform (ICTRP)

Host: https://trialsearch.who.int/
Date of search: 24 Feb 2025
Searcher location: London, UK.

N=38
((CardioMEMS) OR (("Micro-Electro-Mechanical System" OR MEMS) AND (heart failure)))

N=6
((Cordella OR myCordella OR CorPASS) OR (CHFS AND heart failure))

### Websearching

We searched the websites of both manufactures for study reports or data that would be eligible for inclusion in our reviews. Below we tabulate the reports or data identified and how we processed this.

CardioMEMS
Date of search: 27 Feb 2025
Searcher location: London, UK.
We searched the clinical studies page via the following link:
https://www.cardiovascular.abbott/us/en/hcp/products/heart-failure/pulmonary-pressure-monitors/CardioMEMS/clinical-evidence.html#ClinicalData

**Table 27 Results of CardioMEMS websearches**

| Citation | Action |
|---|---|
| Lindenfeld J, Zile MR, Desai AS, et al. Haemodynamic-guided management of heart failure (GUIDE-HF): a randomized controlled trial. *The Lancet*. 2021;398:991-1001. | Identified in our searches<br><br>Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| Abraham J, et al. Association of Ambulatory Hemodynamic Monitoring with Clinical Outcomes in a Concurrent Matched Cohort Analysis. *JAMA Cardiology*. 2019;4(6):556-563. | Identified in our searches<br><br>Excluded Clinical (Matched cohort analysis)<br><br>Excluded Economic (not a model/no UK costs data) |
| Givertz MM, Stevenson LW, Costanzo MR, et al., on behalf of the CHAMPION Trial Investigators. Pulmonary artery pressure–guided management of patients with heart failure and reduced ejection fraction. *Journal of the American College of Cardiology*. 2017; 70:1875–86 | Identified in our searches<br><br>Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| Abraham WT, Stevenson LW, Bourge RC, et al. (2016). Sustained efficacy of pulmonary artery pressure to guide adjustment of chronic heart failure therapy: Complete follow-up results from the CHAMPION randomised trial. *The Lancet*, 387(10017), 453-461. | Identified in our searches<br><br>Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| Shavelle D, et al. Lower rates of heart failure and all-cause hospitalizations during pulmonary artery pressure-guided therapy for ambulatory heart failure: One year outcomes from the CardioMEMS Post- Approval Study. *Circulation: Heart Failure*. 2020; e006836. | Identified in our searches<br><br>Excluded Clinical (Single-arm study)<br><br>Excluded Economic (not a model/no UK costs data) |
| Angermann, C, Aßmus, B, et al. Pulmonary-Artery-Pressure-Guided Therapy in Ambulatory Patients with Symptomatic Heart Failure: The CardioMEMS European Monitoring Study for Heart Failure (MEMS-HF). *European J of Heart Failure*. 2020. 10.1002/ejhf.1943. | Identified in our searches<br><br>Excluded Clinical (Single-arm study)<br><br>Excluded Economic (not a model/no UK costs data) |
| Heywood JT, Jermyn R, Shavelle D, et al. Impact of practice-based management of PA pressures in 2000 patients implanted with the CardioMEMS sensor. *Circulation*. 2017; 135: 1509–17. | Identified in our searches<br><br>Excluded Clinical (Retrospective cohort study)<br><br>Excluded Economic (not a model/no UK costs data) |
| Desai AS, et al. Ambulatory Hemodynamic Monitoring Reduces Heart Failure Hospitalizations in "Real-World" Clinical Practice. *J Am Coll Cardiol*. 2017; 69(19):2357–65. | Identified in our searches<br><br>Excluded Clinical (Retrospective cohort study) |

| Citation | Action |
|---|---|
| | Excluded Economic (not a model/no UK costs data) |
| Lindenfeld, J, Costanzo, M, Zile, M. et al. Implantable Hemodynamic Monitors Improve Survival in Patients With Heart Failure and Reduced Ejection Fraction. *J Am Coll Cardiol*. 2024 Feb, 83 (6) 682–694. | Identified in our searches<br><br>Excluded Clinical (Review (references screened))<br><br>Excluded Economic (not a model/no UK costs data) |
| Mehra M, Costanzo MR, Zile M, et al; GUIDE-HF Trial Investigators. Primary results of the prospective single arm trial of hemodynamic-guided management of heart failure (GUIDE-HF). Presented at: HFSA Conference; October 2023; Cleveland, OH | Not identified in our search as it reports a conference abstract. Added for screening.<br><br>Exclude Clinical (Single arm study)<br><br>Excluded Economic (not a model/no UK costs data) |
| Brugts, J et al. Remote haemodynamic monitoring of pulmonary artery pressures in patients with chronic heart failure (MONITOR-HF): a randomised clinical trial. *The Lancet*. May 20, 2023. https://doi.org/10.1016/S0140-6736(23)00923-6. | Identified in our searches<br><br>Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |

Cordella

Date of search: 27 Feb 2025

Searcher location: London, UK.

We searched the clinical studies via the following link: https://endotronix.com/clinical/

**Table 28 Results of Cordella websearches**

| Study | URL or citation | Action |
|---|---|---|
| PROACTIVE-HF 2 Trial | https://endotronix.com/wp-content/uploads/2024/11/Endotronix-18236-Referring-Physician-Brochure-Digital-FINAL-2024-11-08.pdf | Booklet giving a basic overview of the study. It includes detail but does not include results or links to study reports.<br><br>Excluded. |
| PROACTIVE-HF IDE Trial | Guichard JL, Bonno EL, Nassif ME, Khumri TM, Miranda D, Jonsson O, et al. Seated Pulmonary Artery Pressure Monitoring in Patients With Heart Failure: Results of the PROACTIVE-HF Trial. JACC Heart failure 2024;12(11): | Identified in our searches<br><br>Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| PROACTIVE HF | Klein Liviu. .n.r. (Abstract 653) Seated Pulmonary Artery Pressure Management in Patients with Heart Failure: 12-Month Outcomes in the PROACTIVE-HF Trial. | Not identified in our search as it reports a conference abstract. Added for screening.<br><br>Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| | Guichard JL, Cowger JA, Chaparro SV, Kiernan MS, Mullens W, Mahr C, et al. Rationale and Design of the Proactive-HF Trial for Managing Patients With NYHA Class III Heart Failure by Using the Combined Cordella Pulmonary Artery Sensor and the Cordella Heart Failure System. Journal of Cardiac Failure 2023;29(2): 171-180. | Identified in our searches<br><br>Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| | J. Cowger, J. Guichard, D. Miranda, M. Kiernan, T. Khumri, G. Macaluso, et al. Engaging Patients and Clinicians with Remote Pulmonary Artery Pressures Improves Care: A Substudy of the PROACTIVE-HF Clinical Trial. HFSA Conference 2023; Cleveland, OH., abstract no. 636.) | Not identified in our search as it reports a conference abstract. Added for screening.<br><br>Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| SIRONA 2 | Sharif F, Rosenkranz S, Bartunek J, Kempf T, Asmus B, Mahon NG, et al. Twelve-month follow-up results from the SIRONA 2 clinical trial. ESC heart failure 2024;11(2). | Identified in our searches<br><br>Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| | Sharif F, Rosenkranz S, Bartunek J, Kempf T, Assmus B, Mahon NG, et al. Safety and efficacy of a wireless pulmonary artery pressure sensor: primary endpoint results of the | Identified in our searches<br><br>Included Clinical |

| Study | URL or citation | Action |
|---|---|---|
| | SIRONA 2 clinical trial. ESC heart failure 2022;9(5). | Excluded Economic (not a model/no UK costs data) |
| SIRONA FIH | Mullens W, Sharif F, Dupont M, Rothman AMK, Wijns W. Digital health care solution for proactive heart failure management with the Cordella Heart Failure System: results of the SIRONA first-in-human study. European Journal of Heart Failure 2020;22(10): | Identified in our searches<br><br>Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| | Wilfried Mullens. Proactive Heart Failure Management incorporating ambulatory pulmonary artery pressure monitoring with the Cordella Heart Failure System: Results of the SIRONA First-in-Human Study. American Heart Association; 2019; Philadelphia, PA., https://endotronix.com/wp-content/uploads/2020/01/FINAL-FIH-SIRONA_AHA_2019_FINAL_17NOV2019.pdf | Not identified in our search as it reports a conference abstract. Added for screening.<br><br>Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| Clinician resources | Tejaswini Manavi, Geraldine Stapleton, John Barton, Elizabeth Killeen, Eileen Coen, Haroon Zafar, et al. Successful implementation of a remote patient management system for heart failure patients in West Ireland. 2023. | Not identified in our search as it reports a conference abstract. Added for screening.<br><br>Excluded Clinical (Retrospective single centre analysis of Irish patients)<br><br>Excluded Economic (not a model/no UK costs data) |

## b. Economic evaluation searches

| Resource | N |
|---|---|
| MEDLINE | 427 |
| Embase | 655 |
| Econlit | 1 |
| NHS EED | 0 |
| INAHTA | 4 |
| TUFTS CEA | 9 |
| Total | 1096 |
| - duplicates | -266 |
| Total to screen | 830 |

**Database: MEDLINE (MEDALL)**
Host: Ovid
Data parameters: 1946 to February 27, 2025
Date of search: 28 Feb 2025

| # | Search strategy | Hits | Search narrative |
|---|---|---|---|
| 1 | exp Heart Failure/ | 158591 | **Condition: heart failure.** The search opens with the Medical Subject Headings (MeSH) term for the condition of interest. This is exploded (indicated by exp) to capture sub-indexing terms for types of heart failure. |
| 2 | ((heart or cardiac) adj3 fail*).ti,ab,kf. | 261404 | |

| # | Search strategy | Hits | Search narrative |
|---|---|---|---|
| 3 | 1 or 2 | 296229 | Line 2 are free-text search terms. These terms have been chosen and developed through scoping searches and testing the search against known eligible study reports.<br><br>Free-text lines make use of the functionality of the Ovid platform. For instance, defined adjacency (sometimes known as proximity markers) is used to search between phrases within defined groups. This is represented as adj3 in Line 2. It means that the terms in the left cluster are searched within two words of those terms in the right cluster, and in either direction (e.g., heart failure or failing heart). Truncation (indicated by *) is also used. This searches for root words and alternate word endings (e.g., fail, failing, failed, failure, etc).<br><br>The free-text terms are searched in the following fields:<br>ti—title<br>ab—abstract<br>kf—author chosen keyword (literally terms chosen by authors to describe their own papers)<br><br>Line 3 combines the MeSH line at line 1 with free-text terms at Line 2 using the Boolean connector OR. This means that all concepts within Lines 1 or 2 are searched for. |
| 4 | exp Telemetry/ | 16092 | **Intervention: Remote monitoring.** Lines 4-5 focus on remote monitoring per the NICE scope. We use the MeSH term for telemetry which has the following scope note: '*Transmission of the readings of instruments to a remote location by means of wires, radio waves, or other means. (McGraw-Hill Dictionary of Scientific and Technical Terms, 4th ed)*'<br><br>Line 5 then focuses on terms to describe an eligible device. |
| 5 | ((pulmonar* or arter* or pressure or remote) adj5 (guided or sensor* or monitor* or device)).ti,ab,kf. | 66894 | |
| 6 | 4 or 5 | 81488 | |
| 7 | exp "Costs and Cost Analysis"/ | 276737 | **Economic evaluations and costs:** The CRD NHS EED search filter is used. The filter is available from The InterTASC Information Specialists' Sub-Group Search Filter Resource.<br><br>Researchers commonly amend established search filters to increase sensitivity (i.e., to further reduce |
| 8 | exp Economics, Hospital/ or Financial management, hospital/ | 33401 | |
| 9 | Economics, Medical/ | 9300 | |
| 10 | economics, nursing/ | 4013 | |
| 11 | economics, pharmaceutical/ | 3156 | |

| # | Search strategy | Hits | Search narrative |
|---|---|---|---|
| 12 | (economic* or cost or costs or costly or costing or expense or expenses or financial or price or prices or pricing or pharmacoeconomic* or "pharmaco-economic*" or CEA or CUA or CBA or CMA).ti,ab,kf,kw. | 1375393 | the risk of missing studies). This search was amended to incorporate Line 19 which seeks to identify model types, model designs, or approaches used to report outcomes in the NICE appraisal process.[29] |
| 13 | exp "fees and charges"/ | 31625 | |
| 14 | exp budgets/ | 14322 | |
| 15 | (resource*1 and (allocation or utili* or usage or use*1)).ti,ab,kf,kw. | 315062 | |
| 16 | (expenditure* not energy).ti,ab,kw. | 40749 | |
| 17 | (value adj1 money).ti,ab,kw. | 45 | |
| 18 | (budget* or fiscal or funding or financial or finance*).ti,ab,kw. | 269800 | |
| 19 | ("decision tree" or Markov or "semi Markov" or "partitioned adj2 survival" or "discrete event" or "conceptual* adj2 model*" or (decision adj2 model*) or "outcome model*" or "causal model*" or (simulat* adj2 model*) or "monte carlo" or "decision tree" or QALY*).ti,ab,kf,kw. or Quality-Adjusted Life Years/ or (quality adj2 adjust*).ti,ab,kw,kf. | 192557 | |
| 20 | or/7-19 | 1984612 | |
| 21 | 3 and 6 and 20 | 427 | Line 21 completes our search of Ovid MEDLINE by combining the condition terms (line 3) AND intervention terms (Line 6) AND the search filter for economic evaluations and costs (Line 20). The search is not limited by date, language of publication, or report type. |

### Database: Embase

Host: Ovid

Data parameters: 1974 to 2025 February 27

Date of search: 28 Feb 2025

| # | Search strategy | Results |
|---|---|---|
| 1 | exp Heart Failure/ | 716266 |
| 2 | ((heart or cardiac) adj3 fail*).ti,ab,kf. | 430020 |
| 3 | 1 or 2 | 792113 |

| | | |
|---|---|---|
| 4 | exp Telemetry/ | 45137 |
| 5 | ((pulmonar* or arter* or pressure or remote) adj5 (guided or sensor* or monitor* or device)).ti,ab,kf. | 98374 |
| 6 | 4 or 5 | 136216 |
| 7 | exp "Costs and Cost Analysis"/ | 430674 |
| 8 | exp Economics, Hospital/ or Financial management, hospital/ | 1113337 |
| 9 | Economics, Medical/ | 36983 |
| 10 | economics, nursing/ | 36983 |
| 11 | economics, pharmaceutical/ | 16724 |
| 12 | (economic* or cost or costs or costly or costing or expense or expenses or financial or price or prices or pricing or pharmacoeconomic* or "pharmaco-economic*" or CEA or CUA or CBA or CMA).ti,ab,kf,kw. | 1752967 |
| 13 | exp "fees and charges"/ | 45938 |
| 14 | exp budgets/ | 35850 |
| 15 | (resource*1 and (allocation or utili* or usage or use*1)).ti,ab,kf,kw. | 409386 |
| 16 | (expenditure* not energy).ti,ab,kw. | 54787 |
| 17 | (value adj1 money).ti,ab,kw. | 47 |
| 18 | (budget* or fiscal or funding or financial or finance*).ti,ab,kw. | 407440 |
| 19 | ("decision tree" or Markov or "semi Markov" or "partitioned adj2 survival" or "discrete event" or "conceptual* adj2 model*" or (decision adj2 model*) or "outcome model*" or "causal model*" or (simulat* adj2 model*) or "monte carlo" or "decision tree" or QALY*).ti,ab,kf,kw. or Quality-Adjusted Life Years/ or (quality adj2 adjust*).ti,ab,kw,kf. | 234751 |
| 20 | or/7-19 | 3009358 |
| 21 | 3 and 6 and 20 | 1104 |
| 22 | limit 21 to embase | 655 |

### Database: Econlit

Host: EbscoHost

Data parameters: 1886-Current

Date of search:

| # | Search strategy | Results |
|---|---|---|
| S1 | (TI (((heart OR cardiac) N3 fail*))) OR (AB (((heart OR cardiac) N3 fail*))) | 165 |
| S2 | (TI (((pulmonar* OR arter* OR pressure OR remote) N5 (guided OR sensor* OR monitor* OR device)))) OR (AB (((pulmonar* OR arter* OR pressure OR remote) N5 (guided OR sensor* OR monitor* OR device)))) | 155 |
| S3 | S1 and S2 | 1 |

### Database: NHS EED

Host: https://www.crd.york.ac.uk/CRDWeb/HomePage.asp

Data parameters: unreported

Date of search: 28 Feb 2025

(((heart OR cardiac) AND (fail)) AND ((pulmonar* OR arter* OR pressure OR remote) AND (guided OR sensor* OR monitor* OR device)))

Database: INAHTA
Host: https://database.inahta.org/
Data parameters: unreported
Date of search: 28 Feb 2025

(("chronic heart failure") AND (remote))

**Database: Tufts CEA Register**
Host: https://cevr.tuftsmedicalcenter.org/databases/cea-registry
Data parameters: 1975-current
Date of search: 28 Feb 2025

(("chronic heart failure") AND (remote))

## C. Systematic review of reviews of the CHF population

| Resource | N |
|---|---|
| MEDLINE | 191 |
| Embase | 238 |
| Total | 429 |
| - Duplicates | - 134 |
| To Screen | 295 |

**Database: MEDLINE (MEDALL)**
Host: Ovid
Data parameters: 1946 to February 26, 2025
Date of search: 27 Feb 2025

| # | Search strategy | Hits | Search narrative |
|---|---|---|---|
| 1 | exp Heart Failure/ | 158576 | The search adopts the same rationale and structure as the PAP search for primary studies. |
| 2 | ((heart or cardiac) adj3 fail*).ti,ab,kf. | 261354 | |
| 3 | 1 or 2 | 296178 | |
| 4 | exp "Costs and Cost Analysis"/ | 276700 | Lines 4-7 are adapted from the NHS EED filter, aiming to target systematic reviews reporting decision models. |
| 5 | ((cost* or economic) adj3 (effect* or anal* or model* or evaluat*)).ti,ab,kw,kf. | 283259 | |
| 6 | ("decision tree" or Markov or "semi Markov" or "partitioned adj2 survival" or "discrete event" or "conceptual* adj2 model*" or (decision adj2 model*) or "outcome model*" or "causal model*" or (simulat* adj2 model*) or "monte carlo" or "decision tree").ti,ab,kw,kf | 173018 | |

| | | | |
|---|---|---|---|
| 7 | 4 or 5 or 6 | 627678 | |
| 8 | "Systematic Review"/ | 284831 | A targeted search is taken to identity systematic reviews. Lines 8-9 align with PRISMA reporting guidance item #1: that systematic reviews should report that they are systematic reviews. |
| 9 | Systematic Review.ti,ab,kw,kf. | 341431 | |
| 10 | 8 or 9 | 380740 | |
| 11 | (2015* or 2016* or 2017* or 2018* or 2019* or 2020* or 2021* or 2022* or 2023* or 2024* or 2025*).dt,dp,ed,ep,yr. | 14785832 | Line 11 reports the date limit for this review. |
| 12 | 3 and 7 and 10 and 11 | 191 | Line 12 completes the targeted search for systematic reviews. It combines the condition terms (Line 3) AND terms for economic evaluations (Line 7) and terms for systematic review (Line 10) with the date limit of the review (Line 11). |

### Database: Embase

Host: Ovid

Data parameters: 1974 to 2025 February 26

Date of search: 27 Feb 2025

| # | Search strategy | Results |
|---|---|---|
| 1 | exp *Heart Failure/ | 283775 |
| 2 | ((heart or cardiac) adj3 fail*).ti,ab,kf. | 429916 |
| 3 | 1 or 2 | 530151 |
| 4 | exp economic evaluation/ | 381131 |
| 5 | ((cost* or economic) adj3 (effect* or anal* or model* or evaluat*)).ti,ab,kw,kf. | 382832 |
| 6 | ("decision tree" or Markov or "semi Markov" or "partitioned adj2 survival" or "discrete event" or "conceptual* adj2 model*" or (decision adj2 model*) or "outcome model*" or "causal model*" or (simulat* adj2 model*) or "monte carlo" or "decision tree").ti,ab,kw,kf. | 204424 |
| 7 | 4 or 5 or 6 | 755043 |
| 8 | "systematic review"/ | 513110 |
| 9 | Systematic Review.ti,ab,kw,kf. | 406340 |
| 10 | 8 or 9 | 609175 |
| 11 | 3 and 7 and 10 | 524 |
| 12 | (2015* or 2016* or 2017* or 2018* or 2019* or 2020* or 2021* or 2022* or 2023* or 2024* or 2025*).yr. | 17428337 |
| 13 | 11 and 12 | 359 |
| 14 | limit 13 to embase | 238 |

# Appendix 2

# Tables of included, on-going, or excluded studies

## Studies included in the review showing primary and secondary reports

Primary reports are the primary publication for the study and are used to refer to that study throughout text and tables.

## On-going studies

**Table 29 On-going studies**

| Citation | Study design | Estimated completion | Device |
|---|---|---|---|
| NCT05934487. A Prospective, Multi-Center, Open Label, Randomized Control Clinical Trial Evaluating the Safety and Efficacy of the Cordella™ Pulmonary Artery Sensor System in New York Heart Association (NYHA) Class II-III Heart Failure Patients.2023. URL: https://clinicaltrials.gov/study/NCT05934487 | RCT | 09-2028 | Cordella |
| NCT05428631. Evaluation of the Tolerability and Safety of the CARDIOMEMS™ Intracardiac Continuous Cardiac Hemodynamic Monitoring Device in Patients with Cardio Renal Syndrome with Severe Renal Impairment.2022. URL: https://clinicaltrials.gov/study/NCT05428631 | Single arm | 08-2026 | CardioMEMS |
| NCT05284955. Efficacy of Pulmonary Pressure Guided Therapy in Stable Outpatients With Advanced Heart Failure - A Randomized Controlled Clinical Trial.2022. URL: https://clinicaltrials.gov/study/NCT05284955 | RCT | 12-2025 | CardioMEMS |
| NCT04441203. Patient SELF-management With HemodynamIc Monitoring: Virtual Heart Failure Clinic and Outcomes (the SELFIe-HF Trial): Program.2020. URL: https://clinicaltrials.gov/study/NCT04441203 | RCT | 12-2025 | CardioMEMS |
| NCT04398654. Pulmonary Artery Sensor System Pressure Monitoring to Improve Heart Failure (HF) Outcomes.2020. URL: https://clinicaltrials.gov/study/NCT04398654<br><br>Stork S, Bernhardt A, Bohm M, Brachmann J, Dagres N, Frantz S, et al. Pulmonary artery sensor system pressure monitoring to improve heart failure outcomes (PASSPORT-HF): rationale and design of the PASSPORT-HF multicenter randomized clinical trial. Clinical Research in Cardiology 2022;1111245–1255 | RCT | 06-2026 | CardioMEMS |
| NCT06526195. Trial to Evaluate Safety and Effectiveness of Mechanical Circulatory Support in Patients with Advancing Heart Failure.2024. URL: https://clinicaltrials.gov/ct2/show/NCT06526195 | RCT | 09-2029 | CardioMEMS |

## Studies included in manufacturers' submissions

Below we tabulate decisions made and reasons for inclusion or exclusion from the systematic reviews of clinical effectiveness and cost-effectiveness, where applicable, for studies reported in submissions from manufacturers.

**Table 30 Studies included in submission from Endotronix/Edwards Lifesciences**

| Study Name | Reference | Decision |
|---|---|---|
| SIRONA | Mullens W, Sharif F, Dupont M, Rothman AMK, Wijns W. Digital health care solution for proactive heart failure management with the Cordella Heart Failure System: results of the SIRONA first-in-human study. European Journal of Heart Failure 2020;22(10): 1912-1919. | Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| SIRONA 2 | Sharif F, Rosenkranz S, Bartunek J, Kempf T, Assmus B, Mahon NG, et al. Safety and efficacy of a wireless pulmonary artery pressure sensor: primary endpoint results of the SIRONA 2 clinical trial. ESC heart failure 2022;9(5): 2862–2872. | Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| | Sharif F, Rosenkranz S, Bartunek J, Kempf T, Asmus B, Mahon NG, et al. Twelve-month follow-up results from the SIRONA 2 clinical trial. ESC heart failure 2024;11(2): 1133–1143. | Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| PROACTIVE-HF | Bennett M. Seated Pulmonary Artery Pressure Response Patterns and Heart Failure Outcomes. Presented at: CRF Technology and Heart Failure Therapeutics; February 11-13, 2025; Boston, MA | Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| | Engaging Patients and Clinicians with Remote Pulmonary Artery Pressures Improves Care: A Substudy of the PROACTIVE-HF Clinical Trial Academic in Confidence (unpublished but presented at HFSA 2023 conference) | Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| | Guichard JL, Cowger JA, Chaparro SV, Kiernan MS, Mullens W, Mahr C, et al. Rationale and Design of the Proactive-HF Trial for Managing Patients With NYHA Class III Heart Failure by Using the Combined Cordella Pulmonary Artery Sensor and the Cordella Heart Failure System. Journal of Cardiac Failure 2023;29(2): epub. | Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |

| Study Name | Reference | Decision |
|---|---|---|
| | Guichard JL, Bonno EL, Nassif ME, Khumri TM, Miranda D, Jonsson O, et al. Seated Pulmonary Artery Pressure Monitoring in Patients With Heart Failure: Results of the PROACTIVE-HF Trial. JACC Heart failure 2024;12(11): 1879-1893. | Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| | Guichard JL. Time in Target Seated Pulmonary Artery Pressure Range is Associated with HF Outcomes. Presented at: CRF Technology and Heart Failure Therapeutics; February 11-13, 2025; Boston, MA | Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| | Seated Pulmomary Artery Pressure Management in Patients with Heart Failure: 12-Month Outcomes in the PROACTIVE-HF Trial Academic in Confidence (unpublished but presented at HFSA 2024 conference) | Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| NA | Dauw J, Sokolski M, Middleton JT, Nijst P, Dupont M, Forouzan O, et al. Ambulatory haemodynamic-guided management reduces heart failure hospitalizations in a multicentre European heart failure cohort. ESC heart failure 2022;9(6): 3858-3867. | Excluded Clinical (Data not stratified by device)<br><br>Excluded Economic (not UK costs, but used as a source of costs in the economics section) |
| NA | Guichard JL, Sharif F, Forouzan O, Martina J, Klein L. A Procedural Guide for Implanting the Cordella Pulmonary Artery Pressure Sensor. The Journal of invasive cardiology 2023;35(2): epub. | Excluded Clinical (Procedural guide)<br><br>Excluded Economic (not a model/no UK costs data) |
| NA | Mullens W, Rosenkranz S, Sharif F, Asmus B, Mahon NG, Kempf T, et al. Feasibility of Continuous Noninvasive Pulmonary Artery Pressure Monitoring via the Cordella Implantable Pulmonary Artery Sensor. JACC Heart failure 2024;12(4): 785-788. | Excluded Clinical (Not a study design of interest)<br><br>Excluded Economic (not a model/no UK costs data) |

**Table 31 Studies included in submission from Abbott**

| Study Name | Reference | Decision |
|---|---|---|
| CHAMPION | Abraham WT, Adamson PB, Bourge RC, et al. Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial [published correction appears in Lancet. 2012 Feb 4;379(9814):412]. Lancet. 2011;377(9766):658-666. doi:10.1016/S0140-6736(11)60101-3 | Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| | Abraham WT, Adamson PB, Bourge RC, Aaron MF, Costanzo MR, Stevenson LW, et al. Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial. The Lancet 2011;377(9766): 658-666. | Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| | Varma N, Bourge RC, Stevenson LW, Costanzo MR, Shavelle D, Adamson PB, et al. Remote Hemodynamic-Guided Therapy of Patients With Recurrent Heart Failure Following Cardiac Resynchronization Therapy. Journal of the American Heart Association 2021;10(5): 13. | Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| GUIDE-HF | Lindenfeld J, Zile MR, Desai AS, Bhatt K, Ducharme A, Horstmanshof D, et al. Haemodynamic-guided management of heart failure (GUIDE-HF): a randomised controlled trial. The Lancet 2021;398(10304): 991-1001. | Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| MONITOR-HF | Brugts JJ, Radhoe SP, Clephas PRD, Aydin D, van Gent MWF, Szymanski MK, et al. Remote haemodynamic monitoring of pulmonary artery pressures in patients with chronic heart failure (MONITOR-HF): a randomised clinical trial. The Lancet 2023;401(10394): 2113-2123. | Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| | Clephas PRD, Zwartkruis VW, Malgie J, van Gent MWF, Brunner-La Rocca HP, Szymanski MK, et al. Pulmonary artery pressure monitoring in chronic heart failure: effects across clinically relevant subgroups in the MONITOR-HF trial. European heart journal 2024;45(32): 2954-2964. | Included Clinical<br><br>Excluded Economic (not a model/no UK costs data) |
| PASSPORT-HF | Stork S, Bernhardt A, Bohm M, Brachmann J, Dagres N, Frantz S, et al. Pulmonary artery sensor system pressure monitoring to improve heart failure outcomes (PASSPORT-HF): rationale and design of the PASSPORT-HF multicenter randomized clinical trial. Clinical Research in Cardiology 2022;1111245–1255. | Excluded Clinical (ongoing/no results)<br><br>Excluded Economic (not a model/no UK costs data) |
| TEAM-HF | NCT06526195. Trial to Evaluate Safety and Effectiveness of Mechanical Circulatory Support in Patients with Advancing Heart Failure.2024. URL: https://clinicaltrials.gov/study/NCT06526195 | Excluded Clinical (ongoing/no results) |

| Study Name | Reference | Decision |
|---|---|---|
| | | Excluded Economic (not a model/no UK costs data) |
| COAST | 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 Failure. 2022;9(1):48-56. | Included for device related outcomes<br><br>Excluded Economic (not a model/no UK costs data) |
| | de Groote P, Thuny F, Blanchart K, Gueffet J-P, Habib G, Salvat M, et al. Remote haemodynamic-guided heart failure management in France: Results from the CardioMEMS HF System Post-Market Study (COAST) French cohort. Archives of Cardiovascular Diseases 2024;117(11): 624-632. | Included for device related outcomes<br><br>Excluded Economic (not a model/no UK costs data) |
| MEMS-HF | Angermann CE, Assmus B, Anker SD, Asselbergs FW, Brachmann J, Brett M-E, et al. Pulmonary artery pressure-guided therapy in ambulatory patients with symptomatic heart failure: the CardioMEMS European Monitoring Study for Heart Failure (MEMS-HF). European Journal of Heart Failure 2020;22(10): 1891-1901. | Included for device related outcomes<br><br>Excluded Economic (not a model/no UK costs data) |
| CardioMEMS Post-Approval Study | Shavelle DM, Desai AS, Abraham WT, Bourge RC, Raval N, Rathman LD, et al. Lower Rates of Heart Failure and All-Cause Hospitalizations During Pulmonary Artery Pressure-Guided Therapy for Ambulatory Heart Failure: One-Year Outcomes From the CardioMEMS Post-Approval Study. Circulation Heart failure 2020;13(8): e006863. | Included for device related outcomes<br><br>Excluded Economic (not a model/no UK costs data) |
| NA | Abraham J, Bharmi R, Jonsson O, et al. Association of ambulatory hemodynamic monitoring with clinical outcomes in a concurrent matched control analysis. JAMA Cardiology. 2019;4(6):556-563. | Excluded Clinical (Matched cohort analysis)<br><br>Excluded Economic (not a model/no UK costs data) |
| NA | Clephas PRD, Radhoe SP, Boersma E, Gregson J, Jhund PS, Abraham WT, et al. Efficacy of pulmonary artery pressure monitoring in patients with chronic heart failure: a meta-analysis of three randomized controlled trials. European heart journal 2023;44(37): 3658-3668. | Excluded Clinical (Review (references screened)) |

| Study Name | Reference | Decision |
|---|---|---|
| | | Excluded Economic (not a model/no UK costs data) |
| NA | Codina P, Vicente Gómez JÁ, Hernández Guillamet G, et al. Assessing the impact of haemodynamic monitoring with CardioMEMS on heart failure patients: a cost-benefit analysis. ESC Heart Fail. 2024;11(4):1955-1962. | Exclude clinical (economic)<br><br>Include economic |
| NA | Cowie MR, Simon M, Klein L, Thokala P. The cost-effectiveness of real-time pulmonary artery pressure monitoring in heart failure patients: a European perspective. European Journal of Heart Failure 2017;19(5): 661-669. | Exclude clinical (economic)<br><br>Include economic |
| NA | Cowie MR, Thokala P, Ihara Z, Adamson PB, Angermann C. Real-time pulmonary artery pressure monitoring in heart failure patients: an updated cost-effectiveness analysis. ESC heart failure 2023;10(5): 3046-3054. | Exclude clinical (economic)<br><br>Include economic |
| NA | Desai AS, Bhimaraj A, Bharmi R, et al. Ambulatory hemodynamic monitoring reduces heart failure hospitalizations in “real-world” clinical practice. JACC. 2017;69(19):2357-2365. | Excluded Clinical (Retrospective cohort study)<br><br>Excluded Economic (not a model/no UK costs data) |
| NA | Flett A, Lindenfeld J, Shah H, et al. Consistent heart failure hospitalization reduction throughout studies and geographies: a pooled analysis of the CardioMEMS HF System trials over the last decade. Presented at:Heart Failure 2025 Congress, May 17-20, Serbia. | Excluded Clinical (Pooled analysis of real-world studies)<br><br>Excluded Economic (not a model/no UK costs data) |
| NA | Heywood JT, Jermyn R, Shavelle D, Abraham WT, Bhimaraj A, Bhatt K, et al. Impact of Practice-Based Management of Pulmonary Artery Pressures in 2000 Patients Implanted With the CardioMEMS Sensor. Circulation 2017;135(16): 1509 - 1517. | Excluded Clinical (Retrospective cohort study)<br><br>Excluded Economic (not a model/no UK costs data) |
| NA | Kapelios CJ, Liori S, Bonios M, Abraham WT, Filippatos G. Effect of pulmonary artery pressure-guided management on outcomes of patients with heart failure outside clinical trials: A systematic review and meta-analysis of real-world evidence with the CardioMEMS Heart Failure System. European journal of heart failure. 2025 May 13. Epub. | Excluded Clinical (Review (references screened))<br><br>Excluded Economic (not a model/no UK costs data) |

| Study Name | Reference | Decision |
|---|---|---|
| NA | Lindenfeld J, Costanzo MR, Zile MR, Ducharme A, Troughton R, Maisel A, et al. Implantable Hemodynamic Monitors Improve Survival in Patients With Heart Failure and Reduced Ejection Fraction. Journal of the American College of Cardiology 2024;83(6): 682-694. | Excluded Clinical (Review (references screened))<br><br>Excluded Economic (not a model/no UK costs data) |
| NA | Mokri H, Clephas PRD, de Boer RA, van Baal P, Brugts JJ, Rutten-van Mölken MPMH. Cost-effectiveness of remote haemodynamic monitoring by an implantable pulmonary artery pressure monitoring sensor (CardioMEMS-HF system) in chronic heart failure in the Netherlands. European Journal of Heart Failure. 2024;26(5):1189-1198. | Exclude clinical (economic)<br><br>Include economic |
| NA | Zile MR, Abraham WT, Stevenson LW, Costanzo MR, Angermann CE, Mehra MR, et al. Relationship Between Remote, Ambulatory Pulmonary Artery Pressures, and All-Cause Mortality in Patients With Chronic Heart Failure. Circulation: Heart Failure.18(6):e012754. | Excluded Clinical (Not a primary study)<br><br>Excluded Economic (not a model/no UK costs data) |

## Studies excluded at full-text screening

### Table 32 Studies excluded at full-text screening

| Citation | Reason for exclusion |
|---|---|
| NCT01162707. A Multi-Center, Non-Randomized, Prospective Trial to Evaluate the Safety and Feasibility of Wireless, Intermittent Monitoring of Right Heart Pressures in Adult Heart Failure Subjects.2010. URL: https://clinicaltrials.gov/study/NCT01162707 | CARDIOMEMS SIngle Arm - no relevant outcomes |
| 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 Cardiology. 2019;4(6):556-563. | CARDIOMEMS SIngle Arm - no relevant outcomes |
| Abraham W, Adamson P, Hasan A, et al. Safety and accuracy of a wireless pulmonary artery pressure monitoring system in patients with heart failure. American Heart Journal. 2011;161(3):558-566. | CARDIOMEMS SIngle Arm - no relevant outcomes |
| Alam A, Van Zyl J, Nayyar N, Hall S, Jermyn R. Improvement in Metabolic Co-Morbidities after Implantation of CardioMEMS in Patients with Heart Failure with Preserved Ejection Fraction Phenotype. Journal of clinical medicine. 2021;10(19): 4308. | Retrospective cohort study |
| NCT03623165. An Observational, Prospective, Single Arm, Multi-Center Registry to Evaluate the Cordella™ Heart Failure System in New York Heart (NYHA) Class III Heart Failure Patients (PRODIGY Registry).2018. URL: https://clinicaltrials.gov/study/NCT03623165 | Terminated/withdrawn |
| Ana MD-S, Bionat S, Creamer A, Bhimaraj A. Utilization And Implementation Of Inpatient Transmission Of Pa Pressures Using Cardiomems Sensor During Heart Failure Admission- A Single Center Experience. Journal of Cardiac Failure 2022;28(5): S32. | Case Report |
| Anuwatworn A, Sethi P, Thompson P, Jonsson O. 141 - The Effects of Timing in Measurement of Pulmonary Artery Diastolic Pressure with CardioMEMS Hemodynamic Monitoring. Journal of Cardiac Failure 2017;23(8): S54. | Single centre experience of CardioMEMS |
| Assaad M, Sarsam S, Naqvi A, Zughaib M. CardioMems R device implantation reduces repeat hospitalizations in heart failure patients: A single center experience. JRSM cardiovascular disease. 2019;8. | Retrospective cohort study |
| Baginski BN, Byrne KA, Vaz DG, Barber R, Blackhurst D, Tibbett TP, et al. Development and implementation of a remote patient monitoring program for heart failure: a single-centre experience. ESC heart failure 2021;8(2): 1349-1358. | Single centre experience of CardioMEMS |
| Bhimaraj A, Benjamin T-A, Guglin M, Volz E, Shah H, Guha A, et al. Translating Pressure Into Practice: Operational Characteristics of Ambulatory Hemodynamic Monitoring Program in the United States. Journal of Cardiac Failure 2023;29(11): 1571-1575. | Economic |
| Brinkley DM, Guglin ME, Bennett MK, Redfield MM, Abraham WT, Brett M-E, et al. Pulmonary Artery Pressure Monitoring Effectively Guides Management to Reduce Heart Failure Hospitalizations in Obesity. JACC Heart failure 2021;9(11): 784–794. | CARDIOMEMS SIngle Arm - no relevant outcomes |
| Brugts JJ, Manintveld OC, van Mieghem N. Remote monitoring of pulmonary artery pressures with CardioMEMS in patients with chronic heart failure and NYHA class III: first experiences in the Netherlands. Netherlands heart journal : monthly journal of the Netherlands Society of Cardiology and the Netherlands Heart Foundation 2018;26(2): 55-57. | Case Report |
| NCT06779552. CardioMEMS HF System Coverage with Evidence Development Study.2025. URL: https://clinicaltrials.gov/ct2/show/NCT06779552 | CARDIOMEMS SIngle Arm - no relevant outcomes |
| NCT03020043. CardioMEMS Registry of the Frankfurt Heart Failure Center.2017. URL: https://clinicaltrials.gov/study/NCT03020043 | Single centre experience of CardioMEMS |

| Citation | Reason for exclusion |
|---|---|
| NCT06306573. CardioMEMS™ HF System Real-World Evidence Post-Approval Study.2023. URL: https://clinicaltrials.gov/study/NCT06306573 | CARDIOMEMS SIngle Arm - no relevant outcomes |
| Carey S, Bass K, Dormer A, et al. 391 - Our Experience with CardioMEMSTM in a Large Advanced Heart Failure Program. Journal of Cardiac Failure. 2016;22. | Retrospective cohort study |
| Caruso M, Droogan C, Nesfeder J, Domsky S, Anouti K, O'Regan K. 305 - Heart Failure and All Cause Hospitalization Prior to and Following Implantation of the CardioMEMS Heart Failure System. Journal of Cardiac Failure. 2017;23. | Retrospective cohort study |
| Case L, Deibert J, Jonsson O, Preister S. Treating PA Pressures with Use of a CardioMems Device Affects Quality of Life Measures By Improving Kansas City Cardiomyopathy Questionnaire (KCCQ) and 6 Minute Walk Test (6mwt). Heart & Lung. 2020;49(2). | Single centre experience of CardioMEMS |
| Chilcote JL, Summers RP, Vaz DG, Barber R, Wariar R, Guichard JL. Concurrent Assessment of the CardioMEMS HF System and HeartLogic HF Diagnostic: A Retrospective Case Series. Journal of Cardiac Failure 2022;28(1): 44-55. | Single centre experience of CardioMEMS |
| Clincial Evidence Division. CardioMEMS HF System. CardioMEMS HF System.[websearch] | Single centre experience of CardioMEMS |
| Codina P, Altisent OA-J, Santiago-Vacas E, Domingo M, Lupon J, Bayes-Genis A. A new option for monitoring heart failure. First experience in Spain with CardioMEMS. Medicina clinica 2021;156(1): 26-28. | Single centre experience of CardioMEMS |
| Comment on: Safety and feasibility of hemodynamic pulmonary artery pressure monitoring using the CardioMEMS device in LVAD management. Journal of Cardiac Surgery 2021;36(9): 3281-3282. | Not a primary study |
| Cordella. PROACTIVE HF-2. [Data on File] | Not a primary study |
| Craig W, Ohlmann S. The Benefits of Using Active Remote Patient Management for Enhanced Heart Failure Outcomes in Rural Cardiology Practice: Single-Site Retrospective Cohort Study. Journal of medical Internet research. 2024;26. | Retrospective cohort study |
| Cuellar S, Karnkowska B, Alnajjar H, et al. Impact Of Pulmonary Artery Wireless Monitoring (CardioMEMS) Guided Interventions On Renal Function In Heart Failure Patients. Journal of Cardiac Failure. 2025;31(1). | Retrospective cohort study |
| Dale A, Drysdale H, Heneghan C. The CHAMPION trial outcomes were not adequately prespecified. Lancet (London, England). 2016;388(10044). | Background |
| Dauw J, Sokolski M, Middleton J, et al. Ambulatory haemodynamic-guided management reduces heart failure hospitalizations in a multicentre European heart failure cohort. ESC heart failure. 2022;9(6). | Data not stratified by device |
| Davidovich D, Jonsson O, Pelzel J, et al. Effect of pulmonary pressure monitoring (cardiomems heart failure system, st. Jude medical) on hospital admissions and emergency department visits: a multicenter real world experience. Journal of the American College of Cardiology (JACC). 2017;69. | Retrospective cohort study |
| DeFilippis E, Axsom K, Henderson J, et al. Hemodynamic Monitoring Equally Reduces Heart Failure Hospitalizations in Women and Men in Clinical Practice: CardioMEMS Post-Approval Study. Journal of Cardiac Failure. 2020;26(10). | CARDIOMEMS SIngle Arm - no relevant outcomes |
| Desai A, Bhimaraj A, Bharmi R, et al. Ambulatory Hemodynamic Monitoring Reduces Heart Failure Hospitalizations in "Real-World" Clinical Practice. Journal of the American College of Cardiology. 2017;69(19). | Retrospective cohort study |
| NCT05284955. Efficacy of Pulmonary Pressure Guided Therapy in Stable Outpatients With Advanced Heart Failure - A Randomized Controlled Clinical Trial.2022. URL: https://clinicaltrials.gov/study/NCT05284955 | Include - ongoing/no results |
| NL-OMON24459. HEMOdynamic guidance with CardioMEMS in LVAD patients.2017. URL: https://onderzoekmetmensen.nl/en/trial/24459 | Not in the population of interest |

| Citation | Reason for exclusion |
|---|---|
| NL-OMON46145. HEMOdynamic guidance with PA-sensor CardioMEMS in patients with an left ventricular assist device (LVAD).2017. URL: https://onderzoekmetmensen.nl/en/trial/46145 | Not in the population of interest |
| NL-OMON52937. Hemodynamic Monitoring with the CardioMEMS PA sensor and Quality of Life in Patients with Chronic Heart Failure: The MONITOR HF Trial.2019. URL: https://onderzoekmetmensen.nl/en/trial/52937 | Duplicate |
| NCT05428631. Tolerability and Safety of CARDIOMEMS™ Intracardiac Continuous Cardiac Hemodynamic Monitoring Device in Patients with Cardio Renal Syndrome with Severe Renal Impairment.2022. URL: https://clinicaltrials.gov/ct2/show/NCT05428631 | Include - ongoing/no results |
| Gallagher B, Moise N, Haerizadeh M, Ye S, Medina V, Kronish I. Telemonitoring Adherence to Medications in Heart Failure Patients (TEAM-HF): A Pilot Randomized Clinical Trial. Journal of cardiac failure. 2017;23(4). | Did not evaluate intervention of interest |
| Goel A, Malik A, Gupta R, et al. Impact of age on the utility of CardioMEMS device in reducing heart failure readmissions. Progress in cardiovascular diseases. 2022;74. | Background |
| Guazzi M. The CHAMPION trial. Giornale Italiano di Cardiologia. 2017;18(2). | Duplicate |
| Guazzi M. The CHAMPION trial. Giornale Italiano di Cardiologia. 2017;18(2). | Not a primary study |
| Heywood J, Jermyn R, Shavelle D, et al. Impact of Practice-Based Management of Pulmonary Artery Pressures in 2000 Patients Implanted With the CardioMEMS Sensor. Circulation. 2017;135(16). | Retrospective cohort study |
| Hussain B, Mahmood A, Dahal K, Kanmanthareddy A, Alexander T, Kassier A. Impact of COVID-19 Era on Pulmonary Artery Pressure Monitoring Device (CardioMEMS) Readmissions. Cardiovascular Revascularization Medicine. 2024;65. | Retrospective cohort study |
| NCT02862197. Invasive Monitoring of Pulmonary Artery Pressure (PAP) Among Dialysis Treated Patients.2016. URL: https://clinicaltrials.gov/study/NCT02862197 | Not in the population of interest |
| Jermyn R, Alam A, Kvasic J, Saeed O, Jorde U. Hemodynamic-guided heart-failure management using a wireless implantable sensor: Infrastructure, methods, and results in a community heart failure disease-management program. Clinical Cardiology. 2017;40(3):170-176. | Single centre experience of CardioMEMS |
| Joy P, Kumar G, Jermyn R, et al. Heart Failure Admission Outcomes: CardioMEMS Compared. Journal of Cardiac Failure. 2023;29(4). | Acute heart failure |
| Joy P, Kumar G, Jermyn R, et al. Heart Failure Admissions Outcomes in Patients With CardioMEMS. The American journal of cardiology. 2023;207. | Not a primary study |
| Kanat N, Nichols M. 6 CardioMEMS for Effective Management of Heart Failure: Reducing Healthcare Utilization and 30 Day Readmissions. Heart & Lung. 2017;46(3). | Single centre experience of CardioMEMS |
| Kishino Y, Kuno T, Malik A, et al. Effect of pulmonary artery pressure-guided therapy on heart failure readmission in a nationally representative cohort. ESC heart failure. 2022;9(4). | Retrospective cohort study |
| Kittipibul V, Fudim M, Silver M, Yaranov D. Discordant Pressure-Volume Trends During CardioMEMS Monitoring. JACC. Heart failure. 2023;11(8 Pt 2). | Not a primary study |
| Larkin M. CardioMEMS boosts QoL, curbs HF hospitalizations: MONITOR-HF. Cardiology News. 2023. | Not a primary study |
| Late-Breaking Data Shows the CardioMEMS HF System is Effective in Reducing Heart Failure Hospitalizations and Cost of Care. EP Lab Digest. 2017;17(4). | Not a primary study |
| Leahy N, O'Brien C, Alsubai S, Coen E, Murphy D, Sharif F. Clinical Characteristics and Outcomes in Heart Failure Patients with Implantable Pulmonary Artery Pressure Monitors: A Single Centre Irish Experience. Journal of cardiovascular development and disease. 2025;12(1). | Single centre experience of CardioMEMS |
| Legha S. CardioMEMS Device: Sensing the Heart's Clues and Redefining the Management of Heart Failure. Indian Journal of Cardiovascular Disease in Women - WINCARS. 2024;9(2). | Not a primary study |

| Citation | Reason for exclusion |
|---|---|
| Leslie Steinkamp. Management of CardioMEMS Patients: A Nursing Perspective. Management of CardioMEMS Patients: A Nursing Perspective. [CHAMPION report – data on file] | Not a primary study |
| Levy W, Hauptman P, Gilbert E, et al. Is The Benefit Of CardioMEMS Lessened In Elderly Patients With Heart Failure?. Journal of Cardiac Failure. 2022;28(5). doi:10.1016/j.cardfail.2022.03.230. | CARDIOMEMS Single Arm - no relevant outcomes |
| Lin A, Hu G, Dhruva S, Kinard M, Redberg R. Quantification of Device-Related Event Reports Associated With the CardioMEMS Heart Failure System. Circulation. Cardiovascular quality and outcomes. 2022;15(10). doi:10.1161/circoutcomes.122.009116. | Post-marketing AEs - no denominator |
| Man S, Lazdam M, Clayton L, Loke I, Somani R. Cardiomems predicts heart failure decompensation from recent onset frequent premature ventricular complexes: improvement in pulmonary artery pressure and symptoms after radiofrequency ABLATION. Journal of the American College of Cardiology (JACC). 2019;73(9). doi:10.1016/s0735-1097(19)33396-0. | Case Report |
| Markson F, Abe T, Adedinsewo D, et al. Sex Differences in CardioMEMS Utilization and Impact on Readmissions and Mortality in Heart Failure Patients. JACC. Heart failure. 2023;11(12). doi:10.1016/j.jchf.2023.08.021. | CARDIOMEMS Single Arm - no relevant outcomes |
| Mehra MR, Costanzo MR, Zile MR, et al.; GUIDE-HF Trial Investigators. Primary results of the prospective single-arm trial of hemodynamic-guided management of heart failure (GUIDE-HF). Paper presented at: Heart Failure Society of America Annual Scientific Meeting; October 6–9, 2023; Cleveland, OH. | CARDIOMEMS Single Arm - no relevant outcomes |
| Milligan G, Minniefield N, Raju B, et al. Effectiveness and Safety Profile of Remote Pulmonary Artery Hemodynamic Monitoring in a "Real-World" Veterans Affairs Healthcare System. The American journal of cardiology. 2022;184. | Single centre experience of CardioMEMS |
| Milligan G, Patel N, Alam A, et al. CardioMEMS Device Implantation Reduces Repeat Hospitalizations In A Veterans Affairs Patient Population: A Single Center Experience. Journal of Cardiac Failure. 2020;26(10). | Single centre experience of CardioMEMS |
| Min J, Srivastava A. CARDIOMEMS AND BARIATRIC SURGERY: A NOVEL SOLUTION FOR OBESE HFPEF. Journal of the American College of Cardiology (JACC). 2022;79(9). | Case Report |
| Morgan J, Kitt S, Gill J, et al. Remote management of heart failure using implantable electronic devices. European Heart Journal. 2017;38(30):2352-2360. | Did not evaluate intervention of interest |
| Morris K, Haleem A, Garcia-Cortes R, et al. A Single-center Experience of CardioMEMS in Patients With Left Ventricular Assist Devices. ASAIO journal (American Society for Artificial Internal Organs : 1992). 2022;68(7). | Single centre experience of CardioMEMS |
| Mullens W, Rosenkranz S, Sharif F, et al. Feasibility of Continuous Noninvasive Pulmonary Artery Pressure Monitoring via the Cordella Implantable Pulmonary Artery Sensor. JACC. Heart failure. 2024;12(4). | Background |
| New Long-term Data Published Further Demonstrate Superiority of the CardioMEMS HF System over Standard of Care. EP Lab Digest. 2015;15(12). | Not a primary study |
| Nguyen T, Soni A, Phan R, et al. GW27-e1216 Mechanism of Success in the Management of Heart Failure with the CardioMEMS? HF System. Journal of the American College of Cardiology (JACC). 2016;68. | Single centre experience of CardioMEMS |
| Ni Y, Heywood J, Mohan R, et al. THE DOCTOR-PATIENT-DEVICE COLLABORATIVE: A CARDIOMEMS QUALITY IMPROVEMENT PROJECT. Journal of the American College of Cardiology (JACC). 2022;79(9). | Did not evaluate intervention of interest |
| O'Brien D, Wolfson A, Fong M, et al. 166 - Hemodynamic Guided Therapy for Heart Failure: Initial Clinical Experience with the CardioMEMSTMHF System. Journal of Cardiac Failure. 2016;22. | Single centre experience of CardioMEMS |
| Ollendorf D, Sandhu A, Pearson S. CardioMEMS HF for the Management of Heart Failure-Effectiveness and Value. JAMA internal medicine. 2016;176(10). | Review |

| Citation | Reason for exclusion |
|---|---|
| NCT03581032. Optimization of Cardiac Pacing Using CardioMEMS.2018. URL: https://clinicaltrials.gov/show/NCT03581032 | Did not evaluate intervention of interest |
| NCT04441203. Patient SELF-management With HemodynamIc Monitoring: Virtual Heart Failure Clinic and Outcomes.2020. URL: https://clinicaltrials.gov/ct2/show/NCT04441203 | Include - ongoing/no results |
| Paul L, Moinul S, Urina-Jassir M, Gopal D, Ayalon N. Expanding pulmonary artery pressure monitoring to racially and socially diverse populations: A pilot CardioMEMS program. The American journal of the medical sciences. 2024;368(4). | Single centre experience of CardioMEMS |
| Pike E, Bjerkan AM, Fagerlund BC, Hamidi V, Harboe I, Klemp M. Continuous monitoring of pulmonary artery pressure via an implanted leadless and battery-less pressure sensor for the management of patients with moderate to severe heart failure (New York Heart Association Class III). Oslo, Norway: Norwegian Institute of Public Health (NIPH); 2016 Oct. Report No. 2016-04. https://www.ncbi.nlm.nih.gov/books/NBK482062/ | Review |
| Preister S, Case L, Deibert J, Jonsson O. 6 Pulmonary Artery Sensor (CardioMEMS) effect on Hospital Admissions and Emergency Department Visits. Heart & Lung. 2017;46(3). | Single centre experience of CardioMEMS |
| NCT04977310. Prospective, Randomized-controlled, Non-blinded, Multi-center, Pilot Trial to Compare Standard-of-care LVAD Unloading Plus Heart Failure Medications Reverse-modeling Management Versus Hemodynamics-guided LVAD Unloading with the Use of the Wireless Monitoring System CardioMEMS Plus Heart Failure Medications Reverse-remodeling Management.2021. URL: https://clinicaltrials.gov/study/NCT04977310 | Terminated/withdrawn |
| Pudlo M, Estep J, Trachtenberg B, Park M, Ketkar S, Bhimaraj A. 277 - Describing Our Heart Failure (HF) CardioMEMS Program: Our Experience at a Single Center Academic Institution. Journal of Cardiac Failure. 2017;23. | Single centre experience of CardioMEMS |
| NCT04398654. Pulmonary Artery Sensor System Pressure Monitoring to Improve Heart Failure (HF) Outcomes.2020. URL: https://clinicaltrials.gov/study/NCT04398654 | Include - ongoing/no results |
| Quinn J. Keeping PAPs down: Implementation of a Nurse-Led Pulmonary Artery Pressure Monitoring Program to Reduce Heart Failure Readmissions. Heart & Lung. 2020;49(2). | Did not evaluate intervention of interest |
| Raina A, Abraham W, Adamson P, Bauman J, Benza R. Limitations of right heart catheterization in the diagnosis and risk stratification of patients with pulmonary hypertension related to left heart disease: insights from a wireless pulmonary artery pressure monitoring system. The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation. 2015;34(3). | Retrospective cohort study |
| Rathman L, Fiorini D, Nissley K, Kurtz K, Small R, Roberts J. 147 - Holding Up Both Ends of the Bargain: Ambulatory Hemodynamic Monitoring Using CardioMEMS. Journal of Cardiac Failure. 2016;22. | Retrospective cohort study |
| Raval N, Shavelle D, Bourge R, et al. 060 - Significant Reductions in Heart Failure Hospitalizations with the Pulmonary Artery Pressure Guided HF System: Preliminary Observations From the CardioMEMS Post Approval Study. Journal of Cardiac Failure. 2017;23. | Single centre experience of CardioMEMS |
| Raval N, Valika A, Adamson P, Williams C, Brett M, Costanzo M. Pulmonary Artery Pressure-Guided Heart Failure Management Reduces Hospitalizations in Patients With Chronic Kidney Disease. Circulation. Heart failure. 2023;16(5). | CARDIOMEMS Single Arm - no relevant outcomes |
| NCT02729922. Registry of Patients With CardioMEMS.2016. URL: https://clinicaltrials.gov/ct2/show/NCT02729922 | CARDIOMEMS Single Arm - no relevant outcomes |
| Söllner B. Fernüberwachung mit CardioMEMS™ verbessert die Überlebensrate von Herzinsuffizienz-Patienten. Perfusion (0935-0020) 2023;36(2):1-12 | Not a primary study |
| Saeyeldin A, Chugh Y, Banerjee S, Alam A. CardioMEMS Device Release Failure Necessitating Percutaneous Retrieval. Journal of the Society for Cardiovascular Angiography & Interventions. 2023;2(5). | Case Report |

| Citation | Reason for exclusion |
|---|---|
| Salavitabar A, Bradley E, Chisolm J, et al. Implantable pulmonary artery pressure monitoring device in patients with palliated congenital heart disease: Technical considerations and procedural outcomes. Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions. 2020;95(2). | Background |
| Shavelle D, Desai A, Stevenson L. Response by Shavelle et al to Letters Regarding Article, "Lower Rates of Heart Failure and All-Cause Hospitalizations During Pulmonary Artery Pressure-Guided Therapy for Ambulatory Heart Failure: One-Year Outcomes From the CardioMEMS Post-Approval Study". Circulation. Heart failure. 2021;14(1). | Not a primary study |
| Sherrod C, Smith S, Kennedy K, et al. Rehospitalization Following Inpatient Cardiomems Implantation: Insights From The Nationwide Readmissions Database. Journal of Cardiac Failure. 2022;28(5). | Retrospective cohort study |
| Singh R, Varjabedian L, Kaspar G, Zughaib M. CardioMEMS in a Busy Cardiology Practice: Less than Optimal Implementation of a Valuable Tool to Reduce Heart Failure Readmissions. Cardiology research and practice. 2018;2018. | Retrospective cohort study |
| Sollner B. Heart failure: CardioMEMSTM Sensor improves quality of life and reduces risk of hospitalization. Perfusion (Germany). 2023;36(3). | Duplicate |
| Stork S, Bernhardt A, Bohm M, et al. Pulmonary artery sensor system pressure monitoring to improve heart failure outcomes (PASSPORT-HF): rationale and design of the PASSPORT-HF multicenter randomized clinical trial. Clinical research in cardiology : official journal of the German Cardiac Society. 2022;111(11). | Include - ongoing/no results |
| Suhocki P, Perry W. Abstract No. 61 - The CardioMEMSâ„¢ sensor: a novel, permanent intravascular wireless device for providing ambulatory porto-systemic pressures. Journal of Vascular & Interventional Radiology. 2017;28. | Not in the population of interest |
| Manavi T, Stapleton G, Barton J, et al. Successful implementation of a remote patient management system for heart failure patients in West Ireland. Poster presented at: National Prevention Conference. May 2023; University Hospital Galway, Ireland. | Single centre experience of Cordella |
| The Effect of a Nurse-Driven Program Utilizing Implantable Pulmonary Artery Pressure Monitoring to Reduce Hospitalizations in Low-Socioeconomic Urban Patients with Heart Failure...15th American Association of Heart Failure Nurses (AAHFN) Annual Meeting, June 27-29, 2019, Austin, Texas. Heart & Lung. 2019;48(5). | CARDIOMEMS SIngle Arm - no relevant outcomes |
| NCT06783335. The Real-World Effectiveness of The Cordella Pulmonary Artery Sensor System in Patients With Chronic Heart Failure: A Comparative Analysis to Standard of Care Pharmacologic Therapy.2025. URL: https://clinicaltrials.gov/study/NCT06783335 | Retrospective cohort study |
| Thohan V, Abraham J, Burdorf A, et al. Use of a Pulmonary Artery Pressure Sensor to Manage Patients With Left Ventricular Assist Devices. Circulation. Heart failure. 2023;16(6). | CARDIOMEMS SIngle Arm - no relevant outcomes |
| Tinnemans A. Improvement of the quality of life and reduction of hospitalization with the CardioMEMS sensor: Outcomes of the MONITOR-HF trial. Journal fur Kardiologie. 2023;30(9-10). | Not a primary study |
| Tolia S, Khan Z, Gholkar G, Zughaib M. Simultaneous measurement of pulmonary artery diastolic pressure by CardioMEMS device and left atrial pressure measurement by transthoracic echocardiography in a heart failure population. Journal of the American College of Cardiology (JACC). 2018;71(Suppl):A31479. doi:10.1016/S0735-1097(18)31479-7. | Accuracy evaluation |
| Tran J, Wolfson A, O'Brien D, Yousefian O, Shavelle D. 062 - Patient and Health Care Provider Utilization Practices of a Remote Hemodynamic Monitoring Device are Major Determinants of Patient Outcomes: A Single Center Experience with the CardioMEMS HF Device. Journal of Cardiac Failure. 2017;23. | Retrospective cohort study |
| Tran J, Wolfson A, O'Brien D, Yousefian O, Shavelle D. A Systems-Based Analysis of the CardioMEMS HF Sensor for Chronic Heart Failure Management. Cardiology research and practice. 2019;2019. | Retrospective cohort study |

| Citation | Reason for exclusion |
|---|---|
| Vaduganathan M, DeFilippis E, Fonarow G, Butler J, Mehra M. Postmarketing Adverse Events Related to the CardioMEMS HF System. JAMA cardiology. 2017;2(11). | Post-marketing AEs - no denominator |
| Valika A, Sulemanjee N, Pedersen R, Heidenreich D. Reduction in 90 day readmission rates utilizing ambulatory pulmonary pressure monitoring. ESC heart failure. 2023;10(1). | Single centre experience of CardioMEMS |
| Verdejo H, Castro P, Concepcion R, et al. Comparison of a radiofrequency-based wireless pressure sensor to swan-ganz catheter and echocardiography for ambulatory assessment of pulmonary artery pressure in heart failure. Journal of the American College of Cardiology. 2007;50(25). | Accuracy evaluation |
| Wolfson A, Grazette L, Saxon L, Nazeer H, Shavelle D, Jermyn R. Baseline diastolic pressure gradient and pressure reduction in chronic heart failure patients implanted with the CardioMEMS TM HF sensor. ESC heart failure. 2018;5(3). | Retrospective cohort study |
| Zakeri R, Morgan J, Phillips P, et al. Impact of remote monitoring on clinical outcomes for patients with heart failure and atrial fibrillation: results from the REM-HF trial. European Journal of Heart Failure. 2020;22(3):543-553. | Did not evaluate intervention of interest |
| Zoler M. CardioMEMS shows real-world success as use expands. Chest Physician. 2018;13(1). | Not a primary study |

### Table 33 Studies excluded at full-text screening (Review of Cost-effectiveness)

| Citation | Reason for exclusion |
|---|---|
| Azari S, Mousavi SH, Markazi Moghaddam N, Rezapour A, Zargar Balaye Jame S, Kolivand P, et al. Cost-Effectiveness of Remote Cardiac Monitoring With the CardioMEMS Heart Failure System: A Systematic Review. Medical journal of the Islamic Republic of Iran 2023;37(1): 2-2023. | Systematic review (not economic evaluation) |
| Dauw J, Sokolski M, Middleton JT, Nijst P, Dupont M, Forouzan O, et al. Ambulatory haemodynamic-guided management reduces heart failure hospitalizations in a multicentre European heart failure cohort. ESC heart failure 2022;9(6): 3858-3867. | Costs study (not UK) |
| Klersy C, De Silvestri A, Gabutti G, Raisaro A, Curti M, Regoli F, et al. Economic impact of remote patient monitoring: an integrated economic model derived from a meta-analysis of randomized controlled trials in heart failure. European Journal of Heart Failure 2011;13(4): 450-459. | Not PAP monitoring |
| Morgan JM, Dimitrov BD, Gill J, Kitt S, Ng GA, McComb JM, et al. Rationale and study design of the REM-HF study: remote management of heart failure using implanted devices and formalized follow-up procedures. European Journal of Heart Failure. 2014;16(9): 1039-1045.<br><br>Morgan JM, Kitt S, Gill J, McComb JM, Ng GA, Raftery J, et al. Remote management of heart failure using implantable electronic devices. European heart journal 2017;38(30): 2352-2360. | Economic evaluation planned was not reported |
| Odrobina I. Clinical Predictive Modeling of Heart Failure: Domain Description, Models' Characteristics and Literature Review. Diagnostics (Basel, Switzerland) 2024;14(4): .n.r.. | No cost-effectiveness outcomes |
| Rasoul D, Chattopadhyay I, Mayer T, West J, Stollar H, Black C, et al. Economic evaluation of the Liverpool heart failure virtual ward model. European Heart Journal - Quality of Care and Clinical Outcomes 2025;11(2): 197-205. | Not PAP monitoring |
| Reed SD, Li Y, Kamble S, Polsky D, Graham FL, Bowers MT, et al. Introduction of the tools for economic analysis of patient management interventions in heart failure costing tool a user-friendly spreadsheet program to estimate costs of providing patient-centered interventions. Circulation: Cardiovascular Quality and Outcomes 2012;5(1): epub. | Not PAP monitoring |
| The Knowledge Centre for the Health Services. Norwegian Cardiovascular Disease Model (NorCaD) – a simulation model for estimating health benefi ts and cost consequences of cardiovascular interventions.2016. URL: https://www.fhi.no/en/publ/2009-and-older/norwegian-cardiovascular-disease-model-norcad--a-simulation-model-for-estim/ (Accessed 12 April 2025). | Not PAP monitoring |

# Appendix 3

# Included study details

## Study characteristics

**Table 34 Overview of studies included in the review**

| Study Name | Study Design | Number with device implanted | Duration | Funding Sources | Study Location | Device | Inclusion criteria |
|---|---|---|---|---|---|---|---|
| **Studies that provided full quantitative outcome data** | | | | | | | |
| CHAMPION[43] | RCT | 550 | Randomised access period: 18 months (mean 15 months, SD 7) | Industry | USA | CardioMEMS | • Age ≥18 years)<br>• NYHA class III heart failure for ≥ 3 months and hospitalisation for heart failure <12 months<br>• Given drug and device treatments for heart failure at optimum or best-tolerated stable doses, according to national guidelines. |
| GUIDE-HF[45] | RCT | 1000 | 12 months | Industry | USA, Canada | CardioMEMS | • NYHA class II–IV heart failure for ≥ 3 months<br>• Hospitalisation for heart failure <12 months before study consent or elevated natriuretic peptides or N-terminal pro-BNP within 30 days before study consent<br>• Should be on stable, optimally titrated medical therapy for ≥ 30 days |
| MONITOR-HF[44] | RCT | 168 | 48 months (mean: 1.8 years, SD 0.9) | Mixed | Netherlands | CardioMEMS | • Age ≥18 years<br>• Chronic NYHA class III heart failure for ≥3 months and at least 1 HF hospitalization or urgent visit <12 months of baseline visit<br>• Patients with HFrEF should be treated according to National and International (ESC) guidelines for optimal or maximum tolerated doses of GDMT HF medication and evaluated for ICD or CRT therapy, if indicated.<br>• BMI ≤35 kg/m2<br>• BMI >35 kg/m2 will require their chest circumference to be measured at the axillary level <65 inches |
| PROACTIVE-HF[48] | RCT/ Single arm | 456 | 12 months | Industry | USA, Ireland, Belgium | Cordella | • Age ≥18 years<br>• NYHA class III heart failure for ≥3 months |

| Study Name | Study Design | Number with device implanted | Duration | Funding Sources | Study Location | Device | Inclusion criteria |
|---|---|---|---|---|---|---|---|
| | | | | | | | • Patients were to be on stable, optimally titrated GDMT for at least 30 days before screening.<br>• Patients had to have at least 1 HF hospitalization, HF treatment in a hospital day-care setting, or urgent outpatient clinic HF visit within 12 months and/or elevated NT-proBNP |
| SIRONA[46] | Single arm | 15 | 3 months | Industry | Belgium & Ireland | Cordella | • Age ≥18 years<br>• NYHA class III heart failure for ≥3 months with reduced or pre-served ejection fraction treated for a minimum of 3 months and stable for 1 month prior to enrolment with at least one HF-related hospitalization or equivalent within the last year<br>• eGFR of ≥30 mL/min/1.73 m2 and appropriate pulmonary artery anatomy |
| SIRONA 2[47] | Single arm | 70 | 12 months | Industry | Belgium, Germany, Ireland | Cordella | • Age ≥18 years<br>• NYHA class III heart failure for ≥3 months with reduced or preserved ejection fraction treated for a minimum of 3 months and stable for 1month prior to enrolment with at least one HF-related hospitalization or equivalent within the last year<br>• eGFR of ≥30 mL/min/1.73 m2 and appropriate pulmonary artery anatomy |
| **Studies included for device related outcomes only** | | | | | | | |
| MEMS-HF | Prospective, non-randomised, multi-centre | 234 | 12 months | Industry | Germany, Netherlands, Ireland | CardioMEMS | • Age ≥18 years<br>• NYHA class III symptoms over last month and ≥1 HFH in the previous year<br>• Patients with reduced LVEF needed to be on GDMT as tolerated<br>• Patients for heart transplant, ventricular assist device implantation or hospice excluded |
| COAST-UK | Prospective, non-randomised, multi-centre | 100 | 12 months | Industry | UK | CardioMEMS | • Persistent NYHA class III symptoms and at least 1 HFH within 12 months prior to enrolment<br>• Patients with reduced ejection fraction required to be treated with a beta-blocker for 3 months and angiotensin-converting enzyme inhibitor or |

| Study Name | Study Design | Number with device implanted | Duration | Funding Sources | Study Location | Device | Inclusion criteria |
|---|---|---|---|---|---|---|---|
| | | | | | | | angiotensin receptor blocker for 1 month unless intolerant |
| COAST-FRANCE | Prospective, non-randomised, multi-centre | 103 | 24 months | Industry | France | CardioMEMS | • Persistent NYHA class III symptoms and at least 1 HFH within 12 months prior to enrolment<br>• Patients with HFrEF required to be treated with a beta-blocker for 3 months and angiotensin-converting enzyme inhibitor or angiotensin receptor blocker for 1 month unless intolerant |
| CardioMEMS-PAS | Prospective, non-randomised, multi-centre | 1200 | 24 months | Industry | USA | CardioMEMS | • NYHA class III symptoms<br>• HFH within the prior 12 months<br>• HFrEF patients required to take a beta-blocker for 3 months and arenin-angiotensin system (RAS) inhibitor for at least1 month unless intolerant |
| **Studies that reported on patient experience and satisfaction** | | | | | | | |
| Assaad et al.[58] | Survey | 30 | NA | No external funding | USA | CardioMEMS | • CardioMEMS device implanted |
| Haynes et al.[53] | Semi-structured interviews | 12 | 106-1522 days with device | No external funding | USA | CardioMEMS | • UC Davis patients with congestive HF<br>• CardioMEMS device implanted<br>• Cognitively and physically able to participate |

CTPA - computed tomography pulmonary angiogram, GDMT – guideline directed medical therapy, HFrEF – heart failure with reduced ejection fraction, LVEF – left ventricular ejection fraction, NT-proBNP - N-terminal prohormone of brain natriuretic peptide, NYHA – New York heart association

## Included studies and reports

**Table 35 Studies included in the review showing primary and related reports and whether additional data were extracted from related reports**

| Study Name | Report | Additional Data extracted |
|---|---|---|
| **Studies that provided full quantitative outcome data** | | |
| Champion | Primary report[43] | NA |
| | Trial registry entry[152] | NA |
| | Related report - no relevant data[153] | NA |
| | Related report - no relevant data[154] | NA |
| | Related report - data extracted[155] | Intervention characteristics & outcome definitions |
| | Related report - subpopulation[156] | HFH endpoint for MI subgroup |
| | Related report - no relevant data[157] | NA |
| | Related report - subpopulation[158] | HFH endpoint for hAF subgroup |
| | Related report - no relevant data[159] | NA |
| | Related report - subpopulation[160] | HFH endpoint for CKD subgroup |
| | Related report - subpopulation[161] | COPD subgroup |
| | Related report - no relevant data[162] | NA |
| | Related report - data extracted[163] | Change in medication endpoint at 6 months |
| | Related report - no relevant data[164] | NA |
| | Related report - data extracted[91] | Primary & secondary endpoints at 18 months |
| | Related report - no relevant data[165] | NA |
| | Related report - no relevant data[144] | PAPP subgroup |
| | Related report - no relevant data[46] | NA |
| | Related report - no relevant data[166] | NA |
| GUIDE-HF | Primary report[45] | NA |
| | Trial registry entry[167] | NA |
| | Related report - subpopulation[168] | COVID-19 subgroup |
| | Related report - subpopulation[169] | NA |
| | Related report - subpopulation[170] | NA |

| Study Name | Report | Additional Data extracted |
|---|---|---|
| | Related report - no relevant data[171] | NA |
| MONITOR-HF | Primary report[44] | NA |
| | Trial registry entry[172] | NA |
| | Related report - no relevant data[173] | NA |
| | Related report - subpopulation[143] | Primary & secondary endpoints at 12 months for subgroups |
| PROACTIVE-HF | Primary report[48] | NA |
| | Trial registry entry[152] | NA |
| | Related report - no relevant data[174] | Intervention characteristics |
| | Related report - no relevant data[175] | NA |
| | Related report - data extracted[176] | Primary & secondary endpoints at 12 months |
| | Related report - subpopulation[57] | Subpopulation - former control group; Qualitative data |
| | Related report - no relevant data[177] | NA |
| | Related report - no relevant data[178] | NA |
| SIRONA | Primary report[46] | NA |
| | Trial registry entry[179] | NA |
| | Related report - data extracted[180] | KCCQ & NYHA classification endpoints |
| SIRONA 2 | Primary report[47] | Qualitative data – web survey data |
| | Trial registry entry[181] | NA |
| | Related report - data extracted[133] | Funding, Primary & secondary endpoints at 12 months |
| **Studies included for device related outcomes only** | | |
| MEMS-HF | Primary report[49] | NA |
| | Protocol[182] | NA |
| | Related report – no relevant data[183] | NA |
| COAST | Primary report – UK cohort[50] | NA |
| | Primary report – French cohort[56] | NA |
| | Protocol[55] | NA |
| | Related report – no relevant data[184] | NA |
| CardioMEMS-PAS | Primary report[51] | NA |
| | Related report – no relevant data[185] | NA |

| Study Name | Report | Additional Data extracted |
|---|---|---|
| | Related report – no relevant data[186] | NA |
| | Related report – no relevant data[84] | NA |
| **Studies that reported on patient experience and satisfaction** | | |
| Assaad et al. | Primary report[58] | NA |
| Haynes et al. | Primary report[53] | NA |

## Baseline characteristics

### Table 36 Baseline participant details: Quantitative studies only

| Study name | Intervention arm | Number with device implanted | Age Mean (SD) | % Male | % White | % Black | % Asian | % Hispanic | % Other | BMI kg/m2 Mean (SD) | NYHA class (%) | LVEF (≥40%) (%) | | | LVEF Mean % (SD) | eGFR mL/min/1.73 m2 Mean (SD) | PA mean pressure mmHg Mean (SD) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | II | III | IV | | | | |
| **Studies that provided full quantitative outcome data** | | | | | | | | | | | | | | | | | |
| CHAMPION[43] | CardioMEMS | 270 | 61 (13) | 72 | 73 | NR | NR | NR | NR | 31 (7) | 0 | 100 | 0 | 62 (23) | NR | 60 (23) | 29 (10) |
| | Standard care | 280 | 62 (13) | 73 | 73 | NR | NR | NR | NR | 31 (7) | 0 | 100 | 0 | 57 (20) | NR | 62 (23) | 30 (10) |
| GUIDE-HF[45] | CardioMEMS | 497 | 71 (64, 76)* | 62 | 81 | 17 | 0 | 3 | 1 | 32 (27, 38)* | 29 | 65 | 6 | 224 (45) | 38 (25, 55)* | 51 (39, 65)* | 28 (22, 35)* |
| | Standard care | 503 | 70 (64, 77)* | 63 | 80 | 18 | <1 | 3 | 1 | 33 (28, 39)* | 30 | 65 | 5 | 245 (49) | 40 (25, 55)* | 49 (38, 65)* | 29 (22, 35)* |
| MONITOR-HF[44] | CardioMEMS | 176 | 69 (61, 75)* | 78 | NR | NR | NR | NR | NR | 27 (24, 32)* | 0 | 100 | 0 | 48(27) | 30 (23, 40)* | 48 (35, 60)* | 33 (11) |
| | Standard care | 172[$] | 70 (61, 75)* | 73 | NR | NR | NR | NR | NR | 27 (24, 31)* | 0 | 100 | 0 | 49 (29) | 30 (22, 43)* | 48 (38, 63)* | NR |
| PROACTIVE-HF[48] | Cordella | 456 | 64 (13) | 61 | 76 | 18 | 2 | 4 | 2 | 36 (9) | 0 | 100 | 0 | 246 (54) | NR | 55 (19) | 28 (10) |
| SIRONA[46] | Cordella | 15 | 71 | 67 | 100 | 0 | 0 | 0 | 0 | 29 | 0 | 100 | 0 | NR | NR | NR | NR |
| SIRONA 2[47] | Cordella | 70 | 71 (10) | 71 | 94 | NR | NR | NR | NR | 29 (6) | 0 | 100 | 0 | NR | 37 (14) | NR | NR |
| **Studies included for device related outcomes only** | | | | | | | | | | | | | | | | | |
| MEMS-HF[49] | CardioMEMS | 234 | 68(11) | 78 | NR | NR | NR | NR | NR | 29(5) | 0 | 100 | 0 | 64(28) | 33(15) | NR | 30(11) |
| COAST-UK[50] | CardioMEMS | 100 | 69(12) | 70 | NR | NR | NR | NR | NR | 30 (7) | 0 | 100 | 0 | NR | NR | 51(17) | 34(11) |
| COAST-FRANCE[56] | CardioMEMS | 103 | 67(12) | 78 | NR | NR | NR | NR | NR | 28(5) | 0 | 100 | 0 | 30 (29) | NR | 53(22) | 36(11) |
| CardioMEMS-PAS[51] | CardioMEMS | 1200 | 70(12) | 62 | 83 | 14 | 1 | NR | 1.9 | 32(8) | 0 | 100 | 0 | NR | 39(17) | 53(21) | NR |

*median and lower and upper ranges are reported

[$]Device not implanted in control group

## Table 37 Baseline characteristics: medical/surgical history - Studies that provided data on all quantitative outcomes only

| Study name | Intervention arm | Coronary artery disease (%) | COPD (%) | Ischemic cardiomyopathy (%) | Diabetes Mellitus (%) | CKD (%) | Myocardial infarction (%) | Hypertension (%) | Atrial fibrillation (%) | Ischemic cause (%) | Cerebrovascular accident or transient ischaemic (%) | Previous percutaneous coronary intervention (%) | Previous coronary artery bypass graft surgery (%) | Previous implantable cardioverter-defibrillator (%) | Previous cardiac resynchronization therapy (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CHAMPION[43] | CardioMEMS | 182 (67) | 76 (28) | 158 (59) | 130 (48) | 54 (20) | NR | 207 (77) | 120 (44) | NR | NR | NR | NR | 88 (33) | 91 (34) |
| | Standard care | 202 (72) | 83 (30) | 174 (62) | 139 (50) | 54 (19) | NR | 220 (79) | 135 (48) | NR | NR | NR | NR | 98 (35) | 99 (35) |
| GUIDE-HF[45] | CardioMEMS | NR | NR | NR | 243 (49) | NR | 144 (29) | NR | 300 (60) | 207 (42) | 66 (13) | 165 (33) | 135 (27) | 213 (43) | 142 (29) |
| | Standard care | NR | NR | NR | 261 (52) | NR | 158 (31) | NR | 291 (58) | 190 (38) | 65 (13) | 158 (31) | 136 (27) | 205 (41) | 163 (32) |
| MONITOR-HF[44] | CardioMEMS | NR | NR | NR | 66 (38) | NR | 81 (46) | 102 (58) | 100 (57) | NR | 29 (17) | 74 (42.0) | 34 (19) | NR | NR |
| | Standard care | NR | NR | NR | 68 (40) | NR | 65 (38) | 98 (57) | 81 (47) | NR | 39 (23) | 59 (34) | 34 (20) | NR | NR |
| PROACTIVE-HF[48] | Cordella | NR | 92 (20) | NR | 233 (51) | 198 (43) | 118 (26) | 403 (88) | 236 (52) | 143 (31) | NR | 134 (29) | 81 (18) | 160 (35) | 82 (18) |
| SIRONA[46] | Cordella | 7 (47) | 3 (20) | NR | 4 (27) | NR | 7 (47) | 10 (67) | 9 (60) | NR | NR | NR | NR | NR | NR |
| SIRONA 2[47] | Cordella | NR | NR | NR | 32 (46) | 22 (31) | NR | 51 (73) | 46 (66) | NR | NR | NR | NR | 22 (31) | 13 (19) |

## Table 38 Baseline characteristics: treatment history - Studies that provided data on all quantitative outcomes only

| Study name | Intervention arm | Beta blocker (%) | Renin-angiotensin-aldosterone system inhibitor (%) | Angiotensin-converting enzyme inhibitor (%) | Angiotensin-receptor blocker (%) | Angiotensin-receptor neprilysin inhibitor (%) | Hydralazine dinitrate (%) | Mineralocorticoid receptor antagonist (%) | SGLT2 inhibitor (%) | Loop diuretic (%) | Thiazaide diuretic (%) | Loop and thiazide diuretic (%) | Diuretic (%) | Nitrates (%) | Aldosterone antagonist (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CHAMPION[43] | CardioMEMS | 243 (90) | NR | NR | NR | NR | 36 (13) | NR | NR | 248 (92) | NR | NR | NR | 64 (24) | 117 (43) |
| | Standard care | 256 (91) | NR | NR | NR | NR | 33 (12) | NR | NR | 258 (92) | NR | NR | NR | 56 (20) | 114 (41) |
| GUIDE-HF[45] | CardioMEMS | 444 (89) | NR | NR | NR | 145 (29) | 81 (16) | 237 (48) | 2 (<1) | NR | NR | NR | 474 (95) | 99 (20) | NR |
| | Standard care | 442 (88) | NR | NR | NR | 139 (28) | 80 (16) | 216 (43) | 2 (<1) | NR | NR | NR | 478 (95) | 103 (20) | NR |
| MONITOR-HF[49] | CardioMEMS | 150 (85) | 154 (88) | 37 (21) | 26 (15) | 81 (46) | 10 (6) | 143 (81) | 12 (7) | 168 (96) | 11 (6) | 11 (6) | NR | NR | NR |
| | Standard care | 142 (83) | 147 (86) | 32 (19) | 26 (15) | 81 (47) | 8 (5) | 144 (84) | 21 (12) | 167 (97) | 10 (6) | 10 (6) | NR | NR | NR |
| PROACTIVE-HF[48] | Cordella | 365 (80) | 287 (63) | 21 (5) | 65 (14) | 201 (44) | 36 (8) | NR | 259 (57) | 418 (92) | 71 (16) | NR | 422 (93) | 82 (18) | 304 (67) |
| SIRONA[46] | Cordella | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR | NR |
| SIRONA 2[47] | Cordella | 54 (77) | 55 (77) | 19 (27) | 9 (13) | 27 (39) | NR | NR | 12 (17) | NR | NR | NR | 61 (89) | NR | 38 (54) |

# Appendix 4

## Included study results

### Primary outcomes

**Table 39 HFH, urgent visits, HF mortality, all-cause mortality and quality of life**

| Study name | PAP Device | N (Tx/ctrl) | Follow-up (months) | Result | Outcome definition | ROB |
|---|---|---|---|---|---|---|
| **HFH** | | | | | | |
| CHAMPION [91] | CardioMEMS | 270/280 | 18 | **Intervention group:** 182 events (0.46 EPPY))<br>**Control group:** 279 events (0.68 EPPY)<br>**Relative effect: HR 0.67 (95% CI 0.55, 0.80); p < 0.0001)** | Defined by clinical criteria including ≥24-hour admission, new or worsening HF symptoms and signs, and the need for additional HF therapy | Low |
| | CardioMEMS: COPD subgroup | 91/96 | 15 | **Intervention group:** 66 events (0.55 EPPY)<br>**Control group:** 110 events (0.92 EPPY)<br>**Relative effect: HR 0.59 (95% CI 0.44, 0.81), p=0.0009** | | NA |
| | CardioMEMS: CKD subgroup | 150/147 | 6 | **Intervention group:** 0.48 EPPY<br>**Control group:** 0.83 EPPY<br>**Relative effect: HR 0.58, p<0.001** | | NA |
| | CardioMEMS: hAF subgroup | 120/135 | 15 | **Intervention group:** 0.54 EPPY<br>**Control group:** 0.91 EPPY | | NA |
| | CardioMEMS: Baseline PAP Subgroup | | | Relative reduction in HFH between intervention and control:<br>PAP ≤0.583: 27%<br>PAP>0.583: 43%<br><br>Absolute reduction in HFH between intervention and control:<br>PAP ≤0.583: 0.68<br>PAP>0.583: 0.49 | | NA |
| GUIDE-HF [45] | CardioMEMS | 497/503 | 12 | **Intervention group:** 185 events (0.41 EPPY)<br>**Control group:** 225 events (0.50 EPPY)<br>**Relative effect: HR 0.83 (95% CI 0.68, 1.01) ; p = 0.064** | Defined as ≥24-hour hospitalisation primarily due to decompensated HF requiring intravenous diuretics | Low |
| | CardioMEMS: NYHA class III subgroup | [redacted] | 12 | [redacted] | | NA |

| Study name | PAP Device | N (Tx/ctrl) | Follow-up (months) | Result | Outcome definition | ROB |
|---|---|---|---|---|---|---|
| | CardioMEMS: COVID-19 subgroup | 497/503 | 12 | **Pre-COVID-19:**<br>**Intervention group:** 124 events (0.38 EPPY)<br>Control group: 176 events (0.53 EPPY)<br>**Relative effect: HR 0.72 (95% CI 0.57, 0.92); p = 0.0072**<br><br>**During-COVID-19:**<br>**Intervention group:** 61 events (0.49 EPPY)<br>Control group: 49 events (0.41 EPPY)<br>**Relative effect: HR 1.18 (95% CI 0.81, 1.73); p = 0.38** | | NA |
| MONITOR-HF[44] | CardioMEMS | 176/172 | 48 | **Intervention group:** 106 events (0.345 EPPY)<br>**Control group:** 195 events (0.624 EPPY)<br>**Relative effect: HR 0.56 (95% CI 0.38, 0.82); p = 0.0053.** | Defined as a hospitalisation due to heart failure, longer than 6 hours and/or the use of intravenous diuretics for decongestion of the patient | Low |
| | CardioMEMS: Age subgroup | ≥69.4: 174<br><69.4: 174 | 48 | ≥69.4: **HR 0.64 (95% CI 0.38, 1.08)**<br><69.4: **HR 0.49 (95% CI 0.28, 0.87)**<br>**Comparison between groups: p=0.50** | | NA |
| | CardioMEMS: Sex subgroup | Female: 85<br>Male: 263 | 48 | Female: **HR 0.51 (95% CI 0.28, 0.94)**<br>Male: **HR 0.58 (95% CI 0.36, 0.96)**<br>**Comparison between groups: p=0.74** | | NA |
| | CardioMEMS: eGFR subgroup | ≥60mL/min: 95<br><60 mL/min: 253 | 48 | ≥60mL/min: **HR 0.40 (95% CI: 0.16-0.99)**<br><60 mL/min: **HR 0.61 (95% CI: 0.39-0.95**<br>**Comparison between groups: p=0.43** | | NA |
| | CardioMEMS: DM subgroup | Yes: 134<br>No: 214 | 48 | Yes: **HR 0.42 (95% CI 0.23, 0.77)**<br>No: **HR 0.67 (95% CI 0.40, 1.12)**<br>**Comparison between groups: p=0.26** | | NA |
| SIRONA[46] | Cordella | 15 | 3 | 1 HF event | Frequency of HFH, HF treatments in a hospital day-care setting or urgent outpatient clinic HF visits | High |
| SIRONA 2[47] | Cordella | 70 | 12 | 18 events in 14 patients<br>Pre-implant vs Post-implant: 1.26 vs 0.27 EPPY, p<0.0001 | Frequency of HFH, HF treatments in a hospital day-care setting or urgent outpatient clinic HF visits | Some concerns |
| PROACTIVE-HF[48] | Cordella: RCT | 72/88 | 12 | **Relative effect: HR 0.61 (95% CI: 0.36, 1.04), p = 0.0685)** | NR | Some concerns |

| Study name | PAP Device | N (Tx/ctrl) | Follow-up (months) | Result | Outcome definition | ROB |
|---|---|---|---|---|---|---|
| | Cordella: single arm | 456 | 6 | 60 events<br>Pre-implant vs post-implant : 0.6 (SD=± 0.7) vs 0.1 (SD=0.4), p<0.0001 (average HFH per patient) | | Some concerns |
| | Cordella: Former control group | 63 | 12 | 12 events in 7 patients (0.24 EPPY)<br>Pre-implant vs post-implant: 1.3 (SD 0.9) vs 0.3 (SD 0.9), p<0.0001 (average HFH) | | NA |
| **All-cause mortality** | | | | | | |
| CHAMPION [43] | CardioMEMS | 270/280 | 18 | **Intervention group**: 50 events<br>**Control group**: 64 events<br>**Relative effect: HR 0.80 (95% CI 0.55, 1.15); p=0.23** | NR | Some concerns |
| | CardioMEMS: Baseline PAP Subgroup | | | **Baseline PAP≤0.583**<br>**Relative effect: HR 0.54 (95% CI 0.31, 0.92)**<br><br>**Baseline PAP≥0.583**<br>**Relative effect: HR 1.18 (95% CI 0.70, 1.99)**<br>**Difference between groups : p=0.02** | | NA |
| GUIDE-HF[45] | CardioMEMS | 497/503 | 12 | **Intervention group:** 40 events (0.094 EPPY)<br>**Control group:** 37 events (0.086 EPPY)<br>**Relative effect: HR 1.09 (95% CI 0.70, 1.70); p=0.71** | Adjudicated by an independent Clinical Events Committee | Low |
| | CardioMEMS: NYHA class III subgroup | [redacted] | 12 | [redacted] | | NA |
| | CardioMEMS: COVID-19 subgroup | Pre-COVID-19: 497/503<br><br>During-COVID-19: 497/503 | 12 | **Pre-COVID-19:**<br>**Intervention group:** 30 events (0.110 EPPY)<br>**Control group:** 25 events (0.088 EPPY)<br>**Relative effect: HR 1.24 (95% CI 0.73, 2.11); p = 0.42**<br><br>**During-COVID-19:**<br>**Intervention group:** 10 events (0.067EPPY)<br>**Control group:** 12 events (0.085 EPPY)**Relative effect: HR 0.79 (95% C: 0.35, 1.83); p = 0.38** | | NA |
| MONITOR-HF[44] | CardioMEMS | 176/172 | 48 | **Intervention group:** 42 events (0.137 EPPY)<br>**Control group:** 45 events (0.144 EPPY) | Deaths classified and presented in all-cause mortality or CV-mortality | Some concerns |

| Study name | PAP Device | N (Tx/ctrl) | Follow-up (months) | Result | Outcome definition | ROB |
|---|---|---|---|---|---|---|
| | | | | **Relative effect: HR 0.96 (95% CI 0.63, 1.46); p=0.846** | | |
| SIRONA 2[47] | Cordella | 70 | 12 | 5 events | NR | |
| PROACTIVE -HF[48] | Cordella: RCT | 72/88 | 12 | **Relative effect: HR 0.51 (95% Wald CI: 0.20 – 1.32), p = 0.167)** | NR | Some concerns |
| | Cordella: Single arm | 456 | 6 | 10 events | | NA |
| | Cordella: Former control group | 63 | 12 | 2 events, 0.03 EPPY | | NA |
| **HRQoL: KCCQ** | | | | | | |
| GUIDE-HF[45] | CardioMEMS | 421/408 | 12 | **Intervention group:** Mean difference in overall score: 5.20 (SD 21.35), p<0.0001<br>**Control group:** Mean difference in overall score: 4.12 (SD 22.50), p=0.0002<br>**Mean difference between groups in change from baseline:** 1.08<br><br>**Between groups**: p=0.48 | KCCQ-12 Overall Summary Score<br><br>KCCQ scale 0-100:<br>0 = worst health status<br>100 = best health status | Some concerns |
| MONITOR-HF[44] | CardioMEMS | 176/172 | 12 | **Mean difference between groups in change from baseline:** 7.13 (95% CI: 1.51-12.75), p=0.013 | Mean change in KCCQ overall summary (OS) score from baseline to 12 months. Differences in mean KCCQ-OS changes between the treatment groups assessed.<br><br>KCCQ scale 0-100:<br>0 = worst health status<br>100 = best health status | Some concerns |
| | CardioMEMS: Age subgroup | ≥69.4: 131<br><69.4: 148 | 12 | **≥69.4:** Mean difference 0.52 (−6.42−7.45)<br>**<69.4:** Mean difference 12.64 (4.16−21.13) | | NA |
| | CardioMEMS: Sex subgroup | Female: 74<br>Male: 205 | 12 | **Female:** Mean difference 1.76 (−9.31−12.83)<br>**Male:** Mean difference 8.89 (2.34−15.44) | | NA |
| | CardioMEMS: eGFR subgroup | ≥60mL/min: 81<br><60 mL/min: 198 | 12 | **≥60mL/min:** Mean difference 4.51 (−4.79−13.82)<br>**<60 mL/min:** Mean difference 8.28 (1.31−15.26) | | NA |
| | CardioMEMS: DM subgroup | Yes: 105<br>No: 138 | 12 | **Yes**: Mean difference −3.06 (−12.77−6.65)<br>**No:** Mean difference 13.42 (6.56−20.28) | | NA |
| SIRONA[46] | Cordella | 15 | 3 | **Mean score:** 66 (SD 27); mean difference change from baseline of 5 points | KCCQ scale 0-100:<br>0 = worst health status<br>100 = best health status | High |
| SIRONA 2[47] | Cordella | 70 | 12 | **Baseline:** mean score - 60.4 (SD 24.2)<br>**12 months:** mean score - 59.4 (SD 23.8)<br>**Change from baseline:** p = 0.82 | Out of 23-items, 10 scores calculated. Presented as absolute values and change from baseline by visit. | Some concerns |

| Study name | PAP Device | N (Tx/ctrl) | Follow-up (months) | Result | Outcome definition | ROB |
|---|---|---|---|---|---|---|
| | | | | | KCCQ scale 0-100:<br>0 = worst health status<br>100 = best health status | |
| PROACTIVE -HF[48] | Cordella | 456 | 12 | **Baseline:** mean score – 52.8 (SD 22.8)<br>**12 months:** mean score – 58.5 (SD 24.4)<br>p<0.0001 | KCCQ scale 0-100:<br>0 = worst health status<br>100 = best health status | Some concerns |
| **HRQoL: EQ-5D-5L VAS** | | | | | | |
| GUIDE-HF[45] | CardioMEMS | 421/409 | 12 | **Intervention group:** mean difference in scores 0.94 (SD 20.17), p = 0.34<br>**Control group:** mean difference in scores 2.90 (SD 20.71), p = 0.0048<br>**Mean difference between groups in change from baseline:** -1.96 (-4.72, 0.80)<br><br>**Between groups**: p=0.17 | EQ-5D-5L scale 0-100:<br>0 = worst health state<br>100 = health state | Some concerns |
| MONITOR-HF[44] | CardioMEMS | 176/172 | 12 | **Mean difference between groups in change from baseline**: 6·0 (95% CI 1.1, 10.9; p=0·016) in favour of the intervention group (+3·0 in the intervention group and –3·0 in the control group) | Mean difference in EQ-5D-5L VAS score.<br><br>EQ-5D-5L scale 0-100:<br>0 = worst health state<br>100 = health state | Some concerns |
| **HRQoL: MLHFQ** | | | | | | |
| CHAMPION [43] | CardioMEMS | 270/280 | 12 | **Intervention group:** 47.0 score<br>**Control group:** 56.5 score<br>p=0.0267 | MLHFQ total score range 0-105:<br>Lower score=better health status<br>Higher score=worse health status | High |

CI – confidence interval, CKD – chronic kidney disease, COPD – chronic obstructive pulmonary disease, Ctrl – control, DM – diabetes mellitus, EPPY – events per patient-year, EQ-5D-5L-VAS - European Quality of Life Five-Dimensions Five-Level Visual Analogue Scale, hAF – history of atrial fibrillation, HF – heart failure, HFH – heart failure hospitalisations, KCCQ - Kansas City Cardiomyopathy Questionnaire, MD – mean difference, MLHFQ - Minnesota Living with Heart Failure questionnaire NA – not applicable, NR – not reported, Pt – patient, SD – standard deviation, SoC – standard of care, Tx - treatment

## Table 40 Device related outcomes: failure of sensor implantation, sensory failure, and device related complications

| Study name | PAP Device | Number of devices | Follow-up (months) | Result | Outcome definition | ROB |
|---|---|---|---|---|---|---|
| **Failure of sensor implantation** | | | | | | |
| CHAMPION[43] | CardioMEMS | Attempted implant: 575 | 6 | 25 implant failure: 19 devices not opened; 2 sensors did not release; successfully removed; 1 transient ventricular tachycardia; 1 difficulty maintaining guide-wire position due to severe chronic cough; 1 transient left bundle branch block; 1 discovery of pre-existing deep vein thrombosis or pulmonary embolism during pulmonary angiogram | NA | Low |
| GUIDE-HF[45] | CardioMEMS | Attempted implant: 1022 | 12 | 22 implant failures; reasons NR | NA | Low |
| MONITOR-HF[44] | CardioMEMS | Attempted implant: 168 | 48 | 4 failures to implant on 1st attempt:1 unexpected abnormal anatomy, 3 operator or (tech.) facility related. All implanted on second attempt. | NA | Low |
| MEMS-HF[49] | CardioMEMS | Attempted implant: 234 | 12 | None | NA | Low |
| COAST-UK[50] | CardioMEMS | Attempted implant: 103 | 12 | 3 implant failures due to: haemoptysis, anatomical constraints and inability to gain venous access. | NA | Low |
| COAST-FRANCE[56] | CardioMEMS | Attempted implant: 103 | 24 | None | NA | Low |
| CardioMEMS -PAS[51] | CardioMEMS | Attempted implant: 1214 | 24 | 14 implant failures, reason NR | NA | Low |
| SIRONA[46] | Cordella | Attempted implant: 15 | 3 | None | NA | High |
| SIRONA 2[47] | Cordella | Attempted implant: 70 | 12 | None | NA | Low |
| PROACTIVE-HF[48] | Cordella | Attempted implant: 493 | 6 | 37 implants aborted due to: adherence to IFU (out of range PA diameter), prior undiagnosed comorbidities, procedural skills/challenges | NA | Low |

| Study name | PAP Device | Number of devices | Follow-up (months) | Result | Outcome definition | ROB |
|---|---|---|---|---|---|---|
| **Sensor failure** | | | | | | |
| CHAMPION[43] | CardioMEMS | Implanted: 550 | 6 | No sensor failures | Pressure-sensor failure was defined as an inability to obtain readings | Low |
| MONITOR-HF[44] | CardioMEMS | Implanted: 168 | 48 | 2 sensor failures:<br>• 1 pt lost signal due to complex posture – no re-implant attempted<br>• 1 pt lost signal due to displacement - reimplanted<br>No events required removal of sensor. | Sensor failure was defined as any longstanding inability to obtain readings due to malfunction of the sensor (resulting in signal loss/no readings). | Low |
| MEMS-HF[49] | CardioMEMS | Implanted: 234 | 12 | 1 sensor failure | Inability to obtain readings after troubleshooting the system to exclude problems with external electronics | Low |
| COAST-UK[50] | CardioMEMS | Implanted: 100 | 12 | 1 sensor failure | A sensor failure occurs when no readings can be obtained from after troubleshooting the system to rule out any problems with the external electronics. | Low |
| COAST-FRANCE[56] | CardioMEMS | Implanted: 103 | 24 | No sensor failures | | Low |
| CardioMEMS-PAS[51] | CardioMEMS | Implanted: 1200 | 24 | 1 sensor failure | NR | Low |
| SIRONA[46] | Cordella | Implanted: 15 | 3 | No sensor failures | NR | High |
| SIRONA 2[47] | Cordella | Implanted: 70 | 12 | No sensor failures | NR | Low |
| PROACTIVE-HF[48] | Cordella | Implanted: 456 | 6 | 1 sensor failure<br>Freedom from sensor failure: 99.8% (95% CI: 98.6, 100%) | NR | Low |
| **Device/system or procedure related complications** | | | | | | |
| CHAMPION[43] | CardioMEMS | Attempted implant: 575 | 6 | 15 SAEs<br>• 8 (1%) were DSRC<br>• 7 (1%) were procedure-related AEs<br>SAEs included:<br>• 4 bleeding events | An AE that was definitely or was potentially related to the wireless pressure sensor or external electronics, and was treated with invasive means other than intramuscular administration of drugs or a right-heart catheterisation | Low |

| Study name | PAP Device | Number of devices | Follow-up (months) | Result | Outcome definition | ROB |
|---|---|---|---|---|---|---|
| | | | | • 3 hospitalisations related to anticoagulation intervention<br>• 2 exacerbations of pre-existing atrial dysrhythmias during right heart catheterisation<br>• 2 febrile illnesses<br>• 1 pulmonary insitu thrombus during right-heart catheterisation<br>• 1 cardiogenic shock<br>• 1 atypical chest pain<br>• 1 delivery-system failure that required a snare to remove the delivery system | NR | |
| GUIDE-HF[45] | CardioMEMS | Attempted implant: 1022 | 12 | 8 (0.8%) DSRC | An AE that is related or possibly related to the system (CardioMEMS™ PA Sensor or other components of the CardioMEMS™ HF System) and has at least one of the following characteristics: is treated with invasive means (other than intramuscular medication or a right heart catheterization which is used for diagnostic purposes) or resulted in the death of the subject or resulted in the explant of the device | Low |
| MONITOR-HF[44] | CardioMEMS | Attempted implant: 168 | 48 | 4 (2.4%) DSRC events:<br>• 2 haemoptysis with invasive measures<br>• 2 arrythmias<br>No DSRC resulted in death or explant of the device. | An AE that was definitely or possibly related to the wireless pressure sensor or external electronics, and was treated with invasive means (other than intramuscular medication or right heart catheterization which is used for diagnostic purposes), resulted in death of the subject or resulted in the explant of the device | Low |
| MEMS-HF[49] | CardioMEMS | Attempted implant: 234 | 12 | 21 SADEs of which:<br>4 were DSRC events<br>• Lead dislodgement or migration | (serious) AE definitely or possibly related to the PAP sensor or external electronics that was | Low |

| Study name | PAP Device | Number of devices | Follow-up (months) | Result | Outcome definition | ROB |
|---|---|---|---|---|---|---|
| | | | | • Haemoptysis<br>• Infection<br>• Endocarditis | treated invasively or resulted in patient death or explant of the device. | |
| | | | | 21 procedure-related AEs in 18 pts:<br>• 2 abnormal heart rate or rhythm<br>• 2 bleeding<br>• 1 cardiac decompensation<br>• 2 haemoptysis<br>• 4 infection<br>• 3 lead dislodgment or migration<br>• 1 pulmonary artery perforation<br>• 3 renal failure<br>• 3 other<br>• 1 endocarditis<br>• 1 pseudoaneurysm formation<br>• 1 sudden death | | |
| COAST-UK[50] | CardioMEMS | Attempted implant: 103 | 12 | No DSRC events | An AE that is or is possibly related to the system (wireless pressure sensor or external electronics), and has at least one of the following characteristics: Is treated with invasive means (other than intramuscular medication or a right heart catheterization that is used for diagnostic purposes), results in the death of the subject or results in the explant of the device | Low |
| COAST-FRANCE[56] | CardioMEMS | Attempted implant: 103 | 24 | No DSRC events | | Low |
| CardioMEMS -PAS[51] | CardioMEMS | Attempted implant: 1214 | 24 | 5 DSRC events; details NR | Defined based on the criteria of the CHAMPION study: An AE that was definitely or was potentially related to the wireless pressure sensor or external electronics, and was treated with invasive means other than intramuscular administration of drugs or a right-heart catheterisation | Low |
| SIRONA[46] | Cordella | Attempted implant: 15 | 3 | No DSRC events. | Defined as invasive treatment, device explant or death | High |

| Study name | PAP Device | Number of devices | Follow-up (months) | Result | Outcome definition | ROB |
|---|---|---|---|---|---|---|
| | | | | 4 (27%) AEs related to the use of the device:<br>• 1 sensor was dislodged from the target location of deployment into the main pulmonary artery during withdrawal of the delivery system<br>• 1 pt experienced a transient complete heart block as the sensor passed through the right heart<br>• 2 pts post-procedure minor haemoptysis<br><br>All events resolved without clinical sequelae or impairment of device function. | NR | |
| SIRONA 2[47] | Cordella | Attempted implant: 70 | 12 | 1(1.4%) DSRC event:<br>• 1 LV lead dislodgement* | NR | Low |
| PROACTIVE-HF[48] | Cordella | Attempted implant: 493 | 6 | 4 (0.8%) DSRC events | Defined as an adverse event that is, or is possibly, related to the device/system (Cordella PA Sensor or electronic components) and is either treated invasively (other than intramuscular medication or diagnostic RHC) or results in patient death or explant of the device | Low |
| | | | 6 | 26 (5.7%) procedure-related AE | SAEs - defined as the event is serious when the patient outcome is: death, life-threatening, hospitalization (initial or prolonged), disability or permanent change, congenital anomaly/birth defect, required intervention to prevent permanent impairment or damage, other serious (important medical events) | |

SADE – serious adverse device effects

**Table 41 Overview of GRADE ratings for each of the primary outcome included in the review**

| Outcome | Device (study design) | Provisional GRADE | RoB | Imprecision | Inconsistency | Indirectness | Publication Bias | Final GRADE |
|---|---|---|---|---|---|---|---|---|
| Heart failure hospitalisation | CardioMEMS (RCT) | High | NC | NC | NC | NC | NC | ⊕⊕⊕⊕ High |
| | Cordella (RCT) | High | -1 (some concerns) | -1 (wide CI, crossing 1) | Unable to assess (1 study) | NC | NC | ⊕⊕⊖⊖ Low |
| | Cordella (Single arm) | Low | NC | NC | NC | NC | NC | ⊕⊕⊖⊖ Low |
| All-Cause Mortality | CardioMEMS (RCT) | High | NC | -1 (wide CI, crossing 1) | NC | NC | NC | ⊕⊕⊕⊖ Moderate |
| | Cordella (RCT) | High | -1 (some concerns) | -1 (wide CI, crossing 1) | Unable to assess (1 study) | NC | NC | ⊕⊕⊖⊖ Low |
| HRQoL: EQ-5D | CardioMEMS (RCT) | High | NC | -1 (wide CI, crossing 0)) | -1 ($I^2$ = 89%) | NC | NC | ⊕⊕⊖⊖ Low |
| | Cordella | No studies | No studies | No studies | No studies | No studies | No studies | No studies |
| HRQoL: KCCQ | CardioMEMS (RCT) | High | NC | -1 (wide CI, crossing 0) | -1 ($I^2$ = 71%) | NC | NC | ⊕⊕⊖⊖ Low |
| | Cordella (Single arm) | Low | NC | Unclear | -1 Differences across studies | NC | NC | ⊕⊖⊖⊖ Very low |
| Failure of sensor implantation | CardioMEMS (Single arm) | Low | NC | NC | -1 ($I^2$=76%) | NC | NC | ⊕⊕⊕⊕ High |
| | Cordella (Single arm) | Low | NC | NC | -1 (visual inspection) | NC | NC | ⊕⊕⊕⊕ High |
| Sensor failure | CardioMEMS (Single arm) | Low | NC | NC | -1 ($I^2$=45%) | NC | NC | ⊕⊕⊕⊕ High |
| | Cordella (Single arm) | Low | NC | NC | -1 (visual inspection) | NC | NC | ⊕⊕⊕⊕ High |
| DSRC | CardioMEMS (Single arm) | Low | NC | NC | -1 ($I^2$=50%) | NC | NC | ⊕⊕⊕⊕ High |
| | Cordella (Single arm) | Low | NC | NC | -1 (visual inspection) | NC | NC | ⊕⊕⊕⊕ High |

## Secondary outcomes

### Table 42 Secondary outcomes: Urgent care for HF, cardiovascular mortality, changes to clinical management, functional capacity, change in NYHA class and adherence to device

| Study name | PAP Device | N (Tx/ctrl) | Follow-up (months) | Result | Outcome definition |
|---|---|---|---|---|---|
| **Urgent care for HF** | | | | | |
| GUIDE-HF[45] | CardioMEMS | 497/503 | 12 | **Intervention group:** 28 events (0.065 EPPY)<br>**Control group:** 27 events (0.063 EPPY)<br>**Relative effect: HR 1.04 (95% CI 0.61, 1.77) ; p = 0.89)** | Defined as an unscheduled or unplanned admission to the emergency department, hospital outpatient observation visit, or hospital inpatient visit (< 24 hours) determined to be due to heart failure and requiring intravenous diuretics. |
| | CardioMEMS: NYHA class III subgroup | [redacted] | 12 | [redacted] | |
| | CardioMEMS: COVID-19 subgroup | Pre-COVID-19: 497/503<br><br>During-COVID-19: 497/503 | 12 | **Pre-COVID-19:**<br>**Intervention group:** 23 events (0.074 EPPY)<br>**Control group:** 23 events (0.073 EPPY)<br>**Relative effect: HR 1.02 (95% CI 0.57, 1.82); p = 0.95)**<br><br>**During-COVID-19:**<br>**Intervention group:** 5 events (0.048 EPPY)<br>**Control group:** 4 events (0.041 EPPY)<br>**Relative effect: HR 1.19 (95% CI 0.32, 4.45); p = 0.80)** | |
| MONITOR-HF[44] | CardioMEMS | 176/172 | 48 | **Intervention group:** 11 events (0.036 EPPY)<br>**Control group:** 17 events (0.054 EPPY)<br>**Relative effect: HR 0.65 (95% CI 0.23, 1.88), p = 0.44)** | Defined as unscheduled hospitalisation for heart failure shorter than 6 h and the use of intravenous diuretics for decongestion of the patient |
| PROACTIVE-HF[48] | Cordella: | 456 | 6 | 17 events in 14 patients (0.04 EPPY, 95% CI 0.02, 0.06) | NR |
| | Cordella: Former control group | 63 | 12 | 4 events (0.07 EPPY) | |
| **Cardiovascular mortality** | | | | | |
| CHAMPION[43] | CardioMEMS | 270/280 | 18 | **Intervention group:** 40 events (0.099 EPPY)<br>**Control group:** 48 events (0.114 EPPY) | NR |

| Study name | PAP Device | N (Tx/ctrl) | Follow-up (months) | Result | Outcome definition |
|---|---|---|---|---|---|
| | | | | **Relative effect: 0.87 (95% CI: 0.51, 1.49) (calculated from EPPY)** | |
| GUIDE-HF[45] | CardioMEMS | 497/503 | 12 | **Cardiovascular mortality:**<br>**Intervention group:** 30 events (0.10 EPPY)<br>**Control group:** 24 events (0.086 EPPY)<br>**Relative effect: 1.16 (95% CI: 0.77, 1.77) (calculated from EPPY)**<br><br>**HF mortality:**<br>**Intervention group:** 17 events (0.034 EPPY)<br>**Control group:** 15 events (0.030 EPPY)<br>**Relative effect: HR 1.13 (95% CI: 0.57, 2.27)** | NR |
| MONITOR-HF[44] | CardioMEMS | 176/172 | 48 | **Intervention group:** 25 events (0.081 EPPY)<br>**Control group**: 31 events (0.099 EPPY)<br>**Relative effect: HR 0.83 (95% CI: 0.49, 1.39), p=0.485** | Deaths classified and presented in all-cause mortality or CV-mortality |
| **Changes to medication** | | | | | |
| CHAMPION[43] | CardioMEMS | 270/280 | 6 | **Total HF medication changes**: intervention group: 2468 changes (mean 9.1 per pt, SD 7.4: 1.52 per pt per month) Vs control group: 1061changes (mean 3.8 per pt, SD 4.5: 0.63 per pt per month); p<0.0001<br><br>**Mean difference in medication changes per patient per month:** 0.89<br><br>**Dose increases vs decreases:** Frequency of decreases in medication doses from baseline to 6 months greater in the intervention group than in the standard of care group (p <0.05).<br><br>**Change to diuretics:** intervention group:1547 changes Vs control group: 585 changes; p<0.0001 | Total daily doses for each HF drug therapy class were also calculated at baseline and after 6 months, converting to equivalents for enalapril, carvedilol, AA spironolactone, furosemide, and metolazone.<br><br>Outpatient medication changes were tracked during the 6 months of follow-up, including whether the dose was increased or decreased. |
| GUIDE-HF[45] | CardioMEMS | 497/503 | 12 | **Total HF medication changes:** Intervention group**:** 1.031 changes per month per patient<br><br>Control group: 0.608 changes per month per patient<br><br>**Mean difference in medication changes per patient per month**: 0.42 | NR |

| Study name | PAP Device | N (Tx/ctrl) | Follow-up (months) | Result | Outcome definition |
|---|---|---|---|---|---|
| | | | | **Change to diuretics:** Proportion of pts on GDMT at baseline & 12 months<br>Intervention group: 95% at baseline vs 94% at 12 months<br>Control group: 95% at baseline vs 93% at 12 months | |
| MONITOR-HF[44] | CardioMEMS | 176/172 | 48 | **Total HF medication changes:** Intervention group: 0.73 per pt-month (rate)<br><br>Control group: 0.47 per pt-month (rate)<br><br>**Mean difference in medication changes per patient per month:** 0.26 | NR |
| SIRONA 2[47] | Cordella | 70 | 12 | **Change HF medication**: total monthly change rate: 0.71<br>**Change to diuretics**: average monthly changes: 0.29 | HF related medication change collected and summarised by visit presenting the percentage of subjects with and without any change in HF related medication |
| PROACTIVE-HF[48] | Cordella | 456 | 6 | **Change HF medication**: 2956 HF medication changes (mean 1.1 (SD 1.4) changes per month per patient)<br>Months 0-3 vs months 4-6 (Mann-Whitney U Test p<0.001).<br><br>**Dose increases vs decreases**: mean 0.6 (SD 0.8) vs 0.5 (SD 0.7), Mann-Whitney U test p=0.04<br><br>**Change to diuretics**: total 2,041 changes (69%)<br>Increase in dose: total 153 pts (33.5%)<br>Decrease in dose: total 104 pts (22.8%) | Days where the total dosage went up were noted as up-titrations and days when the total dosage went down were marked as down-titrations. Medication stops and starts were identified as days in which medication dosage reached 'zero' after having been above 'zero' or days in which medication dosage became above 'zero' after having previously been 'zero,' respectively |
| | Cordella: Baseline PAP subgroup | mPAP >20: 206<br><br>mPAP ≤20: 247 | 6 | **Change HF medication:** mPAP >20: 1.4 (SD 1.7) changes per month<br>mPAP ≤20: 0.9 (SD 1.1) changes per month<br>Mann-Whitney U test p=0.001 | |
| **Changes to the frequency of contact with healthcare professionals** | | | | | |
| CHAMPION[43] | CardioMEMS | 270/280 | 6 | **Total number of contacts:** Intervention group: 1024 office visits, 723 telephone calls<br>Control group: 1042 office visits, 686 telephone calls<br><br>**Mean number of contacts**: Intervention group: 6.5 per patient | NR |

| Study name | PAP Device | N (Tx/ctrl) | Follow-up (months) | Result | Outcome definition |
|---|---|---|---|---|---|
| | | | | Control group: 6.4 per patient | |
| GUIDE-HF[45] | CardioMEMS | 497/503 | 12 | **Mean number of contacts:** Intervention group: 1.89 (SD 0.79) per patient-month<br>Control group: 1.65 (SD 0.59) per patient- month | Contacts included site initiated contacts, subject study visits, subject initiated contacts and other contacts. |
| | CardioMEMS: COVID-19 subgroup | 497/503 | 12 | **Mean number of contacts:** Intervention group: 2.13 (SD 0.89) per patient-month<br>Control group: 1.85 (SD 0.73) per patient- month | |
| MONITOR-HF[44] | CardioMEMS | 176/172 | 48 | **Total number of contacts:** Intervention group: 4872<br>Control group: 3539<br><br>**Mean number of contacts:** Intervention group: 1·55 (SD 1.06) per patient-month<br>Control group: 1.04 (SD 0.77) per patient-month | Contacts included site initiated contacts, subject study visits and subject initiated contacts. |
| **Functional capacity: 6 minute walk test** | | | | | |
| GUIDE-HF[45] | CardioMEMS | 288/291 | 12 | Intervention group: change in mean score -12.83 metres (SD 100.08), within group p=0.030<br><br>Control group: change in mean score -6.46 (SD 106.57), within group p=0.30<br><br>Between groups: p=0.46<br><br>**Mean difference between groups:** -6.37 | Six Minute Hall Walk (6MHW) test at baseline, 6, and 12 months post-implantation |
| MONITOR-HF[44] | CardioMEMS | 176/172 | 12 | Intervention group: change in mean score: 29.3 metres (2.4-56.2), within group p=0.033<br><br>Control group: change in mean score: 9.8 metres (-20.4-40.1) within group p=0.52<br><br>**Mean difference between groups:** 19.5 | 6 minute walk test (6MWT) |
| SIRONA 2[47] | Cordella | 70 | 12 | Baseline: mean distance: 301.2 metres (SD 140.3)<br>12 months: mean distance: 324.7 metres (SD 116.1)<br><br>MD change from baseline: p=0.005 | 6 minute walk test (6MWT). Total distance walked (metres) collected and analyzed |

| Study name | PAP Device | N (Tx/ctrl) | Follow-up (months) | Result | Outcome definition |
|---|---|---|---|---|---|
| PROACTIVE-HF[48] | Cordella | 456 | 12 | Baseline: mean distance: 259.5 metres (SD 121.1)<br>12 months: mean distance: 294.1 metres (SD 132.9)<br><br>MD change from baseline: p=0.0004 | 6 minute walk test (6MWT) measured in metres |
| **Change in NYHA** | | | | | |
| SIRONA[46] | Cordella | 15 | 3 | NYHA class improvement: 53% from NYHA III to NYHA II | NR |
| SIRONA 2[47] | Cordella | 70 | 12 | Improvement in NYHA from baseline to 12 months: 41 of 59 subjects (69.5%, p<0.001)<br><br>**1 patient (1.4%) went from NYHA class III to NYHA Class IV** | Shifts in NYHA functional classification from baseline over all post-baseline visits |
| PROACTIVE-HF[48] | Cordella | 456 | 12 | Improvement in NYHA 12 months post-implant: 165 pts (p<0.0001) | NR |
| **Adherence to using the device** | | | | | |
| GUIDE-HF[45] | CardioMEMS | 497/503 | 12 | Adherence to daily measurement and transmission: 80-90% in both groups | Patient compliance in obtaining and transmitting daily pulmonary artery pressure readings |
| MONITOR-HF[44] | CardioMEMS | 176 (tx group) | 48 | Adherence to daily measurement and transmission: 84.3% | Frequency of (daily) pulmonary artery uploads |
| SIRONA[46] | Cordella | 15 | 3 | Adherence to daily measurement and transmission: 99% | NR |
| SIRONA 2[47] | Cordella | 70 | 12 | Adherence to daily measurement and transmission: 95% | Data transmission ≥5 out of 7 days |
| PROACTIVE-HF [48] | Cordella | 456 | 6 | Adherence to daily measurement and transmission: 88% | Transmitting clinical data at least 5 of 7 days per week (did not need to be consecutive). |

CKD – chronic kidney disease, COPD – chronic obstructive pulmonary disease, Ctrl – control, EPPY – events per patient-year, hAF – history of atrial fibrillation, HF – heart failure, HFH – heart failure hospitalisations, MD – mean difference, NA – not applicable, NR – not reported, PAP – pulmonary artery pressure, Pt – patient, SD – standard deviation, SoC – standard of care, Tx - treatment

## Table 43 Overview of study participants and withdrawals

| Study name | Group | Number | | | | | | Withdrawal prior to implant reasons | Withdrawals post randomisation |
|---|---|---|---|---|---|---|---|---|---|
| | | Enrolled | Device attempted implanted | Device implanted | Randomised | ITT population | Full follow-up data | | |
| CHAMPION[43] | Total | 575 | 575 | 550 | 550 | 570 | 347 | NR | 203 |
| | CardioMEMS | | | 270 | 270 | 270 | 177 | | 93 (34.4%): 50 death, 21 withdrew consent, 9 investigator decision, 7 non-compliance, 6 lost to follow-up |
| | Control | | | 280 | 280 | 280 | 170 | | 110 (39.3%): 64 death, 27 withdrew consent, 9 investigator decision, 6 non-compliance, 4 lost to follow up |
| GUIDE-HF[45] | Total | 1022 | 1022 | 1000 | 1000 | 1000 | 931 | NR | 69 |
| | CardioMEMS | | | | 497 | 497 | 472 | | 25 (5.0%): 9 withdrew consent, 3 lost to follow-up, 6 non-compliance, 7 withdrew for other reasons |
| | Control | | | | 503 | 503 | 459 | | 44 (8.7%): 19 withdrew consent, 9 lost to follow-up, 6 non-compliance, 10 withdrew for other reasons |
| MONITOR-HF[44] | Total | 348 | 168 | 168 | 348 | 348 | 247 | NR | 99 |
| | CardioMEMS | | 168 | 168 | 176 | 176 | 119 | | 49 (27.8%): 7 withdrew informed consent, 40 died, 2 stopped active monitoring |
| | Control | | NA | NA | 172 | 172 | 122 | | 50 (29%): 5 withdrew informed consent, 45 died |
| MEMS-HF[49] | CardioMEMS | 239 | 234 | 234 | NA | 236 | 180 | 2 not implanted: 1 no longer met inclusion/exclusion criteria at implant visit, 1 withdrawn during the procedure | 31: 18 died, 6 withdrew consent, 6 discontinued measurements, 1 had sensor removed |
| COAST-UK[50] | CardioMEMS | 103 | 103 | 100 | NA | 100 | 85 | NR | 15: 10 died, 5 withdrew consent |
| COAST-FRANCE[56] | CardioMEMS | 103 | 103 | 103 | NA | 103 | 61 | NR | 49: 37 died, 10 missed visit, 2 withdrawn by investigator |
| CardioMEMS -PAS[51] | CardioMEMS | 1214 | 1214 | 1200 | NA | NR | 710 | 14: reasons NR | 490: 326 died, 38 withdrew consent, 21 lost to follow-up, 43 non-compliance, 48 terminated by investigator, 14 other |

| Study name | Group | | Number | | | | | Withdrawal prior to implant reasons | Withdrawals post randomisation |
|---|---|---|---|---|---|---|---|---|---|
| | | Enrolled | Device attempted implanted | Device implanted | Randomised | ITT population | Full follow-up data | | |
| SIRONA[46] | Cordella | 19 | 15 | 15 | NA | 15 | 15 | 4 not implanted: 1 with drew consent, 1 anatomical reasons, 1 major surgery, 1 hospitalisation | 0 |
| SIRONA 2[47] | Cordella | 81 | 70 | 70 | NA | 75 | 68 | 11 not implanted: 6 withdrew consent prior to device implantation, implant aborted in 5 patients (3 withdrew consent, 2 met exclusion criteria while awaiting implant, 1 withdrawn by physician) | 2 (2.9%): Reasons not reported |
| PROACTIVE-HF[48] – randomised phase | Total | NR | NR | 160 | 148 | NR | NR | Unclear | Unclear |
| | Cordella | | NR | NR | 88 | NR | NR | Unclear | Unclear |
| | Control | | NR | NR | 72 | NR | 66 | Unclear | 8: 2 withdrew after implant. 2 died. 4 lost to follow-up |
| PROACTIVE-HF[48] | Cordella | 541 | 493 | 456 | NA | 493 | 425 | 48 withdrawal prior to implant (21 withdrawals of consent, 3 death, 5 adverse events, 12 exclusion criteria, 3 physician decision, 3 insurance denial and 1 loss to follow-up). | 16 (3.5%): 10 death, 2 withdrew consent/patient decision, 2 adverse event, 1 physician decision, 1 lost to follow-up |

## Table 44 Other adverse events

| Study name | PAP Device | N (Tx/ctrl) | Follow-up (months) | Result | Outcome definition |
|---|---|---|---|---|---|
| GUIDE-HF[45] | CardioMEMS | 497/503 | 12 | **Intervention group:** 282 pts (57%) had a SAE<br><br>**Control group**: 268 pts (53%) had a SAE<br><br>**Relative effect: RR 1.06 (95% CI: 0.95-1.19)** | **SAEs** - were classified as an AE that led to death or a serious deterioration in the health of the subject |
| SIRONA 2[47] | Cordella | 75 | 1 | 4pts had 6 AEs:<br>Skin irritation, haemoptysis, vessel trauma and haematoma<br>1pt had 2 SAEs: related to the implant procedure, with 1 being adjudicated as DSRC (left ventricle lead dislodgement)<br>All observed complications recovered without lasting effects | NR |
| PROACTIVE-HF[48] | Cordella | 493 | 6 | 196 pts had a SAE | SAEs - defined as the event is serious when the patient outcome is: death, life-threatening, hospitalization (initial or prolonged), disability or permanent change, congenital anomaly/birth defect, required intervention to prevent permanent impairment or damage, other serious (important medical events) |

* originally classed as a SAE but then adjudicated as a DSRC

AE – adverse event, Ctrl – control, DSRC – device/system-related complications, EPPY - events per patient-year, IFU – Instructions for use, NA – not applicable, NR – not reported, PA – pulmonary artery, Pt – patient, SAE – serious adverse event, Tx – treatment

## Patient experience and satisfaction data

### Cordella device

**Table 45 Web survey results from SIRONA 2**

| Question | Respondents (N) | Very Easy n (%) | Somewhat Easy n (%) | Neutral n (%) | Somewhat Difficult n (%) | Very Difficult n (%) |
|---|---|---|---|---|---|---|
| How easy is it to use the myCordella Patient Kit? | 36 | 27 (75) | 7 (19) | 2 (6) | 0 (0) | 0 (0) |
| How has the myCordella Patient Kit changed how you feel about your health? | 37 | 10 (27) | 8 (22) | 19 (51) | 0 (0) | 0 (0) |
| How has the myCordella Patient Kit changed how you communicate with your physician about your health? | 36 | 17 (47) | 4 (11) | 15 (42) | 0 (0) | 0 (0) |
| How easy was the initial setup of the myCordella Patient Kit in your home? | 37 | 25 (68) | 9 (24) | 3 (8) | 0 (0) | 0 (0) |
| Would you recommend the myCordella Patient Kit to others? | 34 | 33 (97) | 1 (3) | | | |
| How much of a burden is taking your readings? | 37 | 28 (76) | 7 (19) | 2 (5) | 0 (0) | |
| Do you take notice and monitor your daily measurements? | 37 | 16 (43) | 9 (24) | 12 (33) | | |
| Do you make changes to your lifestyle based on the daily measurement you see? | 37 | 10 (27) | 7 (19) | 20 (54) | | |
| Are you seated and lying flat PA pressure measurements taken in the same room? | 37 | 37 (100) | 0 (0) | 0 (0) | | |
| When taking a lying flat PA pressure measurement – is this location totally flat? | 37 | 19 (51) | 11 (30) | 7 (19) | 0 (0) | |

| Question | Respondents (N) | Sitting n (%) | Lying flat n (%) |
|---|---|---|---|
| Which PA pressure measurement position do you prefer, lying flat or seated? | 37 | 31 (84) | 6 (16) |

### Table 46 Patient engagement with daily PA pressures from PROATIVE-HF

| Question | Response |
|---|---|
| Do you understand PAP and it is important | Yes - 88%<br>No - 12% |
| Do you notice and monitor your PAP trends | Yes, I know what my normal range is – 55%<br>No, I leave that to my clinician – 45% |
| Do you make changes to your lifestyle based on your PAP trends | Regularly – 45%<br>Sometimes – 33%<br>No – 23% |
| Rate the impact of PAP readings and resulting clinician care on your health | Very good/excellent – 73%<br>Good – 13%<br>Fair – 13%<br>Poor – 3% |

## CardioMEMS

### Table 47 Telephone survey results

| Question | Yes | No | |
|---|---|---|---|
| Have you received phone calls from your doctor regarding your device? | 15 | 15 | |
| Has your cardiologist changed your heart medications since you received your device? | 13 | 17 | |
| Have you made any changes to your lifestyle since you received the device? | 10 | 20 | |
| Has your dyspnea improved since you received the device? | 17 | 13 | |
| Have you made improvements to your diet since you received the device? | 21 | 9 | |
| Have you increased your physical activity since you received the device? | 13 | 17 | |
| | Easy | Acceptable | Difficult |
| How would you describe using the equipment to transmit the numbers as instructed? | 21 | 7 | 2 |

**Table 48 Summary of main categories and themes**

| Category | Theme | Sub-theme | Quote(s) | Interpretative summary |
|---|---|---|---|---|
| Engagement | Health literacy | Not knowing what's going on | "I was becoming quite frustrated with not really knowing necessarily what I should do…it was a constant up and down not really knowing if I was doing the right thing". "What was hard was that I had no idea what was going on. Just no idea…my weight was going up but I didn't know it was because of fluid. It gets quite frustrating, to sit there and watch this happening to you and there's nothing you can do about it." | Not understanding heart failure, particularly the link between behaviors and signs and symptoms of decompensation, can make patients feel frustrated and even helpless. |
| | | Learning how heart failure affects your body | "Once I got the CardioMEMS I was able to manage a little better knowing that when I felt bad I could tell my readings were high and I'd get a phone call. So I started being able to judge based on my physical condition and abilities what my CardioMEMS was going to report." "The symptoms and the pressures definitely correlate so I know when I'm going to get a phone call". "I know when the readings are high because of the way I feel: I'm bloated in my stomach area, my feet are swollen, I know I have a problem." "The CardioMEMS keeps me more connected with what's going on in my body on a daily basis." | CardioMEMS teaches patients about their bodies by providing nearly instant feedback. Over time, many patients see connections between their behavior, their symptoms, and their CardioMEMS readings, which helps them to manage more effectively. |
| | Seeing the value of the device | No sub-themes identified | "I had one situation where my pressures were up and I didn't even realize…and had I not had that reading I would have been in the hospital." "Without the machine I wouldn't know that I have a problem because I have other things that are distracting me." "Sometimes it's a surprise and I can't detect it…with-out the machine I would go on my merry way and be totally oblivious that there's a problem." | Most patients had experienced a time when their pressure readings were high even though they didn't have any symptoms; this served to reinforce patients' belief that CardioMEMS is helping them stay out of the hospital. |
| | Being engaged in healthcare | No sub-themes identified | "Having the readings would help me a lot. It would allow me to be more proactive than reactive" "Isn't there a way for them or for you or somebody to set up something that I can go look at the data on? So I can see based on my meals and my diet and fluid intake for the last day did this to me on this day". | Two-thirds of patients indicated that they were interested in seeing their readings because they like to track their health and are accustomed to recording their weight, blood pressure, or other measurements. |

| Category | Theme | Sub-theme | Quote(s) | Interpretative summary |
|---|---|---|---|---|
| Management | Self-concept | Identifying as a person who does things well, follows rules | "I'm a person who commits. I've always been religious about doing [the readings]…I committed to do it so I'm gonna do it." "I've got a lot of years left and I'm trying my best to live them the best way that I can. I'm not a quitter. I don't give up on things. I've always been that way, I've never been a quitter." "I'm one of those people where if the doctor says do it this way, I do it. And I keep on doing it until the doctor says it's not necessary. That also goes for medications. I'm very medication compliant. I'm very compliant without thinking well it doesn't matter if I don't take it. I do take this seriously you know." | Some patients self-identified as independent people who follow the rules and commit to doing the CardioMEMS readings. |
| | | Identifying as a person who does "their own thing" | "When I get a notification I know that I've gotta do some-thing for a few days to make it better. And I'll do that and hopefully it all works out." "My wife doesn't put any added salt into her cooking. She uses low-salt products. So that's as best we can do. But meat's got what meat's got…And then when you go out …It's like my nurse says, [Patient]'s gonna do what [Patient]'s gonna do." "It would be nice to know the numbers because I would know ahead of time, if its high, let me lesser my salt, lesser my drinks. It would probably make me use it more because I would want to see the number. I'm good at checking my blood sugar because I can see the number right away and I'm curious to know if it's ok." | Some patients self-identified as independent people who "do their own thing". These patients were focused on fitting HF management into their cur-rent lifestyle. These patients indicated that the Car-dioMEMS helped them to maintain their current lifestyle by letting them know when they abso-lutely needed to make an adjustment to their behavior in order to avoid a negative outcome. These participants were named "integrators". |
| Underlying motivation for sustained use of the device | Avoiding hospitalization | No sub-themes identified | "I use [the CardioMEMS] because I want to have the best quality of life and to me that means not living in the hospital. I don't want to be in the hospital. I want to be as far away as I can. That's no life being in that hospital. It's no life whatsoever." "And I need to do [the readings] for me because other-wise I'm gonna be in the hospital, where I don't want to be. I don't like being here. I was here last year for two months and I was going nuts." | Patients expressed that their overall goal for CardioMEMS was to stay out of the hospital, which they associated with a poor quality of life. This motivation was one of the driving factors behind continued use. |
| | Peace of mind | No sub-themes identified | "My mind is a little bit more relaxed. Knowing that they are keeping track of my heart makes | Patients said that CardioMEMS reduced anxiety around HF |

| Category | Theme | Sub-theme | Quote(s) | Interpretative summary |
|---|---|---|---|---|
| | | | me more relaxed, knowing that at least I'm getting checked somehow instead of ending up in the emergency room or the hospital." "I have peace of mind that I have something right here that helps me in the long run." "I know I got a bad heart so it lets me live life without worrying about it. That's all I can say. I have a lot of faith in the doctors and nurses at UC Davis. I'll be doing even better with this new machine." | management; they liked the feeling that someone is watching over them. |

# Appendix 5

## Results from review of cost-effectiveness studies and models

We used the Philips checklist to evaluate the three models with a UK focus. Each criterion was assessed as:

- **Y (Yes):** The criterion is directly satisfied in the report, or it is clear that the model addresses it explicitly.
- **PY (Probably Yes):** The report does not explicitly confirm it, but it is reasonable to assume the model addresses the criterion based on the data or context.
- **NI (No Information):** The report provides no information related to the criterion.
- **N (No):** The report or model does not address the criterion.

**Table 49 Philips quality assessment checklist for studies that include an economic model**

| Assessment Criteria | Cowie 2017[65] | Cowie 2023[68] | HTA Wales[73] |
|---|---|---|---|
| 1 Is there a clear statement of the decision problem? | Y | Y | Y |
| 2 Is the objective of the model specified and consistent with the stated decision problem? | Y | Y | Y |
| 3 Is the primary decision maker specified? | Y | Y | Y |
| 4 Is the perspective of the model stated clearly? | Y | Y | Y |
| 5 Are the model inputs consistent with the stated perspective? | Y | Y | Y |
| 6 Has the scope of the model been stated and justified? | Y | Y | Y |
| 7 Are the outcomes of the model consistent with the perspective, scope and overall objective of the model? | Y | Y | Y |
| 8 Is the structure of the model consistent with a coherent theory of the health condition under evaluation? | Y | Y | Y |
| 9 Are the sources of the data used to develop the structure of the model specified? | Y | Y | Y |
| 10 Are the causal relationships described by the model structure justified appropriately? | Y | Y | Y |
| 11 Are the structural assumptions transparent and justified? | Y | Y | Y |
| 12 Are the structural assumptions reasonable given the overall objective, perspective and scope of the model? | Y | Y | Y |
| 13 Is there a clear definition of the options under evaluation? | Y | Y | Y |
| 14 Have all feasible and practical options been evaluated? | Y | Y | Y |
| 15 Is there justification for the exclusion of feasible options? | NA | NA | NA |
| 16 Is the chosen model type appropriate given the decision problem and specified casual relationships within the model? | Y | Y | Y |

| Assessment Criteria | Cowie 2017[65] | Cowie 2023[68] | HTA Wales[73] |
|---|---|---|---|
| 17 Is the time horizon of the model sufficient to reflect all important differences between the options? | Y | Y | Y |
| 18 Are the time horizon of the model and the duration of treatment described and justified? | Y | Y | Y |
| 19 Do the disease states or pathways reflect the underlying biological process and the impact of interventions? | PN | PN | PN |
| 20 Is the cycle length defined and justified in terms of the natural history of disease? | PY | PY | NR |
| 21 Are the data identification methods transparent and appropriate? | Y | Y | Y |
| 22 Where choices have been made between data sources are these justified appropriately? | Y | Y | Y |
| 23 Has particular attention been paid to identifying data for the important parameters of the model? | Y | Y | Y |
| 24 Has the quality of the data been assessed appropriately? | NR | NR | Y |
| 25 Where expert opinion has been used are the methods described and justified? | NA | NA | NA |
| 26 Is the data modelling methodology based on justifiable statistical and epidemiological techniques? | Y | Y | Y |
| 27 Is the choice of baseline data described and justified? | Y | Y | Y |
| 28 Are transition probabilities calculated appropriately? | Y | Y | Y |
| 29 Has a half-cycle correction been applied to both costs and outcomes? | PY | Y | NR |
| 30 If not, has the omission been justified? | NR | NA | NR |
| 31 If relative treatment effects have been derived from trial data, have they been synthesised using appropriate techniques? | Y | Y | Y |
| 32 Have the methods and assumptions used to extrapolate short-term results to final outcomes been documented and justified? | NR | NR | Y |
| 33 Have alternative extrapolation assumptions been explored through sensitivity analysis? | Y | Y | Y |
| 34 Have assumptions regarding the continuing effect of treatment once complete been documented and justified? | Y | Y | NI |
| 35 Have alternative assumptions regarding the continuing effect of treatment been explored through sensitivity analysis? | N | PY | N |
| 36 Are the costs incorporated into the model justified? | Y | Y | Y |
| 37 Has the source for all costs been described? | Y | Y | Y |
| 38 Have discount rates been described and justified given the target decision maker? | Y | Y | Y |
| 39 Are the utilities incorporated into the model appropriate? | Y | Y | Y |
| 40 Is the source of utility weights referenced? | Y | Y | Y |
| 41 Are the methods of derivation for the utility weights justified? | Y | Y | Y |

| Assessment Criteria | Cowie 2017[65] | Cowie 2023[68] | HTA Wales[73] |
|---|---|---|---|
| 42 Have all data incorporated into the model been described and referenced in sufficient detail? | Y | Y | Y |
| 43 Has the use of mutually inconsistent data been justified? | NA | NA | NA |
| 44 Is the process of data incorporation transparent? | Y | Y | Y |
| 45 If data have been incorporated as distributions, has the choice of distributions for each parameter been described and justified? | Y | Y | Y |
| 46 If data have been incorporated as distributions, is it clear that second order uncertainty is reflected? | Y | Y | Y |
| 47 Have the four principal types of uncertainty been addressed? | PY | PY | PY |
| 48 If not, has the omission of particular forms of uncertainty been justified? | N | N | N |
| 49 Have methodological uncertainties been addressed by running alternative versions of the model? | Y | Y | Y |
| 50 Is there evidence that structural uncertainties have been addressed via sensitivity analysis? | Y | Y | Y |
| 51 Has heterogeneity been dealt with by running the model separately for different subgroups? | N | N | N |
| 52 Are the methods of assessment of parameter uncertainty appropriate? | Y | Y | Y |
| 53 If data are incorporated as point estimates, are the ranges used for sensitivity analysis stated clearly and justified? | Y | Y | Y |
| 54 Is there evidence that the mathematical logic of the model has been tested thoroughly before use? | N | N | N |
| 55 Are any counterintuitive results from the model explained and justified? | NI | NI | NI |
| 56 If the model has been calibrated against independent data, have any differences been explained and justified? | NA | NA | NA |
| 57 Have the results been compared with those of previous models and any differences in results explained? | Y | Y | Y |

**Table 50 Overview of systematic reviews included in the Economic Review of Reviews**

| Review citation | Research question | PICOS | N of studies | Models structures identified |
|---|---|---|---|---|
| Azari 2024[111] | To assess the cost-effectiveness of remote cardiac monitoring with the CardioMEMS Heart Failure System. | **Population:** HF patients<br><br>**Intervention**: CardioMEMS<br><br>**Comparator:** Standard of Care<br><br>**Limitations:** searches limited to English language | Five studies | All five models were Markov and decision tree models. |
| Beese 2024[112] | To assess the clinical and cost-effectiveness of a left ventricular assist device compared to medical management for patients with advanced heart failure ineligible for heart transplantation (destination therapy) | **Population:** AHF patients (age > 16 years) who are ineligible for HT and are receiving a LVAD intended as DT<br><br>**Intervention**: Any LVAD irrespective of type, mechanism or generation. Studies of participants with biventricular assist devices, or RVADs were not eligible for inclusion.<br><br>**Comparator:** MM or different generation or type of devices or no comparator.<br><br>**Limitations:** none. | 19 studies from 20 articles.<br><br>Five cost analyses and 14 economic evaluations. | Markov (8 models)<br><br>[the types of models used in other evaluations was not reported]. |
| Zakiyah 2024[113] | To systematically review the economic evaluations that assess the adoption of DHIs in the management and treatment of HF. | **Population:** adult patients with HF (aged ≥18 y)<br><br>**Intervention**: any DHI for patients with HF comprising a digital intervention for transmitting medical information to improve patients' health status<br><br>**Comparator:** Standard of Care<br><br>**Limitations:** searches limited to English language and excluding experimental or observational studies unspecific to HF. Conference abstracts and editorials exclude. | 27 studies<br>13 using a model. | Markov<br>Discrete event simulation<br><br>[the types of models used in other evaluations was not reported]. |

| Review citation | Research question | PICOS | N of studies | Models structures identified |
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| Autore 2024[114] | To conduct a systematic review on studies which examined the application of health economic modelling to CMR. | **Population:** not reported<br><br>**Intervention**: cardiac magnetic resonance (CMR)<br><br>**Comparator:** not reported<br><br>**Limitations:** not reported | 38 'studies' | Markov (16 models)<br><br>[the types of models used in other evaluations was not reported]. |
| Kuan 2023[115] | To summarize and critically appraise the EEs of guideline-directed medical therapies (GDMTs) for HFrEF. | **Population:** people with HFrEF.<br><br>**Intervention**: use of a guideline-directed medical therapy.<br><br>**Comparator:** not reported<br><br>**Limitations:** searches limited to English language | 59 studies from 74 reports. | Markov (was the most commonly used DAM and its use increased considerably from 2015 onward. The simple Markov model (2-5 states) was more commonly used than the complicated one (>7 states).[115] |
| Albuquerque 2018[116] | To systematically review the literature on decision-analytical models used for the economic evaluation of early warning systems for the management of chronic HF patients and to describe the general and methodological characteristics of those models. | **Population:** diagnosed HF >18 yrs old.<br><br>**Intervention**: early warning systems.<br><br>**Comparator:** any.<br><br>**Limitations:** searches limited to English language and peer reviewed articles. | 7 studies | Markov (5)<br>Decision Trees (2) |
| Di Tanna 2019[118] | To conduct a systematic literature review (SLR) of published economic models for the management of HF and describe their general and methodological features. | **Population:** Adult HF >18 yrs old.<br><br>**Intervention**: pharmacologic treatment for HF<br><br>**Comparator:** Not reported<br><br>**Limitations:** studies that were observational, experimental, preclinical, pharmacokinetic or pharmacodynamic in nature; a case report or case series (ten or fewer patients); a letter to the editor, opinion piece or review article; or published before 1997, were excluded. | 64 Studies | Markov (28)<br>Trial-based analytic (22)<br>Discrete-event simulation (6)<br>Survival analytic (n7)<br>Decision-tree modelling (1) |

| Review citation | Research question | PICOS | N of studies | Models structures identified |
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| Di Tanna 2020[117] | To identify model drivers that emerge from a systematic review of cost-effectiveness models in HF treatment. | **Population:** Adult HF >18 yrs old.<br><br>**Intervention**: pharmacologic treatment for HF<br><br>**Comparator:** Not reported<br><br>**Limitations:** studies that were observational, experimental, preclinical, pharmacokinetic or pharmacodynamic in nature; a case report or case series (ten or fewer patients); a letter to the editor, opinion piece or review article; or published before 1997, were excluded. | 72 studies | Markov modelling (53%) and a trial or registry-based analysis (28%) were the most common approaches used. Discrete-event simulation (8%) and survival analysis (7%) were the only other approaches used by more than one study. |
| Febrinasari 2023[119] | To compare cost-effectiveness of sacubitril/valsartan with angiotensin-converting enzyme (ACE) inhibitors for treating chronic heart failure patients with reduced ejection fraction (HFrEF) from the published articles and explore the methodology applied in the studies. | **Population:** HFrEF patients<br><br>**Intervention**: assessed sacubitril/valsartan as the main drug in the study<br><br>**Comparator:** Not reported<br><br>**Limitations:** studies eligible if conducted between 2016-2020 and written in English. | 15 Studies | Markov (11)<br>Decision analytic (4) |
| Nam 2023[121] | Systematic review of economic evaluation studies of SGLT2 inhibitors for the treatment of patients with reduced ejection fraction (HFrEF) and preserved ejection fraction (HFpEF). | **Population:** patients with reduced ejection fraction (HFrEF) and preserved ejection fraction (HFpEF).<br><br>**Intervention**: SGLT2 inhibitors<br><br>**Comparator:** Not reported<br><br>**Limitations:** studies which did not focus on cost, burden of illness or budget impact, or did not report a CEA or CUA, and which reported abstracts or published in languages other than English were excluded. | 27 Studies | Markov (All) |
| Proudfoot 2023[122] | To summarize cost-effectiveness (CE) evidence of sacubitril/valsartan for the treatment of heart failure (HF) | **Population:** Chronic HF<br><br>**Intervention**: sacubitril/valsartan | 44 studies and 5 HTA reports | Markov (44%)<br>Markov with regression-based models. |

| Review citation | Research question | PICOS | N of studies | Models structures identified |
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| | patients with reduced ejection fraction (HFrEF). | **Comparator:** Not reported<br><br>**Limitations:** Not reported. | | |
| Teimourizad 2021[123] | To systematically review cost-effectiveness of CRT combined with an implantable cardioverter-defibrillator (ICD) versus ICD in patients with HF. | **Population:** Patients with HF<br><br>**Intervention**: CRT combined with an ICD versus ICD<br>alone<br><br>**Comparator:** Not reported<br><br>**Limitations:** studies published in English language during 2000-2020. | 5 studies | Markov (2)<br>Cohort survival (1)<br>Decision model (1)<br>No model (1) |
| Tomini 2016[124] | To systematically review decision models evaluating the cost-effectiveness of CRT-D for patients with DHF, compare the structure and inputs of these models and identify the main factors influencing the ICERs for CRT-D. | **Population:** HF patients with NYHA II, III or IV, LVEF B 35 %<br><br>**Intervention**: Not reported<br><br>**Comparator:** CRT-D<br><br>**Limitations:** studies published in English language during 2000-2014. | 8 Studies | Markov (4)<br>Markov and decision tree (4) |

**Health Tech Programme**

**DG10087 Pulmonary artery pressure technologies for remote monitoring of chronic heart failure**

**External Assessment Report - Comments collated table**

Any confidential sections of the information provided should be underlined and highlighted. Please underline all confidential information, and separately highlight information that is 'commercial in confidence' in blue and all that is 'academic in confidence' in yellow

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| 1 | Edwards Lifesciences | 23 | | Cordella has now received CE mark approval and should not be classified as investigational | We have edited the text to remove statements that state that Cordella is an investigational device. |
| 2 | Edwards Lifesciences | 99 | 6.2.6 Paragraph 1 | Possible typographical error "in puts" | Corrected. |
| 3 | Edwards Lifesciences | 128 | 7.4.3 Paragraph 5 | Possible typographical error "That, howeverThat meant" | Corrected. |
| 4 | Abbott Medical | 117 | 6.3.3.2 | Mortality rates – inaccurate assumptions and data used<br><br>We note that "Due to there being no statistical evidence for an effect of CardioMEMS on all-cause mortality, and clinical advice that the main benefit of remote PAP monitoring is a reduction in HFHs, we follow the approach taken in the Cowie 2023 model by assuming the hazard ratio for mortality is 1"<br><br>We would note that the Cowie model (2023) predates the publication of the results of Guide-HF and Monitor-HF and while, neither were powered for mortality there | Our meta-analysis for all cause mortality gives an estimated hazard ratio of [redacted], which is consistent with our statement that there is no statistical evidence for an effect of CardioMEMS on all-cause mortality. Whilst we use a hazard ratio of 1 in our model, this does not mean that there is no effect of CardioMEMS on all-cause mortality. This is because in our model the mortality rate increases with the number of HFHs that a patient has had, and CardioMEMS reduces the rate of HFHs, and hence reduces mortality. This means that |

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| | | | | is a signal of impact. We would also like to draw to your attention to three publications, two of which have entered the public domain in the past 6 months.<br><br>1. Implantable Hemodynamic Monitors Improve Survival in Patients With Heart Failure and Reduced Ejection Fraction https://www.jacc.org/doi/10.1016/j.jacc.2023.11.030<br><br>2. Relationship Between Remote, Ambulatory Pulmonary Artery Pressures, and All-Cause Mortality in Patients With Chronic Heart Failure https://doi.org/10.1161/CIRCHEARTFAILURE.124.012754<br>3. Early Reduction of Pulmonary Artery Pressures Is Associated With Improved Mortality Among Medicare Beneficiaries With Heart Failure Early Reduction of Pulmonary Artery Pressures Is Associated With Improved Mortality Among Medicare Beneficiaries With Heart Failure \| JACC: Heart Failure<br><br>In these papers management of PAP pressures alone is shown to have an impact on mortality. Outcome differs between control and treatment arm (Lindenfeld 2023) and is also associated with PA pressure at implant as well as the subsequent PA pressure response to the optimisation of GDMT that is possible through the use of a CardioMEMS PA pressure monitor. | there is an indirect effect on mortality. Including an additional mortality benefit may therefore double-count the benefit to some extent. To explore the possibility that is an additional mortality benefit over-and-above the indirect effect, we provide a scenario analysis using the hazard ratio from our meta-analysis (scenario 3), but stress that this will double-count the mortality benefit to some extent.<br><br>The pooled meta-analysis by Lindenfeld et al. 2023 combined patient level data from 3 trials: GUIDE-HF, CHAMPION, and LAPTOP-HF. LAPTOP-HF was for a different device (HeartPOD LAP) and so not directly relevant to this appraisal. The analysis also did not include MONITOR-HF, which is included in our meta-analysis. Lindenfeld 2023 found heterogeneity between studies, with a mortality effect found in CHAMPION and LAPTOP-HF, but not in GUIDE-HF. The results from MONITOR-HF were in line with GUIDE-HF. We therefore consider the results from Lindenfeld 2023 to be misleading for this appraisal. We prefer to use the results from our meta-analysis as used in our scenario 3, which includes all the relevant trials for Cardio-MEMS. |

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| | | | | **We would request that the hazard ratio for mortality when using CardioMEMS is 0.75.** | |
| 5 | Abbott Medical | 118 | 6.3.4.3 | Inappropriate comparison, data selection.<br><br>DSRC – selection of studies to derive DSRC rates.<br><br>We note the following. "For Cordella the fixed effect model was used due to insufficient evidence to estimate heterogeneity, giving an estimate of 0.001 (95%CI 0.000, 0.009) ". We would question the inclusion, in this calculation, of a small study, of limited duration, where there was a change in the design of the device during the evaluation. *"A change of nitinol anchors was developed during the study to accommodate a broader range of patient and vessel anatomy and sizes and to improve stability of the device. The iteration lengthened and angulated the distal anchor to stabilize the device on the inferior-posterior inflection of the pulmonary artery."*<br><br>In addition, DSRC, in the majority of studies, also includes the external electronics "definitely or possibly related to the wireless pressure sensor or external electronics, and was treated with invasive means other than intramuscular administration of drugs or a right-heart catheterisation;" A short duration study may well include bias in this reporting as insufficient time has elapsed for evaluation, and as a first in human captured events only for the first 30 days and did not | We have added a sensitivity analysis for the DSRC outcome to the results:<br><br>"We conducted a sensitivity analysis by removing the SIRONA study from the analysis for the Cordella studies due to its very small sample size and short follow-up time. The proportion of DSRC for this analysis increased slightly to 0.7% (95% CI 0.1, 0.17%)."<br><br>We have also added a scenario to the economic model with the DSRC rate for Cordella with the SIRONA study removed (scenario 9b). |

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| | | | | include interaction with the external electronics as part of its DSRC definition.<br><br>**We would therefore request that DSRC rates are reviewed and a standardised definition and minimum trial duration are used.** | |
| 6 | Abbott Medical | 121 | 6.3.6.1 | Cordella model<br><br>On multiple occasions throughout the document a statement similar to this is made: "We therefore could not robustly assess the cost-effectiveness of Cordella" and yet, a model has been derived and the following statement made "While Cordella may offer similar benefits and could be more cost-effective than CardioMEMS, the certainty of evidence is lower due to the reliance on non-comparative data for some outcomes" as well as in the Table 25 "Strictly dominated by Cordella". We question the appropriateness of modelling Cordella given the assumptions used (costs= CardioMEMS, DSRC derived from 175 patients and HR for HFH derived from 88 patients in RCT element that was terminated early).<br><br>**We would therefore request that either the model for Cordella is revised and the uncertainty around the model is clear, and no conclusions should be stated regarding that model versus CardioMEMS given the different levels of evidence used or that no model for Cordella is generated.** | NICE requested that we present results for Cordella, and highlight the limitations with the evidence, which is what was done in the report. We have discussed this further with NICE and have been advised to retain the results for Cordella, but add further text to the results section to make it even clearer that the results are illustrative only. |
| 7 | Abbott Medical | 121 | 6.3.6.1 | Implantation failure rate: Incorrect data | The company has misunderstood. This text / section is describing the cost of implant |

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| | | | | It is stated that "Devices were assumed to be opened but unusable in 6/25 (24%) (based on CHAMPION data), with recharges (the full device cost) applied in half of these cases. "<br><br>We believe that this is an incorrect statement. In CHAMPION there were 575 patients who underwent a RHC and intended implant. (Lancet 2011; 377: 658–66 Figure 2: Trial profile) Of these, 25 patients did not receive an implant for different reasons. 6 devices were opened but not implanted. This would equate to 6/575 (1%) of devices opened but unusable.<br><br>Moreover, sensitivity analysis about the implantation failure rate, which indicate significantly increasing the cost of the device, does not seem to impact the results.<br><br>**We therefore request the model be adapted to take into account the correct implant failure rate.** | failure **conditional** on implant failure having occurred, and so only applies to the 0.017 proportion of patients with implant failed (which is taken from our meta-analysis – see section 5.5.1.3 and 6.3.4.1). We therefore believe that we have used the correct denominator to estimate the rate of recharge **conditional on** an implantation having failed. In 19 of the 25 implantation failures, the device was not opened and could therefore be used at a later date, but 6 of the 25 were wasted. In our base case we assumed that half of the wasted devices were charged, and conducted scenario analyses in which all 6 of the wasted devices were charged at full rate (the worst case scenario) and all 6 fees were waived (the best case scenario).<br><br>We have reworded to make it clear that this is conditional on implant failure:<br><br>"Of those cases with implantation failure, devices were assumed to be opened but unusable in 6/25 (24%) of cases (based on CHAMPION data), with recharges (the full device cost) applied in half of these cases." |
| 8 | Abbott Medical | 121 | 6.3.6.1 | Clarification: Impact of device price and implantation failure on model sensitivity<br><br>We also note that in the Tornado plot the device price does not seem to interact with the model even though | Tornado plots are used to present the impact of parameter uncertainty. Device price and implantation failure costs are fixed costs which do not have uncertainty, and so |

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| | | | | sensitivity analysis has been carried out using the above assumption and would question why this is the case.<br><br>**We request that scenario analysis around device and implantation failure costs be captured in the Tornado plot.** | are not appropriate to display in a tornado plot. |
| 9 | Abbott Medical | 122 | 6.3.6.1 | Potential additional costs under standard care<br><br>We note in the standard care arm that standard care is defined as a single annual consultant review of the patient (clinician advice), this was costed using National Cost Collection data for a consultant led cardiology attendance (non-admitted, face-to-face). According to both the 2018 (published) and the 2025 (draft) NICE guideline a review should take place at least every 6 months.<br><br>This interval does not take into account that NYHA III patients are symptomatic and, by the nature of their NYHA III classification defined have advancing heart failure.<br><br>The guideline (NG106) Recommendations \| Chronic heart failure in adults: diagnosis and management \| Guidance \| NICE states:<br>*More detailed monitoring will be needed if the person has significant comorbidity or if their condition has deteriorated since the previous review.*<br>*The frequency of monitoring should depend on the clinical status and stability of the person. The monitoring interval should be short (days to 2 weeks) if the clinical condition or medication has changed, but* | We based the number of appointments on clinical advice on current practice, rather than the NICE guidelines. However, we have now added a scenario where patients receive 6 out-patient appointments per year (scenario 11).<br><br>Note that for CardioMEMS and Cordella, the usual care costs are also incurred but with additional costs for monitoring of the device. |

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| | | | | *is needed at least 6-monthly for stable people with proven heart failure.*<br><br>In Monitor-HF (Supplemental Table S8b Comparison of patient contacts and medication changes between 3 trials) in the standard care arm it was reported that there were 1.14 (0.82) mean (SD) patient contacts per month. Alternatively, the standard care arm experienced 0.55 medication changes per month during the 12 months follow up or 0.47 during the follow up period. Based on NG106 this suggests that a medication change should trigger a follow up contact. (Table S8a Frequency of Contact between Sites and Subjects). Monitor-HF (Table S8a Frequency of Contact between Sites and Subjects) also demonstrated that in the standard care arm there were 0.49 out-patient clinic appointments per month.<br><br>**We would therefore request that the standard care arm reflects the interaction required to manage this more advanced disease patient cohort.** | |
| 10 | Abbott Medical | 123 | 6.3.6.3 | Clarification of data used<br><br>Table 20 Summary of model inputs, values and distribution assumed in base-case analysis, and source of evidence. Each parameter was estimated separately, and so model parameters assumed to be independent in the PSA.<br><br>Hazard ratio for hospitalisation Cordella vs standard care 0.61 Hazard ratio from comparative phase of | PROACTIVE-HF is the best available data for Cordella, and the limitations of the trial being small and ending early are captured to some extent in the effect estimates with the wide CIs.<br>Table 20 is a summary of the model inputs that have been described in detail in the earlier sections of the report, where the limitations of the data for Cordella are |

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| | | | | PROACTIVE-HF. It is our understanding that this reference is unpublished data from the comparator phase of Proactive-HF which did not meet its power calculation or the primary outcome of the original study.<br><br>**We would therefore ask if this hazard ratio is to be used then an appropriate comment included regarding its use and limitation.** | clearly highlighted. We have added a further comment on this in section 6.3.2.3.<br>"As previously noted, the model results for Cordella are illustrative only due to the limitations with the available evidence."<br><br>We also discuss limitations of Cordella data in the discussion and evidence is rated as low certainty based on GRADE. |
| 11 | Abbott Medical | 54 | 5.5.1.5 | Device/system or procedure related complications and procedure related complications<br>(Figure 6 & Table 7)<br><br>"The proportion of DSRC were very low across studies for both CardioMEMS and Cordella (range 0.8 to 2.4%). The summary proportion of DSRC across trials was 0.7% (95% CI 0.3, 1.3%) for CardioMEMS and 0.1% (0.0, 0.09%) for Cordella. There was moderate heterogeneity for the CardioMEMS studies (I2 = 44%) and so results are presented for the random effects model. For Cordella, results are presented for the fixed effects model. We considered this more appropriate due to the small number of studies, difficulties in estimating heterogeneity, and the disproportionate weight given to the small SIRONA study by the random effects model."<br><br>Note that availability of DSRC evidence for CardioMEMS is a lot more extensive in comparison to Cordella.<br>DSRC follow-up ranges towards Cordella are really short (Example – Sirona, 0,000 (0,000, 0,204) 3 | See response to comment #5. We have added a scenario to the economic model with the DSRC rate for Cordella with the SIRONA study removed (scenario 9b). |

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| | | | | months) and likely do not capture sufficient development of DSRC rates across such a short patient pathway.<br><br>**We would therefore request that DSRC rates are reviewed and a standardised definition and minimum trial duration are used.** | |
| 12 | Abbott Medical | 137 | 7.1 | Statement of principal findings<br><br>"We did not have the device cost for Cordella, and there was limited comparative evidence for Cordella. We therefore could not robustly assess the clinical-or cost-effectiveness of Cordella."<br><br>The statement confirms clear lack of evidence towards inclusion of Cordella within the cost-effectiveness model. However, despite this statement a model has been created, assessment made and conclusions stated. It is therefore contradictory that Cordella is still being assessed as part of cost-effectiveness analysis based on the available evidence and the number of underlying assumptions.<br><br>**We would request that if a cost effectiveness model for Cordella is to be estimated and underpinned using the current clinical evidence, including a single unfinished trial, this should be made clear and no comparison made with CardioMEMS.** | See response to comment #6. |
| 13 | Abbott Medical | 139 | 7.3 | Overview of findings from the assessment of cost-effectiveness | See response to comment #6. We have edited the results section to reiterate that |

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| | | | | "We did not have the device cost for Cordella, and there was limited comparative evidence for Cordella. We therefore could not robustly assess the cost-effectiveness of Cordella. For illustrative purposes only we conducted an analysis where we assumed the device cost for Cordella was the same as for CardioMEMS. Under this assumption the base-case analysis estimated a deterministic ICER for Cordella of £31,257, a probabilistic ICER of £31,541, and Cordella strictly dominated CardioMEMS. These results were driven by the slightly more favorable hazard ratio for HFH for Cordella compared with CardioMEMS, which increased QALYs and reduced costs. We stress, however, that these results are very uncertain and no robust conclusions can be drawn for Cordella."<br><br>Statements in this section are directly linked to 7.1 and contradictory use of evidence and inclusion of Cordella as part of cost-effectiveness analysis.<br><br>**We would request that if a cost effectiveness model for Cordella is to be estimated and underpinned using the current clinical evidence, including a single unfinished trial, this should be made clear and no comparison made with CardioMEMS.** | the results for Cordella are illustrative only and based on limited data and assumptions. |
| 14 | Abbott Medical | 112 | 6.2.4 | Definition of health-related quality of life<br><br>"An NHS and personal social services (PSS) perspective was taken with a lifetime horizon where | We do use EQ-5D in the model, and CardioMEMS is associated with a HRQoL benefit. This occurs because EQ-5D decreases with the number of HFHs in the |

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| | | | | costs and QALYs were discounted at an annual rate of 3.5%. The model included the impact on health-related quality of life on patients, however due to a lack of evidence the impact on HRQoL of carers was not included (see section 6.3.5.3)."<br><br>Evidence to support improvements towards HRQoL is available yet excluded:<br><br>1. Remote pulmonary artery pressure-guided management of patients with heart failure: A clinical consensus statement of the Heart Failure Association (HFA) of the ESC 10.1002/ejhf.3619<br><br>"The cost-effectiveness of CardioMEMS is another critical consideration. Previous studies have shown that while the initial investment in the technology may be significant, the long-term savings from reduced hospitalizations and emergency visits are substantial.[68-71] Moreover, improved QoL and patient satisfaction are benefits that complement the financial advantages.[28]<br><br>2. Effect of pulmonary artery pressure-guided management on outcomes of patients with heart failure outside clinical trials: A systematic review and meta-analysis of real-world evidence with the CardioMEMS Heart Failure System https://doi.org/10.1002/ejhf.3687<br><br>"Other outcomes were changes in PAP, New York Heart Association (NYHA) class and quality of life. | model. CardioMEMS reduces HFHs and hence EQ-5D is on average higher.<br><br>We think the point the company are making here may relate to the use of HRQoL data collected in the trials. In our base-case we do not use this data and instead model changes in EQ-5D via number of HFHs. As noted above this does give an improved QoL in line with the findings of the papers listed. We do also present scenarios 6a – 6c where trial HRQoL data is used for the 12 month period where it is available. The question then is how to extrapolate beyond 12 months, and for that the best evidence we found was to link this to HFHs. On reflection, we prefer scenario 6c as the most appropriate way to combine both the short-term trial data and state-based HRQoL for the long-term. |

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| | | | | Quantitative analysis was performed by generating forest plots and calculating pooled means, mean differences and incidence rate ratio (IRR) by random-effect models, as appropriate. Eight studies with a total of 3306 patients were included. Four studies were single-arm, open-label, industry-funded studies and four real-world practice studies. Four studies were performed in the US and four in Europe. Significant decreases in systolic PAP (−7.8 mmHg [−10.1 mmHg; −5.6 mmHg]), mean PAP (−5.2 mmHg [−6.7 mmHg; −3.8 mmHg]) and diastolic PAP (−4.4 mmHg [−5.5 mmHg; −3.3 mmHg]) were demonstrated. One year after CardioMEMS implantation, 56% [43%; 67%] of patients were NYHA class I/II with EQ-5D-5L visual analogue scale scores being significantly improved from baseline (7.2 [3.5; 10.9]). PAP-guided HF management was associated with a significant, 61% decrease in HFHs at 1 year (IRR 0.39 [0.31; 0.47]).”<br><br>**We would request that health related quality of life includes EQ-5D and is not limited HFH.** | |
| 15 | Abbott Medical | 38 | 5.3.2 | Incorrect information.<br><br>COAST study aimed to enrol 800 and not 8000 patients from 85 sites across the UK, Europe and Australia.55. DOI: 10.1002/ehf2.12646<br><br>**We would request that the text in the report is updated.** | Apologies, this was a typo and has been corrected. |
| 16 | Abbott Medical | 6 | Methods | Clarification of comparator analysis<br><br>“For outcomes with comparative evidence available for both devices (CardioMEMS and Cordella) against | This is clear in the text where we describe the comparator arm of Cordella (section 5.3.1): |

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| | | | | a common comparator (standard care), we conducted an indirect comparison using the Bucher method."<br><br>We would question if this is appropriate given the different evidence levels and associated confidence intervals that exist between the two approaches. In addition, should the comparison be made it should be clear that the Cordella arm includes blood pressure (BP), heart rate (HR), body weight, blood oxygen saturation (SpO2), and symptoms from HF patients in addition to the sensor derived PAP as this the system that was evaluated in the published evidence and therefore the comparison is not between two sensors.<br><br>**We would request that if a comparison is carried out, that the relative evidence levels are clearly stipulated as well as the comparison being made. In this instance, CardioMEMS sensor vs Cordella system comprising sensor, blood pressure, body weight, blood oxygen saturation.** | "*The control arm in PROACTIVE-HF involved standard heart failure management with additional telemonitoring of daily data on patients vital signs (but not PAP measurements), which reflects more intensive monitoring than current monitoring*"<br><br>And also in the discussion:<br>*"This assumes that control arms in trials of the two devices are equivalent. However, the control arm for the PROACTIVE-HF trial that evaluated Cordella includes enhanced monitoring in the control arm, and so this assumption does not fully hold. The results of this comparison should therefore be treated with some caution."* |
| 17 | Abbott Medical | 23 | 2.1 | Clarification<br><br>"Additional peripheral devices that connect to the Cordella "myCordellaHub" are required to provide these measurements."<br><br>Given the pricing assumption that Cordella will be the same as CardioMEMS, did the modelling team take into account the cost of the additional peripherals as part of such assumption as the Cordella evidence is predicated on their use? | We describe this in section 6.3.6.1 under the heading "**Device and equipment costs**" "Costs for Cordella are unknown as yet, but will include delivery system and sensor, patient reader and reader dock, access to the Cordella Heart Failure System, and *ad hoc* training on implantation and the Cordella Heart Failure System."<br><br>As requested by NICE we included Cordella in the model, but had to make some strong assumptions, including for the cost. With nothing else to go on, we assumed these |

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| | | | | **We request Bristol TAG to clarify what is included in the Cordella pricing.** | were the same as for CardioMEMS, but as stated clearly in the report this is only for illustration, and conclusions on relative cost-effectiveness cannot be drawn. |
| 18 | Abbott Medical | 43 | 5.4 | Clarification<br><br>"For device-related outcomes (failure of sensor implantation, sensor failure, and device/system related complications), we considered single-arm data to be the most appropriate source of evidence. The SIRONA-2 and PROACTIVE-HF studies were therefore judged to have low concerns for these outcomes. Although the three RCTs evaluating CardioMEMS were comparative in design, they only contributed single-arm data for these outcomes and so were assessed accordingly using the JBI checklist. The same checklist was also applied to the three additional studies included specifically for the device-related outcomes. All six CardioMEMS studies were judged as low risk of bias for these outcomes"<br>**In CHAMPION and GUIDE-HF patients were randomised post implant and therefore experienced "device-related outcomes" we would request these data to be included in the above calculation.** | These data are included. This is explained in section 4.4.1.3:<br>*"Device related outcomes were analysed as the proportion of participants who experienced an event. Outcomes considered were device implant failure, device failure, and device and system related complications. Where devices were implanted in both intervention and control arms but information was only acted on for the intervention arm, data were used for the two arms combined. Data for these outcomes were effectively single arm, non-comparative data*" |
| 19 | Abbott Medical | 74 | 5.5.2.4 | Clarification<br><br>What is meant by the following statement "However, the two comparative studies reported no difference in change from baseline compared to the control groups (MD = 4.12, 95% CI -20.8, 29.0; Figure)." | This statement is based on meta-analysis of the difference in change from baseline between the two treatment groups as shown in Figure 10.<br><br>We have edited the text to clarify as follows: |

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| | | | | **We would request clarification on this statement. It is stated that GUIDE-HF and MONITOR-HF provide these data. MONITOR-HF states "*The mean 6MWT scores from baseline to 12 months significantly improved by 29·3 m (2·4 to 56·2; p=0·033) in the CardioMEMS-HF group but not in the standard care group (9·8 m [–20·4 to 40·1]; p=0·52). "Similarly, in GUIDE-HF pre-specified COVID analysis at 12 months mean 6MWT scores treatment group 19.46+/- 87.63 p=0.017, control group –9.78+/- 112.7 p=0.33.* We therefore question the above statement and its source.** | "However, **a meta-analysis of the** two comparative studies reported no difference in change from baseline compared to the control groups (MD = 4.12, 95% CI -20.8, 29.0; **Error! Reference source not found.**)." |
| 20 | Abbott Medical | 77 | 5.5.2.8 | Clarification<br><br>"Table 43 in Appendix 4). The proportion of withdrawals ranged from 0 to 39% across studies. Withdrawal rates were similar across treatment arms in the CardioMEMS RCTs and were highest in CHAMPION and MONITOR-HF, these studies also had the longest duration of follow up (18 and 48 months respectively). There were 110 withdrawals (39%) in the control arm and 93 (34%) in the CardioMEMS arm in the CHAMPION trial. In MONITOR-HF there were 50 withdrawals in the control arm (29%) and 49 (28%) in the CardioMEMS arm. The most common reasons for withdrawals in both trials were death followed by withdrawal of consent. There were fewer withdrawals in the GUIDE-HF RCT: 25 (5%) in the CardioMEMS arm and 33 (9%) in the control arm. There were fewer deaths in this trial with most withdrawals due to withdrawal of consent." | We are unclear what is meant here. The text already shows that these data include withdrawals due to deaths and that there are more deaths due to longer follow-up. |

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| | | | | Where clarification and justification as to the withdrawal rates in Cordella studies have been provided no equivalent commentary has been provided for CardioMEMS studies.<br><br>**We would request clarification of the text. In the context of the CardioMEMS studies withdrawal includes patients unable to provide follow up data due to death. Their data, will of course, be included in any mortality calculation. Following up patients with advancing heart failure for longer periods will naturally increase the withdrawal rate. The higher numbers in MONITOR-HF and CHAMPION reflect the longer duration of study as well as a difference in inclusion criteria of more advanced/ symptomatic disease and NYHA III classification vs NYHA II plus NYHA III patients.** | |
| 23 | Abbott Medical | 125 | 6.3.6.3 | Clarification<br><br>Table 20 Summary of model inputs, values and distribution assumed in base-case analysis, and source of evidence. Each parameter was estimated separately, and so model parameters assumed to be independent in the PSA.<br><br>There are a number of items model parameters and values defined in Table 20 and we would seek clarification around the source/ use.<br><br>Cordella device: assumed to be equal to CardioMEMS. Does this assumption include the additional items used as part of the Cordella system | **Cordella device:** The assumption includes all parts of the Cordella system apart from the calibration unit.<br><br>**Implantation failure:** This is described in section 6.3.6.1, under the heading "**Procedure costs to implant the device**". It is made up of £1631 for the repeat day case insertion based on National Cost Collection data, plus an allowance for wasted devices, as explained in comment number #7 above. This cost is **conditional on** having an implantation failure, and so in |

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| | | | | (weights, blood pressure etc) that have been evaluated alongside the PAP sensor within the referenced evidence?<br><br>Implantation failure (CardioMEMS) £2,771. What is the source of this value? Is it a calculation based on the quoted implantation failure rate of 24% that we believe is factually incorrect and should read 1% (item 6 above)<br><br>**We request that implantation failure rate costs are reviewed and commentary provided as to its composition and additional commentary provided around what is included in the costs of Cordella.** | the model is multiplied by the probability of having an implantation failure (0.017). |
| 24 | Abbott Medical | 129 | 6.5.1 | Deterministic base-case analyses<br><br>Table 22 Results from the deterministic base case<br><br>In both Table 22 and Table 23 results are presented for a cost effectiveness model of Cordella that is predicated on results produced in a single, unfinished clinical study (n=88) and yet there is no commentary associated with these tables.<br><br>**We would request that associated commentary is provided but also that, given the significantly different levels of available evidence that no comparison is made between the two methods in line with the statement made in Section 7.1 "We did not have the device cost for Cordella, and there was limited comparative evidence for Cordella. We therefore could not robustly assess the clinical-or cost-effectiveness of Cordella."** | We have edited the text in the cost-effectiveness results section to make the limitations with the data for Cordella clear, and caution against comparisons between CardioMEMS and Cordella. |

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| 25 | Abbott Medical | 137 | 7.2 | Definition of HRQoL<br><br>"CardioMEMS appeared to be associated with improvements in HRQoL in some studies, but findings were inconsistent, and the overall effect remains uncertain. The impact on HRQoL was all uncertain for Cordella due to the lack of comparative evidence.<br><br>We would question this statement. Of the CardioMEMS RCTs, CHAMPION HRQoL was measured using the MLFHQ and a p=0.02 observed in favour of CardioMEMS, MONITOR-HF trial was explicitly powered to evaluate the impact on HRQoL and determined a 7·05 (2·77 to 11·33) improvement in KCCQ and a p value of 0.013. The only RCT that did not show a statistically significant impact on HRQoL was GUIDE-HF where a less sick population was being investigated and therefore the impact of CardioMEMS in this group might be anticipated to be a less in a NYHA II cohort where their disease is already defined as "having mild symptoms and slight limitation on function capacity"<br><br>**We would request health related quality of life includes EQ-5D as well as HFH.** | We are unsure what is meant here. The data reported in this comment match the data included in our report, but the EQ-5D results are not mentioned here. We report data for all QoL scales reported including EQ-5D. We consider that this statement supports what the data shows. We have added a note to highlight that the GUIDE-HF data relates to the full study population:<br><br>"However, data were only available for the full trial population which includes those with NYHA class II who are likely to be a less ill population."<br><br>See also response to comment #14 regarding the use of the HRQoL data in the model. |
| 26 | Abbott Medical | 137 | 7.2 | Inconsistency<br><br>For device-related outcomes, there was high-certainty evidence that sensor implantation failure was uncommon, occurring in less than 2% of people in whom implantation was attempted for CardioMEMS and approximately 5% for Cordella. Sensor failure and DSRC were rare for both devices." | We agree that sensor implantation failure is uncommon, and this is reflected in the probability of implantation failure of 0.017 used in the model. However, as described above in comment number 7, the wasted device calculation is relevant solely to cases in which the implantation has actually failed. In these cases, 6/25 devices could not be |

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| | | | | In section 6.3.6.1, and within the model, “Devices were assumed to be opened but unusable in 6/25 (24%) of cases (based on CHAMPION data), with recharges (the full device cost) applied in half of these cases”. The above contradicts this but more accurately reflects the published data. Contradicts their 24%<br><br>**We would request that the model and commentary reflect the first paragraph rather than a second which includes incorrect data.** | inserted into the patient at a later date. We must therefore include an amount to allow for the number of these devices that are charged at full rate. |
| 27 | Abbott Medical | 137 | 7.2 | Clarification<br><br>Change in New York Heart Association (NYHA) class was not reported for CardioMEMS but was assessed in all Cordella studies, which showed improvement; again, without a comparator, the clinical significance is uncertain.<br><br>In Brugts 2023 Appendix page 33 exploratory analysis of the change in NYHA class is reported for the treatment group (below). Furthermore, Kapelios CJ et al. European Journal of Heart Failure (2025) doi:10.1002/ejhf.3687 go further and analysing the Real World studies suggest that 56% (43%; 67%) of patients had improved to NYHA classes I/II (Figure 4) with EQ-5D-5L-VAS also being significantly improved compared with baseline (7.2 [95% CI 3.5; 10.9], p<0.001)<br><br>**We would request that the text is updated to reflect these CardioMEMS publications.** | Real world studies were not eligible for inclusion as RCT data were available. The data on p.33 of Brugts are stratified by improvement in KCCQ scores in the treatment group. It is unclear how the ORs were calculated, what data were included for the control group (presumably only data for those with each improvement in QoL in the intervention group included) and so were considered of limited value and not included in our report. |

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| 28 | Abbott Medical | 139 | 7.3 | Source of assumption<br><br>"If 10% of patients stop adhering to using the device after 12 months then the ICER increases to £47,934. However, we heard that adherence drop-off would likely be lower than this, although adherence may be better with Cordella due to ease of use."<br><br>We question both statements. There is no data to suggest that patients stop using their devices at 12 months. We would also ask for the evidence around "though adherence may be better with Cordella due to ease of use."<br><br>If real world data is used to estimate adherence rates the US post approval study of 2000 patients and follow up time of 333 ± 125 days demonstrated days between transmissions ranged from 1.07 in the first 30 days after implantation to 1.27 days after 6 months. Utilization of the system was observed at a median of 98.6% (IQ Range 82.9% to 100.0%). Median utilization for patients aged < 65 was 96.9% (IQ range 72.7% to 100.0%) and those aged > 65 was 100% (IQ range 87.5% to 100.0%), p value < 0.001.<br><br>**We would request that references for these statements are provided.** | We agree that adherence is likely to be good, as found in section 5.5.2.6, and that is why we assume 100% adherence in our base-case, as described in section 6.3.4.4. This scenario was included purely to give an indication of the impact of lack of adherence, and the 10% figure is not based on any evidence. The statement that drop off in adherence is likely to be better than 10% was from our clinical advisors. The comment on Cordella was based on the findings of the clinical review, although we acknowledge that this is very uncertain. We have reworded this text in the report to: "In our scenario where 10% of patients stop adhering to using the device after 12 months then the ICER increases to £47,934. However, we heard from our clinical advisors that adherence drop-off would likely be better than this. The clinical review found that adherence may be better with Cordella due to ease of use, but more evidence is required to assess this." |
| 29 | Abbott Medical | 143 | 7.4.3 | Clarification<br><br>"There was also no information supplied by Abbott about the cost of the calibration unit for CardioMEMS, | We apologise for the oversight in missing the cost of the calibration system at the outset. To explore the impact of this cost we have run an additional scenario (scenario 12) with a rough estimate of this cost per |

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| | | | | so there is also some uncertainty around the cost of CardioMEMS."<br><br>We question this. In the DAP request for information form provided in December 2024 the following was stated.<br>[redacted]<br><br>No follow up request was made to Abbott to provide the costs of the calibration unit.<br><br>**We request that the model reflects this previously provided data and that it includes calibration of Cordella for consistency.** | patient. To estimate this we estimated the annual number of eligible patients per hospital per year to be 56.24 based on patients who survived an index heart failure admission across 335 NHS hospitals between Jan 1, 2019, and Dec 31, 2022 NHS data (Fletcher et al 2024). If the calibration unit lasts for 10 years, then this would give a per patient cost of [redacted] which is approximately [redacted]. This is based on some strong assumptions and doesn't account for the proportion of eligible patients who decline the implantation or annuitizing the case. However, the results from scenario 12 show that it has a negligible effect on the ICER for CardioMEMS.<br><br>We describe this scenario in section 6.3.6.1. |

## Section B Economic model - Comments

| Stakeholder | Comment | Description of problem | Description of proposed amendment | Result of amended model or expected impact on the result (if applicable) | EAG response |
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| Abbott Medical | 1 | Inappropriate adaptation to existing Markov model on HFH state<br><br>The Markov model available in best available evidence has a recurrent HFH state in a 3-state model (stable, HFH, death).<br><br>However, the present model in EAR broke down the HFH state into further hospitalisation states and applies identical probabilities for subsequent heart failure hospitalizations (HF2, HF3, HF4) across both treatment and control arms, despite published evidence showing that CardioMEMS reduces HFH.<br><br>HFH input parameters:<br><br>• HF_hosp: -0.153<br>• LHR_CM_hosp: -0.4155154 | We propose to follow the existing model structure as HTW, Cowie 2023, and Mokri 2024 in assessing the risk of HFH or mortality when in a stable heart failure state. This relies on the existing evidence fully without making assumptions based on evidence that does not exist. | We expect the result to lead to a lower incremental cost for the treatment arm and a higher QALY gained. We were not able to amend the model and test this hypothesis as it would require a significant alteration by adapting the Markov model and its health states. Instead, we are basing the reduced ICER off of the existing cost-effectiveness analyses (HTW, Cowie 2023, and Mokri 2024). | The company has misunderstood our model. **Under usual care**, the rate of HFH increases based on the number of previous HFHs. This effect is based on data and clinical advice. So, for example the parameter LHR_hosp_for_HF2 is the logHR of hospitalisation for a patient on usual care who has had a recurrent HFH compared to a patient on usual care who has not had a recurrent HFH. These LHRs are used to get the HFH rate for each of the states in the model **under usual care**.<br><br>The hazard ratio for CardioMEMS is then applied to all the usual care HFH rates to get the HFH rates for CardioMEMS in each state. In other words, the treatment effect continues throughout the model, reducing the rate of HFH at each state in the model. |

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| | | • LHR_Cordella_hosp: -0.4942963<br>• LHR_hosp_for_HF2: 0.532<br>• LHR_hosp_for_HF3: 0.619<br>• LHR_hosp_for_HF4: 1.134<br><br>While assessing the impact of repeated HFHs on outcomes such as mortality and cost is a sensible approach, using the same probabilities for both groups disregards the demonstrated benefit of CardioMEMS. This assumption inflates the hospitalization risk for the treatment arm, leading to an overestimated incremental cost and underestimated QALYs gained.<br><br>The available clinical evidence also relates to any HFH following implantation of a PAP sensor and not the impact on defined HF1 HF2 HF3 and HF4. Accurately determining the likelihood of experiencing the additional HF2, HF3, HF4 states cannot be | | | We are effectively assuming that the treatment effect of the CardioMEMS device is the same regardless of how many previous HFHs a patient has had, and it does not wane with more HFHs. |

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| | | determined for the intervention arm. | | | |
| Abbott Medical | 2 | The model applies identical utility values to both treatment and control arms, with decrements following each HFH. This approach overlooks the quality-of-life improvements demonstrated in the MONITOR-HF RCT for patients using CardioMEMS. As a result, the model fails to capture the treatment's true benefit in terms of patient-reported outcomes. | We propose to include the utility improvements thanks to CardioMEMS as proven in MONITOR-HF for patients with stable HF1 before any HFH has occurred in the base case analysis. | CardioMEMS vs SC ICER: £ 25,667 | As explained in section A comment #14, there is a utility benefit of CardioMEMS in the model, resulting from a reduced rate of HFHs, because the HRQoL depends on the number of previous HFHs. However, we acknowledge that there may be additional HRQoL benefits over and above those via HFH, and so we explored the impact of this in our scenario 6c where we used the HRQoL data from MONITOR-HF for 12 months, with the state-based utilities beyond 12 months. This scenario gave an ICER of £35,596. The ICER the company give is from Scenario 6b, where utilities are extrapolated linearly based purely on assumption. |
| Abbott Medical | 3 | CardioMEMS mortality benefit ignored<br>The model assumes no mortality benefit for CardioMEMS compared to standard care, disregarding two meta- | We propose to amend the base case model to include the mortality benefit (HR 0.75) found in the meta-analysis of 3 RCTs by Lindenfeld et al. 2024 (CHAMPION trial, | Base case analysis mortality HR 0.75: CardioMEMS vs SC ICER: £ 21,342 | See response to Section A comment #4. The model does include a mortality benefit via the HFH states because mortality increases with number of previous HFHs, and CardioMEMS reduces HFH rate. |

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| | | analyses of three RCTs that demonstrated a significant mortality reduction. Excluding this evidence solely because it wasn't validated against UK national data is not a sufficient justification. We also disagree with the indirect modeling of mortality using a hazard ratio of 1, which fails to reflect the reduced HFH rates after the first event. This approach underestimates the clinical benefit of CardioMEMS and misrepresents its impact on long-term outcomes. | GUIDE-HF, LAPTOP-HF).<br><br>We further propose to amend the scenario analysis to include the mortality benefit (HR 0.70) found in the propensity matched cohort analysis by Abraham et al. 2019.<br><br>We agree with the use of including the meta-analysis of the three RCTs for scenario analysis 3.<br><br>*Lindenfeld J, Costanzo MR, Zile MR, Ducharme A, Troughton R, Maisel A, et al. Implantable Hemodynamic Monitors Improve Survival in Patients With Heart Failure and Reduced Ejection Fraction. Journal of the American College of Cardiology 2024;83(6): 682-694.*<br><br>*Abraham J, Bharmi R, Jonsson O, et al. Association of ambulatory hemodynamic monitoring with clinical outcomes in a concurrent matched control analysis. JAMA* | Scenario analysis mortality HR 0.70: CardioMEMS vs SC ICER: £ 19,817<br><br>Scenario analysis mortality HR 0.91: CardioMEMS vs SC ICER: £ 29,986 | Furthermore, we included a scenario using the mortality HR from our meta-analysis as an additional mortality benefit over and above the benefit due to number of HFHs (scenario 3).<br><br>We do not understand the comment that our approach "fails to reflect the reduced HFH rates after the first event". We think this may be related to the misunderstanding of our model noted in our response to section B comment #1. In our model the treatment effect for CardioMEMS is applied throughout the model for each HFH transition, and so does reduce HFH rates after the first event (and in fact for all events). |

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| | | | *Cardiology. 2019;4(6):556-563.* | | |
| Abbott Medical | 4 | CardioMEMS incorrect wasted device rate and clarification on scenario analysis 8a and 8b<br><br>The model assumes a wasted implant rate of 24% which is not correct as stated in comment no. 4. The referenced trial, CHAMPION, had 575 patients who underwent a RHC and intended implant. (Lancet 2011; 377: 658–66 Figure 2: Trial profile) Of these, 25 patients did not receive an implant for different reasons. 6 devices were opened but not implanted. This would equate to 6/575 (1%) of devices opened but unusable.<br><br>Furthermore, it is unclear how scenario 8a and 8b on wasted and no wasted devices were calculated in the model as there were almost no changes in the resulting ICER for either analysis. | We propose to amend the model with the correct wasted device rate of 1% applied to the base case analysis instead of 24%.<br><br>Moreover, we propose a clear explanation as to how wasted devices affects the cost-effectiveness analysis<br><br>. | We were not able to model the change in wasted device rates as it was not clear how this was calculated in the base case or scenario analysis. | Please see our response to Section A comments #7, #23, and #26. These values are **conditional** on having an implant failure, and multiplied by the probability of implant failure. We have reworded 6.3.6.1 to make this clearer:<br><br>“Of those cases with implantation failure, devices were assumed to be opened but unusable in 6/25 (24%) of cases” |

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| Abbott Medical | 5 | Cost of usual care<br><br>As explained in Comment No. 6 in Section A of the EAR and model comments, the annual rate of consultant-led follow-up is unrealistic and too sporadic. The cost of usual care should reflect a more realistic follow-up rate.<br><br>According to the NICE Guidelines (NG106) for chronic heart failure, patients should be monitored at short intervals of two weeks until their condition stabilizes, followed by follow-up every six months. We acknowledge that heart failure characteristics vary among patients. Therefore, we recommend adopting the follow-up rate used in the MONITOR-HF standard care arm—every two months. This recommendation is based on the average monthly rate of outpatient clinic contact, which was 0.44 over the entire follow-up period and 0.49 during the 12-month follow-up in | We propose amending the cost of usual care to reflect consultant-led outpatient cardiology follow-up (WF01A Cardiology Service) every two months in the standard care arm of the base case analysis. This corresponds to a monthly usual care cost of £144.50, calculated as £91 + (£107 ÷ 2).<br><br>We recommend assigning the control arm its own follow-up cost of £144.50, as the current model double-counts follow-up and monitoring costs for the treatment arm. These costs should be separated to ensure accurate representation of usual care. | We were unable to amend the model to include a separate follow-up cost for usual care, as this would require the creation of a new cost variable. We anticipate that, once follow-up and monitoring costs are correctly separated, the total cost of usual care will increase, while the total cost for the treatment arms will decrease. | See response to comment section A #9. We based our estimate of usual care on clinician advice that a single annual outpatient appointment was typical. However, we have now added a scenario analysis (Scenario 11) in which each patient has 6 outpatient appointments per year. The cost of a single WF01A consultant-led cardiology appointment is £180 in the National Cost Collection data for 2023/24. Medication costs are £907, leading to a monthly follow-up cost of £166 in Scenario 11. We note that patients could have more follow-up appointments in the treatment arm than in the control arm if the device is leading to more medication changes.<br><br>Note that the usual care cost is applied to both the intervention and control arms, because it relates to medications and follow-up appointments for the patient. The monitoring costs cover clinician time to examine |

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| | | MONITOR-HF (See MONITOR-HF Supplemental File Table S8a).<br><br>Additionally, we note that the model does not differentiate the cost of follow-up between the treatment and control arms. As a result, it currently double counts the cost of follow-up and monitoring for the treatment arm. These costs should be separated, and usual care should be assigned its own follow-up cost. | | | PAP data from the device (ie not with the patient), and are therefore only applied to the treatment arms. We do not think that the costs are double counted. |
| LeadTeam | | Requested a scenario where the disutility due to HFH lasts longer than 1 month | | | We have added scenarios where the disutility due to HFH lasts for 2 months |