**SMARTS- project**

**Smartphone Atrial fibrillation testing post stroke**

Version 1.0

06/04/2021

MAIN SPONSOR: Chelsea and Westminster NHS Foundation Trust

FUNDERS: CW+ Charity (Chelsea and Westminster NHS Foundation Trust)

STUDY COORDINATION CENTRE: West Middlesex University Hospital

IRAS Project ID: 299122

REC reference: xxx

**Protocol authorised by:**

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| --- | --- | --- |
| **Name & Role** | **Date** | **Signature** |
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**This protocol has regard for the HRA guidance.**

# SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor’s SOPs, and other regulatory requirement.

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 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 and breaches of GCP from the study as planned in this protocol will be explained.

|  |  |  |
| --- | --- | --- |
| **For and on behalf of the Study Sponsor:** | | |
| Signature:  ...................................................................................................... |  | Date: ....../....../...... |
| Name (please print):  ...................................................................................................... |  |  |
| Position: ...................................................................................................... |  |  |
| **Chief Investigator:** | | |
| Signature: ...................................................................................................... |  | Date: ....../....../...... |
| Name: (please print):  ...................................................................................................... |  |  |

**Study Management Group**

Chief Investigator: Dr Sadia Khan

Co-investigators: Dr Pavidra Sivanandarajah, Dr Fu Siong Ng , Dr Ravneeta Singh

**Study Coordination Centre**

For general queries, supply of study documentation, and collection of data, please contact:

Study Coordinator: Dr Pavidra Sivanandarajah

Address: West Middlesex Hospital, Twickenham Road, Isleworth, TW7 6AF

**Registration:**

Tel:

E-mail: pavidra.sivanandarajah1@nhs.net

Fax:

Web address:

**Clinical Queries**

Clinical queries should be directed to Dr Sadia Khan who will direct the query to the appropriate person.

**Sponsor**

Chelsea and Westminster NHS Foundation Trust is the main research Sponsor for this study.

For further information regarding the sponsorship conditions, please contact:

Chelsea and Westminster Hospital NHS Foundation Trust  
Research & Development Office  
Unit G2, Harbour Yard  
Chelsea Harbour  
London  
SW10 0XD

**Telephone number:** 020 3315 6825  
**Email:** [research.development@chelwest.nhs.uk](mailto:research.development@chelwest.nhs.uk)

**Funder**

CW+ Charity (Chelsea and Westminster NHS Trust) are funding this study.

This protocol describes the SMARTS project and provides information about procedures for entering participants. Every care was taken in its drafting, but corrections or amendments may be necessary. These will be circulated to investigators in the study. Problems relating to this study should be referred, in the first instance, to the Principal Investigator.

This study will adhere to the principles outlined in the UK Policy Framework for Health and Social Care Research It will be conducted in compliance with the protocol, Data Protection Act 2018, and General Data Protection Regulations (Europe) and other regulatory requirements as appropriate.

**Keywords**

# Atrial fibrillation, Screening, Cryptogenic Stroke

**LIST OF ABBREVIATIONS**

**Define all unusual or ‘technical’ terms related to the trial. Add or delete as appropriate to your trial. Maintain alphabetical order for ease of reference.**

**AE Adverse Event**

**AF Atrial fibrillation**

**AR Adverse Reaction**

**CI Chief Investigator**

**ECG Electrocardiogram**

**GCP Good Clinical Practice**

**ICF Informed Consent Form**

**ISRCTN International Standard Randomised Controlled Trials Number**

**NHS R&D National Health Service Research & Development**

**PI Principal Investigator**

**PIC Participant Identification Centre**

**PIS Participant Information Sheet**

**PPG Photoplethysmography**

**QA Quality Assurance**

**QC Quality Control**

**QP Qualified Person**

**REC Research Ethics Committee**

**SAE Serious Adverse Event**

**SAR Serious Adverse Reaction**

**SDV Source Data Verification**

**SOP Standard Operating Procedure**

**SSI Site Specific Information**

**SUSAR Suspected Unexpected Serious Adverse Reaction**

**Study Summary**

|  |  |
| --- | --- |
| **TITLE** | SMARTS- project: Smartphone atrial fibrillation screening post stroke |
| **DESIGN** | Prospective observational study |
| **AIMS** | To evaluate the benefit of Fibricheck in atrial fibrillation screening of post stroke patients  To evaluate the patient experience and satisfaction of usage of the Fibricheck App |
| **OUTCOME MEASURES** | Detection of AF  Diagnostic yield of Fibricheck for AF detection  Patient satisfaction |
| **POPULATION** | Patients who have had a stroke in last 6 months with a diagnosis of AF |
| **SAMPLE SIZE** | ~ 50-70 post stroke patients |
| **ELIGIBILITY** | **Inclusion criteria**  Aged 18 years old or above  Had a cryptogenic stroke within the last 6 months  Able to provide verbal or signed written informed consent  Access to smartphone  **Exclusion criteria**  Have already a diagnosis of atrial fibrillation prior to study enrolment  Unable to provide verbal or signed written informed consent  Below the age of 18 years old  Presence of cardiac electronic implantable device |
| **duration** | 1 year |

# STUDY FLOW CHART

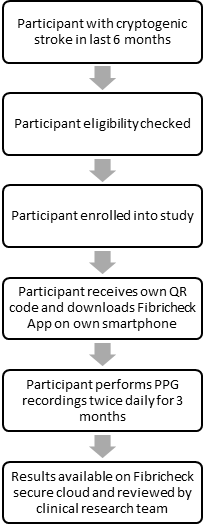
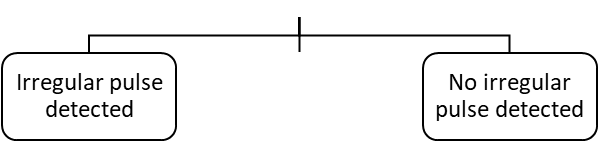
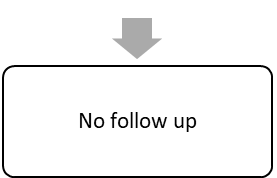
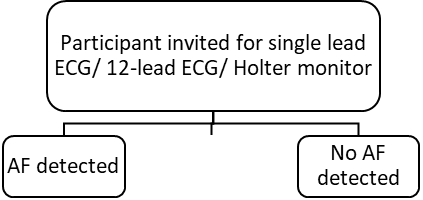
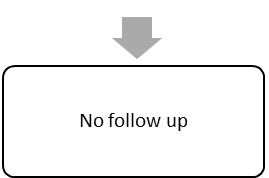
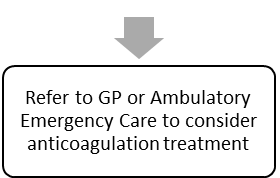


Figure 1: Study flow chart- SMARTS- project

1. **INTRODUCTION**

Atrial fibrillation (AF) is the most common heart rhythm disturbance (arrhythmia). Individuals with atrial fibrillation have a five-fold increased risk of developing strokes. AF can be persistent or paroxysmal (intermittent). People with AF can be unaware that they have the condition as they may not display any symptoms. This results in many people presenting with AF at the time they present to hospital with a stroke. Strokes are debilitating, cause significant permanent disability and are a burden to the healthcare system.

Many patients with undiagnosed AF present to hospital with a stroke. The AF can remain undiagnosed due to paroxysmal nature of the rhythm and the patient being asymptomatic. AF has been shown to account for up to 25% of ischaemic stroke patients presenting to hospital. People who have AF related strokes are at risk of further strokes without treatment for the AF in the form of a blood thinner (known as anticoagulation). Appropriate anticoagulation can reduce risk of a further stroke by 64% and mortality by 25%.

In an ideal world, we would want to monitor patients with electrocardiograms (ECGs) continuously to detect AF, but this requires invasive treatment. As more people have smartphones and smartwatches, this provides us with opportunities to monitor patients for longer and more frequently and ultimately, diagnose AF earlier. We propose to use a CE marked smart phone App (Fibricheck) that uses photoplethysmography, which measures pulse pressure signals from blood pressure pulses travelling along arterial blood vessels. It therefore can discern irregularities in pulse pressure signals that would be present as result of AF.

This App has been validated in previous studies for the detection of AF. The App is supported by almost all smartphones and has cross platform compatibility. It is easy to use for both patients and clinicians. It is non-invasive.

The ability of this App to detect AF in post stroke patients will be analysed. Patient experience and satisfaction with using this App will also be assessed.

1. **STUDY OBJECTIVES**

**AIMS**

1) To evaluate the benefit of Fibricheck in atrial fibrillation screening of post stroke patients

2) To evaluate the patient experience and satisfaction of usage of the Fibricheck App

1. **STUDY DESIGN**

This will be 1 year study in which participants will be recruited prospectively from secondary care. Participants will be identified as those who have a cryptogenic stroke in the last 6 months without a diagnosis of AF. They will be recruited from the stroke ward or stroke clinics.

Participants will be given the Fibricheck App and shown how to use the App. They will be asked to perform twice daily recordings lasting 1 minute each using the camera light of their smartphone. If they have symptoms, they can also make further recordings. The recordings will be performed over a period of 3 months.

If an irregular pulse is identified from one of the recordings, the participant will be invited to have a single lead ECG, 12-lead ECG or a Holter monitor. If AF is detected following this, the participant will be referred to their general practice or through the ambulatory emergency care for review of suitability to start anticoagulation via existing clinical pathways.

An electronic participant questionnaire will be sent to participants to review patient experience and satisfaction with using the App.

Participation in this study will be entirely voluntary and will not affect participants’ current or future care. Participants will be free to withdraw from the study at any time without having to provide a reason. Participants will be recruited prospectively from stroke ward and stroke clinic, on a first-come first-serve basis, to minimise bias. Recruitment will continue throughout the study.

Data collected from participants prior to drop out or loss to follow-up will be included in the data analysis. We are not aware of any ongoing studies that are competing for the same group of participants or whose results may affect recruitment. Similarly, our study will not jeopardise other studies either.

**3.1 STUDY OUTCOME MEASURES**

The primary endpoint will be the detection of atrial fibrillation with a one-off ECG. The diagnostic yield of the Fibricheck will be analysed.

The secondary analysis will involve assessing patient experience and satisfaction with using the Fibricheck App.

**4. PARTICIPANT ELIGIBILITY CRITERIA**

Prospective participants will only be recruited from stroke wards and stroke clinics. They will need to fulfil the inclusion criteria to enrol into the study.

**4.1 INCLUSION CRITERIA**

To take part in the study, participants must meet all the following requirements:

1. Aged 18 years old and above
2. Had a cryptogenic stroke within the last 6 months
3. Able to provide verbal and signed written informed consent
4. Access to a smartphone

Definition of Cryptogenic stroke: brain infarction not attributable to definite cardioembolism, large artery atherosclerosis or small artery disease despite extensive vascular, cardiac, and serologic evaluation (stroke of unknown cause according to TOAST criteria).

The stroke diagnosis will have to made from stroke physician or neurologist following brain and neurovascular imaging.

**4.2 EXCLUSION CRITERIA**

Participants with any of the following will not be able to take part in the study:

1. Have already a diagnosis of atrial fibrillation prior to study enrolment
2. Unable to provide verbal or signed written informed consent
3. Below the age of 18 years old
4. Presence of cardiac electronic implantable device

**4.3 WITHDRAWAL CRITERIA**

Participants will be withdrawn from the study if they fulfil one of the following:

1. Unable to use their screening App
2. Withdrawal of consent
3. Presence of cardiac electronic implantable device

**5. ADVERSE EVENTS**

**5.1 DEFINITIONS**

**Adverse Event (AE):** any untoward medical occurrence in a patient or clinical study subject.

**Serious Adverse Event** **(SAE):** any untoward and unexpected medical occurrence or effect that:

* **Results in death**
* **Is life-threatening** – *refers to an event in which the subject 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.*
* **Requires hospitalisation, or prolongation of existing inpatients’ hospitalisation**
* **Results in persistent or significant disability or incapacity**
* **Is a congenital anomaly or birth defect**

Medical judgement should be exercised in deciding whether an AE is serious in other situations. Important AEs that are not immediately life-threatening or do not result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, should also be considered serious.

**5.2 REPORTING PROCEDURES**

All serious & non serious adverse effects, whether expected or not, will be recorded. Depending on the nature of the event the reporting procedures below will be followed. Any questions concerning adverse event reporting will be directed to the Chief Investigator in the first instance.

**Non serious AEs**

All such events, whether expected or not, will be recorded.

**Serious AEs**

An SAE form will be completed and faxed to the Chief Investigator within 24 hours. However, relapse and death due to any pre-existing medical or surgical conditions and hospitalisations for elective treatment of a pre-existing conditions will not be reported as SAEs.

All SAEs will be reported to the \*\*\*\* REC where in the opinion of the Chief Investigator, the event was:

* ‘related’, i.e., resulted from the administration of any of the research procedures; and
* ‘unexpected’, i.e., an event that is not listed in the protocol as an expected occurrence

The Chief Investigator will inform the sponsor of the study of all SAEs. Reports of related and unexpected SAEs will be submitted within 15 days of the Chief Investigator becoming aware of the event.

Local investigators will report any SAEs as required by their Local Research Ethics Committee and/or Research & Development Office.

**Contact details for reporting SAEs.**

**CI email (Dr Sadia Khan; sadia.khan@chelwest.nhs.uk)**

**6. ASSESSMENT AND FOLLOW-UP**

Upon enrolment to the study, the participant will be provided with a QR code to scan for the prescription of 3- month monitoring period. The participant will need to download the Fibricheck App on their own smartphone from the App store. They will then need to scan the QR code with the Fibricheck App. The participant will then be able to start making recordings by placing their finger on the camera for 1 minute. Figure 1 demonstrates how to set the Fibricheck App on a smartphone and Figure 2 shows how to take a recording with the App.



**Figure 1: How to set up Fibricheck App on smartphone**

**Figure 2: How to take a recording using the Fibricheck App**



As mentioned earlier, participants will be asked to perform twice daily recordings lasting 1 minute each using the camera light of their smartphone. If they have symptoms, they can also make further recordings. They will also be able to annotate the recording afterwards with their symptoms. The recordings will be performed over a period of 3 months. Following each recording, feedback will be given. The recordings will be sent to Fibricheck’s secure cloud. Irregular results will be reviewed by Fibricheck’s monitoring center under the supervision of cardiologists. The clinical research team will have access to all participant’s data via the physician dashboard. They will regularly review the data on a weekly basis and will inform the participant if irregular results are seen which warrant further management.

An electronic participant questionnaire will be sent one month after using the App and 3 months after to explore patient experience and satisfaction.

The end of the study will be defined as last follow-up required for the purposes of the study.

Data and all appropriate documentation will be stored for a minimum of 10 years after the completion of the study, including the follow-up period.

**7. REGULATORY ISSUES**

**7.1 ETHICS APPROVAL**

**The Study Coordination Centre has obtained approval from \*\*\* Research Ethics Committee (REC) and Health Research Authority (HRA).**

The study has obtained confirmation of capacity and capability from Chelsea and Westminster NHS Foundation Trust to accept participants into the study for the purposes of research.

This study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964, and later revisions.

**7.2 CONSENT**

A member of the stroke team or the clinical research team will approach prospective participants to offer participation in the study.

Consent to enter the study will be sought from each participant only after a full explanation has been given, an information leaflet (patient information sheet) offered, and time allowed for consideration. Signed written and verbal informed consent will be obtained from every participant at the beginning of the study at the point of enrolment. Participants’ suitability to partake will be checked prior to enrolment, according to inclusion and exclusion criteria. The right of the participant to refuse to participate or withdraw from the study at any point without giving reasons will be always respected.

After the participant has entered the study, their stroke or general practice clinician(s) remain free to give an alternative treatment or monitoring to that specified at the start of the research study, at any stage if they feel it is in the participant’s best interest. The reasons for doing so will be recorded. In these cases, the participants can remain within the study for the purposes of data collection, follow-up, and data analysis if they wish.

All participants are free to withdraw at any time from the study without giving reasons and without prejudicing current, further, or future treatment.

**7.3 CONFIDENTIALITY**

The Chief Investigator will preserve the confidentiality of participants taking part in the study and is registered under the Data Protection Act.

All participants will have an anonymous identifier that will be generated by the research team during the recruitment process. Participants will be entered into a study database which will contain all research records. This database can be accessed at the West Middlesex University Hospital. It will be password protected and will have restricted access to specific members of the research team only. Anonymised data will be available to researchers. Similarly, during the study, all medical history, ECG recordings, PPG recordings, Holter monitor recordings and any other clinical data for the study will be stored in an anonymised format and securely on a password protected study database at West Middlesex University Hospital. This will also only be accessible by the research team.

Chelsea and Westminster NHS Foundation Trust retention schedule states that all study data should be retained for 10 years after completion of the study. This will include some identifiable data such as consent forms and will be stored in a secure Chelsea and Westminster NHS Foundation Trust archiving facility, in-line with institutional policy. All other personal data, such as contact details that will be kept securely during the study, will be irretrievably deleted, and disposed at the end of the study.

Fully anonymised data from the database may be shared with approved research collaborators, if required during the course of the study.

In the event that a research participant loses capacity to consent during the study, their identifiable samples and data will be withdrawn from the study. Any samples or data that is not identifiable may be retained and used for the purpose of which they consented to.

**7.4 INDEMNITY**

Chelsea and Westminster NHS Foundation Trust holds standard NHS Hospital Indemnity and insurance cover with NHS Litigation Authority for NHS Trusts in England, which apply to this study.

**7.5 SPONSOR**

Chelsea and Westminster NHS Foundation Trust will act as the main Sponsor for this study.

**7.6 FUNDING**

CW+ Charity **(**Chelsea and Westminster NHS Foundation Trust) are funding this study.

**7.7 AUDITS AND INSPECTION**

The study may be subject to inspection and audit by Chelsea and Westminster NHS Foundation Trust under their remit as sponsor and other regulatory bodies to ensure adherence to GCP and the UK Policy Framework for Health and Social Care Research.

**8. STUDY MANAGEMENT**

The day-to-day management of the study will be co-ordinated through the research team and clinical research fellow (Dr Pavidra Sivanandarajah) with overview from the chief investigator (Dr Sadia Khan).

**9. PUBLICATION POLICY**

All publications and data-sharing will be in accordance with the current guidance provided by Chelsea and Westminster NHS Foundation Trust.