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Assessment Group's Protocol

Algorithm-based remote monitoring of heart failure risk data in people with cardiac implantable electronic devices

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Note on the text

All commercial-in-confidence (CIC) data have been highlighted in blue and underlined, all academic in-confidence (AIC) data are highlighted in yellow and underlined, all depersonalised data (DPD) are highlighted in pink and underlined.

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Plain English Summary

Heart failure (HF) is a clinical syndrome caused by the impaired ability of the heart to cope with the metabolic needs of the body. This results in breathlessness, fatigue, and fluid retention. HF is often the result of several problems affecting the heart at the same time. Conditions that can lead to HF include coronary heart disease (when the arteries that supply blood to the heart become clogged up with fatty substances), high blood pressure, conditions affecting the heart muscle, heart rhythm problems, damage or other problems with the heart valves and congenital heart disease (birth defects that affect the normal workings of the heart). Sometimes anaemia, drinking too much alcohol, an overactive thyroid or high pressure in the lungs can lead to HF. HF is, in most cases, a progressive condition with a poor prognosis which has substantial effects on health-related quality of life.

Cardiac implantable electronic devices (CIEDs) are recommended as treatment options for specific people who have or are at high risk of HF. These devices include pacemakers, implantable cardiac defibrillators or cardiac resynchronization therapy devices. Monitoring is recommended for people who have CIEDs. Some CIEDs come with remote monitoring systems, which are capable of identifying new onset acute HF or worsening signs of HF using measurements captured by CIEDs. The CIED may send an alert, which will be seen by clinicians, which could help them to identify people who need a review. These remote monitoring systems are optional extras to the CIED that come with an additional cost. When used within a monitoring pathway alongside standard care, earlier identification of people at risk of HF could ensure earlier access to care. This could help to prevent symptoms occurring or worsening, reducing cardiac (heart-related) events, improving health outcomes and resulting in fewer hospitalisations. Remote monitoring could also reduce the number of unnecessary follow-up appointments or face-to-face reviews, freeing up NHS resources and patient travel, stress and anxiety for people with CIEDs.

The aim of this project is to review the clinical scientific evidence, and to assess the costs and benefits associated with the use of four remote monitoring systems (CorVue and Merlin.net Patient Care Network, HeartInsight and BIOTRONIK Home Monitoring, HeartLogic and LATITUDE NXT Heart Failure Management system, and TriageHF and CareLink remote monitoring (Triage HF Plus) that use predictive algorithms for identifying HF risk.

1. Decision Problem

1.1 Purpose of the decision to be made

Patients who have cardiac implantable electronic devices (CIEDs) due to heart failure or who are at risk of heart failure (HF) may have a remote monitoring system incorporated in the device. The remote monitoring system includes a predictive algorithm for heart failure. The system can send alerts and/or the stored data can be reviewed. There is an additional cost to access and utilise the remote monitoring system. The decision question is whether the algorithm-based remote monitoring of heart failure risk data in people with CIEDs represent a clinical and cost-effective use of NHS resources and should be recommended for use.

The purpose of this assessment is to investigate the predictive accuracy of the predictive algorithms and the clinical, health-related quality of life (HRQoL), cost and cost-effectiveness outcomes of remote monitoring systems that include the incorporated predictive algorithms for people with cardiac implantable electronic devices (CIEDs). The assessment will be conducted for four CIEDs with remote monitoring systems separately, comparing the outcomes for the individual CIEDs with and without the remote monitoring system: CorVue and Merlin.net Patient Care Network, HeartInsight and BIOTRONIK Home Monitoring, HeartLogic and LATITUDE NXT Heart Failure Management system, and TriageHF and CareLink remote monitoring (Triage HF Plus).

1.2 Place of technology

CIEDs are recommended as treatment options for specific people who have or are at high risk of HF. These devices include pacemakers, implantable cardiac defibrillators (ICDs) or cardiac resynchronization therapy (CRT) devices. Monitoring is recommended for people who have CIEDs. As a minimum, monitoring currently includes a clinical assessment, a review of medication, and renal function assessments. The frequency of the reviews varies according to the person's condition. Clinical experts highlighted that currently reviews are commonly triggered by worsening symptoms reported by the person with the CIED.

Remote monitoring systems capable of identifying new onset acute HF or worsening signs of HF (decompensation) using measurements captured by CIEDs could help clinicians identify people who need a review. When used within a monitoring pathway

alongside standard care, earlier identification of people at risk of new onset acute HF or worsening signs of HF (decompensation) could ensure earlier access to interventions. This could help to prevent symptoms occurring or worsening, reducing cardiac events, improving health outcomes and resulting in fewer hospitalisations. Remote monitoring could also reduce the number of unnecessary follow-up appointments or face-to-face reviews, freeing up NHS resources, and travel, stress and anxiety for people with CIEDs.

1.3 Interventions

This assessment will evaluate remote monitoring systems, consisting of data collection, heart failure predictive algorithms and the software and data management platforms to send, receive, store and present data and alerts for implanted cardiac devices. These remote monitoring systems are only compatible with specific devices manufactured by the same company. The CIED remotely monitors physiological parameters measured by an implanted cardiac device. The predictive algorithm determines whether an alert should be sent to healthcare professionals via the remote monitoring system software and data management platform when HF metrics worsen. All the technologies are intended for use within a single person with an implanted device, none are reprogrammable for use with another person. All require an internet connection to access their relevant data management platforms.

Every CIED has its own remote monitoring system with its own unique heart failure predictive algorithm for sending alerts. Monitoring patients utilising the remote monitoring system will be compared to monitoring patients without the remote monitoring system for each CIED. Remote monitoring systems will not be compared with each other as that would require either the effectiveness of the CIEDs to be the same or for the relative effectiveness of the CIEDs to also be reviewed. The CIEDs would also need to be considered for use in the same population.

Four CIEDs and their remote monitoring systems will be assessed. For each of these CIEDs, the CIED:

- is intended for use in people with an implanted cardiac device
- is available in the UK
- holds a CE-mark

- is therapeutic, not just monitoring

The identified technologies are summarised in Table 1.

1.3.1 HeartInsight and BIOTRONIK Home Monitoring

The BIOTRONIK Home Monitoring system (HMSC) and HeartInsight algorithm are intended for monitoring cardiac function in people who have implanted BIOTRONIK pacemakers, implantable cardiac defibrillators (ICDs) or cardiac resynchronization therapy (CRT) devices. It is indicated for heart failure patients with NYHA Class II or III. The HeartInsight algorithm is integrated within the HMSC and has a Class III CE-mark.

The system includes the handheld CardioMessenger device which transmits data from the implanted cardiac device to the BIOTRONIK HMSC via a mobile phone network. The system has an integrated HeartInsight algorithm to identify people with a higher risk of decompensation and predict HF hospitalisations.

The HeartInsight algorithm combines seven parameters into one composite score (calculated daily): atrial burden, heart rate variability, general activity, thoracic impedance, heart rate, heart rate at rest and premature ventricular contractions, with an optional additional baseline rate parameter. HeartInsight triggers an alert to healthcare professionals (via text message and/or email) once the threshold is exceeded for three consecutive values (days), indicating higher risk of worsening heart failure. The system is set to raise an alert to health professionals according to customised parameters and the reports use a traffic light system for prioritising alerts. Information collected by HeartInsight can be accessed and reviewed by healthcare professionals on the BIOTRONIK HMSC website platform.

Following an alert, the person is automatically sent a Heart Failure Screening Questionnaire (HFQ) via the BIOTRONIK Patient App to report any relevant behaviours and symptoms. The BIOTRONIK Patient App is an optional tool to use as an electronic symptom diary or self-monitoring device information. The app is free of charge and can be downloaded to the person's smartphone.

There are no known contraindications with its use; however, HeartInsight is not recommended in patients without a lead capable of atrial sensing, with a deactivated atrial lead or with permanent atrial fibrillation. It is also not recommended in patients with

insufficient mobile network coverage or the inability to use BIOTRONIK Home Monitoring.

1.3.2 HeartLogic and LATITUDE NXT Heart Failure Management system

The HeartLogic algorithm and LATITUDE NXT HF Management system (Boston Scientific) is intended for remote monitoring of HF in people who have compatible implanted devices. The HeartLogic algorithm is integrated within the implanted device and has a Class III implantable CE-mark.

It is intended to be used alongside in-person or remote clinical evaluations. The HeartLogic device has an integrated HeartLogic algorithm which automatically analyses measurements. In addition to the implanted device, the LATITUDE NXT HF Management system includes a wireless LATITUDE transmitter and optional weighing scales and a blood pressure monitor. The LATITUDE NXT system is further described in the NICE Medtech innovation briefing MIB67.[1] HeartLogic is currently in use in 13 NHS Trusts.

Measurements including heart sounds, thoracic impedance, respiration, heart rate and activity are collected by the implanted device, which the HeartLogic algorithm combines into 1 composite index that indicates decompensation. The data are transferred to the LATITUDE NXT patient management system via the LATITUDE transmitter. The system has daily data transfers to the clinical team. The transmitter can use a mobile phone connection or an internet connection to relay the data. The system is configured to send an alert to a health professional when the index is over a set threshold (customisable by the clinician). Health professionals need to log on to the LATITUDE NXT website to receive alerts. Secondary notification of alerts may be through email or text message.

1.3.3 TriageHF and CareLink remote monitoring (Triage HF Plus)

TriageHF Plus is a monitoring system for identifying and managing an increased risk of HF or worsening HF in people with CIEDs. The TriageHF algorithm is integrated within the implanted device and has Active Implantable Medical Devices (AIMD) classification.

TriageHF is an alert-based algorithm that is hosted on the Medtronic CareLink network platform for collaborative patient management between clinical teams. CareLink uses a plug-in monitor or a smartphone app for transmitting data. Using a mobile or landline connection, data are transmitted from the CIED to the CareLink network where it can be accessed by healthcare professionals. Data can be transmitted manually by patients if they perceive symptoms, automatically based on TriageHF algorithm alert triggers, or through a scheduled transmission based on a predefined date to replace a routine check. For each day the data is transmitted, the TriageHF algorithm generates a daily risk status of a heart failure event occurring in the next 30 days (low, medium or high risk) based on the maximum daily risk status for the previous 30 days. A heart failure management report is generated on the daily risk status.

TriageHF algorithm uses physiological parameters measured by the CIED (compatible Medtronic devices that monitor the OptiVol Fluid Status [thoracic impedance over time]) to create a hospitalisation risk score. The following parameters factor into the algorithm: atrial tachycardia (AT) or atrial fibrillation (AF) burden, ventricular rate during AT or AF, OptiVol fluid index (which tracks changes in thoracic impedance over time), general activity, night ventricular rate, heart rate variability, percent of ventricular pacing, treated ventricular tachycardia or ventricular fibrillation, and defibrillator shocks.

The CareLink network sends an alert for people who have high risk score so that they are contacted for a telephone consultation with a heart failure nurse. A set of standardised questions are used to distinguish between worsening heart failure and other issues. Healthcare professionals can also be notified of alerts via text messaging or email. The manual states that there are no known contraindications for the use of TriageHF Plus. The TriageHF Plus care pathway is currently in use in 12 NHS Trusts, of which over 80% already have the CareLink platform installed.

1.3.4 CorVue and Merlin.net patient care network

The CorVue algorithm and Merlin.net patient care network (PCN) platform are intended for the remote monitoring of early signs of heart failure in people who have compatible implanted devices. The CorVue algorithm is integrated with the implanted device and has Active Implantable Medical Devices (AIMD) classification.

The CorVue algorithm collects intrathoracic impedance (ITI) data from the implanted device and transmits to the Merlin.net PCN platform via the mobile app (myMerlinPulse) using Bluetooth technology and an internet or mobile network connection to generate an alert. Alternatively, a remote monitoring unit (Merlin@Home) connected via wifi, mobile or landline connection, can be provided by the company instead of using the app-based smartphone transmitter. Healthcare professionals can view the data transmitted by the algorithm and device on the Merlin.net PCN platform. Access to Merlin.net and the mobile transmitter is provided as part of the CIED, and the CorVue algorithm comes free of charge with the CIED devices.

The CorVue algorithm automatically calculates the mean daily impedance (from 12 measurements taken daily) and collects reference impedance data based on the previous 12-14 days which changes continuously based on new impedance readings. If a consistent drop of daily impedance values is detected (13 or 14 consecutive days in congestion) then a congestive event is reported and detected during device check-up. Patient alerts can be activated via remote monitoring if the person wishes. Any medical condition that causes ITI to decrease (for example, a chest infection) may create a false positive. CorVue is suitable for people who have a CIED and congestive heart failure with ventricular dyssynchrony.

Table 1: Product properties

Algorithm-based remote monitoring system	Manufacturer	Components	Compatible CIEDs
CorVue and Merlin.net Patient Care Network	Abbott Medical	• CorVue algorithm (integrated within CIED) • Transmitter mobile app (myMerlinPulse) or remote monitoring unit (Merlin@Home) if app-based smartphone transmitter not used • Management system (Merlin.net PCN platform)	Abbott devices: Gallant Single Chamber ICD, Gallant Dual Chamber ICD, Gallant HF, Quadra Allure MP CRT-P Pacemaker, Quadra Assura MP CRT-D, Ellipse Single, Chamber ICD, Ellipse Dual Chamber ICD, Fortify Assura Single Chamber ICD, Fortify Assura Dual Chamber ICD, Unify Assura CRT-D, Assurity Dual Chamber PPM, Assurity Single Chamber PPM
HeartInsight and BIOTRONIK	Biotronik	• Management system (BIOTRONIK Home Monitoring Service Centre)	BIOTRONIK heart devices: Acticor/Rivacor, Ilivia Neo/Intica Neo, Ilivia/Intica

Home Monitoring		• HeartInsight algorithm (integrated within management system) • Transmitter (CardioMessenger) • Optional BIOTRONIK mobile app	/Inlexa -5 and -7 series ICD DX/DC and CRT-D
HeartLogic and LATITUDE NXT Heart Failure Management system	Boston Scientific	• Transmitter (LATITUDE) • HeartLogic algorithm (integrated within the CIED) • LATITUDE NXT Patient Management system • Optional MyLATITUDE mobile app	Boston Scientific devices: Perciva, Momentum EL, Resonate EL, Vigilant EL, and CRT-Ds: Resonate X4, Vigilant X4, Momentum X4 and Momentum
TriageHF and CareLink remote monitoring (TriageHF Plus)	Medtronic	• TriageHF risk algorithm (integrated within CIED) • CareLink monitoring platform • Optional MyCareLink heart mobile app	Medtronic CIEDs with OptiVol measurement capability

1.4 Population and relevant subgroups

1. This research will be conducted for two populations. Each of these have subgroups. These are as follows: People who have a CIED and do not have a diagnosis of chronic heart failure but are at high risk of new onset acute heart failure

   If data allow, analyses on the following subgroups will be included. People who:

   a) have a CRT-P device

   b) have a CRT-D device

   c) have an ICD device

   d) have a pacemaker device

2. People who have a CIED and have a diagnosis of chronic heart failure

If data allow, analyses on the following subgroups will be included. People who:

a) have a CRT-P device
b) have a CRT-D device
c) have an ICD device
d) have a pacemaker device
e) have a diagnosis of heart failure New York Heart Association (NYHA) class I and II, or III and IV (at study recruitment)

f) have a prior heart failure hospitalisation or urgent care visit within the last 12-months

1.5 Place of intervention in the treatment pathway

1.5.1 Heart failure

HF 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 HF are breathlessness, fatigue, and oedema. Conditions that can cause HF 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 coexist, and they can cause or exacerbate each other.[2]

HF may present as acute or chronic, depending on whether a person has an established diagnosis of HF and speed of symptom onset. People with chronic HF may experience sudden deterioration in heart function and worsening of symptoms, which is known as acute decompensated HF.

The British Heart Foundation website[3] explains that HF 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), HF may be classed as the following:[3]

- HFpEF - HF with preserved ejection fraction (>50%)
- HFmrEF - HF with mildly reduced ejection fraction (40% - 49%)
- HFmrEF – HF with reduced ejection fraction (<40%)

HF may also be grouped by symptom severity and limitation of physical activity according to the New York Heart Association (NYHA) functional classification of HF, 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).

HF 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 HF, which increases to 1 in 15 of people aged 75–84 years, and to just over 1 in 7 people those aged above 85 years.[4]

Around 920,000 people in the UK were living with HF in 2018 with an estimated 200,000 new diagnoses each year.[5] The incidence of HF in the UK is 140 per 100,000 men and 120 per 100,000 women.[6] The prevalence of HF is increasing over time because of population ageing and a rise in the prevalence of associated comorbidities.

HF has a poor prognosis - estimates of 1-year mortality vary, but a long-term registry of people with HF found a mortality rate of 23.6% for people with acute HF and 6.4% for those with chronic HF across Europe.[7] A UK-based population study conducted between 2000 and 2017 found that patients diagnosed with HF had a 1 year survival rate of 75.9%, 5-year survival of 45.5% and 10-year survival of 24.5%.

HF accounts for a total of 1 million inpatient bed days – 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 HF in 2021/22 compared with 86,474 in 2018/19.[8, 9]

This is at significant cost to the NHS – a 2016 All Party Parliamentary Group (APPG) report on HF found that the condition costs the NHS around £2 billion per year, or approximately 2% of the total NHS budget.[10]

1.5.2 Current methods of assessing and monitoring of heart failure symptoms

The NICE guidelines for diagnosis and management of chronic HF in adults recommend that monitoring of people with chronic HF should include a clinical assessment of functional capacity, fluid status, cardiac rhythm (minimum of examining the pulse), cognitive status and nutritional status, a review of medication, and an assessment of renal function.[4] The European Society of Cardiology (ESC) guidelines for the diagnosis and treatment of acute and chronic HF add that HF management may involve in-person service models or home-based telemonitoring, and that the COVID-19 pandemic has highlighted some of the potential advantages of the latter.[2] While care is usually followed up by HF clinics, suitable patients may be followed up by community HF nurses or a GP

with a special interest in HF - a clinical expert commented that there is no standard HF service model.

People should have additional monitoring if they have comorbidities, 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. Reviews are offered every 6 months for people whose condition is stable. Early follow up visits are recommended at 1-2 weeks following hospital discharge to assess signs of congestion and drug tolerance. Levels of NT-proBNP (N-terminal pro-B-type natriuretic peptide) may be monitored as a surrogate biomarker for HF in people under 75 who have HF with reduced ejection fraction and an estimated glomerular filtration rate above 60 ml per minute per 1.73 m^2.

Clinical experts highlighted that in practice a combination of the ESC guidelines and the NICE guidelines are followed in the NHS. The ESC guidelines for the diagnosis and treatment of acute and chronic HF recommend that an ECG should be done annually to detect prolonged QRS duration, so that conduction disturbances and atrial fibrillation may be recognised and to identify people with prolonged QRS duration who may become candidates for cardiac resynchronisation therapy.[2] Repeat ECGs are also advised if there has been a deterioration in clinical status, and 36 months after optimisation of standard therapies for HFrEF.

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

Pressure sensors placed in the pulmonary artery that work in combination with an external monitor may also be used to wirelessly monitor symptoms of HF. NICE's interventional procedures guidance states that the evidence on efficacy and safety of percutaneous implantation of pulmonary artery pressure sensors for monitoring treatment of chronic HF is sufficient to support standard arrangements for use.[11]

Implantable loop recorders which are placed under the skin are capable of continuous monitoring of heart rate and rhythm and last around three years, with data checked at regular intervals by a clinician. A clinical expert commented that most newer devices

allow for remote monitoring, but older devices may require the patient to attend an in-person appointment so that data collected from the device may be downloaded. The British Heart Rhythm Society's clinical standards and guidelines for the follow up of cardiac implantable electronic devices (CIEDs) for cardiac rhythm management states that most modern implantable pulse generators are also equipped with algorithms that provide reliable pacing threshold management.[12]

1.5.3 Follow up of people with CIEDs

Clinical experts explained that people at risk of HF or worsening HF who have a CIED are usually managed in multiple clinics. For example, a HF clinic manages the medication review, and a cardiac physiologist led clinic manages the follow up of the CIED. The extent to which these services overlap varies between centres.

The British Heart Rhythm Society's (BHRS) clinical standards and guidelines for the follow up of cardiac implantable electronic devices (CIEDs) for cardiac rhythm management state that managing HF is a multidisciplinary process and recommends that monitoring includes a regular technical review of device function, monitoring of symptoms, and management of new and changing conditions. The guidelines also state that clear local protocols should be in place for suspected worsening HF.[12]

The BHRS standards also state that alert-based remote follow up should be considered as standard care for CIED patients, including those with pacemakers, and annual in-person follow up is not mandated for all CIED patients. However, device follow up may also include in person evaluation and can differ according to clinic policies, the capabilities and maintenance needs of the CIED, and patient needs or preferences.

1.5.4 Current treatments for chronic heart failure

NICE guidelines for diagnosis and management of chronic HF in adults recommend the use of pharmacological treatments including routine use of diuretic therapy, which should be started using a bolus or infusion strategy.

In cases where people have potentially reversible cardiogenic shock, inotropes or vasopressors may also be recommended if given in a cardiac care unit or high dependency unit or an alternative setting where at least level 2 care can be provided.

People with acute onset heart failure may also require ventilation. If a person has cardiogenic pulmonary oedema with severe dyspnoea and acidaemia consider starting non-invasive ventilation without delay, while invasive ventilation may be appropriate where heart failure is leading to or is complicated by either respiratory failure or reduced consciousness or physical exhaustion.

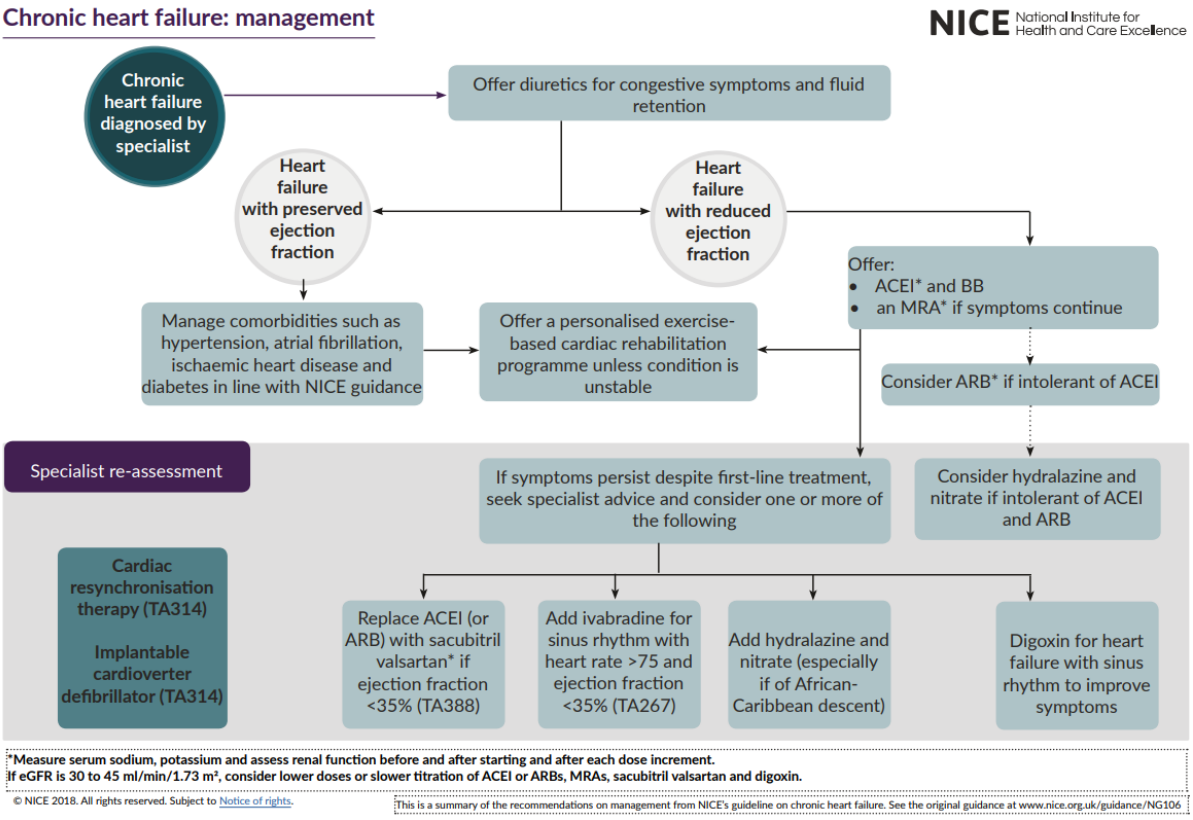

Figure 1: NICE guidelines on chronic heart failure management[4]

In the case of HF with reduced ejection fraction, the NICE guidelines for diagnosis and management of chronic HF in adults recommend that an angiotensin-converting enzyme (ACE) inhibitor, or angiotensin II receptor blockers (ARBs) licensed for HF if the person is intolerant to ACE inhibitors, should be offered as a first line treatment in combination with a beta-blocker licensed for HF.[4] If people are continuing to experience symptoms, mineralocorticoid receptor antagonists (MRAs) may be used in addition to first line therapies. The ESC guidelines also recommend the use of sodium-glucose cotransporter-2 (SGLT2) inhibitors as a first line therapy in people with reduced ejection fraction.[4] The NICE technology appraisal guidance on Dapagliflozin for treating chronic heart failure

with reduced ejection fraction also supports the use of an SGLT2 inhibitor in these people,[13] 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 ESC guidelines 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.[2]

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

- Severe HF (NYHA class IV)
- HF that does not respond to treatment in primary care or can no longer be managed in the home setting
- HF 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 HF with reduced ejection fraction may include ivabradine, sacubitril valsartan, hydralazine in combination with nitrate and digoxin.

In people with both reduced ejection fraction and chronic kidney disease, lower doses of pharmacological treatments being offered should be considered. Specialist referral for transplantation should be considered for HF 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.

1.5.5 Treatment for acute heart failure

Acute HF can present as acute decompensation of chronic HF in addition to new-onset HF in people without known cardiac dysfunction. The NICE guidelines for diagnosis and management of acute HF in adults recommend that people requiring immediate treatment for acute HF should be offered intravenous diuretic therapy, which should be started using a bolus or infusion strategy.[14]

In cases where people have potentially reversible cardiogenic shock, inotropes or vasopressors may also be recommended if given in a cardiac care unit or high dependency unit or an alternative setting where at least level 2 care can be provided.

People with acute onset HF may also require ventilation. If a person has cardiogenic pulmonary oedema with severe dyspnoea and acidaemia consider starting non-invasive ventilation without delay, while invasive ventilation may be appropriate where HF is leading to or is complicated by either respiratory failure or reduced consciousness or physical exhaustion.

1.5.6 Devices and surgical procedures 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 HF who have left ventricular dysfunction with a left ventricular ejection fraction (LVEF) of 35% or less depending on NYHA functional classification, QRS duration and presence of left bundle branch block (LBBB) (see Table 2).[6]

Table 2: Recommended cardiac implantable electronic devices for people with different symptoms and QRS intervals where LVEF is 35% or less

	NYHA classification of symptoms			
QRS interval	**I**	**II**	**III**	**IV**
<120 milliseconds	**ICD if there is a high risk of sudden cardiac death**			**ICD and CRT not clinically indicated**
120–149 milliseconds without LBBB	ICD	ICD	ICD	CRT-P
120–149 milliseconds with LBBB	ICD	CRT-D	CRT-P or CRT-D	CRT-P
≥150 milliseconds with or without LBBB	CRT-D	CRT-D	CRT-P or CRT-D	CRT-P

NYHA: New York heart association, ICD: Implantable cardiac device, CRT-P: Cardiac resynchronisation therapy with pacing, CRT-D: Cardiac resynchronisation therapy with defibrillation, LBBB: Left bundle branch block

1.6 Patient issues and preferences

HF 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.

Experts highlighted that some technologies in the assessment could produce false-positive alerts, and this could lead to unnecessary contact with healthcare specialists, leading to increased patient anxiety. Alternatively, remote monitoring could reduce anxiety because people with CIEDs know that their condition is being closely monitored. This could provide reassurance when an individual's condition is stable and early warning signs when their condition worsens enabling them to modify lifestyle behaviours.

Objective monitoring of physiological metrics could help people who are unable to advocate for themselves, for example people with cognitive impairment who are less

likely to recognise or describe their symptoms. Clinicians highlighted that the technologies could also help monitor the condition of people who are less likely to engage with the healthcare system.

Patient experts explained that having access to objective monitoring of data could also give people with CIEDs or their carers the confidence to request a clinical review appointment, especially if there are communication barriers.

Remote monitoring systems could predict the signs, symptoms and behaviours associated with worsening HF. This may enable earlier and more appropriate intervention potentially reducing hospital admissions and improving outcomes and quality of life. In addition, avoiding hospital admissions could reduce hospital acquired infections. Remote monitoring could reduce the number of face-to-face appointments and the potential stress and travel costs associated with these appointments.

1.7 Relevant comparators

The current standard of care for monitoring HF risk for people who have CIEDs is periodic reviews of device function with a cardiac physiologist or cardiologist, and ad-hoc reviews of symptoms with a GP, specialist nurse, cardiologist or a heart failure team . Clinicians explained that reviews can be over the telephone or in-person, and that they are most commonly triggered by self-reporting of symptoms from the person with the CIED. The number and timing of the reviews varies in practice depending on patient symptoms. Clinical experts explained that reviews can be over the telephone or in-person, and that they are most commonly triggered by self-reporting of worsening symptoms from the person with the CIED. The organisation of heart failure monitoring pathways varies in practice between different trusts, and even between different hospitals.

1.8 Key outcomes to be addressed

Four key types of outcomes will be considered (for further detail, see Table 3). Firstly, intermediate measures of prognostic accuracy and usage of the equipment. Secondly, clinical outcomes concerned with mortality and morbidity (including adverse events from treatments). Thirdly, patient-reported outcomes, such as health-related quality of life, and finally, cost-effectiveness of the intervention.

1.9 Objectives

The aim of the project is to determine the clinical and cost-effectiveness of remote monitoring devices for identifying new onset acute HF or worsening signs of HF in people with CIEDs, in particular, of the four technologies described in Section 1.3. To achieve this, the following objectives are proposed:

Clinical effectiveness

- To perform a systematic review, narrative synthesis and, if feasible, a meta-analysis of the prognostic accuracy of the four remote monitoring systems
- To perform a systematic review, narrative synthesis and, if feasible, a meta-analysis of the clinical impact, such as morbidity and mortality, of the remote monitoring systems
- To perform a systematic review and narrative synthesis of patient and physician opinions on the value and ease-of-use of the remote monitoring systems

Cost effectiveness

- To conduct a systematic review of existing economic evaluation studies of the remote monitoring systems for identifying new onset acute HF or worsening signs of HF in people with CIEDs.
- To develop an in-house decision model to estimate the cost-effectiveness of remote monitoring systems for identifying new onset acute HF or worsening signs of HF in people with CIEDs.

2. Methods for synthesising evidence of clinical effectiveness

2.1 Search strategy

Search strategies will be undertaken to identify studies evaluating remote monitoring systems for implanted cardiac devices (described in Table 1), as recommended in the Centre for Reviews and Dissemination (CRD)[15] guidance for undertaking reviews in health care and the latest Cochrane Handbook for Diagnostic Test Accuracy Reviews.[16]

Candidate search terms will be identified from target references, browsing database thesauri (e.g. MEDLINE MeSH and Embase EMTREE), and existing reviews identified

during the initial scoping searches. Strategy development will involve an iterative approach, testing candidate text and indexing terms across a sample of bibliographic databases, aiming to reach a satisfactory balance of sensitivity and specificity. Search strategies will be developed specifically for each database and the keywords and thesaurus terms will be adapted according to the configuration of each database.

The following databases will be searched for relevant studies:

- MEDLINE (Ovid)
- MEDLINE In-Process Citations (Ovid)
- MEDLINE Daily Update (Ovid)
- MEDLINE Epub Ahead of Print (Ovid)
- EMBASE (Ovid)
- CINAHL (Cumulative Index to Nursing and Allied Health Literature) (EBSCO)
- PROSPERO (International Prospective Register of Systematic Reviews) (Internet) (http://www.crd.york.ac.uk/prospero/)
- International Platform of Registered Systematic Review and Meta-analysis Protocols (Internet) (Home - INPLASY)
- Cochrane Database of Systematic Reviews (CDSR) (Wiley)
- Cochrane Central Database of Controlled Trials (CENTRAL) (Wiley)
- Database of Abstract of Reviews of Effects (DARE) (CRD)
- International HTA database (INAHTA) Publication (Internet) (https://www.inahta.org/hta-database/)
- NIHR Health Technology Assessment Programme (Internet) (https://www.nihr.ac.uk/)

Completed and ongoing trials will be identified by searches of the following resources:

- NIH ClinicalTrials.gov (Internet) (http://www.clinicaltrials.gov/)
- EU Clinical Trials Register (Internet) (https://www.clinicaltrialsregister.eu/ctr-search/search)
- WHO International Clinical Trials Registry Platform (ICTRP) (Internet) (http://www.who.int/ictrp/en/)
- ScanMedicine (Internet) (https://scanmedicine.com/)

To identify conference proceedings, searches in Embase will not be restricted to exclude conference abstracts. Key conference proceedings, not indexed in Embase and identified in consultation with clinical experts will also be screened for the last five years.

An additional search of the medRxiv PrePrint server will be undertaken. All results retrieved from this resource will be treated with due caution as these are preliminary reports of work that have not been certified by peer review.

- MedRxiv (Internet) (https://www.medrxiv.org)

No restrictions on language, publication status or date will be applied. Searches will include generic and other product names for the intervention.

The main MEDLINE (Ovid) strategy (included in Appendix 1) will be independently peer reviewed by a second Information Specialist based on the CADTH Peer Review checklist.[17]

References in retrieved articles will be checked for additional studies to identify any additional relevant papers not retrieved by the searches and clinical experts will be consulted to identify ongoing or un-published studies. Forwards and backwards citation chaining will be conducted on all included studies. In addition, we will review company submissions for relevant articles.

2.2 Study selection

Two reviewers will independently screen all titles and abstracts. Full papers of any records that may be relevant will be obtained where possible and independently screened by two reviewers according to the inclusion criteria listed below. Any disagreements will be resolved through discussion and, where necessary, consultation with a third reviewer.

2.3 Inclusion criteria

Population

People who have one of the CIEDs listed in Table 1 and do not have a diagnosis of chronic HF but are at high risk of new onset acute HF; and people who have a CIED and have a diagnosis of chronic HF.

Interventions

Algorithm-based remote monitoring systems for heart failure risk data in people with CIEDs (including Implantable cardioverter defibrillators [ICD] and Cardiac Resynchronization Therapy [CRT] devices):

- CorVue and Merlin.net patient care network (Abbott Medical)
- HeartInsight and BIOTRONIK home monitoring system (Biotronik)
- HeartLogic and Latitude NXT heart failure management system (Boston Scientific)
- TriageHF and CareLink remote monitoring (Triage HF Plus; Medtronic)

Comparators

The comparator is standard care. The current standard of care for monitoring heart failure for people who have CIEDs is without use of remote monitoring. It includes periodic reviews of device function with a cardiac physiologist or cardiologist, and ad-hoc reviews of symptoms with a GP, specialist nurse, cardiologist or a heart failure team. The number and timing of the reviews varies depending on patient symptoms. The organisation of heart failure monitoring pathways varies in practice between different trusts, and even between different hospitals. For prognostic accuracy studies a reference standard will be implemented. This may vary between the studies and the definition of the reference standard will be extracted from the individual included studies.

Outcomes

See Table 3 for the full list of intended outcomes.

Healthcare setting

Secondary care

Study designs

We will consider all study designs that provide relevant outcome data as listed in Table 3.

2.4 Data Extraction

Data will be extracted by one reviewer using a standardised data extraction form, and independently checked for accuracy by a second reviewer. Information extracted will include details of the study's design and methodology, intervention and comparator or reference standard (for prognostic accuracy studies) details, baseline characteristics of participants, and outcome measures, including clinical outcome efficacy and any adverse events. Where there is incomplete information, if time allows, attempts will be made to contact authors with a request for further details. Discrepancies will be resolved by discussion, with involvement of a third reviewer if necessary.

2.5 Quality assessment

The quality of prognostic test accuracy studies will be assessed using the PROBAST (Prediction model Risk Of Bias Assessment Tool) tool.[18, 19] The quality of clinical effectiveness studies will be assessed based on their study design: randomised controlled trials will be assessed using Cochrane risk of bias tool (Rob);[20] non-randomised studies will be assessed using the Risk Of Bias In Non-randomized Studies-of Interventions (ROBINS-I) tool;[21] All quality appraisal assessments will be carried out by one reviewer and verified by another independently, with disagreements resolved by discussion or the involvement of a third reviewer, if necessary.

2.6 Methods of analysis/synthesis

Details of results on clinical effectiveness and quality assessment for each included study will be presented in structured tables and as a narrative summary. Should clinically and methodologically homogenous studies be identified for each individual technology, data will be synthesised using appropriate meta-analytic techniques. Clinical, methodological and statistical heterogeneity will be investigated. For test accuracy data, absolute numbers of true positive, false negative, false positive and true negative test results, as well as sensitivity and specificity values, with 95% confidence intervals will be presented for each study. Other measures of test accuracy data will be presented if reported. If the data allow, we will also undertake the following sensitivity analyses: by study design (of randomised controlled trials and observational studies) and by removing high risk of bias studies.

Table 3: Outcomes of interest

Outcome type	Outcome assessed
Intermediate outcomes	• Prognostic accuracy (including the number of false positive alerts) • Changes to clinical management (including non-pharmacological treatment and medications) • Time between an alert and a heart failure event • Alert response rates (including time between an alert, clinical review and change in clinical management) • Number of heart failure and all cause hospitalisations • Number of emergency or urgent care visits • Length of hospital stay • Software failure rate (including failed data transmissions) • Number of monitoring reviews (remote and face-to-face)
Clinical outcomes	• Rate of heart failure events • Rate and category of atrial fibrillation (subclinical, paroxysmal or persistent/permanent) • Morbidity (including adverse events from treatments) • Changes in NYHA classification of symptoms • Mortality (cardiac and all-cause mortality)
Patient reported outcomes	• Health-related quality of life

	• Patient reported outcome measures such as satisfaction, anxiety and stress • Patient adherence to treatment (as agreed between the prescriber and the person taking the medication)

3. Methods for synthesising evidence of cost effectiveness

The economics-related objectives are:

- To conduct a systematic review of existing economic evaluation studies of remote monitoring systems identifying new onset acute HF or worsening signs of HF in people with CIEDs. The systematic reviews of published existing economic evaluations studies (if any) will be used to inform the conceptualisation and development of a de novo economic model.

- To develop an in-house decision model to assess the cost-effectiveness of remote monitoring systems in identifying new onset acute HF or worsening signs of HF in people with CIEDs listed in Table 1 versus standard follow-up care without these remote monitoring systems. The model will provide estimates of the incremental cost per quality adjusted life years (QALY) gained of remote monitoring systems plus current standard follow-up care compared with standard follow-up care alone.

3.1 Identifying and systematically reviewing economic evaluation studies

The External Assessment Group (EAG) will conduct a systematic review to identify economic evaluations of remote monitoring systems for identifying new onset acute HF or worsening signs of HF in people with CIEDs. The aim of the systematic review is to help design the de novo economic model structure. Studies included in the systematic review may also inform resources to cost in the model and sources of evidence for parameters other than effectiveness evidence.

The search strategies will combine terms capturing the interventions (remote monitoring systems) or current clinical pathway and the target population (people fitted with CIEDs: and at risk of new onset acute HF or with chronic HF). A validated search filter designed to identify full economic evaluations (e.g., cost-minimisation, cost-effectiveness, cost-consequence, cost-utility, and cost-benefit analyses) will be applied to search strategies in non-economic electronic databases (e.g., MEDLINE, Embase and Cochrane Library). No restrictions on language, setting, geographical location, publication status or date will be applied to the search strategy.

In addition, the EAG will contact clinical experts in the field for details of published and unpublished studies (grey literature) which they may be aware of. Furthermore, references in

retrieved articles and company submissions will be searched for any additional relevant references not retrieved by the searches.

The main MEDLINE (Ovid) strategy will be independently peer reviewed by a second Information Specialist based on the CADTH Peer Review checklist.[17] The following databases will be searched to find relevant studies:

- MEDLINE (OVID), MEDLINE In-Process Citations (Ovid), MEDLINE Daily Update (Ovid) and MEDLINE Epub Ahead of Print (Ovid)
- Embase (OVID)
- NHS Economic Evaluation (NHSEED) (Centre for Review and Dissemination, CRD)
- Database of Abstract of Reviews of Effects (DARE) (CRD)
- Cochrane databases of systematic reviews (CDSR) (Wiley)
- Cochrane Central Database of Controlled Trials (CENTRAL) (Wiley)
- CEA Registry (Internet) (http://www.cearegistry.org)
- Research Papers in Economics (RePEc) (Internet) (http://repec.org/)
- CRD Health Technology Assessment Database (HTAD) (Internet) (https://www.crd.york.ac.uk/CRDWeb/)
- International HTA database (INAHTA) Publication (Internet) (https://www.inahta.org/hta-database/)
- NIHR Health Technology Assessment Programme (Internet) (https://www.nihr.ac.uk/)

The EAG will produce and utilise standardised forms to conduct data extraction from included studies. The data will be extracted by one reviewer from each study and then checked by a second reviewer. In case of any discrepancy, a third reviewer will be asked to check the findings. Main findings from the studies identified from the SLR will be presented and discussed with a narrative synthesis and structured tables. Specifically, information will be extracted on the interventions and comparators, study population and setting, main analytic approaches (e.g. patient-level data analysis/ decision-analytic modelling), primary/secondary outcome specified for the economic analysis, details of adjustment (e.g., mapping) for quality of life, direct costs and indirect costs, estimates of incremental cost-effectiveness and approaches to quantifying decision uncertainty (e.g. deterministic/probabilistic sensitivity analysis). In term of outcomes, the EAG will include all

possible intermediate outcomes (e.g. cost per HF hospitalisations prevented), clinical outcomes (e.g cost per cardiovascular deaths avoided, cost per HF events avoided) and patient health related quality of life (HRQoL) outcomes (e.g., incremental cost per Quality adjusted Life year (QALYs) gained). The EAG will also use the consolidated health economic evaluation reporting standards (CHEERS) checklist for quality assessment of full economic evaluation methodology of retrieved studies.[22]

Any variation of the results from the systematic review of economic evaluations and their applicability to the NICE scope will be narratively discussed.

3.2 Identifying additional literature

Separate focused literature searches on utility, costs and resource utilisation will be conducted. The search strategy will combine terms capturing the interventions (remote monitoring systems) or current clinical pathway and the target population (people fitted with CIEDs; and at risk of new onset acute HF or with chronic HF). A validated filter (e.g. NICE filter for health economic and quality of life searches,[23] Cochrane filter for cost-of-illness studies[24] will be applied to search strategies in electronic databases (e.g. Medline, Embase and Cochrane library) to capture any study designs reporting cost-effectiveness, cost and quality of life and health state utility values (HSUVs). In addition to the databases listed in section 3.1, ScHARRHUD[25] will also be searched to find relevant studies. No restrictions on language, setting, geographical location, publication status or date will be applied to the search strategy. References from retrieved articles and company submissions will be searched for any additional studies not identified by database searching.

The EAG will produce and utilise standard forms to conduct data extraction from included studies. The data will be extracted by one reviewer from each study and then checked by a second reviewer. The extracted utility, resource utilisation and cost data will be summarised in structured tables.

3.3 Development of a health economic model

Following the completion of the systematic review of economic evaluations, the EAG will develop a de novo economic model in an appropriate software package (e.g., Microsoft® Excel or R package). The model will assess the cost-effectiveness of remote monitoring systems in identifying new onset acute HF or worsening signs of HF in people with CIEDs and will provide a comparison with standard follow-up care without remote monitoring systems in the NHS.

The model will be developed according to standard modelling guidelines.[26, 27] The face validity of the economic model will be checked by clinical and patient experts by reviewing its structure and whether the model incorporates all the significant outcomes affected by the technology. The model structure will be reviewed by our clinical and methodological experts for appropriateness to the current NHS clinical and diagnostic pathways. The internal validity will be checked using built-in internal validity checks and by varying dummy parameter values. The literature will be searched for estimates of hospitalisation and mortality rates and the model predicted outcomes will be assessed using these and clinical expert opinion.

Model parameters (e.g., outcome probabilities, utilities, cost data) will be populated from the results of the systematic review of effectiveness (section 2) and focused literature searches (section 3.2). Estimates of resource utilisation will be combined with unit costs from NHS reference costs,[28] Personal Social Services Research Unit[PSSRU],[29, 30] the British National Formulary (BNF),[31] and other relevant publications of UK health care costs as appropriate. The EAG will also utilise the cost of remote monitoring system supplied by the device manufacturers wherever appropriate to do so. Wherever needed, costs will be inflated to price year 2023/2024.

The EAG will elicit expert opinion if published data are not available to inform any model parameters.

3.3.1 General structure of the model

The decision-analytic model will be designed to reflect the potential health and economic benefits of introducing remote monitoring systems into current practice for identifying new onset acute HF or worsening signs of HF in people with CIEDs. The model will be developed to compare the remote monitoring system plus standard follow-up (intervention) with standard follow-up alone (comparator) for each of the CIEDs:

- CorVue and Merlin.net patient care network (Abbott Medical)
- HeartInsight and BIOTRONIK home monitoring system (Biotronik)
- HeartLogic and Latitude NXT heart failure management system (Boston Scientific)
- TriageHF and CareLink remote monitoring (Triage HF Plus; Medtronic)

Each CIED has their own specific remote monitoring system. For each CIED, the CIED plus the remote monitoring system will be compared to the CIED alone.

The model structure will take into consideration the designs of any economic models of remote monitoring systems for identifying new onset acute HF or worsening signs of HF in people with CIEDs identified in the systematic review and the characteristics of the outcome evidence identified in the literature. The model structure will be reviewed by clinical experts.

It is expected that RCT and observational evidence on key cost and clinical outcomes will be available. Therefore, it is anticipated that a Markov cohort model will be an appropriate design to capture the costs and benefits associated with remote monitoring systems. A Markov model with 2 states (Alive and Dead), as shown in Figure 2, where hospitalisation rates and clinic visit rates (and their associated costs and HRQoL effects) are modelled each cycle may be sufficient. An appropriate cycle length that accounts for hospitalisations and clinic visits will be used. A hypothetical cohort of people with one of the CIEDs can either transition from "Alive" to "Dead" (absorbing state) or continue to remain in the "Alive" state. Whether disease severity should be incorporated in the model will be considered during the review of the published economic evaluations and discussion with clinical experts.

The outcomes in a clinical study will be associated with the monitoring and treatment protocol followed in the clinical study centres. These monitoring and treatment protocols will be costed where possible. While it will not be possible to adjust the outcomes accordingly, the cost of any recommended pathway that individuals will follow in the UK NHS will be incorporated in scenario analysis. The generalisability of patient follow-up in the control cohorts of clinical study evidence will be assessed.

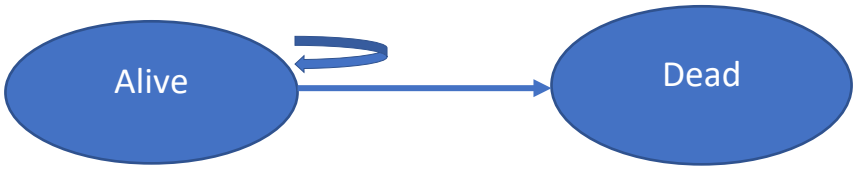

Figure 2: Markov model

3.4 Evaluation of costs, QALYs and cost-effectiveness

The resource utilisation and costs associated with the care pathway of identifying new onset acute HF or worsening signs of HF in people with CIEDs with and without the remote monitoring systems, are expected to include costs of clinical management of HF events

(including treatment costs and healthcare utilisation e.g. review appointments (routine or additional), costs of hospitalisation, further tests and any treatment related adverse events). The care pathway with a remote monitoring system will also include the cost associated with the use of the remote monitoring system (e.g. acquisition, operational costs, system alerts and data review).

The cost-utility of the remote monitoring systems in identifying new onset acute HF or worsening signs of HF in people with CIEDs compared to standard practice (without these remote monitoring systems) will be estimated. Intervention costs, follow-up visit costs, hospitalisations, mortality outcomes will be summarised. The analysis will be run and results will be reported for each population (at risk of new onset acute HF and with chronic HF) and for each CIED (listed in Table 1).

The economic assessment will be undertaken from the perspective of UK NHS and Personal Social Services (PSS). The model time horizon will be set to patient lifetime and both costs and benefits will be discounted at 3.5% per annum.

Assuming appropriate preference-based utility values are identified, the output of the economic model will be incremental cost per quality-adjusted life year (ICER) gained using QALYs as the measure of effectiveness. Scenario analyses, where feasible, will be conducted using the sub-groups listed in Section 1.4. Various sensitivity analyses will be conducted to test the robustness of the model to changes in parameter assumptions and potentially also to alternative data sources. To assess the overall uncertainty in the model estimates, both deterministic sensitivity analysis (DSA) and probabilistic sensitivity analysis (PSA) will be conducted by sampling from appropriate probability distributions for the parameters in the model for which this is feasible. The impact of uncertainty in the model parameters will be presented as a cost-effectiveness acceptability curve (CEAC) and tornado diagram. Key drivers of the cost-effectiveness results will be identified and described.

4. Handling information from the companies

The EAG will consider any data or evidence supplied by the companies involved. If the data meet the inclusion criteria for the review they will be extracted, quality assessed and synthesised in accordance with the procedures outlined in this protocol. It may not be possible to include data received later than 27 October 2023.

All commercial-in-confidence (CIC) data will be highlighted in blue and underlined, all academic in-confidence (AIC) data will be highlighted in yellow and underlined, all depersonalised data (DPD) will be highlighted in pink and underlined.

Confidential data will be stored securely and will only be accessible to members of the project team. 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.

5. Competing interests of authors

None of the authors have any conflicts of interest.

6. Timetable/Milestones

Milestone	Date to be completed
Submission of the final protocol	5th June 2023
Submission of progress report	1st September 2023
Submission of draft Diagnostic Assessment Report	27th October 2023
Submission of final Diagnostic Assessment Report	24th November 2023

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Appendix 1: Medline search strategy

Database(s): **Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions** 1946 to May 31, 2023
Search Strategy:

#	Searches	Results
1	(TriageHF* or CareLink Network* or MyCareLink* or "00763000351656").ti,ab,kw,kf.	16
2	(Latitude* NXT or Mylatitute* or HeartLogic* or "00802526562105" or "00802526573408" or "00802526584107" or "00802526590306" or "00802526592102" or "00802526613876").ti,ab,kf,kw.	42
3	(biotronik home monitor* or CardioMessenger* or HeartInsight* or "04035479139360" or "04035479159115" or "04035479177768").ti,ab,kw,kf.	20
4	(CorVue* or mymerlinimpact or "merlin@home").ti,ab,kw,kf.	6
5	or/1-4	83
6	Optivol.ti,ab,kw,kf.	57
7	viva.ti,ab,kw,kf.	849
8	acticor.ti,ab,kw,kf.	0
9	rivacor.ti,ab,kw,kf.	0
10	ilivia.ti,ab,kw,kf.	0
11	intica.ti,ab,kw,kf.	0
12	inlexa.ti,ab,kw,kf.	0
13	resonate.ti,ab,kw,kf.	1357
14	vigilant.ti,ab,kw,kf.	6917
15	momentum.ti,ab,kw,kf.	24408
16	perciva.ti,ab,kw,kf.	0
17	gallant.ti,ab,kw,kf.	82
18	quadra.ti,ab,kw,kf.	148
19	ellipse.ti,ab,kw,kf.	3111
20	assura.ti,ab,kw,kf.	19
21	assurity.ti,ab,kw,kf.	7
22	(biotronik or medtronic or "boston scientific" or abbott or "merlin.net").ab,in,go,ci.	47802
23	or/6-22	84497
24	(remote monitoring and heart failure).ti,ab,kw,kf.	594
25	23 and 24	106
26	5 or 25	171