Pulmonary artery pressure technologies for remote monitoring of chronic heart failure [DG10087] Protocol

Diagnostic Assessment Report commissioned by the NIHR Evidence Synthesis Programme on behalf of the National Institute for Health and Care Excellence

NIHR Reference No	NIHR172941
Version Number	1.0
Date	17/2/25
External Assessment Group:	Bristol Technology Assessment Group
Project & Clinical Lead:	Penny Whiting Professor of Clinical Epidemiology Bristol TAG
Health Economics Leads:	Nicky Welton Professor in Statistical and Health Economic Modelling Bristol TAG Joanna Thorn Senior Research Fellow in Health Economics Bristol TAG

Team members

NAME	ROLE ON PROJECT	AFFILIATION
Rachel James	Reviewer	Bristol TAG
Chris Cooper	Reviewer & Information Specialist	Bristol TAG
Joe Carroll	Health Economist	Bristol TAG
Mary Ward	Health Economist	Bristol TAG
Hayley Jones	Statistician	Bristol TAG
Angus Nightingale	Clinical Advisor	University of Bristol
John Walsh	Patient Representative	University of Bristol
Francesco Palma	Patient Representative	University of Bristol

1 Plain English Summary

What is the problem?

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 hands and feet, feeling light headed and fainting.

CHF is usually diagnosed by a doctor based on your signs and symptoms, physical examination and assessments. Once CHF has been confirmed it requires regular monitoring to identify any worsening symptoms and to make sure you are receiving the best treatment.

One of the early signs of worsening CHF is a change in pressure in the arteries that carry blood from the heart to the lungs. Sensors can be used to monitor changes in this pressure. These sensors are inserted into the pulmonary artery (the arteries that supply blood to each lung) and record the pressure within the artery. This data is sent to an external monitor in the person's home that can then be accessed remotely by the CHF team.

What are we trying to find out?

We want to know whether use of these sensors will mean people get better treatment and have fewer visits to hospital. We also want to know whether introducing these sensors is a good use of NHS money.

What are we going to do

We will look at existing research and create cost models to study both the health benefits and costs of using pressure sensors to see how well they work and if they are good value for money.

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%	Often associated with 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. The clinical characteristics and outcomes of HFmrEF are subjects of ongoing research.
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. 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,[4] with an analysis of over 4 million primary care records reporting a UK prevalence of 1.6% in 2014.[5] The European Society of Cardiology long-term outpatient registry reports that 55% of patients have HFrEF, 21% have HFmrEF, and 24% have HFpEF.[6] 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.[5] 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.[5] 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.[5] The overall prevalence of CHF is increasing as a result of an ageing population and increasing rates of obesity.

CHF is a leading cause of hospitalisation in people aged over 65 years and accounts for 1–2% of all NHS hospital admissions.[4] On average, a 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 11 days)[7] 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.[8, 9] Five year survival rates are around 50%.[9] 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.[10]

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. National Institute for Health and Care Excellence (NICE) guideline NG106 provides comprehensive guidelines for diagnosing and managing CHF in adults.[11] These recommend that a core specialist heart failure multidisciplinary team (MDT) should work in collaboration with the primary care team to diagnose CHF.[11] 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.[12] 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.[11]

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. 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 rests (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.[11] Invasive haemodynamic assessment via right heart catheterisation is occasionally used in complex cases.[13]

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[11] recommend regular (6-monthly) reviews to manage the condition effectively and prevent exacerbations, although monitoring for CHF is currently highly variable across the NHS. At a minimum, these 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.[11] Monitoring of patients with CHF is often done by specialist nurses and pharmacists.[14, 15]

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. 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.[16]

1.3.3 Treatment of CHF

Management of CHF involves a combination of pharmacological treatments, lifestyle modifications, and, in certain cases, device therapies.[11, 17] 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 all patients with CHF should be offered diuretics to relieve congestive symptoms and fluid retention. [11] Other treatments are dependent on whether patients have reduced or preserved ejection fraction. Management is more conservative for those with preserved ejection fraction, where 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, but they should additionally be offered the following pharmacological interventions:

- **Angiotensin-Converting Enzyme Inhibitors (ACEIs) and 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.
- **Angiotensin II Receptor Blockers (ARBs):** Considered for patients intolerant to ACEIs.
- **Hydralazine and nitrate:** for those intolerant of ACEI and ARB

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

- **Angiotensin receptor–neprilysin inhibitor (ARNI) (Sacubitril or Valsartan):** To replace ACEI or ARB in those with ejection fraction <35%[18]
- **Ivadribine:** added to other interventions to control sinus rhythm in those with heart rate >75 and ejection fraction <35%[19]
- **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
- **Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors:** Dapagliflozin or empagliflozin have been recommended by NICE for treating CHF if symptom persist despite first line treatment.[20]

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.

As NICE guidelines have not been updated since 2018, the more recent European Society of Cardiology (ESC) guidelines are often followed in the NHS.[17] An update to the NICE guidance is expected In 2025, ESC guidance is also currently being updated. A "four pillar" approach is usually taken based on ESC guidance where clinicians aim to get patients in HFeEF established on treatments from each of the following four classes – a key difference from NICE guidance is taking an SGLT2 inhibitor earlier than currently recommended:

- ACE, ARB or ARNI
- Beta-blocker
- MRA
- SGLT2 Inhibitor

Patients with HFpEF are also usually offered SGLT-2 inhibitors. Diuretics may also be given to treat fluid retention. 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.

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 technolgoies. **CardioMEMS HF System** (Abbott)[21] and **Cordella Pulmonary Artery Sensor System and Cordella Heart Failure System** (Endotronix/Edwards Lifesciences).[22] These are referred to as "CardioMEMS" and "Cordella" PAP monitoring technologies from here.

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 retention 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.[23]

Cordella is an investigational device 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 vital signs such as blood pressure, heart rate, weight, and oxygen saturation. 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. This system aims to assist healthcare providers in assessing and managing heart failure, potentially reducing hospitalisations. However, the Cordella PA Pressure Sensor System is currently an investigational device and is not approved for clinical use in any region.[22]

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.[24]

2.2 Comparator

The comparator for this appraisal is current 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 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 Methods for the clinical effectiveness review

A systematic review will be conducted to summarise the evidence on the clinical effectiveness of remote PAP monitoring technologies for CHF. The systematic review will follow 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.[25, 26]

4.1 Inclusion and exclusion criteria

Studies that meet the following criteria will be eligible for inclusion:

4.1.1 Participants

People with CHF. Studies in all sub-populations will be eligible for inclusion. Inclusion into the systematic review will not be restricted by NYHA classification.

4.1.2 Technology

Remote PAP monitoring technologies:

- **CardioMEMS HF System** (Abbott)[21]
- **Cordella Pulmonary Artery Sensor System and Cordella Heart Failure System** (Endotronix/Edwards Lifesciences)[22]

4.1.3 Comparator

Any comparator intervention, including standard care, no monitoring or no comparator, will be eligible for inclusion.

4.1.4 Outcome

Studies will be required to report at least one of the following outcomes to be included:

- Changes to clinical management (including medication changes)
- Failure of sensor implantation or sensor
- Hospitalisation for heart failure
- Urgent care for heart failure (hospital attendance for i.v. diuretics)
- Worsening of heart failure (e.g., decompensation, change of NYHA symptom class)
- Functional capacity
- Improvement in co-morbidities
- Mortality due to heart failure
- All-cause mortality
- Adverse events
    - Complications associated with sensor implantation (including hospitalisation, complications associated with vascular procedures, infection, complications associated with anticoagulant/dual antiplatelet therapy post-implantation)
- Patients lost to follow-up
- Health-related quality of life
- Adherence to using the device
- Adherence to treatment (adherence to adjusted medication triggered by changes in PAP trend data, adherence to usual heart failure medication)
- Qualitative data of patient experience of using the technology

4.1.5 Study design

Randomised controlled trials; where randomised controlled trials are not available for one or more of the technologies of interest, then comparative non-randomised studies of interventions (NRSI) will be eligible. Where NRSI are not available, single arm studies will be eligible. Qualitative studies that report data on patient or clinician experience of using the technology will also be included.

4.2 Study identification

Studies will be identified using bibliographic and non-bibliographic search methods following guidance in the NICE technology appraisal manual and recent guidance specific to technologies.[26, 27]

4.2.1 Bibliographic searching

The following databases will be searched:

- MEDLINE (Ovid SP)
- EMBASE (Ovid SP)
- CINAHL (Cumulative Index to Nursing and Allied Health Literature) (EBSCOhost)

We will use a sensitive search strategy based on terms for each of the technologies eligible for inclusion. A draft search strategy is reported in Appendix 0.

4.2.2 Non-bibliographic search methods

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

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

Additional relevant studies will be 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
- Information submitted by test manufacturers

4.2.3 Managing the searches

Search results will be exported to EndNote 20 for deduplication using the default deduplication settings and manual review of records. Search results will be exported to Nested Knowledge for screening.

4.3 Review strategy

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

4.3.1 Study selection

Two reviewers will independently screen titles and abstracts identified by the searches. Full copies of all reports considered potentially relevant will be obtained and two reviewers will independently assess these for inclusion. Any disagreements will be resolved by consensus or discussion with a third reviewer.

4.3.2 Data extraction

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

Data will be 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
- Outcomes at timepoints closest to 1 year, 2 year or 5 year follow-up
  - Changes to clinical management (including medication changes)
  - Failure of sensor implantation or sensor
  - Hospitalisation for heart failure
  - Urgent care for heart failure (hospital attendance for i.v. diuretics)
  - Worsening of heart failure (e.g., decompensation, change of NYHA symptom class)

- Functional capacity
- Improvement in co-morbidities
- Mortality due to heart failure
- All-cause mortality
- Adverse events
    - Complications associated with sensor implantation (including hospitalisation, complications associated with vascular procedures, infection, complications associated with anticoagulant/dual antiplatelet therapy post-implantation)
- Patients lost to follow-up
- Health-related quality of life
- Adherence to using the device
- Adherence to treatment
    - Adherence to adjusted medication triggered by changes in PAP trend data
    - Adherence to usual heart failure medication
- Patient experience of using the technology (qualitative data only)

We will consider the PROGRESS-Plus population factors, where reported.[28] 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 will extract 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 will extract 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 reports results data stratified by the factor. Where stratified data are reported, these will be extracted.

Dichotomous data will be 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 will be extracted as the proportion of participants with events in each treatment arm, and as hazard ratios (HR) and 95% confidence intervals. If reported, Kaplan-Meier plots will be digitized and IPD reconstructed using the Guyot method.[29] These reconstructions will be used to test the proportional hazards assumption and distributional

assumptions of time-to-event outcomes in the economic model. For categorical data, we will extract details on the categories assessed, the total number of patients in each treatment arm and the number of patients in each outcome category. For continuous data we will extract 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, summary effect estimates together with 95% CIs and p-values for comparisons between groups together with details on the methods of analysis, any variables controlled for in the analysis and the test statistic will be extracted.

Study findings will be extracted from qualitative studies. Where appropriate we will extract direct quotes to support the qualitative findings.

4.3.3 Quality assessment strategy

The methodological quality of included RCTs will be assessed using the updated Cochrane Risk of Bias Tool (ROB 2.0).[30] NRSI will be assessed using the ROBINS-I tool.[31] Detailed guidance for reviewers on how to complete the assessments for studies included in the review will be produced prior to starting the quality assessment. Where other types of studies are included, we will use the LATITUDES Network to identify the most appropriate tool to assess these studies.[32] Quality assessment will be undertaken by one reviewer and checked by a second reviewer. Any disagreements will be resolved by consensus or discussion with a third reviewer.

4.4 Synthesis methods

A narrative summary of all of the included studies will be presented. This will include a summary of the study characteristics, outcomes reported and study quality. The synthesis will be stratified by technology evaluated.

If sufficient data are available for any reported outcome, meta-analysis will be carried out to summarise effect estimates. For studies of effectiveness where there is only a single comparison (i.e. technology versus comparator), fixed and random effects meta-analysis will be performed, and an appropriate model selected. A restricted maximum likelihood (REML) approach will be used to estimate the between-study heterogeneity parameter, tau. Heterogeneity and inconsistency across studies will be quantified using the tau and I^2 statistics.[33]

Where sufficient data are available, we will stratify analyses and/or perform meta-regression, to explore potential variation by:

- 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 II
    - Class III
    - Class IV

If data are not available for thresholds reported above, we will explore subgroups for which data are available.

If there are sufficient data on both CardioMEMS and Cordella then a Bayesian network meta-analysis will be conducted to indirectly compare them. We anticipate a lack of randomised evidence for Cordella. In this situation, we will explore methods to synthesise RCT and single-arm evidence to produce indirect comparisons, adjusting for potential confounders where possible.[34]

If two or more qualitative studies are identified that report data on the same outcomes, we will use the meta-aggregative approach to qualitative synthesis based on guidance from the Joanna Briggs Institute (JBI).[35] This involves extracting study findings, often as a direct quote, then creating conceptual categories of findings and, where possible, pooling the categories of findings into synthesised findings. Synthesised findings aim to convey the overall meaning of the categorised findings. Where conflicted information, or negative cases, are identified, these will be pursued further to enhance methodological rigour.

5 Methods for the cost effectiveness analysis

5.1 Review of economic evaluations

We will conduct a systematic review of economic evaluations comparing remote PAP monitoring technologies to usual care. The systematic review will follow 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.[25, 26]

The objectives of the review are:

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 will also review 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 of models for CHF, we will undertake a review of systematic reviews (umbrella review) of economic analyses in CHF published within the last ten years. The objectives of this review are to summarise the main model structures and health states used in economic models of heart failure.

5.1.1 Inclusion and exclusion criteria

Studies will be included that meet the criteria for each of the two reviews outlined in Table 2.

Table 2 Inclusion criteria for the cost-effectiveness reviews

	Systematic review of remote PAP monitoring	Systematic review of systematic reviews of heart failure
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) Cost and resource studies reporting UK data.	Published economic models Systematic Review
Limits	None	Reported in English and published since 2015.

5.1.2 Study identification

Studies will be identified using bibliographic and non-bibliographic search methods following guidance in the NICE technology appraisal manual and recent guidance.[26, 27]

5.1.2.1 Bibliographic searching

The MEDLINE search strategies are detailed in Appendix 1 using a search narrative.[36]

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

- MEDLINE (MEDALL, Ovid)
- Embase (Ovid)
- EconLit (EBSCO)
  - NHS EED database via: www.crd.york.ac.uk/CRDWeb/ (the archive will be searched as the database is no longer supported and has not been updated since 2016)
- INAHTA database via: www.inahta.org/hta-database/

- Tufts CEA Registry via: https://cear.tuftsmedicalcenter.org/

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

- MEDLINE (MEDALL, Ovid)
- Embase (Ovid)

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

5.1.2.2 Non-bibliographic searching

- Eligible studies or systematic reviews identified in the systematic review of clinical effectiveness will be reviewed for inclusion.
- The references of studies included at full-text will be reviewed for any studies eligible for inclusion in this review. At the same time, studies will be checked for any post-publication amendment (e.g., Errata/Corrections, Retractions, Expressions of concern, Editorial notes).
- Hand searching the websites of the manufacturer/or licence holders for each test
- Information submitted by test manufacturers

5.1.2.3 Managing the searches

Search results will be exported to EndNote 20 for deduplication using the default deduplication settings and manual review of records.

5.1.3 Review strategy

Two reviewers will independently screen titles and abstracts identified by the searches against the criteria set out in Table 2. Full copies of all reports considered potentially relevant will be obtained and two reviewers will independently assess these for inclusion. Any disagreements will be resolved by consensus or discussion with a third reviewer. Studies excluded at full-text will be tabulated and reported alongside reasons for exclusion.

Data extraction forms will be piloted on a small sample of reports and adapted as necessary. Data will be extracted by one reviewer and checked in detail by a second reviewer. Any disagreements will be resolved by consensus or discussion with a third reviewer. The following data will be extracted:

For the review of remote PAP;

- 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.

For the systematic review of reviews;

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

5.1.4 Quality assessment strategy

The methodological quality of included evaluations for the remote PAP review will be assessed using the Drummond checklist.[37] Any economic models identified will be appraised using the Philips checklist.[38] We will not appraise the quality of the systematic reviews included in the systematic review of reviews of heart failure, as these will be used only to inform our choice of model structure. Quality assessment will be undertaken by one reviewer and checked by a second reviewer. Any disagreements will be resolved by consensus or discussion with a third reviewer.

5.1.5 Synthesis methods

A narrative summary of all of the included economic evaluation studies comparing remote PAP monitoring technologies will be presented. This will include a summary of the study characteristics, outcomes reported, and study quality. The synthesis will be stratified by technology evaluated.

5.2 Evaluation of costs, quality of life and cost-effectiveness

A decision-analytic model will be developed to estimate the incremental costs and quality-adjusted life years (QALYs) of remote PAP monitoring technologies compared with usual monitoring.

5.2.1 Population

We consider a population of patients with CHF, focusing on patients classified as NYHA class III at time of assessment, regardless of whether they subsequently change class.

If sufficient evidence is identified, subgroup analyses will be presented for:

- Baseline PAP
- Age (<75 , >=75 or other age group shown to impact outcomes by the clinical effectiveness review)
- Impact of renal impairment

5.2.2 Strategies for monitoring CHF patients

We aim to compare the following different strategies for monitoring HF patients:

- CardioMEMS HF System (Abbott)
- Cordella PA Sensor System (Endotronix/Edwards Lifesciences), if sufficient evidence is available to populate the model
- Usual monitoring (no device), as described in section 1.3.2.

5.2.3 Model structure

The model structure will be developed to capture the short- and long-term costs and benefits of remote PAP monitoring technologies, and will be informed by the findings of our review of clinical and cost-effectiveness studies and discussions with our clinical advisors and expert committee members.

Recent reviews of cost-effectiveness models of PAP monitoring for CHF,[39, 40] show that the previous models used a Markov model with 2 states (Heart Failure (HF) and Death), where transient hospitalisation events may occur at each cycle of the model which incur costs, utility decrements, and a risk of death, such as the model used by Cowie et al.[41] A recent review of economic models for CHF more generally, found that Markov models were most common, but partitioned survival models and discrete event simulation models have also been used.[40] Health states and events included in these models include, NYHA class, alive/death, hospitalisation, and cardiovascular events. Appendix 2 shows a selection of common model structures used for CHF. We will develop a model that has sufficient detail to capture the key costs and benefits, but that can be estimated from the evidence available.

An NHS and personal social services (PSS) perspective will be taken with a life time horizon where costs and QALYs are discounted at an annual rate of 3.5%. The model will include all relevant health effects, including patients and other relevant people (such as carers), where evidence can be identified.

Probabilistic sensitivity analysis where parameter uncertainty is captured with probability distributions and simulation will be used to estimate incremental cost-effectiveness ratios and expected net benefits at commonly used NICE willingness to pay thresholds. Uncertainty will be presented using cost-effectiveness planes and cost-effectiveness acceptability frontiers. One way sensitivity analyses will be performed for all key model parameters.

5.2.4 Model inputs

Model inputs will be derived from the clinical and cost-effectiveness reviews where possible, supplemented by targeted literature searches. Where there is insufficient evidence available we will base parameters on expert opinion and conduct scenario analyses to explore the impact of these assumptions on the results.

5.2.5 Scenario analyses

Scenario analyses will be conducted to explore the sensitivity of results to key model assumptions. For example, we will explore the impact of adherence to provision of data dropping off over time.

5.2.6 Health outcomes

The model will include the impact of the different monitoring strategies for HF patients on mortality and health-related quality of life (HRQoL). The model will include the HRQoL impact of hospitalisation, and procedure and device-related complications. The impact on carers will be included in the model if evidence is available, and will be discussed if no evidence is identified.

5.2.7 Costs

Costs will be considered from an NHS and Personal Social Services perspective. Costs will be 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 will include the following costs:

- device cost and equipment costs, including hardware/software, connections, maintenance
- procedure to implant the device
- staff training for monitoring and interpreting results
- Patient/carer training in device use
- HF-related and non-HF related hospitalisation and re-hospitalisation
- treatment costs
- disease management costs
- management of implant-related complications

We will not include costs that are incurred regardless of monitoring strategy.

6 Handling information from the companies

All data submitted by the manufacturers/sponsors will be considered if received by the EAG no later than 30 June. Data arriving after this date will not be considered. If the data meet the inclusion criteria for the review they will be extracted and quality assessed in accordance with the procedures outlined in this protocol.

Any 'commercial in confidence' data provided by manufacturers, and specified as such, will be highlighted in blue and underlined in the assessment report (followed by company name in parentheses). Any 'academic in confidence' data provided by manufacturers, and specified as such, will be highlighted in yellow and underlined in the assessment report. Any confidential data used in the cost-effectiveness models will

also be highlighted. If confidential information is included in economic models then a version using dummy data or publicly available data in place of confidential data will be provided.

7 Competing interests of authors

None of the authors have any competing interests.

8 Timetable/milestones

Milestone	Date to be completed
Draft protocol	7 February 2025
Final protocol	17 February 2025
Draft assessment report	15 July 2025
Final assessment report	11 August 2025

9 References

1. National Institute for Health and Care Excellence. *Heart failure - chronic*.2025. URL: https://cks.nice.org.uk/topics/heart-failure-chronic/ (Accessed 17/01/2025).
2. Bozkurt B, Coats AJS, Tsutsui H, Abdelhamid M, Adamopoulos S, Albert N*, et al.* Universal Definition and Classification of Heart Failure: A Report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure. *Journal of Cardiac Failure* 2021;**27**(4): 387-413
3. The Criteria Committee of the New York Heart Association. *Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels*. 9th edn. Boston: LIttle Brown & Co.; 1994. http://dx.doi.org/10.7326/0003-4819-80-5-678_2
4. Groenewegen A, Rutten FH, Mosterd A, Hoes AW. Epidemiology of heart failure. *European Journal of Heart Failure* 2020;**22**(8): 1342-1356
5. Conrad N, Judge A, Tran J, Mohseni H, Hedgecott D, Crespillo AP*, et al.* Temporal trends and patterns in heart failure incidence: a population-based study of 4 million individuals. *Lancet* 2018;**391**(10120): 572-580
6. Savarese G, Gatti P, Benson L, Adamo M, Chioncel O, Crespo-Leiro MG*, et al.* Left ventricular ejection fraction digit bias and reclassification of heart failure with mildly reduced vs reduced ejection fraction based on the 2021 definition and classification of heart failure. *American Heart Journal* 2024;**267**52-61
7. Braunschweig F, Cowie MR, Auricchio A. What are the costs of heart failure? *EP Europace* 2011;**13**(suppl_2): ii13-ii17
8. Emmons-Bell S, Johnson C, Roth G. Prevalence, incidence and survival of heart failure: a systematic review. *Heart* 2022;**108**(17): 1351
9. Jones NR, Roalfe AK, Adoki I, Hobbs FDR, Taylor CJ. Survival of patients with chronic heart failure in the community: a systematic review and meta-analysis. *European journal of heart failure* 2019;**21**(11): 1306-1325
10. BMJ Best Practice. *Heart failure with preserved ejection fraction*.2025. URL: https://bestpractice.bmj.com/topics/en-gb/953 (Accessed 05/02/2025).

11. National Institute for Health and Care Excellence. *[NICE guideline NG106] Chronic heart failure in adults: diagnosis and management*.2018. URL: https://www.nice.org.uk/guidance/ng106 (Accessed 28/01/2025).
12. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M*, et al.* 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. *European Heart Journal* 2021;**42**(36): 3599-3726
13. Cochran JM, Alam A, Guerrero-Miranda CY. Importance of right heart catheterization in advanced heart failure management. *Reviews in Cardiovascular Medicine* 2022;**23**(1):
14. Jasińska-Stroschein M, Waszyk-Nowaczyk M. Multidimensional Interventions on Supporting Disease Management for Hospitalized Patients with Heart Failure: The Role of Clinical and Community Pharmacists. *Journal of clinical medicine* 2023;**12**(8):
15. Paul F, Susan Y, Kirsty H, Ruby J, Cheryl O, Ruth K*, et al.* Multiprofessional heart failure self-development framework. *Open Heart* 2024;**11**(1): e002554
16. National Institute for Health and Care Excellence. *[DG61] Heart failure algorithms for remote monitoring in people with cardiac implantable electronic devices*.2024. URL: https://www.nice.org.uk/guidance/dg61 (Accessed 04/2/2025).
17. European Society of Cardiology. *2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure*.2023. URL: https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Focused-Update-on-Heart-Failure-Guidelines (Accessed 29/01/2025).
18. National Institute for Health and Care Excellence. *[TA388] Sacubitril valsartan for treating symptomatic chronic heart failure with reduced ejection fraction*.2016. URL: https://www.nice.org.uk/guidance/ta388 (Accessed 29/01/2025).
19. National Institute for Health and Care Excellence. *[TA267] Ivabradine for treating chronic heart failure*.2012. URL: https://www.nice.org.uk/guidance/ta267 (Accessed 04/02/2025).
20. National Institute for Health and Care Excellence. *Heart failure - chronic: SGLT2 Inhibitors*.2024. URL: https://cks.nice.org.uk/topics/heart-failure-chronic/prescribing-information/sglt-2-inhibitors/ (Accessed 29/01/2025).
21. Abbott. *CardioMEMS HF System* 2025. URL: https://www.cardiovascular.abbott/us/en/hcp/products/heart-failure/pulmonary-pressure-monitors/cardiomems/about.html (Accessed 28/01/2025).
22. Endotronix. *Cordella*.2025. URL: https://endotronix.com/hemodynamic-monitoring/ (Accessed 29/01/2025).
23. Abbott. *How CardioMEMS HF System Remote PA Pressure Monitoring Works*.2025. URL: https://www.cardiovascular.abbott/int/en/hcp/products/heart-failure/pulmonary-pressure-monitors/cardiomems/about/how-it-works.html (Accessed 17/01/2025).
24. National Institute for Health and Care Excellence. *[Interventional procedures guidance Reference number PG711] Percutaneous implantation of pulmonary artery pressure sensors for monitoring treatment of chronic heart failure*.2021. URL: https://www.nice.org.uk/guidance/ipg711/chapter/1-Recommendations (Accessed 17/01/2025).
25. Centre for Reviews and Dissemination. *CRD's guidance for undertaking reviews in health care. Centre for Reviews and Dissemination*.2009. URL: https://wwwyorkacuk/media/crd/Systematic_Reviewspdf. (Accessed 28/01/2025).

26. National Institute for Health Care Excellence. *NICE health technology evaluations: the manual*.2023. URL: https://www.nice.org.uk/process/pmg36/ (Accessed 10/01/2025).
27. Cooper C, Dawson S, Lefebvre C. Searching for medical devices – Practical guidance. *Research Synthesis Methods* 2022;**13**(1): 144-154
28. O'Neill J, Tabish H, Welch V, Petticrew M, Pottie K, Clarke M*, et al.* Applying an equity lens to interventions: using PROGRESS ensures consideration of socially stratifying factors to illuminate inequities in health. *Journal of Clinical Epidemiology* 2014;**67**(1): 56-64
29. Guyot P, Ades AE, Ouwens MJNM, Welton NJ. Enhanced secondary analysis of survival data: reconstructing the data from published Kaplan-Meier survival curves. *BMC Medical Research Methodology* 2012;**12**(1): 9
30. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I*, et al.* RoB 2: a revised tool for assessing risk of bias in randomised trials. *Bmj* 2019;**366**l4898
31. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M*, et al.* ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *Bmj* 2016;**355**i4919
32. Whiting P, Wolff R, Savović J, Mallett S, B Devine B, the LATITUDES group. *LATITUDES network*.2023. URL: https://www.latitudes-network.org/ (Accessed 05/02/2024).
33. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *Bmj* 2003;**327**(7414): 557-560
34. Thom H, Leahy J, Jansen JP. Network Meta-analysis on Disconnected Evidence Networks When Only Aggregate Data Are Available: Modified Methods to Include Disconnected Trials and Single-Arm Studies while Minimizing Bias. *Medical Decision Making* 2022;**42**(7): 906-922
35. Hannes K, Lockwood C. Pragmatism as the philosophical foundation for the Joanna Briggs meta-aggregative approach to qualitative evidence synthesis. *Journal of advanced nursing* 2011;**67**(7): 1632-1642
36. Cooper C, Dawson S, Peters J, Varley-Campbell J, Cockcroft E, Hendon J*, et al.* Revisiting the need for a literature search narrative: A brief methodological note. *Research Synthesis Methods* 2018;**9**(3): 361-365
37. Drummond M, Sculpher M, Torrance G, O'Brien B, Stoddart G. *[Drummond checklist] Methods for the economic evaluation of health care programs*. Oxford: Oxford University Press; 2005.
38. Philips Z, Ginnelly L, Sculpher M, Claxton K, Golder S, Riemsma R*, et al.* Review of guidelines for good practice in decision-analytic modelling in health technology assessment. *Health Technology Assessment* 2004;**8**(36): 1-158
39. 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**16
40. Di Tanna GL, Bychenkova A, O'Neill F, Wirtz HS, Miller P, O Hartaigh B*, et al.* Evaluating Cost-Effectiveness Models for Pharmacologic Interventions in Adults with Heart Failure: A Systematic Literature Review. *PharmacoEconomics* 2019;**37**(3): 359-389
41. 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

42. Martinson M, Bharmi R, Dalal N, Abraham WT, Adamson PB. Pulmonary artery pressure-guided heart failure management: US cost-effectiveness analyses using the results of the CHAMPION clinical trial. *European journal of heart failure* 2017;**19**(5): 652-660
43. Schmier JK, Ong KL, Fonarow GC. Cost-Effectiveness of Remote Cardiac Monitoring With the CardioMEMS Heart Failure System. *Clinical cardiology* 2017;**40**(7): 430-436
44. 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
45. Sandhu AT, Goldhaber-Fiebert JD, Owens DK, Turakhia MP, Kaiser DW, Heidenreich PA. Cost-Effectiveness of Implantable Pulmonary Artery Pressure Monitoring in Chronic Heart Failure. *JACC Heart failure* 2016;**4**(5): 368-375
46. Thokala P, Baalbaki H, Brennan A, Pandor A, Stevens JW, Gomersall T*, et al.* Telemonitoring after discharge from hospital with heart failure: cost-effectiveness modelling of alternative service designs. *BMJ open* 2013;**3**(9): e003250
47. 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
48. Health Technology Wales. *Percutaneously implanted pulmonary artery pressure sensors to monitor treatment of people with chronic heart failure*.2023. URL: https://healthtechnology.wales/wp-content/uploads/2023/02/EAR052-PAPS-WEB.pdf (Accessed 06/02/2025).
49. Albuquerque de Almeida F, Corro Ramos I, Rutten-van Mölken M, Al M. Modeling Early Warning Systems: Construction and Validation of a Discrete Event Simulation Model for Heart Failure. *Value in Health* 2021;**24**(10): 1435-1445

10 Appendices

Appendix 1: Literature searches

Search purpose: to identify studies reporting data on the clinical or cost effectiveness of the technologies specified in the scope.

Clinical effectiveness

Database: MEDLINE (MEDALL)
Host: Ovid
Data parameters: 1946 to January 31, 2025
Date of search: 3 Feb 2025

#	Search strategy	Hits	Search narrative
1	1 (CardioMEMS* or (cardi* and ("Micro-Electro-Mechanical System" or MEMS))).ti,ab,kw,kf.	300	The search focuses on the named technologies under review, CardioMEMS and the Cordella device (X/R to Table **). 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. 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	419	
4	(Cordella* or myCordella* or CorPASS or (CHFS and heart fail*)).ti,ab,kw,kf.	38	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 "PROACTIVE-HF 2" or PRODIGY) adj3 (trial* or study or random* or accura*)).ti,ab.	60	
6	4 or 5	93	
7	3 or 6	506	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.

Cost effectiveness (review of Remote PAP)

Database: MEDLINE (MEDALL)

Host: Ovid

Data parameters: 1946 to January 31, 2025

Date of search: 3 Feb 2025

#	Search strategy	Hits	Search narrative
1	exp Heart Failure/	158317	**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. 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. 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). The free-text terms are searched in the following fields: • ti—title • ab—abstract • kf—author chosen keyword (literally terms chosen by authors to describe their own papers) 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.
2	((heart or cardiac) adj3 fail*).ti,ab,kf.	260258	
3	1 or 2	295076	
4	exp Telemetry/	16041	**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)*' 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.	66605	
6	4 or 5	81148	

#	Search strategy	Hits	Search narrative
7	exp "Costs and Cost Analysis"/	276240	**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. Researchers commonly amend established search filters to increase sensitivity (i.e., to further reduce 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.[26]
8	exp Economics, Hospital/ or Financial management, hospital/	33382	
9	Economics, Medical/	9299	
10	economics, nursing/	4013	
11	economics, pharmaceutical/	3154	
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.	1368437	
13	exp "fees and charges"/	31611	
14	exp budgets/	14316	
15	(resource*1 and (allocation or utili* or usage or use*1)).ti,ab,kf,kw.	312976	
16	(expenditure* not energy).ti,ab,kw.	40617	
17	(value adj1 money).ti,ab,kw.	45	
18	(budget* or fiscal or funding or financial or finance*).ti,ab,kw.	268453	
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.	191513	
20	or/7-19	1974597	
21	3 and 6 and 20	425	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.
22	("37591524" or "27647784" or "28272808" or "28176424" or "26874380" or "24048626" or "21193439").ui.	7	Line 21 and 23: The search was compared to a test set of potential eligible studies (n=7). All seven studies were returned so no edits were made to the syntax.[41-47]
23	21 and 22	7	

Cost effectiveness (review of heart failure models)

Database: MEDLINE (MEDALL)

Host: Ovid

Data parameters: 1946 to January 31, 2025

Date of search: 3 Feb 2025

#	Search strategy	Hits	Search narrative
1	exp Heart Failure/	158317	The search adopts the same rationale and structure as the PAP search for primary studies.
2	((heart or cardiac) adj3 fail*).ti,ab,kf.	260258	
3	1 or 2	295076	
4	exp "Costs and Cost Analysis"/	276240	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.	281586	
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	172090	
7	4 or 5 or 6	624899	
8	"Systematic Review"/	286677	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.	338752	
10	8 or 9	381201	
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.	14683476	Line 11 reports the date limit for this review.
12	3 and 7 and 10 and 11	188	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).
13	("37123330" or "36133814" or "34593166" or "30596210" or "29449079" or "25896804" or "24634022" or "27201473").ui.	8	Line 13 and 14: The search was tested against two marker reviews.[39, 40] Both reviews were returned in testing.
14	12 and 13	2	

Appendix 2: Model structures used previously in the disease area

A targeted search of the literature identified 3 types of model structure to assess the cost-effectiveness of heart failure-related monitoring and interventions. The EAG's model structure may contain elements from the following types of heart failure modelling approaches:

- Markov models
- Discrete event simulations
- State transition models built upon New York Heart Association (NYHA) stages

One relevant such Markov model is the model developed by Cowie et al. (2017) and updated in 2023.[41, 44] This model is a typical Markov model in the disease area, and 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 (Figure 1).

This UK-based model was influential in the development of other UK-based heart failure models including Health Technology Wales' (HTW) cost-effectiveness model for percutaneously implanted pulmonary artery pressure sensors to monitor treatment of people with chronic heart failure which employs the same structure.[48] Similar methods have been developed in the USA, for example the Martinson et al. (2017) model for pulmonary artery pressure-guided heart failure management, which uses a four stage Markov model approach where patients in the living health states may occupy the 'stable heart failure', 'heart failure hospitalisation' and 'non-heart failure hospitalisation' health states.[42] This approach would allow for more refined modelling of subgroups in the heterogeneous heart failure population. Markov models are cohort models, and as such they are unable to account for patient heterogeneity as well as an individual patient simulation could, however they do not have the data requirements of a simulation model.

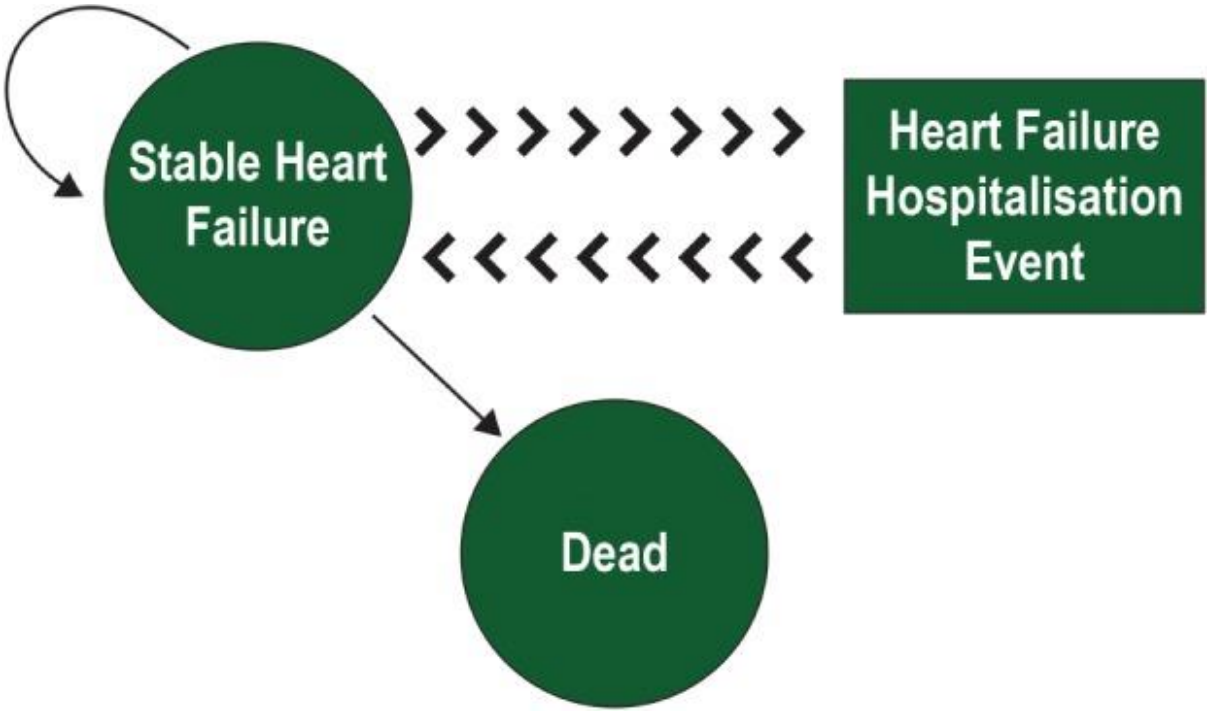

Figure 1 Two State Markov model with health state events [from Cowie et al. (2017)][41, 44]

Another model structure which the EAG will explore for feasibility is discrete event simulations. Discrete event simulation models have also been employed to model the cost-effectiveness of monitoring in the disease area before. One such model from a European perspective includes the model for early warning systems by Albuquerque de Almeida et al. (2021).[49] This model uses a sample of simulated patients and models their long-term outcomes with the possibility of them experiencing 8 heart failure-related health events (Figure 2. Discrete event simulation is particularly useful in modelling heterogeneous populations who may experience disparate health outcomes and can be well utilised in modelling heart failure, as demonstrated by the Albuquerque de Almeida model. The EAG will consider building a discrete event simulation, however the large data requirements may be a prohibitive factor in model structure selection.

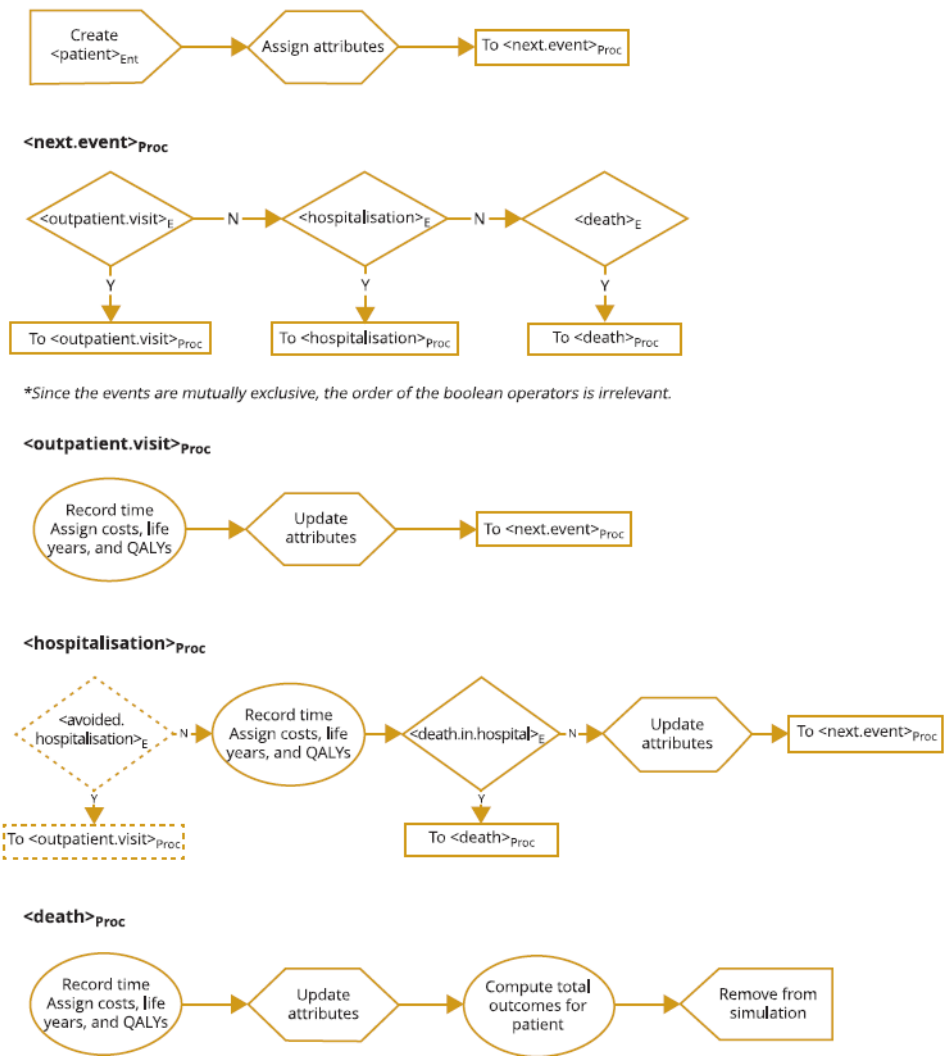

Figure 2 Discrete event simulation diagram [from Albuquerque de Almeida (2021)][49]

Other model structures used outside of the UK include 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. 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.[40] A disadvantage of this modelling approach may be that trial data alone may ignore the costs and benefits not related to the studied intervention. In addition there may be limitations in the data availability of hospital length of stay statistics between treatment groups, as described by Di Tanna et al. As RCTs for clinical trials are more likely to contain time-to-progression data, this modelling approach which has been used in HTA to assess pharmaceutical interventions but it may be inappropriate in a monitoring context where time to NYHA staging progression data is less readily available.[40]