NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology guidance

SCOPE

Zio Service for detecting cardiac arrhythmias

1 Technology

1.1 Description of the technology

Zio ECG monitoring service (Zio Service, iRhythm Technologies) is a remote cardiac monitoring system used to detect cardiac arrhythmias. It is comprised of 3 components:

- Zio biosensor: a wearable single lead ambulatory electrocardiogram (ECG)
- ZEUS: a proprietary, regulated software platform and online portal that stores, analyses and sorts the ECG data to generate a report of the findings
- Zio technical report: a clinically actionable summary of the recorded ECG data

The Zio Service is intended to replace or enhance the current assessment pathway for cardiac arrhythmia detection in people with palpitations, fainting (syncope) and suspected cardiac arrhythmia. The adhesive Zio biosensor is placed on the person's left upper chest and records a continuous beat-to-beat ECG for up to 14 days. The device is designed to facilitate patient compliance and thereby improve data collection. Without external leads or wires, noise artefacts are reduced in the data and the wearer may go about normal daily activities, including light exercise or showering, without required monitor maintenance. Each Zio biosensor is intended for single-patient use. After the monitoring period is completed, the wearer removes the biosensor and sends it to the company by freepost. The ECG recordings are analysed using the artificial intelligence led algorithm within ZEUS and overseen by accredited

cardiac physiologists. A technical report is produced, containing information regarding arrhythmia episodes, wear and analysis time and patient-captured events, and is sent to the prescribing clinician for final analysis and interpretation. There are no patient identifiers in or on the Zio Patch and data cannot be accessed if the Zio Patch were to be physically intercepted.

For the Evidence Standards Framework for digital health technologies, Zio Service is classified as an active monitoring technology and so has a tier 3b evidence level.

1.2 Regulatory status

Zio Service received a CE mark in December 2014 as a Class IIa device.

1.3 Relevant diseases and conditions

Cardiac arrythmias are experienced by more than 2 million people a year in the UK. The term covers a number of conditions in which the heartbeat is irregular, too fast or too slow. Types of arrythmias are categorised by where they originate in the heart (atria or ventricles) and whether they increase (tachycardia) or decrease the heart rate (bradycardia). Important examples of cardiac arrythmia include atrial fibrillation, supraventricular tachycardia, bradycardia, heart block and ventricular fibrillation (NHS, 2018).

Zio Service is intended for use in people suspected of having cardiac arrhythmia, specifically those with symptoms or suspected arrhythmic episodes more than 24 hours apart. Common symptoms include palpitations, dizziness or light-headedness (presyncope) and fainting (syncope) and are known to account for a large number of emergency presentations each year in the UK. Cardiovascular events including arrhythmia are among the most serious causes of syncope.

Atrial fibrillation is the most common sustained cardiac arrhythmia. It causes an irregular and often abnormally fast heart rate which can lead to symptoms such as breathlessness, heart palpitations and dizziness or temporary loss of consciousness. Atrial fibrillation can also be asymptomatic. It has been estimated that 1.4 million people in England have atrial fibrillation, equating to

2.5% of the population (Public Health England, 2017). The likelihood of atrial fibrillation increases with age, with 80.5% of the total estimated atrial fibrillation in the population occurring in people over 65 years. The prevalence of atrial fibrillation is higher in men than women (2.9% compared with 2.0%), with 825,000 men expected to be living with it compared with 580,000 women. Public Health England also estimate that around 425,000 people in England have undiagnosed and untreated atrial fibrillation. Atrial fibrillation is associated with an increased risk of stroke, hospitalisation, and mortality. According to the European Society of Cardiology guidelines for the management of atrial fibrillation, untreated atrial fibrillation is associated with a 5-fold increased risk of stroke and a 3-fold increased risk of heart failure (European Society of Cardiology, 2012).

1.4 Current management

NICE's guidelines on transient loss of consciousness ('blackouts') in over 16s and guidelines on managing atrial fibrillation provide recommendations on current methods of arrhythmia detection.

The NICE guideline on transient loss of consciousness ('blackouts') in over 16s, recommends recording a 12-lead ECG using automated interpretation as the initial assessment. All people with transient loss of consciousness (TLoC) should be referred for specialist cardiovascular assessment, except those with a firm diagnosis after initial assessment of uncomplicated faint, situational syncope or orthostatic hypotension, or people whose presentation is strongly suggestive of epileptic seizure. For people with a suspected cardiac arrhythmic cause of syncope, the guideline recommends offering an ambulatory ECG. The type of device should be chosen on the basis of the patient's history and frequency of TLoC. Holter monitoring (up to 48 hours if necessary) is recommended in people who have TLoC at least several times a week. In those with TLoC every 1 to 2 weeks an external event recorder should be offered. An implantable event recorder should be offered to people with infrequent TLoC (less than once every 2 weeks).

The NICE guideline on managing atrial fibrillation recommends performing manual pulse palpation to assess for the presence of an irregular pulse in people presenting with any of the following:

- breathlessness/dyspnoea
- palpitations
- syncope/dizziness
- chest discomfort
- stroke/transient ischaemic attack

It is recommended that an ECG be performed in all people, whether symptomatic or not, in whom atrial fibrillation is suspected because an irregular pulse has been detected. Arrhythmias may be missed by a 12-lead ECG in people with paroxysmal AF (that is, intermittent atrial fibrillation) because of the occasional nature of the arrhythmic episodes. If arrhythmia is not detected on the initial 12-lead ECG and further assessment of suspected paroxysmal atrial fibrillation is needed, ambulatory ECG monitoring is recommended. The choice of monitor used depends on symptoms and symptom frequency. The guideline recommends the following:

- use a 24-hour ambulatory ECG monitor (such as a Holter monitor) in people with suspected asymptomatic episodes or symptomatic episodes less than 24 hours apart
- use an event recorder ECG (which can be external or implantable) in people with symptomatic episodes more than 24 hours apart.

Zio Service would be used for monitoring up to a 14-day period in place of current methods of cardiac event detection, such as Holter monitoring or event recording (external or implantable) in people suspected of having cardiac arrhythmia. The use of the Zio Service would be prescribed by a clinician, most often a cardiologist or GP, in primary, secondary or tertiary care. It may also be prescribed by a stroke clinician or neurologist.

1.5 Claimed benefits

The benefits to patients claimed by the company are:

- Improved diagnostic yield, minimising the number of repeat tests needed to confirm or rule out arrhythmia
- Greater diagnostic accuracy and efficiency in detecting clinically relevant arrhythmias, including symptomatic and silent atrial fibrillation
- Earlier diagnosis and initiation of preventative treatment (such as anticoagulants), potentially leading to a reduction in the occurrence of clinical sequelae of arrhythmia such as syncope, stroke and heart failure
- Minimal disruption to patients' daily activities leading to improved patient compliance and data collection (wear time, analysable time and signal quality)
- Streamlined patient pathways reduced number of outpatient visits (aligned to NHS Long Term Plan objectives), thereby increasing patient access and reducing health inequalities

The benefits to the health and social care system claimed by the company are:

- Reduction in costs and resources that could be avoided through earlier diagnosis and treatment, such as repeat hospital admissions related to the clinical sequelae of arrhythmia, such as syncope, stroke or heart failure
- Reduction in staff, estate and capital equipment resource use in the ambulatory ECG monitoring pathway, due to reduced repeat testing, reduced in-clinic analysis of ECG recordings and reduced outpatient appointments
- Standardisation and efficiency gains in cardiac diagnostic services within and across NHS trusts through simplified processes, supported by Artificial Intelligence and service evaluation tools
- Ease of implementation; minimal changes in facilities or infrastructure needed when Zio Service adopted in standard practice, including in rural areas

2 Statement of the decision problem

Population	Adults (18 years or older) with suspected cardiac arrhythmia referred for ambulatory ECG monitoring
Intervention	Zio ECG monitoring service (Zio Service)
Comparator(s)	• Current pathway for ambulatory cardiac arrhythmia detection, which includes Holter and/or event monitoring (external and implantable)
Outcomes	The outcome measures to consider include: Procedure-related outcomes: • Diagnostic yield and accuracy (sensitivity and specificity) • Number of symptomatic and asymptomatic arrythmia events detected over total wear time • Ability to quantify atrial fibrillation (AF) burden (amount of time spent in AF) • Time to first arrhythmia event and time to first symptomatic event • Time to return device, analysis and report production • Test failure rate • Signal quality Clinical management outcomes: • Time to diagnosis or rule out of cardiac arrythmia • Time to initiation of preventative treatment • Impact of test results on clinical decision making • Total number of hospital outpatient appointments for testing • Total number of hospital outpatient appointments or admissions for device-related complications • Number of outpatient visits and staff time for undertaking and analyzing diagnostic tests • Morbidity (including stroke, thromboembolism, heart failure, and complications associated with preventative treatment) • Mortality Patient outcomes: • Patient compliance (average wear time and analyzable wear time) • Ease of use (for patients and healthcare professionals), including training requirements • Device acceptability and patient satisfaction • Health-related quality of life • Device-related adverse events

Cost analysis	Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be sufficiently long to reflect any differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers and combinations of devices are needed.	
Subgroups to be considered	• Adults referred for ambulatory ECG monitoring, who experience asymptomatic arrhythmia events • Adults referred for ambulatory ECG monitoring in primary care • Adults referred for ambulatory ECG monitoring in secondary care	
Special considerations, including those related to equality	The area of skin in which the Zio patch is applied will need shaving if hair is present. Some religions forbid cutting or shaving bodily hair. Zio service is not approved for paediatric use. Religion and age are protected characteristics under the Equality Act. Contraindications are listed the instructions for use for Zio Service.	
Special considerations, specifically related to equality	Are there any people with a protected characteristic for whom this device has a particularly disadvantageous impact or for whom this device will have a disproportionate impact on daily living, compared with people without that protected characteristics?	No
	Are there any changes that need to be considered in the scope to eliminate unlawful discrimination and to promote equality?	No
	Is there anything specific that needs to be done now to ensure MTAC will have relevant information to consider equality issues when developing guidance?	No
	Cardiac arrhythmias can develop in people of any age but are more common in people over 60 years. Women tend to be at higher risk of certain arrhythmias, including atrioventricular nodal tachycardia, whereas men are 3 times more likely to develop atrial fibrillation at any age. However, of those people who develop atrial fibrillation, women have a much higher incidence of morbidity and mortality. Age and sex are protected characteristics under the Equality Act. People whose first language is not English or who cannot write may not be able to give written information on their symptoms while using the Zio Service.	

3 Related NICE guidance

Published

- Lead-I ECG devices for detecting symptomatic atrial fibrillation using single time point testing in primary care. NICE diagnostics assessment guidance DG35 (2019).

- Leadless cardiac pacemaker implantation for bradyarrhythmias. NICE Interventional procedures guidance IPG626 (2018).
- Subcutaneous implantable cardioverter defibrillator insertion for preventing sudden cardiac death. NICE Interventional procedures guidance IPG603 (2017).
- Atrial fibrillation and heart valve disease: self-monitoring coagulation status using point-of-care coagulometers (the CoaguChek XS system). NICE Diagnostics guidance DG14 (2017).
- ENDURALIFE powered CRT-D devices for treating heart failure. NICE Medical technologies guidance MTG33 (2017).
- Percutaneous endoscopic laser balloon pulmonary vein isolation for atrial fibrillation. NICE Interventional procedures guidance IPG563 (2016).
- Edoxaban for preventing stroke and systemic embolism in people with non-valvular atrial fibrillation. NICE Technology appraisal guidance TA355 (2015).
- Dual-chamber pacemakers for symptomatic bradycardia due to sick sinus syndrome and/or atrioventricular block. NICE Technology appraisal guidance TA88 (2014).
- Atrial fibrillation: management. NICE Clinical guideline CG180 (2014).
- Implantable cardioverter defibrillators and cardiac resynchronisation therapy for arrhythmias and heart failure. NICE Technology appraisal guidance TA314 (2014).
- Apixaban for preventing stroke and systemic embolism in people with nonvalvular atrial fibrillation. NICE Technology appraisal guidance TA275 (2013).
- WatchBP Home A for opportunistically detecting atrial fibrillation during diagnosis and monitoring of hypertension. NICE Medical technologies guidance MTG13 (2013).
- Dronedarone for the treatment of non-permanent atrial fibrillation. NICE Technology appraisal guidance TA197 (2012).
- Percutaneous balloon cryoablation for pulmonary vein isolation in atrial fibrillation. NICE Interventional procedures guidance IPG427 (2012).

- Rivaroxaban for the prevention of stroke and systemic embolism in people with atrial fibrillation. NICE Technology appraisal guidance TA256 (2012).
- Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation. NICE Technology appraisal guidance TA249 (2012).
- Thoracoscopic exclusion of the left atrial appendage (with or without surgical ablation) for non-valvular atrial fibrillation for the prevention of thromboembolism. NICE Interventional procedures guidance IPG400 (2011).
- Percutaneous occlusion of the left atrial appendage in non-valvular atrial fibrillation for the prevention of thromboembolism. NICE Interventional procedures guidance [IPG349 (2010).
- Percutaneous (non-thoracoscopic) epicardial catheter radiofrequency ablation for atrial fibrillation. NICE Interventional procedures guidance IPG294 (2009).
- Percutaneous (non-thoracoscopic) epicardial catheter radiofrequency ablation for ventricular tachycardia. NICE Interventional procedures guidance IPG295 (2009).
- Thoracoscopic epicardial radiofrequency ablation for atrial fibrillation. NICE Interventional procedures guidance IPG286 (2009).
- High-intensity focused ultrasound for atrial fibrillation in association with other cardiac surgery. NICE Interventional procedures guidance IPG184 (2006).
- Percutaneous radiofrequency ablation for atrial fibrillation. NICE Interventional procedures guidance IPG168 (2006).
- Cryoablation for atrial fibrillation in association with other cardiac surgery. NICE Interventional procedures guidance IPG123 (2005).
- Microwave ablation for atrial fibrillation in association with other cardiac surgery. NICE Interventional procedures guidance IPG122 (2005).
- Radiofrequency ablation for atrial fibrillation in association with other cardiac surgery. NICE Interventional procedures guidance IPG121 (2005).
- Laser sheath removal of pacing leads. NICE Interventional procedures guidance IPG63 (2004).

Under development

NICE is developing the following guidance (details available from www.nice.org.uk):

- Implantable cardiac monitors to detect atrial fibrillation after cryptogenic stroke. NICE diagnostics assessment guidance. Publication expected December 2019.
- TYRX Absorbable Antibacterial Envelope for preventing infection from cardiac implantable electronic devices [ID1440]. NICE technology appraisal guidance. Publication expected February 2020.
- Atrial fibrillation: management. NICE guideline. Publication expected September 2020.
- Atrial fibrillation - idraparinux sodium [ID375]. NICE technology appraisal guidance. Publication expected TBC.
- Atrial fibrillation - vernakalant [ID454]. NICE technology appraisal guidance. Publication expected TBC.

4 External organisations

4.1 Professional organisations

The following societies have been alerted to the availability of the draft scope for comment:

- British Association for Nursing Cardiovascular Care
- British Cardiovascular Society
- British Heart Rhythm Society
- Royal College of Emergency Medicine
- Royal College of General Practitioners
- Royal College of Nursing
- Royal College of Physicians
- Society for Cardiological Science and Technology

4.2 Patient organisations

NICE's Public Involvement Programme contacted the following organisations for patient commentary and alerted them to the availability of the draft scope for comment:

- Arrhythmia Alliance
- Atrial Fibrillation Association
- British Cardiac Patients Association (BCPA)
- British Heart Foundation
- Cardiac Risk in the Young (CRY)
- Cardiovascular Care Partnership
- Children's Heart Federation
- Down's Heart Group
- Heart Rhythm Alliance
- Heart Valve voice
- Pumping Marvellous
- The Ashley Jolly SADS Trust (SADS UK)