Crypto PulseON

A Feasibility Study of a Wearable Arrhythmia Monitoring System (PulseON) in Stroke Patients

PROTOCOL

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MM_02	1.2	30/09/2026	30/09/2026

Confidentiality statement

All information contained within this document is regarded as, and must be kept, confidential. No part of this document may be disclosed to any Third Party without the written permission of the Chief Investigator and/or Sponsor.

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the trial in compliance with the approved protocol and will adhere to the principles outlined in the UK Policy Framework for Health and Social Care Research, the ICH Good Clinical Practice guidelines and the Sponsor's SOPs.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor.

I also confirm that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of the Study Sponsor:

Signature: Date:



11/06/2026

Name:
Ceri Jones

Position:
Head of Research & Development

Chief Investigator:

Signature: Date:



30/09/2026.

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TRIAL SUMMARY

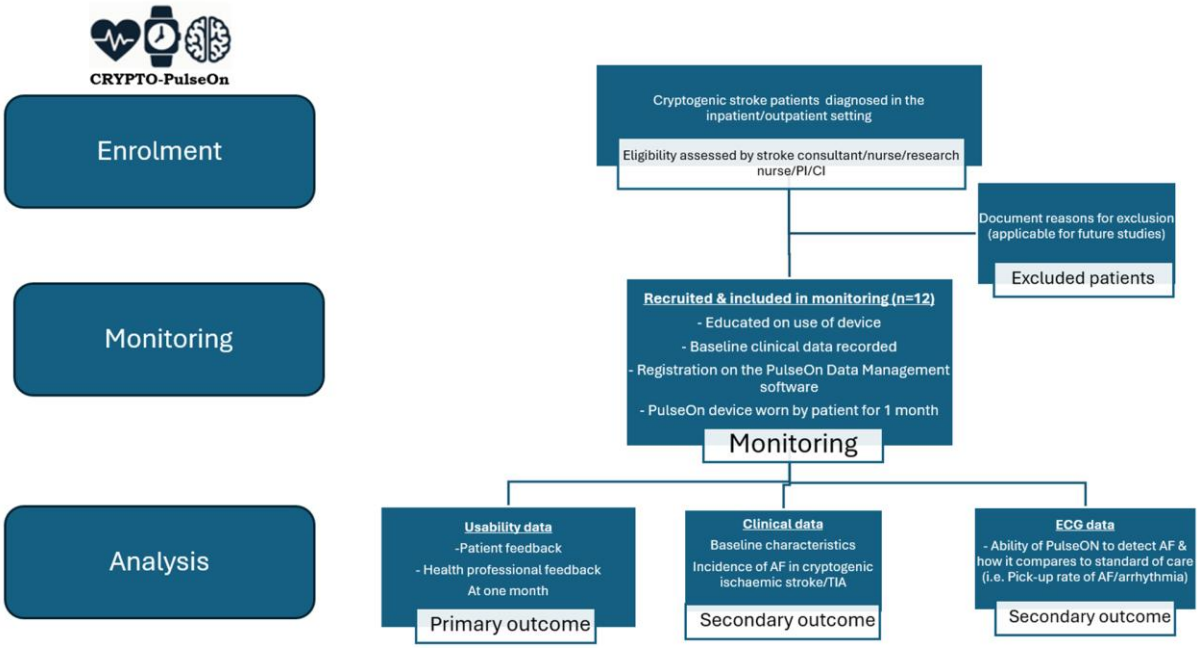
Full study title	*A Feasibility Study of a Wearable Arrhythmia Monitoring System (PulseON) in Stroke Patients*	
Short study title	**CRYPTO-PulseON**	
Study aim	To evaluate the usability of the Pulse ON wearable device in patients with cryptogenic stroke/TIA.	
Trial design	*Single centre feasibility study of a wrist worn device to detect arrhythmia in cryptogenic stroke patients*	
Trial participants	*Patients diagnosed with cryptogenic stroke*	
Trial arms	*Single arm*	
Sample size	*12*	
Planned trial period	*10 Months*	
Follow up duration	*1 Month*	
Planned recruitment start date	*July 2026*	
Planned recruitment end date	*Jan 2027*	
Planned study end date	*March 2027*	
	Objectives	**Outcome Measures**
Primary	The primary objective is to assess patient feedback on the usability of PulseON in patients who have had cryptogenic ischaemic stroke or TIA. To assess professional healthcare feedback	To explore the ease of use, impact on lifestyle, device-specific issues, potential adaptions/ improvements, and satisfaction using primarily a semi-structured online questionnaire and interviews
Secondary	The secondary objectives are:	

	• Assess baseline characteristics of cohort • The incidence of AF in people who have had cryptogenic ischaemic stroke or TIA. • The ability of PulseON in detecting AF on ECG and does this differs from the standard of care (ECG, Holter monitoring or ILR).	Baseline demographic data Number of AF episodes detected by PulseON compared with standard care Ability to detect AF
Investigational Medicinal Product(s)	PulseON arrhythmia monitoring device	
Formulation, Dose, Route of Administration	Wrist worn device	

Key Words: **Cryptogenic stroke, Atrial fibrillation, Non-invasive cardiac monitoring, patient usability, patient experience**

TRIAL FLOW CHART

Figure 1: Flow of participants through the study



SCHEDULE OF EVENTS

Table 1: Schedule of Events

Procedure	Screening	Baseline	Follow-Up 1: Day 1–2	Follow-Up 2: Day 3-40
Eligibility assessment	X			
Patient approach		X		
Informed consent		X		
Demographic, personal and history data collection (DOB, email addresses, sex, ethnicity, height and weight, etc.) *		X		
Blood tests – U&E (sodium, potassium, urea and creatinine), GFR, Glucose, and HbA1c*		X		
Collection of previous cardiac investigation data (including 12 lead ECG, Holter monitor, echocardiogram reports) *		X		
PulseON device given with training		X		
Cardiac rhythm monitoring via the device commences		X		
Usability Questionnaire			X	
Patient follow-up interview**				X
Capture healthcare professional feedback				X

Key

* Part of Standard Care

**Follow up interview can be completed face-to-face or remotely

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LIST OF ABBREVIATIONS

AE	Adverse Event
AF	Atrial Fibrillation
AR	Adverse Reaction
CA	Competent Authority
CI	Chief Investigator
CRF	Case Report Form
CTA	Clinical Trial Authorisation
DMC	Data Monitoring Committee
DSUR	Development Safety Update Report
EC	European Commission
ECG	Electrocardiogram
EU	European Union
GCP	Good Clinical Practice
ICH	International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use.
IMP	Investigational Medicinal Product
MA	Marketing Authorisation
MHRA	Medicines and Healthcare products Regulatory Agency
PI	Principal Investigator
PIC	Participant Identification Centre
PPI	Patient and Public Involvement
REC	Research Ethics Committee
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SOP	Standard Operating Procedure
SmPC	Summary of Product Characteristics
SUSAR	Suspected Unexpected Serious Adverse Reaction
TIA	Transient Ischaemic Attack
TSC	Trial Steering Committee

TRIAL PROTOCOL

The Crypto-PulseOn study

1. INTRODUCTION.

The research project aims to evaluate the usability of a new device for detecting heart rhythm disturbances, especially atrial fibrillation (AF) in people who have had a stroke or mini-stroke (transient ischaemic attack [TIA]) of unknown cause (cryptogenic stroke). AF can be a major cause of disabling strokes and AF-related stroke risk is significantly reduced by starting specific blood thinners called anticoagulants.

Stroke is a major public health concern worldwide, with approximately 100,000 cases annually in the UK alone, making it a leading cause of death and disability.[1] Around 38,000 stroke-related deaths occur each year, and many survivors experience significant long-term impairment. The vast majority (~90%) are ischaemic strokes, yet in 20–40% of cases, no definitive underlying cause is identified, despite extensive evaluation.[1] These cryptogenic stroke cases remain a diagnostic challenge. Cryptogenic strokes are more common in younger stroke patients (<60 years) but can affect all age groups.[1]

AF is the most common arrhythmia and a well-established cause of ischaemic stroke, responsible for 15-30% of cases.[2] However, in cryptogenic stroke, AF often goes undiagnosed because it can come and go (i.e. is paroxysmal) and can be asymptomatic in nature, with episodes that can last for short periods of time but carry high risk of stroke. Early and accurate diagnosis of AF is crucial, as clinical trials have demonstrated the efficacy of oral anticoagulation in significantly reducing stroke risk. Thus, identifying AF in cryptogenic stroke patients can directly impact management by shifting treatment towards anticoagulation.[2]

1.1 Background.

Detecting AF in cryptogenic stroke is a major challenge and many methods fail to capture episodes of AF that come and go (paroxysmal). Conventional AF detection methods, such as in-hospital cardiac monitoring, serial ECGs, Holter monitors, external event recorders, wearable devices and implantable loop recorders (ILRs), vary in effectiveness.[2] ILRs are small devices (the size of a pen-lid) implanted under the skin of the left chest wall and have a battery life of around three years. They have demonstrated superior diagnostic sensitivity, as highlighted in the CRYSTAL-AF trial,[3] which showed their advantage over standard monitoring in cryptogenic stroke (AF detection rate of 12.4% for ILRs vs 2% for standard monitoring at 12 months). However, ILRs are invasive (which comes with its own procedure-related risks), costly, and may not be suitable for all patients.[2] We want to evaluate a different type of AF detection device (the PulseON Arrhythmia Monitor System – see Appendix 1) that is not currently used in standard care, one that's wrist worn and non-invasive.

1.2 Proposed trial

We propose a single centre, single arm feasibility pilot study designed to evaluate how practical and user friendly it is for participants to use the PulseON Arrhythmia Monitor System for detecting AF in addition to their normal standard of care. The study will explore

whether participants can wear the device as intended, respond to alerts and successfully carry out ECG recordings using the system, whilst capturing their user experience and having their heart tracings closely monitored by health care professionals.

1.3 Trial population

At UHCW NHS Trust, we manage approximately 1,400 strokes annually (with 350 classified as cryptogenic), many of whom will need to be monitored for AF. While most patients undergo Holter monitoring for AF, a smaller subset receive ILRs but their use is limited due their cost and invasive nature. The introduction of this PulseON device could significantly enhance AF detection, improving patient outcomes, be more cost-effective and optimise resource utilisation within our hospital and the broader NHS. We plan to evaluate whether cardiac monitoring with the PulseON system is feasible in patients with cryptogenic stroke/TIA. This evaluation project may inform wider research into this device and potential NHS implementation.

1.4 Treatment / Intervention

We aim to recruit twelve patients who have experienced a cryptogenic ischaemic stroke or TIA within the past six months for this project. All patients who participate in the project will receive conventional standard of care investigations (Holter monitoring or ILR) in addition to the PulseON Arrhythmia monitoring system. The data collected will include experience of device usability via an MS forms questionnaire and a follow-up patient interview, baseline demographics, usability data and any newly detected arrhythmia observed from the heart tracing data, in particular AF (defined as an episode of AF lasting $\geq$30seconds). Any arrhythmia documented from the PulseON device will be uploaded and stored in an encrypted and secure cloud-based server.

Participants heart tracing data will be collected and reviewed by a suitably qualified healthcare professional within the study team (primarily the Principal Investigator).The reviewer will assess any detected cardiac events to determine their clinical significance and, when appropriate, will escalate relevant findings to the participant's clinical care team. This process ensures that any new or emerging information arising from the study is used to support and inform the provision of standard clinical care for participants.

1.5 Pre-clinical data

Early and accurate diagnosis of AF is crucial in cryptogenic stroke/TIA, as randomised clinical trials have demonstrated the efficacy of oral anticoagulation in significantly reducing stroke risk.[2] Thus, identifying AF in cryptogenic stroke patients can directly impact management by shifting treatment towards anticoagulation. Conventional AF detection methods, such as in-hospital cardiac monitoring, serial ECGs, Holter monitors, external event recorders, wearable devices and ILRs, vary in effectiveness. ILRs have demonstrated superior diagnostic sensitivity, as highlighted by the CRYSTAL-AF trial,[3] which showed their advantage over standard monitoring in cryptogenic stroke (AF detection rate of 12.4% for ILRs vs 2% for standard monitoring at 12 months). However, ILRs are invasive (which comes with its own procedure-related risks), costly, and may not be suitable for all patients.[2]

1.6 Clinical data

Unfortunately, conventional cardiac monitoring strategies for patients with acute cerebral ischaemia are poor at detecting AF and supporting its possible role in cryptogenic stroke.[2] The appropriate diagnosis of AF is important and has clinical importance, as randomised clinical trials have shown that oral anticoagulation reduces the risk of stroke in patients with AF. However, prior to anticoagulation initiation, it is important to document AF after ischaemic stroke.[1] A diagnosis of AF can influence management of cryptogenic stroke because presence of AF changes the pharmacological therapy towards oral anticoagulation initiation. The risk of stroke in patients with AF is estimated using the CHA2DS2-VA score,[2] but, even in the presence of strong suspicion, AF may not be detected in the acute phase of ischaemic stroke, due to its paroxysmal and asymptomatic nature. For this reason, many strategies have been explored to improve AF detection, ranging from in-hospital monitoring, serial electrocardiography (ECG), Holter monitoring, use of external event recorders or ILRs. Recently, ILRs were found to improve diagnostic sensitivity to detect many arrhythmias, especially AF, in patients with cryptogenic stroke. The CRYSTAL-AF study[3] was the first randomized study demonstrating superiority of ILRs to standard care monitoring in cryptogenic stroke. Increasingly, evidence suggests longer-term monitoring in these patients is important. However, ILRs have several limitations; they require an invasive procedure with significant cost and may not be appropriate for every person.

2. RATIONALE

2.1 Aims and hypothesis

The aim is to evaluate the usability, accessibility and functionality of the Pulse-On device.

2.2 Justification

The PulseON Arrhythmia Monitor System is a wrist-worn device designed to enhance AF detection.[4] Unlike other wearable devices, it continuously monitors pulse irregularities and prompts the user to take a single-channel ECG by placing their hand over the device for at least 30 seconds. AF detection using conventional cardiac monitoring devices (24hour-2week duration of continuous monitoring) is very poor and highly cost-ineffective. Wearable and portable ECG-recording devices are an alternative, but the major limitation is that those technologies require patients to initiate ECG recordings. The paroxysmal and asymptomatic nature of AF compounds this problem, and many patients may miss the opportunity to record an ECG during an AF episode.

The PulseON device is unique in that it monitors the pulse continuously 24/7 and detects irregular heart rhythms using photoplethysmography (PPG). It then alerts the user to take ECG recordings. Data is then transferred securely to the cloud for storage and automated data analysis.[4] The results are then read on a web-interface and the diagnosis communicated to the patient by the health professional. This device is non-invasive, rechargeable and reusable design allows for extended monitoring over days or weeks, making it a highly cost-effective solution for the NHS.

2.3 Assessment and management of risk

Use of the PulseON device is generally considered low risk, as it does not involve a medical procedure and does not involve any medication, radiation, or procedures inside the body that would be in addition to standard of care. However, there are still some potential risks that are highlighted in the table below:

Risk Category	**Description / Comments**
Discomfort or Inconvenience	- Wearing the device for long periods may be uncomfortable or irritating, especially for those with sensitive skin. - The device may vibrate when detecting an irregular pulse which can sometimes be a false alarm and cause worry or anxiety.
Psychological Risks	- The vibration of the device may be Interpreted as a possible heart rhythm problem, which may cause anxiety or concern, even if the issue is not serious. - Constant monitoring may increase awareness or stress about heart health.
Risk of Discovering Unknown Health Issues	The device might detect a previously unknown heart rhythm problem (e.g. atrial fibrillation), potentially leading to further investigations and emotionally difficult decisions about treatment.
Confidentiality and Data Privacy	- Heart rhythm and health data will be collected for research purposes. - Advanced security measures and NHS/research data privacy guidelines will be followed. - Despite safeguards, there is a very small risk of inappropriate data access.
Impact on Insurance	- Discovery of a new health issue (e.g. atrial fibrillation) could affect future insurance applications (health, life, travel, etc.), depending on the provider and policy.

3. OBJECTIVES, ENDPOINTS AND ESTIMANDS

Primary objective:	
Estimand: The aim is to evaluate the usability, accessibility and functionality of Pulse-On	
Treatment: Non-invasive monitoring of cardiac rhythm using a wrist worn device	
ESTIMAND	**ANALYSIS**
Target population: Patients diagnosed with cryptogenic stroke/TIA	**Analysis set:** All patients diagnosed with cryptogenic stroke/TIA at UHCW
Variable: Usability and feasibility of the PulseON device	**Outcome measure:** We will collect patient questionnaires and perform patient interviews to gather data on the

	PulseON device for usability and feasibility data. Formal feedback from health professionals who follow up the trial participants via the PulseON arrhythmia monitoring system online will be obtained.
Population-level summary measure: Quantitative and qualitative data analysis on device useability	**Analysis approach:** Thematic analysis for qualitative datasets and t-testing for qualitative data analysis
Secondary objectives	**Endpoints/outcome measures**
• Assess baseline characteristics of cohort • The prevalence of AF in people who have had cryptogenic ischaemic stroke or TIA. • The ability of Pulse ON in detecting AF on ECG and how it differs from the standard of care (ECG, Holter monitoring or ILR).	Incidence of AF detection

4. TRIAL DESIGN

This is single centre single arm feasibility pilot study evaluating feasibility and usability of the PulseON arrhythmia detection device. Participants will be asked to wear the PulseON Arrhythmia Monitor System for up to four weeks but will be asked to stop using it early if it is deemed appropriate by either the study team or the participants medical treatment team (e.g. the device detects arrhythmia in the participant, there's a heart tracing of medical concern, etc.).

5. STUDY SETTING

This single centre study will take place at University Hospitals Coventry & Warwickshire NHS Trust.

6. ELIGIBILITY CRITERIA

6.1 Inclusion criteria

- Adult patients (>18yrs old) diagnosed with cryptogenic stroke / TIA
- Baseline electrocardiogram (ECG), Holter monitor and echocardiogram as part of the standard of care cardiac work-up in the diagnosis of cryptogenic stroke.

6.2 Exclusion criteria

- Patients unwilling or unable to wear the PulseON arrhythmia detection device.
- Known pre-existing AF or atrial arrhythmia diagnosis.

- Participants without capacity will be excluded from this study.
- Participants who are pregnant will be excluded from this study.

7. TRIAL PROCEDURES

7.1 Recruitment

Recruitment will take place from UHCW NHST Trust follow up clinics, from patients who have been diagnosed with cryptogenic stroke. The patients will be invited to participate in the current study in parallel to their current standard of care. They will be provided with the PulseON device and asked to give feedback on its use.

7.1.1 Patient identification

We work closely with our colleagues from stroke medicine and will identify all eligible patients through the stroke clinic. These patients will then be approached for consenting and recruitment into the study

Identification and eligibility of potential participants for the project will be assessed during standard diagnostic procedures undertaken as part of their standard of care in the stroke clinic, after having suffered a stroke or mini stroke of an unknown cause. Potential participants will then be approached for consenting and recruitment into the study

Baseline data collected through these same diagnostic procedures will be captured following successful patient recruitment.

7.1.2 Screening

Delegated members of the research team, who also serve within the direct clinical care teams in stroke medicine and cardiology, will review the schedules of upcoming follow-up clinics to identify individuals who may meet the study's eligibility criteria. This pre-screening process will involve checking upcoming follow-up clinic lists to determine which patients are potentially suitable for participation based off the studies edibility criteria. Following this review, eligible individuals will be approached during their next routine clinical appointment. At that visit, they will be provided with all necessary study information to support an informed decision about whether they wish to participate.

7.1.3 Payment

As part of the project, we will be conducting a one-hour long follow-up interview with each participant to learn about their patient experience when using the PulseON devices. Each participant taking part in the interview process will receive a £25 reimbursement for their time but will receive no other payments relating to the project.

7.2 Consent

All participants will give written informed consent before any study procedures. The Principal Investigator (PI) is responsible for the consent process and may delegate tasks only to authorised, trained, and competent staff.

Participation is voluntary and individuals may refuse or withdraw at any time without affecting their care. Data collected up to participant withdrawal and during their debrief will still be used to ensure reliable study results.

Participants without capacity will be excluded. All participants must demonstrate capacity during the consent process, including understanding the study's purpose and their own freedom to choose not to participate if they do not want to. If a participant loses capacity during the study, they will be withdrawn. Identifiable data already collected will be retained as described in the consent information and no further data collection will be conducted

7.3 Research Data

Research data, collected during the project by the research team, will include the following information:

- Anonymised patient data
- Baseline demographics
- Clinical data
- Questionnaire/interview responses
- Heart tracing readings.

All data collected during the project will be collated into or linked to a master excel spreadsheet, which will be held on a secure server at UHCW and accessible only via a password protected hospital computer. All data not directly held on the master excel spreadsheet will be held in a restricted research server, only accessible by the study team and other authorised personal.

All paperwork relating to the project will be stored in a locked filing cabinet held in a secured office in the hospital, which will only be accessible to the study team.

7.4 Baseline data

All baseline patient demographic data (including age, email address, gender and comorbidity examination findings where appropriate), baseline blood tests and any previous cardiac investigation data (including 12 lead ECG, Holter monitor, echocardiogram reports) that would have already been collected as part of the standard of care diagnostic work-up of cryptogenic stroke/TIA will be captured from secure hospital systems and transferred to the projects master excel spreadsheet.

7.5 Trial assessments

These will relate to assessments and follow-up questions on the usability and feasibility of the PulseON device at the stated time points. There will be questionnaires posing statements and questions regarding the following themes:

1. Onboarding and Initial Training – assessing the clarity of instructions and patient confidence at the point of device issue.
2. Initial Setup Stage /Baseline Recording – evaluating how easily patients can complete initial device setup and data collection.

3. Daily Use and Interaction – understanding comfort, ease of use, and ability to self-initiate heart monitoring recordings in daily life.
4. Satisfaction and Acceptability – exploring overall satisfaction, trust in the device, and willingness to use or recommend it.
5. Clinical implications – expectations and understanding of arrhythmia management
6. Other – further feedback led by the patient.

Themes 1 and 2 will be adapted into a Microsoft Forms questionnaire to be sent to patients after the device has been given to them and they have received training, whilst the outcomes for Items 3 to 6 will be captured in a in a follow-up interview with the participant.

The questionnaires deliberately contain open-ended questions to allow participants to raise issues and topics spontaneously, which may open new lines of enquiry that may need to be investigated through additional questions. As such, a predetermined question list is not possible. Themes will be guided by participants' experiences and example topic area questions are provided in the accompanying study documents for illustration, rather than as a fixed schedule.

7.6 Withdrawal

Participant Initiated Withdrawal

- Participants may withdraw their consent at any time, without needing to give a reason.

Investigator or Sponsor Initiated Withdrawal

- Participants may be withdrawn from the trial for reasons including, but not limited to, the following:
    - Emerging safety concerns
    - Significant non-compliance with the protocol
    - Abuse of project equipment
    - Pregnancy

All decisions to withdraw a participant will be documented, including the reason if available.

- When a participant is to be withdrawn, the following steps will be followed:
- The Investigator will inform the subject and explain the rationale.
- The Investigator will record the date, circumstances and the reason for withdrawal (if known) in study documents (e.g. the master excel spreadsheet)
- The participant will be asked to stop using the PulseOn device and the return it to the study team at the hospital, where they will also be invited undergo a final safety assessment and for endpoint data to be collected at the time of their visit.
- If the participant withdraws consent for all further data collection, no additional data will be obtained or follow up made after the date of withdrawal. Data collected before consent withdrawal will be retained to be used in the study.

Data to Be Collected for Withdrawn Participants

- The following data will be requested from the participant but they are under no obligation to provide it:

- Reason for withdrawal (if voluntarily provided).
- Date and nature of withdrawal
- Data from the safety assessment performed on their withdraw visit (e.g. adverse events, etc)
- Any trial outcomes already recorded prior to withdrawal.

Recruitment of Additional Participants

- Following the completion of the withdrawal process additional participants may be recruited, to ensure that the study cohort size does not drop below 12 participants and that the full theme saturation required for a qualitative study is achieved.

Loss of Capacity

- If a patient loses the capacity to consent, they will be withdrawn from the study. Identifiable data or tissue already collected with consent would be retained and used in the study. No further data or tissue would be collected or any other research procedures carried out on or in relation to the participant.

7.7 End of study definition

The end of study definition will be the date upon the completion of the follow-up interview for the last patient recruited.

8. SAFETY REPORTING

8.1 Definitions

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence in a participant to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product.
Adverse Reaction (AR)	An untoward and unintended response in a participant to an investigational medicinal product which is related to any dose administered to that participant. The phrase "response to an investigational medicinal product" means that a causal relationship between a trial medication and an AE is at least a reasonable possibility, i.e. the relationship cannot be ruled out. All cases judged by either the reporting medically qualified professional or the Sponsor as having a reasonable suspected causal relationship to the trial medication qualify as adverse reactions. It is important to note that this is

	entirely separate to the known side effects listed in the SmPC. It is specifically a temporal relationship between taking the drug, the half-life, and the time of the event or any valid alternative etiology that would explain the event.
Serious Adverse Event (SAE)	A serious adverse event is any untoward medical occurrence that: • results in death • is life-threatening • requires inpatient hospitalisation or prolongation of existing hospitalisation • results in persistent or significant disability/incapacity • consists of a congenital anomaly or birth defect Other 'important medical events' may also be considered serious if they jeopardise the participant or require an intervention to prevent one of the above consequences. NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.
Serious Adverse Reaction (SAR)	An adverse event that is both serious and, in the opinion of the reporting Investigator, believed with reasonable probability to be due to one of the trial treatments, based on the information provided.
Suspected Unexpected Serious Adverse Reaction (SUSAR)	A serious adverse reaction, the nature and severity of which is not consistent with the information about the medicinal product in question set out in the reference safety information: • in the case of a product with a marketing authorisation, this could be in the summary of product characteristics (SmPC) for that product, so long as it is being used within its licence. If it is being used off label an assessment of the SmPCs suitability will need to be undertaken. • in the case of any other investigational medicinal product, in the investigator's brochure (IB) relating to the trial in question.

NB: "Severe" is often used to describe intensity of a specific event, which may be of relatively minor medical significance. "Seriousness" is the regulatory definition supplied above.

8.2 Definitions for (S)AEs

With the exception of the PulseOn device causing skin irritation in rare cases, no SAEs are anticipated with this study. However, participants will be reviewed at timepoints throughout the project and any inadvertent SAEs will be reported by the CI to the sponsor.
The CI will evaluate (S)AEs and (S)ARs according to standard references for causality and correlation to participation in the project

8.3 Recording and reporting of SAEs, SARs AND SUSARs

Any adverse events will be reported in accordance with the Trusts Standard Operating Procedures.

All SAEs, SARs and SUSARs occurring from the time of written informed consent until the end of the project will be fully documented, with completed documentation being forwarded to the Sponsor within 24 hours of research staff becoming aware of the event.

For each SAEs, SARs and SUSARs the following information will be collected:

- Full details in medical terms and case description event duration (start and end dates, if applicable)
- Action taken
- Outcome
- Seriousness
- Criteria causality (i.e. relatedness to trial drug / investigation),
- In the opinion of the investigator whether the event would be considered anticipated.

8.4 Responsibilities

Principal Investigator (PI):

Checking for AEs and ARs when participants attend for treatment / follow-up.

Using medical judgement in assigning seriousness, causality and whether the event/reaction was anticipated using the trial-approved User Guide for the PulseOn device and in alignment with its CE-marking and MHRA registration.

Using medical judgement in assigning seriousness and causality and providing an opinion on whether the event/reaction was anticipated using the trial-approved User Guide for the PulseOn device and in alignment with its CE-marking and MHRA registration.

Ensuring that all SAEs are recorded and reported to the sponsor within 24 hours of becoming aware of the event and provide further follow-up information as soon as available.
Ensuring that SAEs are chased with Sponsor if a record of receipt is not received within 2 working days of initial reporting.

Ensuring that AEs and ARs are recorded and reported to the sponsor in line with the requirements of the protocol.

Chief Investigator (CI) / delegate or independent clinical reviewer:

Clinical oversight of the safety of patients participating in the trial, including an ongoing review of the risk / benefit.

Using medical judgement in assigning the SAEs seriousness, causality and whether the event was anticipated (in line with the User Guide for the PulseOn device) where it has not been possible to obtain local medical assessment.

Using medical judgement in assigning whether an event/reaction was anticipated or expected in line with the User Guide for the PulseOn device.

Immediate review of all SUSARs.

Review of specific SAEs and SARs in accordance with the trial risk assessment and protocol as detailed in the Trial Monitoring Plan.

Assigning Medical Dictionary for Regulatory Activities (MedDRA) or Body System coding to all SAEs and SARs.

Sponsor:

Central data collection and verification of AEs, ARs, SAEs, SARs and SUSARs according to the trial protocol onto a database.

Reporting safety information to the CI, delegate or independent clinical reviewer for the ongoing assessment of the risk / benefit according to the Trial Monitoring Plan.

Reporting safety information to the independent oversight committees identified for the trial (Data Monitoring Committee (DMC) and / or Trial Steering Committee (TSC)) according to the Trial Monitoring Plan.

Expedited reporting of SUSARs to the Competent Authority (MHRA in UK) and REC within required timelines.

Notifying Investigators of SUSARs that occur within the trial.

9. STATISTICAL CONSIDERATIONS

9.1 Sample size calculation

A group of twelve participants is suitable for this study because, in qualitative research, this number is usually enough to hear all the main ideas and experiences people have to share. Researchers call this “saturation,” which means that after a certain point, more interviews don’t reveal anything new or different. Previous studies have shown that, when everyone in the group has a similar condition or experience, you typically reach this point with around twelve people. Unlike other types of research, where sample sizes are calculated using statistics, qualitative studies focus on collecting rich, detailed information until no new

insights are emerging. For this reason, recruiting twelve participants is expected to give us enough depth and variety in the data to answer the research questions properly and ensure the study is carried out to a high standard

9.2 Planned recruitment rate

Recruitment all 12 consecutive patients with cryptogenic stroke will be completed over a two-to-four-month period

9.3 Summary of baseline data and assessing the baseline characteristics of the cohort

Relevant participant data that is normally collected during routine care for a cryptogenic stroke or TIA (such as age, gender, relevant medical history, blood test results, and any previous heart tests), will be captured from secure hospital systems as baseline data. This will then be added to the master Excel database for the study.

From there, researchers will report on the characteristics of the collected baseline data for the cohort.

9.4 Primary outcome analysis

The primary objective is the usability of PulseON in patients who have had cryptogenic ischaemic stroke or TIA. We will primarily use qualitative research methods to explore the ease of use, impact on lifestyle, device-specific issues, potential adaptions/improvements, and satisfaction using primarily a focus group however people who do not wish to participate in a focus group and have an important perspective will be offered an online semi-structured interview. We will interview up to 12 participants. They will be purposively sampled to ensure equal representation by consecutive unselected recruitment. All data will be audio recorded, transcribed verbatim and coded. Iterative thematic analysis will be used to analyse the data. We expect these interviews will be sufficient to achieve data saturation in identifying usability and satisfaction of use.

In addition, feedback will be collected from health care professionals on the suitability and feasibility of the PulseOn device from their perspective. This will be obtained through a single question:

“What are your views on the use of the PulseOn Arrhythmia Monitoring System for monitoring cryptogenic stroke patients for the detection of arrhythmias?”

When a participant returns their PulseOn device, the trial’s qualitative research and mixed-methods data integration specialist will consult with the health care professionals responsible for that participant’s standard care. The specialist will ask the above question and record the response directly into the master Excel database.

9.4.1 Secondary outcome analysis

The secondary objectives are baseline demographic data analysis using quantitative data, to measure how many AF episodes are detected by the PulseON device and how this differs from the number detected through standard care, and to evaluate how well the PulseON device detects AF and how this differs from standard care. All comparisons will be based on direct numerical result.

10. DATA MANAGEMENT

10.1 Data collection tools, source document identification, data handling and record keeping

Trial data will be collected via Microsoft forms and questionnaire responses, completed by assigned members of the study team (PI, research nurses and the Qualitative research and mixed methods data integration specialist) and the participant, respectively. This information is then inputted into the master excel database stored on secure hospital computers.

Participants will provide feedback on the trial assessment themes described in Section 7.5 at two scheduled follow-up time points:

- Follow-Up 1**:** Participants complete an online Microsoft Forms questionnaire using questions from the “PulseON Usability Questions_Baseline” document. A secure, unique link is emailed to each participant (using the emails collected from them during the collection of baseline data) and their responses are automatically entered into the MS Forms excel database. A member of the study team (PI or research nurse) will then transfer this data into the master excel database.

- Follow-Up 2: Participants take part in recorded follow-up interviews conducted by a qualitative research specialist, using questions from the “PulseON Usability Questions_Interview” document. Interview recordings will be transcribed and the resulting data will be added to the master excel database by the PI or a research nurse

10.2 Access to Data

Only the local the clinical care team and authorised research staff based at the Trust (e.g. PI, delegated research nurses) will have to data held by the project. This data be stored within secure NHS-managed and approved secure systems; including secure network drives, the MS forms and a locked physical storage for paper documents.

Direct access will be granted to authorised representatives from the Sponsor and the regulatory authorities to permit trial-related monitoring, audits, and inspections to ensure the project is in line with participant consent. The anonymised case-studies produced from the trial will be promoted by Health Innovation West Midlands to encourage adoption of the PulseON device into practice if it proves a viable option when compared to standard care. The publication of a project protocol, results and data will be in line with UHCW SOPs.

10.3 Archiving

Essential study documents will be archived for 10 years following the end of the project aligning with the Trusts Standard Operating Procedures. A facility for the storage of records is available within the UHCW Restore contract for Health Record Services. All documents will be stored at box level, and it is the responsibility of the R&D Department to ensure that these are indexed and filed correctly on the boxes, providing document identification, version history, search, and retrieval.

11 TRIAL OVERSIGHT

11.1 Role and responsibilities of the Sponsor

UHCW has agreed to act as sponsor for this trial and will undertake the responsibilities of sponsor as defined by the UK Policy Framework for Health and Social Care Research and ICH Good Clinical Practice. An authorised representative of the Sponsor has approved the final version of this protocol with respect to the trial design, conduct, data analysis and interpretation and plans for publication and dissemination of results. As sponsor, UHCW provides indemnity for this trial and, as such, will be responsible for claims for any negligent harm suffered by anyone as a result of participating in this trial. The indemnity is renewed on an annual basis and will continue for the duration of this trial.

11.2 Role and responsibilities of the Funder

Funding for this trial is provided by West Midlands Health Innovation. The design and management of this trial are entirely independent of the funder

The funding has been obtained to cover all aspects of the trial, including:

- Study setup and conduct
- Regulatory submissions
- Insurance and indemnity
- Data management and analysis
- Reporting and dissemination
- Oversight and Governance by ensuring the study has:
- A qualified sponsor in place
- Appropriate ethical and regulatory approvals
- A clear governance structure
- Regular reporting processes
- Defining Intellectual Property (IP) and Data Rights for
- Study data
- Results and publications
- Any IP generated during the trial

Trial Management Arrangements

11.3 Trial Steering Committee

The role of the Crypto-PulseOn Trial Steering Committee is to provide overall oversight of the project, unblocking any issues that might arise and supporting the implementation of its work packages. Through this oversight, the Pulse-On SC will ensure the delivery of the aims and objectives of the Pulse-On project. The Pulse-On SC will:

- Ensure the Pulse-On Chief Investigator is held accountable for the delivery of the project.
- Review emerging risks and recommend the appropriate actions to mitigate their impact on the project.
- Monitor compliance with Pulse-On Service Level Agreement, Project Plan and timelines.
- Provide assurance to the Health Innovation West Midlands (HIWM) about the activities and progress of the Pulse-On Project, including completion within the agreed timescale
- Provide oversight of the financial arrangements for the Project
- Defining the future direction of the project by reviewing the progress reports, as submitted by the Pulse-On Project Manager.
- Provide strategic planning to accelerate the adoption of the PulseOn arrhythmia monitoring solution for the benefit of patients
- Identifying and exploiting opportunities that could benefit the project
- Be accountable to University Hospitals Coventry and Warwickshire NHS Trust (UHCW), as lead institution and project sponsor

The Steering Committee is made up of the following individuals that the Chair/Deputy Chair have nominated the organisation holding the grant funding; along with representatives from Health Innovation West Midlands, PulseOn Oy and lay members:

Name	Affiliation	Role
Gio Bucci	UHCW	Chairperson
Andrew White	UHCW	Deputy Chairperson, Pulse-On administrator & Pulse-On Project Manager
Faizel Osman	UHCW	Pulse-On Chief Investigator
Ven Gee Lim	UHCW	Pulse-On Principle Investigator
Jari Kaija	PulseON Oy	PulseON Oy representative
Blair Elliott	Health Innovation West Midlands	Health Innovation West Midlands representative

Sabeel Sajid	Health Innovation West Midlands	Health Innovation West Midlands representative
Usman Ghani	UHCW	Stroke Service Lead
Helen Eftekhari	UHCW	Lead Arrhythmia Nurse
Crispin Musicha	UHCW	R&D Medical Statistician
Karen Keates	UHCW	PPI Representative
Angela Flynn	UHCW	PPI Representative

11.4 Trial Co-ordinator / Manager

The Trial Co-ordinator / Manager will have responsibility for overseeing day to day coordination of the trial and reporting regularly to the TSC. The Trial Manager's responsibilities include, but are not limited to:

- Coordinating protocol development, patient and trial management documents
- Correspondence with study funder and tracking of progress against agreed milestones
- Setting up and maintaining the Trial Master File;
- Ensuring necessary approvals are in place before the start of the trial at each site;
- Providing training to trial personnel;
- Providing data management support; including data input, maintenance of the trial database and raising of queries
- Producing trial progress reports and coordinating TSC meetings and minutes;
- Ensuring data security and quality and ensuring data protection laws are adhered to;
- Ensuring complete records are in place for audit and monitoring purposes;
- Ensuring the trial is conducted in accordance with the ICH GCP;
- Archiving all original trial documents including the data forms in line with UHCW NHS Trust policy

12 MONITORING, AUDIT & INSPECTION

Monitoring for research studies will be conducted by the Research & Development Department at UHCW aligning with the Trusts SOPs.

The R&D Office will be responsible for performing a risk-based monitoring assessment to determine level of risk and whether a monitoring plan is required. For studies requiring a monitoring plan the R&D Office will determine the appropriate level, frequency, and target areas of monitoring activity, where the Trust acts as Sponsor.

The study will be monitored by the Research & Development Department at UHCW as representatives of the Sponsor, to ensure that the study is being conducted as per protocol, adhering to Research Governance and GCP.

13. ETHICAL AND REGULATORY CONSIDERATIONS

13.1 Ethical approval and research governance

The study will be conducted in compliance with the principles of the ICH GCP guidelines and in accordance with all applicable regulatory guidance, including, but not limited to, the UK policy framework for health and social care research. Ethical approval for this study will be sought from the Research Ethics Committee combined with Health Research Authority (HRA) approval. No study activities will commence until favourable ethical opinion and HRA, has been obtained. A final report at the conclusion of the trial will be submitted to the approving REC within the timelines defined by the committee. Confirmation of capacity and capability will be obtained from the R&D department prior to commencement of the study and sponsor will provide greenlight once all final checks have been completed.

13.2 Peer review

A peer review of this study was conducted by Dr. Kim Rajappan. an independent cardiology researcher widely recognised as a leader in his field. Dr. Rajappan (a Consultant Cardiologist & Electrophysiologist in the Cardiac Department at the John Radcliffe Hospital), reviewed several critical aspects of the proposed study and offered feedback that was instrumental in shaping it, ensuring it's methodological rigor and alignment with best practices.

13.3 Public and Patient Involvement

We presented our proposed project using PulseON to our patient and public involvement group at UHCW. This was a virtual workshop attended by both patients and patient carers, who had experience of cryptogenic stroke/TIA.

The meeting was also attended by two members of the PulseON company (PulseON Oy), who were able to provide technical details about the device.

The meeting was very helpful and important feedback provided on the development of the proposed project provided by the patient group. Specifically, members of the group were interested in costs associated with the PulseON device and its potential healthcare associated cost-savings longer-term for the NHS. It was confirmed to the group that the device would be provided free of charge by the company for this project and there would be no charge to the NHS. The ILR costs the same regardless of how long it takes to diagnose AF and is not reusable.

As a result of the feedback the PulseON device would only be used until AF was diagnosed. It would then be returned to the hospital for use on another patient. Various aspects of device functionality were discussed and clarified. At the end of the meeting members of the group expressed their support for the proposed project, commenting it appeared to be a 'good idea', 'quite simple and straightforward' and 'worthwhile evaluating its capability if it's going to prevent stroke and medical problems for people.' Group members confirmed they would like to see the project progress and could not see any immediate problems. Please see attached for detail comments from the meeting and reviewers.

Our UHCW PPI group consisted of 6 people who attended a meeting in Sept 2025.

Two were carers of people who had experienced stroke, 4 were stroke patients.

We did not collect demographic data at that meeting as this is not mandated for any of our PPI group meetings. From this meeting there were 3 men, 3 women; 4 were white and 2 were from ethnic minority backgrounds. A further PPI group review was undertaken by 9 members.

We have embedded PPI at multipole levels across the project, including being on the SC and being part of the focus group that has been shaping the project documents.

13.4 Regulatory Compliance

- The trial will not commence until approval from the HRA and REC has been obtained. Please note that the PulseON device is CE-Marked and is being used within its intended purpose, so does not require additional MHRA approvals.
- The study will comply with Good Clinical Practice (GCP) and Medical Device Regulations for safety monitoring and reporting

13.5 Protocol compliance

The trial will hold the following approach to ensure protocol compliance:

- Prospective, planned deviations or waivers to the protocol will not be used
- Accidental protocol deviations will be adequately documented on the relevant forms and reported to the Chief Investigator and Sponsor immediately.
- Deviations will be escalated to the Trial Steering Committee, who will take action if a pattern of deviations occur

13.6 Notification of Serious Breaches to GCP and/or the protocol

Any breach, i.e. a deviation from the approved study protocol, will be reported to sponsor and documented.

Reporting responsibilities:

- Chief Investigator (CI): Ultimately responsible for identifying and reporting breaches.
- Principal Investigator (PI): Must report breaches at their site to the CI.
- Sponsor: Must assess and, if necessary, report serious breaches to the MHRA and REC.

Timeframes:

- Potential Serious Breaches: Must be reported to the Sponsor within 24 hours of awareness by the CI or PI
- Sponsor's Role: The sponsor must assess the breach and, if deemed serious, report it to the appropriate parties within 7 calendar days of confirmation

13.7 Data protection and patient confidentiality

The study will be conducted in accordance with UK data protection legislation, including the UK GDPR and the Data Protection Act 2018. The Sponsor and participating NHS organisation(s) are responsible for ensuring that personal data are handled lawfully, fairly and securely throughout the project. Appropriate organisational and technical measures will be in place, and the study may be monitored by authorised individuals to check that it is being carried out correctly and safely in line with the approved protocol and relevant policies.

When a participant joins the study, they will be assigned a unique study number. This number will be used in place of their name or other direct identifiers wherever possible so that information used for research purposes is pseudonymised. Only members of the direct clinical care team and authorised members of the study team who require access to identifiable data to carry out their role will be able to see information that could directly identify participants. In some circumstances, regulatory authorities or the NHS organisation responsible for the study may review identifiable information to ensure the study is being conducted properly, but they will not use the information for any purpose unrelated to the study.

All personal data will be stored securely. Electronic information will be kept on password protected, encrypted systems approved for NHS research use. Paper documents containing personal data will be stored in locked cabinets within secure access-controlled areas. Access to all information will be strictly limited to individuals who need it to fulfil their study related responsibilities

14. DISSEMINATION

The dissemination of study findings will include the following activities:

- Publications in peer reviewed scientific journals
- Conference presentation
- Website publications
- Publication of case studies (based on the lived experiences of each participant) developed in collaboration with the funder
- A summary of the project's findings will be provided to all participants

15. REFERENCES

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1. APPENDIX 1

Solution – PulseON

A tool for doctors

Not a smartwatch



Suitable for all ages and skills

No need for patient learning, no disturbance of daily life

- Beat-to-beat accurate optical heart-rate technology enables 24/7 detection and monitoring of arrhythmias, e.g. atrial fibrillation (AF)
- Detects even asymptomatic and very short (30 sec) arrhythmia episodes
- Notifies the patient to take an instant ECG measurement with the same device
- Long-time monitoring, can be used for weeks or months



Very cost-efficient solution

Time-savings of medical personnel labor