Evaluation of Huawei Smartwear for Detection of Atrial Fibrillation in a Post-Stroke Population: The Huawei Stroke Study

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Table of Contents

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Abbreviations and definitions

AF	Atrial Fibrillation
ARIC	Atherosclerosis Risk in Communities
C_2HEST	Coronary Artery Disease or COPD, Hypertension, Elderly, Systolic Heart Failure, and Thyroid Disease - Risk Score
CHARGE-AF	Cohorts for Heart and Aging Research in Genomic Epidemiology-AF Risk Score
CRF	Case Report Form
CRN	Clinical Research Network
COPD	Chronic Obstructive Pulmonary Disease
DARS	Data Access Request Service
ECG	Electrocardiogram
EHRA	European Heart Rhythm Association
ESUS	Embolic Stroke of Undetermined Source
EQ-5D-5L	EuroQol-5 Dimension-5 Levels Health-related quality of life scale
GAD-7	General Anxiety Disorder-7
HATCH	Hypertension, Age, TIA or Stroke, COPD, and Heart Failure – Risk Score
HAVOC	Hypertension, Age, Valvular Heart Disease, Peripheral Vascular Disease, Obesity, Congestive Heart Failure, and Coronary Artery Disease - Risk Score
HES	Hospital Episode statistics
LCCS	Liverpool Centre for Cardiovascular Science
MoCA	Montreal Cognitive Assessment
NHS	National Health Service
ONS	Office for National Statistics
PAF	Paroxysmal Atrial Fibrillation
PHQ-9	Patient Health Questionnaire
PPG	Photoplethysmography
PPI	Patient and Public Involvement
PPV	Positive Predictive Value
REDCap	Research Electronic Data Capture
SEFT	Secure Electronic File Transfer
TIA	Transient Ischaemic Attack

Summary

The Huawei Stroke Study aims to determine the clinical effectiveness, cost effectiveness, and acceptability of Huawei Smartwear to detect atrial fibrillation (AF) in patients following an acute ischaemic stroke.

Background and study rationale

Patients admitted with an acute ischaemic stroke are at high-risk of incident adverse cardiovascular outcomes including heart failure, recurrent stroke, and vascular cognitive impairment and dementia[1-3]. AF is the most common heart rhythm disorder, which increases the risk of stroke 5-fold[4]. Alarmingly, an AF-related stroke is associated with greater mortality and morbidity, longer stays in hospital and lower rates of discharge compared to non-AF stroke[5]. Furthermore, clinically diagnosed AF after a stroke and transient ischaemic attack (TIA) is associated with a significantly increased risk of future stroke or systemic embolism, particularly in the presence of additional stroke risk factors[6]. AF often underlies cardioembolic strokes, however paroxysmal AF (PAF) and asymptomatic AF episodes often occur remotely to the stroke/thromboembolic event[7].

Approximately 40% of ischaemic strokes are classified as Embolic Stroke of Undetermined Source (ESUS), with no apparent cause identified following routine clinical or short-term 12-lead electrocardiogram (ECG) evaluation, inpatient monitoring, or 24-hour Holter monitor[8]. Documented AF is required to initiate thromboprophylaxis with oral anticoagulation for secondary stroke prevention, which has proven benefit in reducing recurrent stroke and mortality in AF patients[9]. Although prolonged ECG monitoring is recommended in cases of suspected ESUS, there is currently no consensus on the recommended duration, nor data on patient acceptability or cost effectiveness of this approach.

In general, AF detection is more likely if we *"look longer, look harder and look with more sophisticated methods…."*[10]. Continuous bedside ECG-monitoring during stroke unit admission for 3 days detects AF in approximately 7%, which is higher than 24-hour Holter monitoring, but less suited for ambulant patients with TIA[10-12]. More sophisticated systems have higher detection rates of PAF, but devices such as event-triggered loop recorders are inconvenient, and implantable loop recorders are expensive and require surgical implantation[10-12]. Given AF is prevalent in nearly a quarter of post-stroke patients[13], recent advances in AF-specific mobile health[14], and an increasing variety of AF screening options[6], now is an opportune time to improve AF detection, alleviate patient burden, and reduce

healthcare costs. Indeed, a non-invasive, clinically effective, cost-effective, and patient-acceptable, long-duration ECG-monitoring system post-acute stroke is needed.

Detection of AF post-stroke is critical to initiate appropriate monitoring and treatment to reduce risk of recurrent stroke. Treatment of AF can be guided through the use of the Atrial Fibrillation Better Care (ABC) pathway to A: Avoid strokes with anticoagulants, B: Better symptom management with person-centred decisions of rate and rhythm control and C: Cardiovascular and co-morbidity management[9, 15]. Adherence to the ABC pathway has been associated with fewer major events in patients with AF including patients with multiple comorbidities, polypharmacy, and prior hospitalisation[16].

Photoplethysmography (PPG) involves optically measuring changes in tissue blood volume through the skin. The majority of smart watches and bands measure heart rate with PPG technology, and as such, there are potential benefits of widespread adoption, with easily accessible and user-friendly technology to screen for AF[17]. The Huawei Heart Study monitored over 187,000 people aged 18 years and older in China for suspected AF using PPG signals via Huawei smart watches. The Huawei Heart Study used 14-day monitoring for AF, but the mean age of the participants was only 35 years, therefore, the detection of suspected AF was low (0.23%). Of the participants with suspected AF, 62% were followed-up and compared to clinical evaluation, ECG or 24-hour Holter and the PPG signals had a positive predictive value (PPV) of 91.6% (95% confidence interval (CI) 91.5%-91.8%)[18]. The prevalence and incidence of AF post-stroke has been estimated at 24%[13], therefore, the detection of AF using the Huawei Smart band in the Huawei Stroke Study is expected to be higher than that in the previous Huawei Heart Study.

Several risk prediction models for AF have been developed. These include the C_2HEST risk score,[19, 20] the Atherosclerosis Risk in Communities (ARIC) score,[21] the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE)-AF score,[22] the Framingham Heart Study,[23] the HAVOC[24] and the HATCH[25] scores. Some models include demographic factors and details of cardiovascular disease history only and other models incorporate details of structural changes to the heart. Relatively little research has been conducted to examine risk of AF in post-stroke populations. The C_2HEST score has been shown to perform well in discriminating risk of incident AF in people post-stroke (C index 0.734) and performed significantly better than the Framingham risk score (C index 0.720).[26] The HAVOC score has also shown good discrimination for AF in a population following cryptogenic stroke or TIA.[24] Though, difficulties have been identified in defining cryptogenic stroke[27]. Currently, no single model to stratify people by risk of AF can be recommended for use in clinical practice for people post-stroke. Further research is needed to determine an optimal model that is feasible to use as part of patient-care pathways. Therefore, in this study we will also examine clinical predictors for incident and prevalent AF post-stroke and compare the accuracy of previous risk prediction models for AF in a post-stroke population.

The city of Liverpool in northwest England is a region of comparatively high social deprivation[28] and high levels of cardiovascular disease and stroke. Despite declining deaths attributable to cardiovascular disease, cardiovascular disease and stroke accounts for 20% of all deaths in Liverpool[29]. Compared to the averages for England, the city of Liverpool has higher hospital admissions and higher early mortality rates for cardiovascular conditions and stroke[30]. It is estimated that the Liverpool population of those aged 60 years will increase by 17% from 2017 to 2027[29]. This is particularly important, given the prevalence of AF increases from 2% up to 20% with advancing age[31].

The Liverpool Centre for Cardiovascular Science (LCCS) was established in collaboration with Liverpool Heart and Chest Hospital, Liverpool John Moore's University, Liverpool Health Partners, and the University of Liverpool to address the issue of high cardiovascular disease prevalence within the Liverpool region. The present protocol for the Huawei Stroke Study will focus specifically on identification of AF for people post-stroke using smart wearable technology. Ultimately, the aim is to improve detection of AF to initiate earlier treatment and reduce risk of recurrent stroke in populations post-stroke.

Study details

Aims and objectives

The overarching aim is to conduct a prospective evaluation of Huawei Smartwear to detect prevalent and incident AF in a post-stroke population. The specific objectives are to:

1. Determine **clinical effectiveness** by assessing the accuracy of a Huawei smart band to detect prevalent and incident AF in a post-stroke population.
2. Identify **clinical predictors** of prevalent and incident AF in a post-stroke population and determine the accuracy of risk prediction models for AF in a post-stroke population.
3. Identify **clinical predictors** of other important outcomes in a post-stroke population, such as recurrent stroke, mortality and cognitive impairment.
4. Determine **cost effectiveness** via an economic evaluation of screening procedures with a Huawei smart band.
5. Determine **patient and staff acceptability** of screening procedures through embedded process evaluation.

Study design

Detection of AF with Huawei Smartwear provided to all participants. The study does not fall under the device study regulations and will not be used to achieve CE marking. This is a preliminary, proof-of-concept study and the device will not be used to diagnose AF or influence device manufacture in the future.

Inclusion and exclusion criteria

In order to facilitate inclusion of people who are often excluded from clinical studies, we will keep the inclusion criteria broad and exclusions to a minimum. By collecting comprehensive patient data, we will be able to stratify groups by key characteristics.

Inclusion criteria

- ≥18 years old;
- Current in-patient at the time of baseline data collection for recent ischaemic stroke; confirmed by stroke physician and/or imaging (computerized tomography (CT) or magnetic resonance imaging (MRI)).

Exclusion criteria

- Inability to provide informed consent
- Receiving palliative or end-of-life care.

Patients with AF known at baseline will not be excluded as the aim of the study is to evaluate the Huawei smart band to detect known AF and undetected AF.

Sample size considerations

Conducting research with people following a stroke places a burden on a vulnerable group of people who are recovering from a major health event. Therefore, we will limit the burden on participants by using routinely collected data where possible and link other health datasets available to determine long-term health outcomes. Data already collected for care and quality improvement post-stroke in hospitals in Liverpool are comprehensive. Utilising these existing data will minimise patient burden but may not reduce staff time as a separate electronic case report form (eCRF) will be used.

The primary aim of the project is to evaluate the effectiveness of Huawei Smartwear to identify AF within the first 4-weeks post-stroke. The proportion of those with 'suspected AF' identified from the Huawei smart band will then be referred to an AF clinic for further evaluation at Liverpool Heart and Chest Hospital including a palpation, 12-lead ECG, and if necessary, 14-days of remote cardiac monitoring using a Ziopatch device. The positive predictive value (PPV) of the Huawei smart band will then be determined.

The PPV of the Huawei Smartwear to detect AF was previously shown to be 91.6% in the general population in China.[18] The PPV of the Huawei Smartwear has not been previously examined in a post-stroke population. Previous research in a post-stroke population has estimated the prevalence of AF at approximately 24%.[13] With an expected 24% prevalence of AF and a conservative estimated PPV of 80% for this population, a sample size of 1000 would provide accuracy of ±5%.

Intervention (Huawei smart band)

All participants will be provided with a Huawei smart band (Huawei Band 4/4 pro) and those who do not already have a suitable smart phone to use the Huawei Health App will also be provided with a Huawei smartphone (with settings to allow for Huawei Health App use only). Participants will be asked to wear the Huawei smart band for 4-weeks post-stroke and to transmit the data via the Huawei Health App on their smartphone. As the smartphone application will be the same whether the smart phone is borrowed or owned by the participant this should have no impact on data collection.

Participants with suspected AF, identified via the Huawei smart band, will be invited to attend an AF clinic at Liverpool Heart and Chest Hospital to have more intensive monitoring (including pulse palpation, 12-lead ECG, and if necessary, a 14-day Ziopatch remote monitoring plan) to confirm the suspected AF. If AF is confirmed at the AF clinic at Liverpool Heart and Chest hospital, appropriate treatment will be initiated and a letter will be sent from Liverpool Heart and Chest hospital to the original NHS trust and the participant's GP.

Participants will be able to keep the smart band after the 4-week data collection period but will be asked to return the smartphone (if given) either at their base hospital during a routine visit, or via a prepaid envelope. Participants who did not need to borrow a smartphone, may continue to use the Huawei smart band and continue to provide data for the study for secondary analyses at 6-months, after which, the monitoring of Huawei smart band data will be terminated.

The research team will complete site initiation visits and train all nurses at the participating sites to deliver the intervention and educational resources will be provided. The research nurses will show patients and their family/carers how to use the Huawei smart band, Huawei Health App, and smartphone as required. Family members may be asked to help the participants with using the smart band, Huawei Health App and smartphone once the patient has returned home if needed. A paper print-out of how to use the technology will also be provided. A central phone number will be provided for patients to contact the research team, with an automated line for common queries.

Participant recruitment

Recruitment methods

Recruitment will take place at participating hospitals over a period of 12 months. Potential participants will be assessed against the inclusion and exclusion criteria by a member of the clinical research team. A clinical member of the research team for the participating hospital will assess capacity of each participant to provide consent in consultation with other healthcare professionals with a duty of care to the participant, as appropriate. If the person meets the inclusion and exclusion criteria, they will be given a participant information sheet and will be initially approached to participate by a member of their healthcare team where possible. If the person does not want to be further approached about the study then this will be respected.

If the person is willing to be approached further about the study, a research team member will then provide a brief background to the purpose of the study. After the initial explanation, the research team member will explain to the potential participant that they can take as much time as required to decide. Prior to data collection, all staff involved with patient recruitment will be trained on GCP, the consent process and study protocol to consecutively recruit patients admitted with a stroke.

The project is deemed low risk with utilisation of routinely collected data wherever possible, plus a number of simple validated questionnaires and health measures. Participants will be provided with a Huawei smart band and smartphone (the latter as required). Optional components include consent for linking to other existing datasets within NHS Digital, therefore, we anticipate that recruitment rates will be high.

Overall, we will ensure that the patient is satisfied with the information they have received, and that they understand the study before agreeing to take part. Where possible, participants will be enrolled while they are still in the hospital, to minimise participant burden of additional research appointments. Consent forms will be completed in accordance with ethical approval. Where a patient's first language is not English a hospital translator will be asked to interpret the participant information sheet, where possible. Consent will also be sought to contact the participant's GP and to ask the participant if the research team can approach them about taking part in any related sub-studies.

Baseline and follow-up data collection

The CRF will be used to collect the data from patient healthcare records where available as outlined in Table 1. Questionnaires which are not collected as part of usual care during the participant's current in-patient stay, will be completed as part of the study. The additional questionnaires include: the Patient Health Questionnaire (PHQ)-9,[32] the General Anxiety Disorder (GAD)-7,[33] the EQ-5D-5L quality of life measure[34] and the Fatigue Assessment Scale.[35] The STOP BANG questionnaire[36] and Barthel index[37] may be completed for some patients as part of usual care post-stroke, but if they are not, these will also be in addition. We have trialled these questionnaires with patients who have experienced a stroke and the average completion time was 28 minutes. Additionally, the Modified European Heart Rhythm Association (mEHRA) symptom score[38] and treatment burden questionnaire[39] will be completed for participants with a confirmed diagnosis of AF only. Participants will be advised that they do not have to complete all questionnaires in one go.

For the baseline echocardiogram data, the results of an echocardiogram conducted within the preceding six months will be used for the study, if available. If an echocardiogram has not been completed within the preceding six months, then an echocardiogram will be booked during the participant's in-patient stay. During recruitment, participants will be provided with a unique study ID, Huawei smart band (to keep) and a smartphone (if they do not already have a compatible one) for the first four weeks of the study only.

Follow-ups will take place at 6, and 12-months from the date of admission to hospital with acute stroke. Whenever possible, follow-ups will be conducted remotely via telephone or using Attend Anywhere. The participants will be sent the questionnaires to complete via e-mail, smartphone, online or post (based on preference). If remote follow-up is not possible, these will be conducted at the end of outpatient appointments, where possible. Currently, at the participating sites, patients attend an outpatient appointment at between 4-6 weeks following a stroke and again at 6 months. If it is not possible to link follow-up research appointments with outpatient appointments, the participant will be invited to attend an appointment at their base hospital when convenient within ±2 weeks from the scheduled follow-up date. Follow-up appointments will involve repeating the collection of questionnaires conducted at baseline. The Montreal Cognitive Assessment (MoCA)[40] will be conducted at baseline as part of usual care and at 12-months at a face-to-face interview. Other available electronic data sources will be linked to determine information on clinical outcomes including mortality and Hospital Episode Statistics (HES; including cardiovascular outcomes such as incident stroke, TIA, AF, myocardial infarction, and heart failure) from NHS databases. Optional consent will be sought from the participants for data linkage as part of the initial consent process.

Withdrawal

If the person does not complete the follow-up appointment/questionnaires, the reasons for withdrawal will be recorded where possible and a profile of the participants (e.g. age, sex, ethnicity, base hospital) will be compared to participants who complete all of the follow-ups. All participants are free to withdraw at any time from the study without giving reasons and without prejudicing further treatment.

Table 1. Overview of data to be collected at baseline and follow-up timepoints.

Measures	Baseline	1-month	6-months	12-months
ECG (AF screening) Results include heart rate, ventricular rate, PR Interval, QRS duration, PQ duration and QT duration and PDF of ECG for image analysis using machine learning techniques	X*‡			
Blood pressure	X*‡			
Diagnosed medical conditions	X‡			X
Cardiovascular history	X‡			
National Institutes of Health Stroke Scale (NIHSS)	X‡			
Modified Rankin Scale	X‡			
Cognitive function measured with the Montreal Cognitive Assessment (MoCA)	X‡			X
Blood sample results	X‡			
Echocardiogram results including LVEF, Peak E velocity, LVESD, LVEDD, Diastolic LA diameter, Systolic LA diameter and LA volume	X‡			
Prescribed medications (at time of hospital discharge for baseline)	X‡			
Stroke-related diagnostic tests including CT and MRI imaging and blood samples, where available.	X‡			
Functional independence measured with the Barthel Index	X		X	X
Fatigue Assessment Scale	X		X	X
Depression measured with the Patient Health Questionnaire (PHQ)-9	X		X	X
Anxiety measured with the General Anxiety Disorder (GAD)-7	X		X	X
Health-related quality of life measured with the EQ-5D-5L without the visual analogue scale of the EQ-5D-5L	X		X	X
STOP-BANG sleep apnoea questionnaire	X		X	X
Modified European Heart Rhythm Association (mEHRA) symptom score	X*		X*	X*
Treatment burden questionnaire	X*		X*	X*
Participant 'intervention acceptability' survey		X		
Staff 'intervention acceptability' survey	X			
Participant interviews		X		
Staff interviews			X	

*Collected at baseline and when confirming suspected AF as indicated by Huawei smart band and completed by participants with suspected/confirmed AF.

‡Collected at all participating sites as part of usual care. For the echocardiogram, results will be used if the person had an echocardiogram within the preceding six months. If not, an echocardiogram will be booked and completed post-discharge.

Patient and public involvement (PPI)

A Patient Advisory Group of 4-8 patients and/or their carers will meet throughout the project to advise on study design, participant information sheets, discuss results, and inform dissemination plans. One meeting took place on 21/04/2021 with two people with experience of stroke who gave feedback on the study plans and questionnaires. We plan to expand this group and arrange meetings throughout the project. In addition, a Clinical Advisory Group of stroke clinicians (already developed through the local CRN) will meet bi-monthly throughout the project to provide clinical expertise and support for the study.

Site initiation visits

Prior to participant recruitment, a site initiation visit will be conducted at each site to provide training to the research nurses on the study recruitment procedure, use of the study questionnaires and use of the REDCap system for data collection. The nurses will also be trained to use the smart band and app, so they can in turn train the recruited patients and/or their family members to use the smart band and app.

Outcomes

Primary

Detection of atrial fibrillation. The positive predictive value (PPV) of the Huawei smart band to detect 'suspected AF' will be determined, compared to confirmed AF via clinical evaluation (12-lead ECG and/or 14-day Ziopatch remote monitoring). In addition to detection rates of AF, we will investigate clinical predictors of prevalent and incident AF in a post-stroke population (Table 1). Artificial intelligence (AI) techniques will be used to predict the next episode of AF by using the data collected. The AI model will use all the different types of data (ECG, risk factors, etc) to predict the outcome.

Secondary

Cost-effectiveness. A modelled cost-effectiveness analysis from a UK health funder perspective will be performed comparing the cost of Huawei smart band-based screening for AF compared to diagnosed AF in an un-screened post-stroke population.

Patient and staff acceptability. This will be determined through a mixed-methods process evaluation. Quantitative data will be collected to investigate how long people wore the bands for in total, how many days and for how long they wore them for each day, and whether there are differences in participant characteristics between 'adherers' and 'non-adherers', for example. In addition, a series of surveys and semi-structured interviews will be collected with participants and staff. Participant surveys will be completed at 1-month from baseline to allow for a thorough use of the device. Patient interviews will be conducted with a sub-sample of patients (n=~15) following completion of the surveys at 1-month, with purposive sample to ensure diversity based on age, sex, ethnicity, socioeconomic status, AF diagnosis, whether they adhered to using the intervention and whether they used their own phone or a borrowed phone. Survey questions and interview topic guides will be developed with support from

incorporated PPI activities (as described above), however, they will be iterative in nature and adapted accordingly; informed by any prior interviews and survey responses. Briefly, participant interviews and surveys will explore acceptability of the training and collected measures, acceptability of the intervention (Huawei smart band), perceived challenges, and recommendations for improvement. Staff intervention acceptability will be determined through surveys (baseline) and semi-structured interviews (6-months). All healthcare professionals providing the training and/or managing the intervention will be invited to participate. Staff interviews will explore any challenges in delivery, time taken (to deliver the intervention and ongoing support with the system provided to the patient), unexpected benefits and/or consequences, and recommendations for improvement. Interviews will be audio-recorded and transcribed verbatim. For participation in the surveys and interviews, staff will be provided with a participant information sheet and asked to provide written consent to participate.

12-month clinical outcomes. In addition to measures identified in Table 1, the full cohort will be examined using linkage with other available data sources at one-year follow-up. Outcomes of interest will include all-cause mortality and mortality from cardiovascular causes, as well as cardiovascular outcomes including incident stroke, TIA, AF, myocardial infarction, and heart failure captured from HES.

Statistical analysis

Anonymised data will be analysed by members of the research team at the Liverpool Centre for Cardiovascular Science, University of Liverpool. Continuous variables will be tested for normality with the Shapiro-Wilk test. Data with a normal distribution will be presented as means (standard deviations, SD) and data with a non-normal distribution will be presented as medians (interquartile ranges, IQR). Characteristics of those who do and do not receive a 'suspected AF' notification with the Huawei smart band will be compared with parametric or non-parametric tests as appropriate for continuous variables and chi-squared tests for categorical variables. The positive predictive value (PPV) of 'suspected AF' detected with the PPG algorithm with the Huawei smart band will be calculated by comparison to confirmed diagnosis of AF using clinical evaluation, ECG, and/or 14-day Ziopatch remote monitoring.

Predictors of incident AF will be determined using multivariate competing-risk analyses in order to account for potential high probability of mortality amongst the cohort. The accuracy of risk prediction models for AF developed in previous studies will also be determined in this cohort. Receiver operating characteristic curves will be constructed, and C-statistics (i.e. area under the curve) with 95% confidence intervals will be estimated as a measure of model performance.

Qualitative data will be analysed using a thematic analysis approach,[41] separately for participants and staff. Survey data will be analysed descriptively and reported as frequencies and percentages.

Confidentiality and pseudo-anonymisation of data and data linkage

The Chief Investigator will preserve the confidentiality of participants taking part in the study and will abide by the EU General Data Protection Regulation 2016 and Data Protection Act 2018.

Each record will be pseudo-anonymised by removing identifiable information (name, address, telephone number, NHS number, date of birth). Date of birth will be replaced with decimal age pseudo-anonymisation. Identifiable information will be stored separately to the rest of the data and each record will be assigned a unique, non-identifiable code (participant ID). Identifiable information stored separately will only be used by the direct clinical research team to contact participants to invite them for follow-up, to link data from external data sources including NHS Digital, or regarding any adverse health outcomes that may be identified.

Applications will be made to the relevant bodies to access outcome data routinely collected by the NHS for all participants. This will include mortality information (date and causes of death) from the Office for National Statistics (ONS) and Hospital Episode Statistics (HES) in the central register held by NHS Digital (previously the NHS Health and Social Care Information Centre: HSCIC). Data linkage will continue for up to 5 years from the baseline date. We will request the following datasets from NHS Digital:

- Accident and Emergency
- Admitted Patient Care
- Outpatients
- Adult Critical Care
- ONS mortality data (Date and causes of death)

Data from NHS Digital are provided through the Data Access Request Service (DARS). We will complete an application for the data in the NHS Digital online portal including a Data Sharing Agreement. Upon recruiting participants, they will be asked to consent for their data collected at baseline to be linked to HES and mortality data from NHS Digital. The participant's name, date of birth and NHS number will be sent to NHS Digital through their Secure Electronic File Transfer (SEFT) system. The HES and mortality data will be sent from NHS Digital to the University of Liverpool using the SEFT system, where it will be linked to the participant's pseudo-anonymised data collected at baseline. We have discussed the study with NHS Digital to ensure the consent processes we have put in place will be adequate to facilitate the data linkage.

The monitoring data from the Huawei smart band, such as heart rate, physical activity, and steps, will be synchronised and uploaded to the Amazon Web Service server. These monitoring data will be linked only by the participant ID.

For data acquired during the process evaluation, each record for each patient or staff member will be pseudo-anonymised by removing identifiable information (name and date of birth). Date of birth will be replaced with decimal age pseudo-anonymisation. Identifiable information will be stored separately to the rest of the data and each record will be assigned a unique, non-identifiable code (participant ID). For qualitative work, the audio-file will be transferred from the Dictaphone to the University server (within 48 hours of recording) and then deleted from the Dictaphone. A verbatim transcript will be made from the audio-file with names of staff, hospitals, patients, identifiable information redacted. No identifiable information will be published. Any quotes used in publications/reports will not contain any information that could potentially identify the participant or anyone else and participants will provide explicit consent for quotations to be used. At the end of the study all the audio-files will be securely and permanently erased. Transcripts will be kept (10 years based on UoL policy) on the University server (password-protected).

Data handling and record keeping

Pseudo-anonymised data using the unique, non-identifiable participant ID will be collected by a member of the clinical research team and inputted in an eCRF using Research Electronic Data Capture (REDCap; https://www.project-redcap.org). REDCap is a secure web application for building and managing online surveys and databases. REDCap is specifically designed to support online or offline data capture for research studies and operations. REDCap was selected for this because the University of Liverpool is a member of the REDCap consortium.

Data storage

Identifiable information including the participant's name, address, telephone number and NHS number will not be entered into REDCap. This information will be stored on the Managed (M) computer drive at the University of Liverpool-a secure and daily backed-up protected file-in accordance with University governance procedure. Data will be encrypted using AxCrypt-file encryption software. Only personnel directly involved in participant recruitment or follow-up will have access to the identifiable information. The key file linking the participant ID to patient identifiable information will be kept within NHS hospitals and will be password-protected and will only be accessed by authorised members of the clinical research team.

Anonymised Huawei smart band monitoring data, linked with the participant ID, will be uploaded to the Amazon web service (AWS) cloud storage in the UK or EU. AWS Terms and Conditions are compliant with the UK's G-Cloud Framework, the Data Protection Act, and the European Union's General Data Protection Regulation (AWS Compliance). NHS data is already being stored on AWS cloud storage. In 2019 the NHS e-Referral Service and NHS 111 Directory of Services were migrated to the AWS Cloud Computing Services to save public money and improve the efficiency and security of services (NHS and AWS). Only anonymised monitoring data from the Huawei smart band will be released to Huawei and its affiliates located in the European Economic Area and the UK, along with patient ID, age, sex, height, weight, and skin colour. The demographic data are required to interpret the monitoring data recorded by the Huawei smart band. These data will be anonymised by a member of the University of Liverpool research team. Huawei has agreed not to transfer the anonymised data outside of the European Economic Area and the UK. Huawei will keep the data for 10 years and may use the data for future research with appropriate ethical approval. Figure 2 shows the data flow for the Huawei Stroke Study.

Data archiving

It is the responsibility of each participating hospital to retain copies of all completed paper questionnaires and consent forms for the study on site or at their designated archive facility for a minimum of 10-years after study completion. All hospitals will be asked to complete a log of all patients who are screened for eligibility who do not subsequently take part and the reason for non-participation. Electronic data will be stored for 10 years. Data will be encrypted using AxCrypt- file encryption software. AxCrypt is recommended by the University of Liverpool Research Data Management team and allows the encryption of individual files - including on network/shared drives, which can be useful when sending a specific file to another user or storing files somewhere other than central university storage or a device protected with BitLocker. Once installed, an additional context menu is available in Windows Explorer that allows files and folders to be encrypted (and decrypted) with a key or a passphrase. It also has the added benefit of allowing a "delete and shred" option thereby preventing deleted data from being recovered from the recycle bin etc. Huawei smart band data will be available to Huawei UK and France for a period of 10-years, after which it will be destroyed.

Research ethics

The Chief Investigator will obtain Health Research Authority (HRA) approval. The study will be submitted to each proposed research site for Confirmation of Capacity and Capability. The 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.

Reporting and dissemination

All analyses will be written up and disseminated in appropriate peer-reviewed health and medical journals and submitted for presentation at appropriate conferences. To disseminate the findings to patients and the general public, the findings will be shared with the Stroke Association and an open public lecture will take place at the end of the study. People who have taken part in the study and the general public will be invited to hear the study results. We may also share the results of the study via local media outlets e.g. newspapers and local radio where possible. We will also ask participants if they would like to receive summaries of key findings and copies of journal articles produced from the research.

Indemnity

The University of Liverpool holds Indemnity and insurance cover with Griffiths & Armour, which apply to this study.

Sponsor

The University of Liverpool will act as Sponsor for this study. It is recognised that as an employee of the University the Chief Investigator has been delegated specific duties, as detailed in the Sponsorship Approval letter.

Funding

Huawei Technologies France are funding this study. There are no per participant payments for participation in the study.

Audits

The study may be subject to inspection and audit by the University of Liverpool 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 (v3.2 10th October 2017).

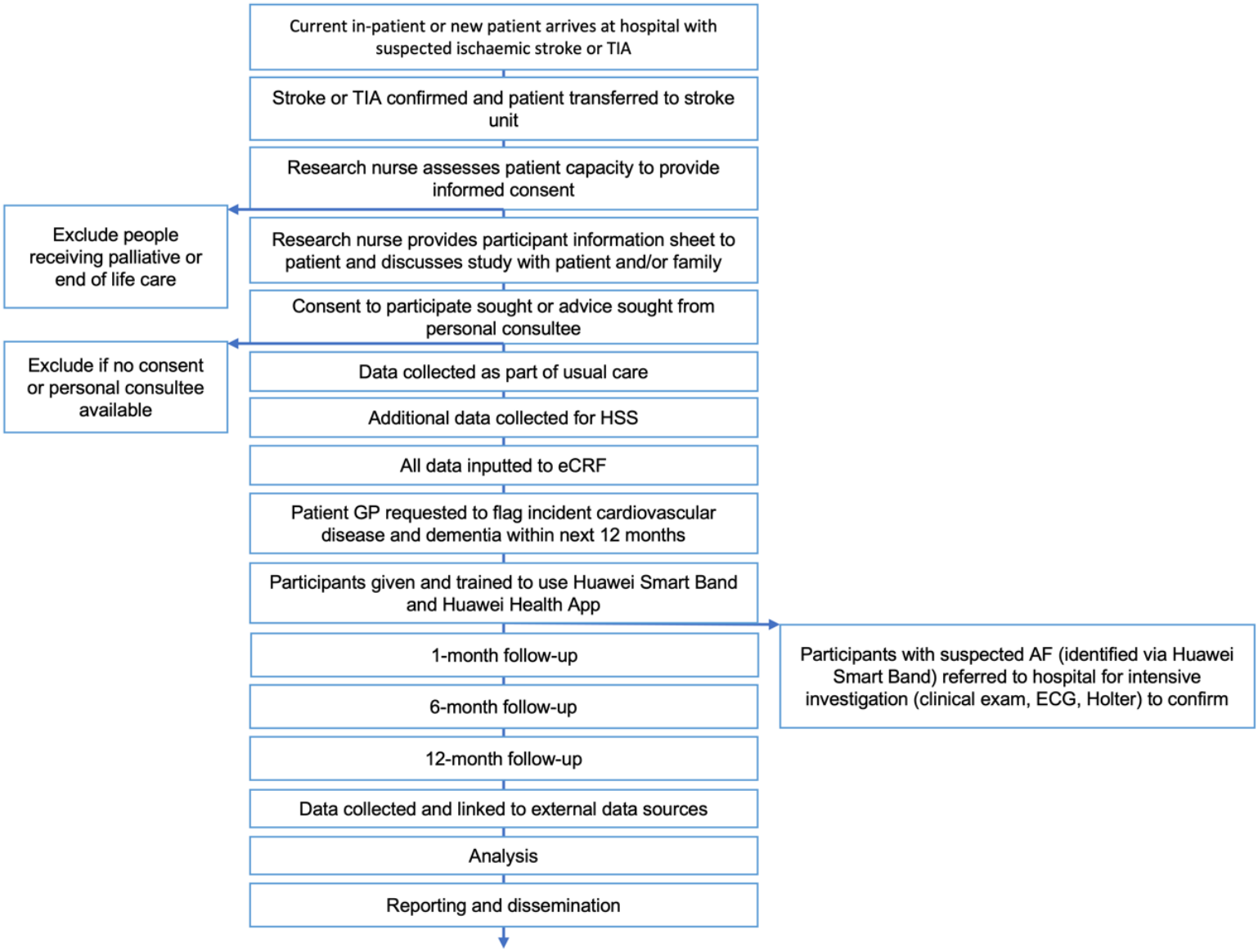


Figure 1. Participant recruitment and study flow for Huawei Stroke Study.

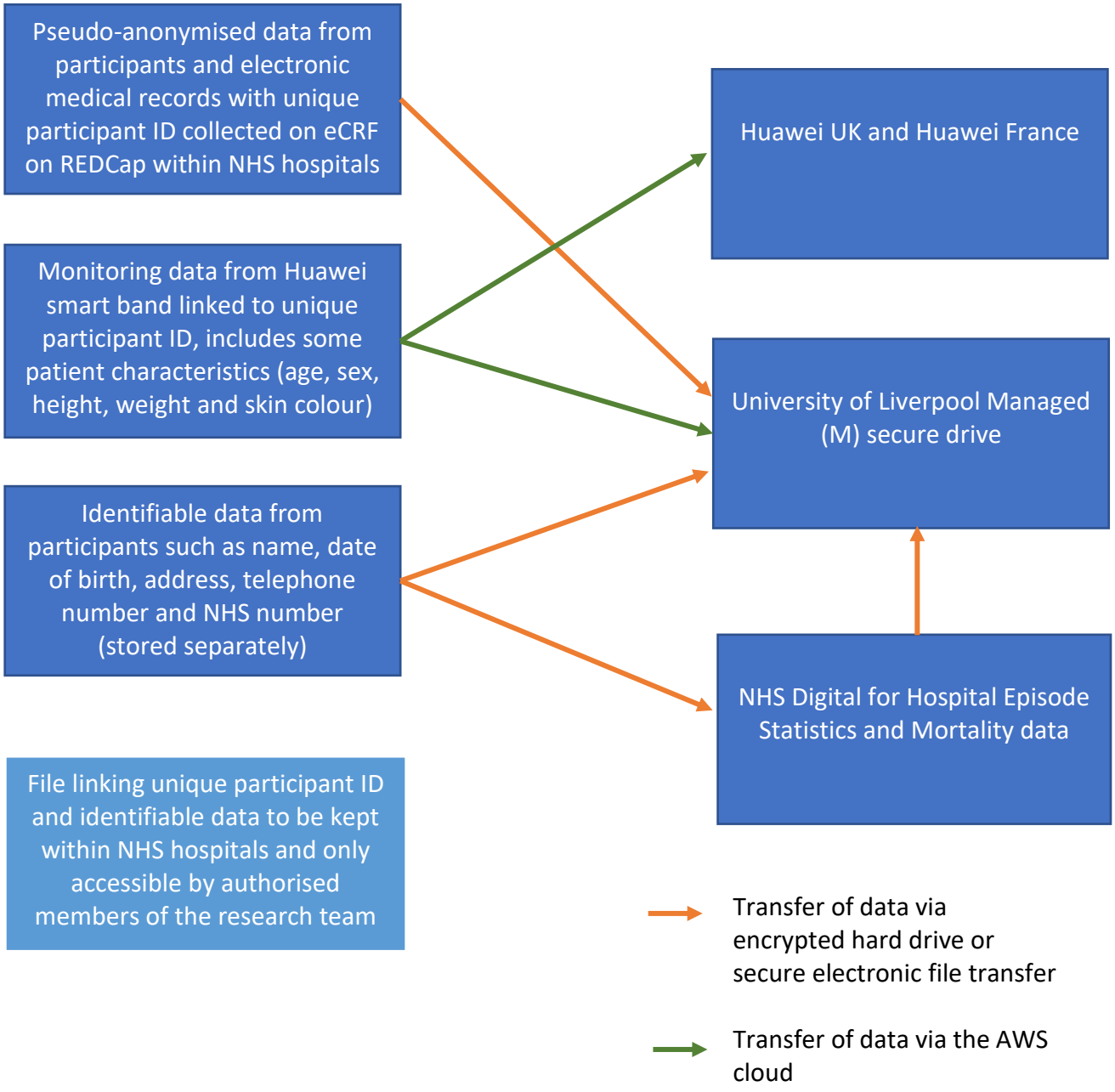
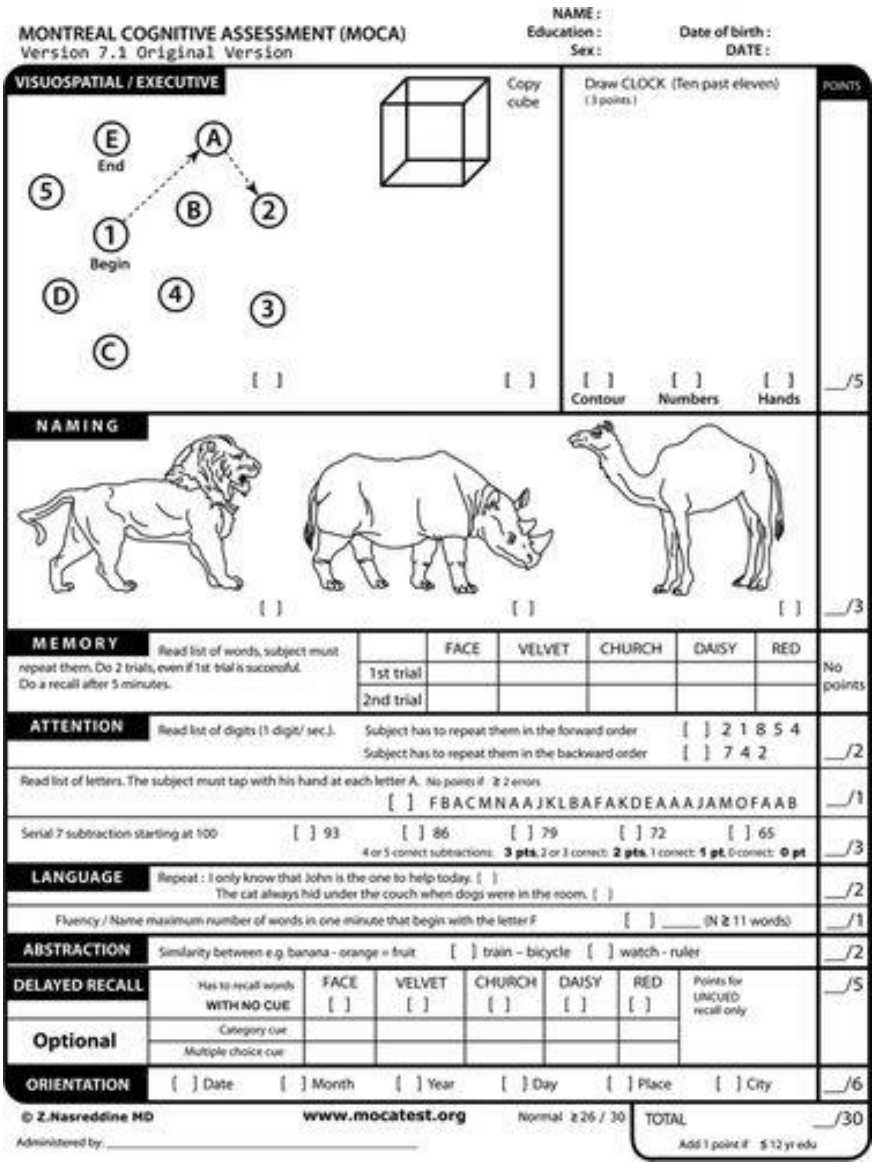


Figure 2. Data flow diagram for the Huawei Stroke Study.

Questionnaires

MoCA[40]



MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

NAME :
Education :
Sex :
Date of birth :
DATE :

VISUOSPATIAL / EXECUTIVE — POINTS

Copy cube

Draw CLOCK (Ten past eleven) (3 points)

[ ] Contour [ ] Numbers [ ] Hands

/5

NAMING

[ ] [ ] [ ]

/3

MEMORY — Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION — Read list of digits (1 digit/ sec.).

Subject has to repeat them in the forward order [ ] 2 1 8 5 4

Subject has to repeat them in the backward order [ ] 7 4 2

/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

/3

LANGUAGE — Repeat : I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ]

/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] ____ (N ≥ 11 words)

/1

ABSTRACTION — Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler

/2

DELAYED RECALL

	Has to recall words WITH NO CUE	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only
Optional	Category cue						
	Multiple choice cue						

/5

ORIENTATION — [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

/6

© Z.Nasreddine MD — www.mocatest.org — Normal ≥ 26 / 30

TOTAL /30

Add 1 point if ≤ 12 yr edu

Administered by: _____

PHQ-9[32]

PATIENT HEALTH QUESTIONNAIRE (PHQ-9)

NAME: _____ **DATE:** _____

Over the last 2 *weeks*, how often have you been bothered by any of the following problems?
(use "✓" to indicate your answer)

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite — being so figety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself	0	1	2	3
	add columns		+	+

(Healthcare professional: For interpretation of TOTAL, please refer to accompanying scoring card). TOTAL:

10. If you checked off *any problems*, how *difficult* have these problems made it for you to do your work, take care of things at home, or get along with other people?

- Not difficult at all _____
- Somewhat difficult _____
- Very difficult _____
- Extremely difficult _____

GAD-7[33]

GAD-7

Over the last 2 weeks, how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3

Total Score ___ = Add Columns ___ + ___ + ___

Barthel Index[37]

Barthel Index of Activities of Daily Living

Instructions: Choose the scoring point for the statement that most closely corresponds to the patient's current level of ability for each of the following 10 items. Record actual, not potential, functioning. Information can be obtained from the patient's self-report, from a separate party who is familiar with the patient's abilities (such as a relative), or from observation. Refer to the Guidelines section on the following page for detailed information on scoring and interpretation.

The Barthel Index

Bowels
0 = incontinent (or needs to be given enemata)
1 = occasional accident (once/week)
2 = continent
Patient's Score: _____

Bladder
0 = incontinent, or catheterized and unable to manage
1 = occasional accident (max. once per 24 hours)
2 = continent (for over 7 days)
Patient's Score: _____

Grooming
0 = needs help with personal care
1 = independent face/hair/teeth/shaving (implements provided)
Patient's Score: _____

Toilet use
0 = dependent
1 = needs some help, but can do something alone
2 = independent (on and off, dressing, wiping)
Patient's Score: _____

Feeding
0 = unable
1 = needs help cutting, spreading butter, etc.
2 = independent (food provided within reach)
Patient's Score: _____

Transfer
0 = unable – no sitting balance
1 = major help (one or two people, physical), can sit
2 = minor help (verbal or physical)
3 = independent
Patient's Score: _____

Mobility
0 = immobile
1 = wheelchair independent, including corners, etc.
2 = walks with help of one person (verbal or physical)
3 = independent (but may use any aid, e.g., stick)
Patient's Score: _____

Dressing
0 = dependent
1 = needs help, but can do about half unaided
2 = independent (including buttons, zips, laces, etc.)
Patient's Score: _____

Stairs
0 = unable
1 = needs help (verbal, physical, carrying aid)
2 = independent up and down
Patient's Score: _____

Bathing
0 = dependent
1 = independent (or in shower)
Patient's Score: _____

Total Score: _____

(Collin et al., 1988)

Scoring:

Sum the patient's scores for each item. Total possible scores range from 0 – 20, with lower scores indicating increased disability. If used to measure improvement after rehabilitation, changes of more than two points in the total score reflect a probable genuine change, and change on one item from fully dependent to independent is also likely to be reliable.

Sources:

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1

EQ-5D-5L[34]

Under each heading, please tick the ONE box that best describes your health TODAY.

MOBILITY

- I have no problems in walking about ❑
- I have slight problems in walking about ❑
- I have moderate problems in walking about ❑
- I have severe problems in walking about ❑
- I am unable to walk about ❑

SELF-CARE

- I have no problems washing or dressing myself ❑
- I have slight problems washing or dressing myself ❑
- I have moderate problems washing or dressing myself ❑
- I have severe problems washing or dressing myself ❑
- I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

- I have no problems doing my usual activities ❑
- I have slight problems doing my usual activities ❑
- I have moderate problems doing my usual activities ❑
- I have severe problems doing my usual activities ❑
- I am unable to do my usual activities ❑

PAIN / DISCOMFORT

- I have no pain or discomfort ❑
- I have slight pain or discomfort ❑
- I have moderate pain or discomfort ❑
- I have severe pain or discomfort ❑
- I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION

- I am not anxious or depressed ❑
- I am slightly anxious or depressed ❑
- I am moderately anxious or depressed ❑
- I am severely anxious or depressed ❑
- I am extremely anxious or depressed ❑

Fatigue Assessment Scale[35]

The following 10 statements refer to how you usually feel. For each statement you can choose one out of five answer categories, varying from *never* to *always*. 1=*never*, 2=*sometimes*; 3=*regularly*; 4=*often*; and 5=*always*.

	Never	Sometimes	Regularly	Often	Always
1. I am bothered by fatigue	1	2	3	4	5
2. I get tired very quickly	1	2	3	4	5
3. I don't do much during the day	1	2	3	4	5
4. I have enough energy for everyday life	1	2	3	4	5
5. Physically, I feel exhausted	1	2	3	4	5
6. I have problems starting things	1	2	3	4	5
7. I have problems thinking clearly	1	2	3	4	5
8. I feel no desire to do anything	1	2	3	4	5
9. Mentally, I feel exhausted	1	2	3	4	5
10.When I am doing something, I can concentrate quite well	1	2	3	4	5

Treatment burden questionnaire (TBQ) adapted for patients with AF[39, 42]

We are interested in finding out about the effort you have to make to look after your health and how this impacts on your day-to-day life.
Please tell us how much difficulty you have with the following: (Please tick the box that most applies to you)
Scale from 0-10 with 0 (Does not apply) to 10 (extremely difficult).

Questions	0	1	2	3	4	5	6	7	8	9	10
Questions about OAC-related treatment burden											
1. The taste, shape or size of your tablets and/or the inconvenience caused by your injections (for example, pain, bleeding, scars)											
2. The number of times you have to take your medication every day											
3. The things you do to remind yourself to take your daily medication and/or to manage your treatment when you are not at home											
4. The specific conditions when taking your medication (for example, taking it at a specific time of the day or meal, not being able to do certain things after taking them like driving or lying down)											
Questions about other drugs-related treatment burden											
1. The taste, shape or size of your tablets and/or the inconvenience caused by your injections (for example, pain, bleeding, scars)											
2. The number of times you have to take your medication every day											
3. The things you do to remind yourself to take your daily medication and/or to manage your treatment when you are not at home											
4. The specific conditions when taking your medication (for example, taking it at a specific time of the day or meal, not being able to do certain things after taking them like driving or lying down)											
Questions about other aspects of treatment burden											
1. Lab tests and other exams (frequency, time spent and inconvenience of these exams)											
2. Self-monitoring (for example, INR controls, taking your blood pressure or measuring your blood sugar yourself: frequency, time spent and inconvenience of this surveillance)											
3. Doctor visits (frequency and time spent for the visits)											
4. Arrange appointments and schedule doctor visits and laboratory tests											
5. How would you rate the burden associated with taking care of paperwork from health insurance agencies, welfare organizations, hospitals and/or social care?											
6. How would you rate the constraints associated with your diet (for example, not being allowed to eat certain foods)?											
7. How would you rate the burden associated with the recommendations from your doctors to practice regular physical exercises?											
8. What is the impact of your healthcare on your social relationships (for example, need for assistance, being ashamed to take your medication in front of people)?											
9. 'Frequent healthcare reminds me of my health problems'											

OAC: Oral anticoagulant therapy; AF: Atrial fibrillation.

Modified EHRA (mEHRA) symptom score[38]

mEHRA score	Symptoms	Description
1	None	
2a	Mild	Normal daily activity not affected, symptoms not troublesome to patient
2b	Moderate	Normal daily activity not affected but patient troubled by symptoms
3	Severe	Normal daily activity affected
4	Disabling	Normal daily activity discontinued

Underlined text represents the modification to the original descriptions of EHRA classes.

STOP-BANG questionnaire

STOP		
Do you **S**NORE loudly (louder than talking or loud enough to be heard through closed doors)?	Yes	No
Do you often feel **T**IRED, fatigued, or sleepy during daytime?	Yes	No
Has anyone **O**BSERVED you stop breathing during your sleep?	Yes	No
Do you have or are you being treated for high blood **P**RESSURE?	Yes	No

BANG		
BMI more than 35kg/m2?	Yes	No
AGE over 50 years old?	Yes	No
NECK circumference > 16 inches (40cm)?	Yes	No
GENDER: Male?	Yes	No

TOTAL SCORE		

High risk of OSA: Yes 5 - 8

Intermediate risk of OSA: Yes 3 - 4

Low risk of OSA: Yes 0 - 2

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