Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please complete the questions in order. If you change the response to a question, please select 'Save' and review all the questions as your change may have affected subsequent questions.

Please enter a short title for this project (maximum 70 characters)
Pharyngeal Electrical stimulation (PES) for Post Stroke dysphagia (PSD

1. Is your project research?

(●) Yes ( ) No

2. Select one category from the list below:

( ) Clinical trial of an investigational medicinal product
(●) Clinical investigation or other study of a medical device
( ) Combined trial of an investigational medicinal product and an investigational medical device
( ) Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice
( ) Basic science study involving procedures with human participants
( ) Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
( ) Study involving qualitative methods only
( ) Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)
( ) Study limited to working with data (specific project only)
( ) Research tissue bank
( ) Research database

If your work does not fit any of these categories, select the option below:

( ) Other study

2a. Is the study sponsored or funded by a device manufacturer or other commercial company?

(●) Yes ( ) No

Please select one of the following:

( ) Clinical investigation for UKCA/CE UKNI/CE marking purposes (includes investigation of a UKCA/CE UKNI/CE marked device outside its current intended purposes or in modified form)
( ) Combined clinical investigation for UKCA/CE UKNI/CE marking purposes and clinical trial of an investigational medicinal product
(●) Post-market clinical study of one or more UKCA/CE UKNI/CE marked devices within intended purposes, involving a change to standard care or randomisation between groups

◯ Registry of a UKCA/CE UKNI/CE marked device in clinical use, involving no change to standard care or randomisation

◯ Performance evaluation of an in vitro diagnostic device (PEIVDD)

2b. Please answer the following question(s):

a) Does the study involve the use of any ionising radiation? ◯ Yes ◉ No

b) Will you be taking new human tissue samples (or other human biological samples)? ◯ Yes ◉ No

c) Will you be using existing human tissue samples (or other human biological samples)? ◯ Yes ◉ No

3. In which countries of the UK will the research sites be located?*(Tick all that apply)*

☑ England
☑ Scotland
☑ Wales
☑ Northern Ireland

3a. In which country of the UK will the lead NHS R&D office be located:

◉ England
◯ Scotland
◯ Wales
◯ Northern Ireland
◯ This study does not involve the NHS

4. Which applications do you require?

☑ IRAS Form
☐ Medicines and Healthcare products Regulatory Agency (MHRA) Devices Division
☐ Confidentiality Advisory Group (CAG)
☐ Her Majesty's Prison and Probation Service (HMPPS)

5. Will any research sites in this study be NHS organisations?

◉ Yes ◯ No

5a. Are all the research costs and infrastructure costs (funding for the support and facilities needed to carry out the research e.g. NHS support costs) for this study provided by a NIHR Biomedical Research Centre (BRC), NIHR Applied Research Collaboration (ARC), NIHR Patient Safety Translational Research Centre (PSTRC), or an NIHR Medtech and In Vitro Diagnostic Co-operative (MIC) in all study sites?

Please see information button for further details.

◯ Yes ◉ No

Please see information button for further details.

5b. Do you wish to make an application for the study to be considered for NIHR Clinical Research Network (CRN)

Support and inclusion in the NIHR Clinical Research Network Portfolio?

Please see information button for further details.

◉ Yes ○ No

The NIHR Clinical Research Network (CRN) provides researchers with the practical support they need to make clinical studies happen in the NHS in England e.g. by providing access to the people and facilities needed to carry out research "on the ground".

If you select yes to this question, information from your IRAS submission will automatically be shared with the NIHR CRN. ***Submission of a Portfolio Application Form (PAF) is no longer required.***

6. Do you plan to include any participants who are children?

○ Yes ◉ No

7. Do you plan at any stage of the project to undertake intrusive research involving adults lacking capacity to consent for themselves?

◉ Yes ○ No

Answer Yes if you plan to recruit living participants aged 16 or over who lack capacity, or to retain them in the study following loss of capacity. Intrusive research means any research with the living requiring consent in law. This includes use of identifiable tissue samples or personal information, except where application is being made to the Confidentiality Advisory Group to set aside the common law duty of confidentiality in England and Wales. Please consult the guidance notes for further information on the legal frameworks for research involving adults lacking capacity in the UK.

8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?

○ Yes ◉ No

9. Is the study or any part of it being undertaken as an educational project?

○ Yes ◉ No

10. Will this research be financially supported by the United States Department of Health and Human Services or any of its divisions, agencies or programs?

○ Yes ◉ No

11. Will identifiable patient data be accessed outside the care team without prior consent at any stage of the project (including identification of potential participants)?

○ Yes ◉ No

Integrated Research Application System
Application Form for Medical Device Study

IRAS Form (project information)

Please refer to the E-Submission and Checklist tabs for instructions on submitting this application.

The Chief Investigator should complete this form. Guidance on the questions is available wherever you see this symbol displayed. We recommend reading the guidance first. The complete guidance and a glossary are available by selecting Help.

Please define any terms or acronyms that might not be familar to lay reviewers of the application.

Short title and version number: (maximum 70 characters - this will be inserted as header on all forms)
Pharyngeal Electrical stimulation (PES) for Post Stroke dysphagia (PSD

Please complete these details after you have booked the REC application for review.

REC Name:
East of England-Essex

REC Reference Number:
21/EE/0252

Submission date:
04/10/2021

PART A: Core study information

1. ADMINISTRATIVE DETAILS

A1. Full title of the research:

Pharyngeal Electrical stimulation for Acute Stroke dysphagia Trial (PhEAST)

A3-1. Chief Investigator:

	Title	Forename/Initials	Surname
	Prof	Philip	Bath
Post	Professor of Stroke Medicine		
Qualifications			
ORCID ID	0000 0003 2734 5132		
Employer	University of Nottingham		
Work Address	Stroke Trials Unit, Mental Health & Clinical Neurosciences University of Nottingham, D Floor, South Block, Queen's Medical Centre, Derby Rd. Nottingham		
Post Code	NG7 2UH		
Work E-mail	philip.bath@nottingham.ac.uk		
* Personal E-mail			
Work Telephone	01158231765		
* Personal Telephone/Mobile			

Fax

** This information is optional. It will not be placed in the public domain or disclosed to any other third party without prior consent.*
A copy of a current CV (maximum 2 pages of A4) for the Chief Investigator must be submitted with the application.

A4. Who is the contact on behalf of the sponsor for all correspondence relating to applications for this project?
This contact will receive copies of all correspondence from REC and HRA/R&D reviewers that is sent to the CI.

	Title	Forename/Initials	Surname
	Ms	Angela	Shone
Address	Research & Innovation, UoN		
	East Atrium, Jubilee Conference Centre		
	Triumph Road, Nottingham		
Post Code	NG8 1DH		
E-mail	sponsor@nottingham.ac.uk		
Telephone	01158467906		
Fax			

A5-1. Research reference numbers. *Please give any relevant references for your study:*

Applicant's/organisation's own reference number, e.g. R & D (if available):	
Sponsor's/protocol number:	21068
Protocol Version:	1.0
Protocol Date:	30/09/2021
Funder's reference number (enter the reference number or state not applicable):	132016

Project website: https://stroke.nottingham.ac.uk/pheast/

Registry reference number(s):
The UK Policy Framework for Health and Social Care Research sets out the principle of making information about research publicly available. Furthermore: Article 19 of the World Medical Association Declaration of Helsinki adopted in 2008 states that "every clinical trial must be registered on a publicly accessible database before recruitment of the first subject"; and the International Committee of Medical Journal Editors (ICMJE) will consider a clinical trial for publication only if it has been registered in an appropriate registry. Please see guidance for more information.

International Standard Randomised Controlled Trial Number (ISRCTN):
ClinicalTrials.gov Identifier (NCT number):

Additional reference number(s):

Ref.Number Description	Reference Number

A5-2. Is this application linked to a previous study or another current application?

○ Yes ◉ No

Please give brief details and reference numbers.

2. OVERVIEW OF THE RESEARCH

To provide all the information required by review bodies and research information systems, we ask a number of

specific questions. This section invites you to give an overview using language comprehensible to lay reviewers and members of the public. Please read the guidance notes for advice on this section.

A6-1. Summary of the study. *Please provide a brief summary of the research (maximum 300 words) using language easily understood by lay reviewers and members of the public. Where the research is reviewed by a REC within the UK Health Departments' Research Ethics Service, this summary will be published on the Health Research Authority (HRA) website following the ethical review. Please refer to the question specific guidance for this question.*

Stroke (brain attack) is common and complicated by swallowing problems (dysphagia) in at least half of patients, many of whom still have abnormal swallowing a year later. Swallowing problems often lead to chest infections, poor nutrition, the need for a feeding tube inserted into the stomach, long hospital stays, disability and so nursing home care after hospital, and death. Patients dislike not being able to eat and drink normally, and they and their family dislike feeding tubes especially when used long-term. These issues reduce stroke survivor quality of life and add much to the physical, mental, emotional and financial cost of stroke. At present, there are no proven treatments for swallowing problems after stroke.

The control of swallowing uses nerves running between the back of the throat and the brain. In volunteers, stimulating these nerves using a tiny electric current has been shown to re-programme the swallowing centres in the brain. Pharyngeal electrical stimulation (PES) is given via a tube inserted through the nose to the back of the throat, and stimulation can barely be felt. In small and medium-sized trials, and summaries of their results, PES was safe, reduced swallowing problems (assessed using a scale called the 'dysphagia severity rating scale') and x-ray evidence of dangerous swallowing, and was acceptable to patients with swallowing problems after stroke. Good results have also been seen in studies in groups of patients with other brain problems and abnormal swallowing.

We would like to do a much larger and simpler trial of PES in 800 patients with recent stroke and needing a feeding tube because of abnormal swallowing. The aim is to see if PES is effective when used in the real-world. Recruitment will take place in 50 sites in 4 European countries (UK, Austria, Denmark, Germany). Following consent, patients will be allocated at random to either receive a treatment catheter and electrical stimulation, or to continue with their normal feeding tube. Treatment will be given for six days by a specially trained researcher, nurse or swallowing therapist. The main outcome will be improvement in swallowing using the dysphagia severity rating scale two weeks after starting treatment, and assessed without knowledge of treatment.

The cost of the treatment against the cost-savings from potentially improved swallowing and reduced stay in hospital will be assessed using health economic analyses. If PES improves swallowing and reduces complications such as pneumonia, and treatment is cost effective as compared to usual care, then it could be used widely after stroke in people with swallowing problems.

A6-2. Summary of main issues. *Please summarise the main ethical, legal, or management issues arising from your study and say how you have addressed them.*

Not all studies raise significant issues. Some studies may have straightforward ethical or other issues that can be identified and managed routinely. Others may present significant issues requiring further consideration by a REC, HRA, or other review body (as appropriate to the issue). Studies that present a minimal risk to participants may raise complex organisational or legal issues. You should try to consider all the types of issues that the different reviewers may need to consider.

Since patients with dysphagia typically have severe stroke and so may have parallel cognitive, language (dysphasia) or wakefulness problems, it is vital that consultee opinion may be sought from a Welfare Guardian/Attorney, nearest relative (as applicable per country) consultee where the patient lacks capacity. We have produced a simplified pictorial information sheet to be help with these issues, bother may still be patients who lack capacity to understand the study.

Post-stroke dysphagia in the hospital setting is associated with poor outcomes. It is known to increase the risk of life threatening and difficult to treat infections as well as increase mortality. If unresolved, dysphagia represents a major long-term disability burden, impacting patient survival, cost of care and quality of life. There are no clinically proven evidence-based treatments for dysphagia.

The Phagenyx® System is a non-signficant risk (NSR) device and its safety profile is well characterized by evidence accumulated from multiple phase II, III and IV clinical studies over a period of 15 years. There are no characteristic device or treatment specific effects that are considered to be serious adverse events. The additional risks associated with the clinical study design are all well understood and can be easily mitigated. None of the protocol-specific assessments are expected to add significant risk over those risks inherent in the care of patients suffering dysphagia in the subacute stroke setting.
Patients participating in this study are expected to be exposed to only marginal incremental risk over standard of care, and some patients may experience more expedient and more successful outcomes associated with their dysphagia

treatment. Hence, the benefits associated with study participation are expected to outweigh any incidental incremental risk

3. PURPOSE AND DESIGN OF THE RESEARCH

A7. Select the appropriate methodology description for this research. *Please tick all that apply*:

- ☐ Case series/ case note review
- ☐ Case control
- ☐ Cohort observation
- ☐ Controlled trial without randomisation
- ☐ Cross-sectional study
- ☐ Database analysis
- ☐ Epidemiology
- ☐ Feasibility/ pilot study
- ☐ Laboratory study
- ☐ Metanalysis
- ☐ Qualitative research
- ☐ Questionnaire, interview or observation study
- ☑ Randomised controlled trial
- ☐ Other (please specify)

A10. What is the principal research question/objective? *Please put this in language comprehensible to a lay person.*

The principal objective is to determine whether using pharyngeal electrical stimulation (PES) over a 6 day course of treatment, speeds up a return to oral feeding and fluids in patients with swallowing problems (dysphagia)following an acute stroke.

A11. What are the secondary research questions/objectives if applicable? *Please put this in language comprehensible to a lay person.*

As the level of swallowing problems (dysphagia) strongly relates to poor outcome because it can lead to pneumonia and malnutrition, the secondary objectives are:
1. Does the PES treatment improve swallowing, reduce the incidence of pneumonia and hence the use of antibiotics and shorten hospital stays?
2. Does the PES treatment increase the quality of life

A12. What is the scientific justification for the research? *Please put this in language comprehensible to a lay person.*

Post Stroke Dysphagia is common, associated with poor outcomes and quality of life, and there are no recognised treatments. As a result, PSD is:

Unpleasant: Although NGT feeding prevents dehydration and malnutrition, it: is disliked by patients and family (distress during tube insertion and irritation when in place); removes the pleasure of drinking/eating; reduces oral health; is complicated by premature NGT removal by confused patients, this needing further NGT(s) (with more chest x-rays, CXR); and often needs replacement with a long-term PEG tube.

Hazardous: PSD is complicated by aspiration, pneumonia and malnutrition, these leading to dependency, disability and death. PSD, with age and stroke severity, is a key determinant of outcome; tube insertion and feeding come with complications.

Logistically challenging and expensive for healthcare: Bed due to extended hospital stay; staff - nursing management of NGT/drugs/feed; speech & language therapy (SLT), dietician management of tube feeding, gastroenterologist insertion of percutaneous endoscopic gastrostomy tubes; drugs – antibiotics for pneumonia; investigations - videofluoroscopy (VFS), fibreoptic endoscopic evaluation of swallowing (FEES), CXR; devices – NGT/PEG, bridles. Importantly, nursing homes rarely take NGT-fed patients so availability and training for PEG determine when and where patients can be discharged.

If PES is effective at reducing dysphagia and returning patients to oral feeding, then it is likely to be cost effective as compared to usual care. PES has a European Conformité Européene (CE) mark and is available across Europe but lacks an adequate evidence base, hence the need for this trial. Public-patient involvement (PPI) representatives confirm the importance of PSD and finding effective treatments.

A13. Please summarise your design and methodology. *It should be clear exactly what will happen to the research participant, how many times and in what order. Please complete this section in language comprehensible to the lay person. Do not simply reproduce or refer to the protocol. Further guidance is available in the guidance notes.*

Design - International prospective randomised open-label blinded-endpoint (PROBE) parallel group superiority phase IV effectiveness trial
Baseline - DSRS FOIS EAT-10 FSS (swallowing scales),NIHSS (stroke scale) and GCS (alertness scale) assessed

Days 1-6 Intervention/sham performed daily for 10 minutes. SAE's collected

Day 14 - DSRS FOIS EAT-10 FSS, NIHSS, GCS Quality of Life scales (EQ-5D5L and EQ VAS) assessed and SAE's collected

Day of discharge or death - Quality of life assesses, resource use and disposition data collected

Day 90 - Swallowing, quality of life, Zung (depression scale), mRS (mobility scale Barthel Index (activities of daily living) and TICS (cognition scale)assessed. Data on death, disposition and resource use also collected

Day 365 - Death data collected

Endpoints will compromise of comparisons between active and sham

Primary at day 14±1
Dysphagia assessed using DSRS, based on bedside clinical assessment/management conducted at days 14±1. Outcome assessment will be assessed by DSRS/FOIS-trained research coordinators, nurses or SLTs who are not involved in treatment.

Secondary at day 7±1
PES threshold, tolerability and stimulation currents; number of catheters used.Secondary at day 14±1
DSRS >3, FOIS, EAT-10 and feeding status score (FSS); NGT/PEG in situ; pneumonia; antibiotic use; weight; EQ5D-5L, EQ-VAS (source recorded - patient or proxy).
Note 1: We have included several measures of dysphagia and feeding: DSRS, FOIS, EAT-10 and FSS to triangulate the presence and magnitude of dysphagia and effects on feeding. These will be analysed together using the Wei-Lachin test.1
Secondary at discharge/death by hospital assessor blinded to treatment: Length of stay; antibiotic use; swallowing therapy contact time; time to removal of NGT/PEG; admitted to ICU; discharged with PEG; disposition (home, residential home, nursing home, hospital, death).
Secondary at day 90±7 by central telephone assessor blinded to baseline, treatment and in-hospital data (or by post): DSRS, FOIS, EAT-10, FSS; home time; dependency (modified Rankin Scale 2), disability (Barthel Index), quality of life (EQ-5D3L/EQ-VAS. SWAL-QOL), cognition (TICS 3), mood (Zung 4);2,5-9 disposition.
Note 1: These outcomes are all sensitive to therapeutic change.
Secondary at day 365 – all cause mortality.
Safety: PES has an excellent safety record in previous trials. Participants with PSD, who usually have severe stroke, will have multiple adverse events and SAEs. Hence, we will limit recording to: SAEs over 0-7 days, procedure/device-related (S)AEs over days 0-14; fatal SAEs over days 8-90 days; and all-cause mortality to day 365.
Costs
Health care resource use at discharge and day 90.

A14-1. In which aspects of the research process have you actively involved, or will you involve, patients, service users, and/or their carers, or members of the public?

- [x] Design of the research
- [x] Management of the research
- [ ] Undertaking the research
- [ ] Analysis of results
- [x] Dissemination of findings
- [ ] None of the above

Give details of involvement, or if none please justify the absence of involvement.
A Patient-Public Involvement (PPI) representative (who is a stroke survivor with residual mild swallowing problems) contributed to the development of the grant application leading to funding of this trial through participating in planning meetings and then leading on the development of PPI text for this application. He provided guidance on issues related to consent and proxy consent with family member consultees, and the need for separate information sheets and consent forms for these. A second PPI member (to be appointed) will be added as an independent member of the TSC.

The PPI member, with support from the Senior Trial Manager, will work with the Independent PPI member of the Trial Steering Committee on areas where there is no conflict of interest. Their focus will be on the writing of the participant and family-facing materials, including participant/consultee information sheets, consent forms (paper and electronic for participants and consultees) and trial leaflets. They will also support development of participant and relative-facing materials on the trial website, including a PowerPoint training slide set. At trial end, they will lead on PPI dissemination of the results.

4. RISKS AND ETHICAL ISSUES

RESEARCH PARTICIPANTS

A15. What is the sample group or cohort to be studied in this research?

Select all that apply:

- [ ] Blood
- [ ] Cancer
- [ ] Cardiovascular
- [ ] Congenital Disorders
- [ ] Dementias and Neurodegenerative Diseases
- [ ] Diabetes
- [ ] Ear
- [ ] Eye
- [ ] Generic Health Relevance
- [ ] Infection
- [ ] Inflammatory and Immune System
- [ ] Injuries and Accidents
- [ ] Mental Health
- [ ] Metabolic and Endocrine
- [ ] Musculoskeletal
- [ ] Neurological
- [ ] Oral and Gastrointestinal
- [ ] Paediatrics
- [ ] Renal and Urogenital

- ☐ Reproductive Health and Childbirth
- ☐ Respiratory
- ☐ Skin
- ☑ Stroke

Gender:	Male and female participants
Lower age limit: 18	Years
Upper age limit:	No upper age limit

A17-1. Please list the principal inclusion criteria (list the most important, max 5000 characters).

Inclusion: 800 hospitalised adults (age >=18) with recent (4-31 days) ischaemic or haemorrhagic anterior or posterior circulation stroke (as diagnosed clinico-radiologically) at a stroke centre, and clinical dysphagia defined as a functional oral intake scale score of 1 (nothing by mouth, feeding by naso-gastric tube [NGT]/percutaneous endoscopic gastrostomy [PEG] tube) or 2 (tube dependent with minimal attempts of food or liquids).

A17-2. Please list the principal exclusion criteria (list the most important, max 5000 characters).

Exclusion: Non-stroke dysphagia, e.g., due to traumatic brain haemorrhage, subarachnoid haemorrhage, brain tumour, Parkinson's disease, multiple sclerosis, severe dementia, head or neck cancer. Pre-stroke dysphagia or dependency (modified Rankin scale, mRS 4/5). Ongoing or anticipated ventilation/intubation/tracheostomy or use of electrical or magnetic stimulation. Malignant middle cerebral artery syndrome. Pregnant. Pacemaker. Need for >2 litres of oxygen. Two or more NGT pulled out unless nasal bridle in place. Investigator feels patient will not tolerate PES catheter.

RESEARCH PROCEDURES, RISKS AND BENEFITS

A18. Give details of all non-clinical intervention(s) or procedure(s) that will be received by participants as part of the research protocol. *These include seeking consent, interviews, non-clinical observations and use of questionnaires.*

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?
3. Average time taken per intervention/procedure (minutes, hours or days)
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
Consent - participant or consultee	1	0	10 minutesutes	Principal investigator or nominated research staff will take consent in hospital
Day 90 and 365 telephone assessment	2	0	30 minutes	Research staff at coordinating centre performed via telephone
Data collection - patient questionnaire	7	0	20 minutes	Performed by research staff

A19. Give details of any clinical intervention(s) or procedure(s) to be received by participants as part of the research protocol. *These include uses of medicinal products or devices, other medical treatments or assessments, mental health interventions, imaging investigations and taking samples of human biological material. Include procedures which might be received as routine clinical care outside of the research.*

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.

2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?

3. Average time taken per intervention/procedure (minutes, hours or days).

4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
Intervention	6	0	10 minutes	Performed by investigator or a trained research nurse/practitioner in hospital
Clinical assessments	4	0	15 minutes	Performed by an investigator in hospital

A20. Will you withhold an intervention or procedure, which would normally be considered a part of routine care?

○ Yes ◉ No

A21. How long do you expect each participant to be in the study in total?

365 days

A22. What are the potential risks and burdens for research participants and how will you minimise them?

For all studies, describe any potential adverse effects, pain, discomfort, distress, intrusion, inconvenience or changes to lifestyle. Only describe risks or burdens that could occur as a result of participation in the research. Say what steps would be taken to minimise risks and burdens as far as possible.

The Phagenyx® System is a non-signficant risk (NSR) device and its safety profile is well characterized by evidence accumulated from multiple phase II, III and IV clinical studies over a period of 15 years. There are no characteristic device or treatment specific effects that are considered to be serious adverse events. The additional risks associated with the clinical study design are all well understood and can be easily mitigated. None of the protocol-specific assessments are expected to add significant risk over those risks inherent in the care of patients suffering dysphagia in the subacute stroke setting.

Patients participating in this study are expected to be exposed to only marginal incremental risk over standard of care, and some patients may experience more expedient and more successful outcomes associated with their dysphagia treatment. Hence, the benefits associated with study participation are expected to outweigh any incidental incremental risk.

A23. Will interviews/ questionnaires or group discussions include topics that might be sensitive, embarrassing or upsetting, or is it possible that criminal or other disclosures requiring action could occur during the study?

○ Yes ◉ No

A24. What is the potential for benefit to research participants?

There may be none. We cannot promise the study will help participants but it might help reduce how badly their current stroke affects them. The information we get from this study will help in deciding the best treatments for stroke.

A25. What arrangements are being made for continued provision of the intervention for participants, if appropriate, once the research has finished? *May apply to any clinical intervention, including a drug, medical device, mental health intervention, complementary therapy, physiotherapy, dietary manipulation, lifestyle change, etc.*

The intervention will only be carried out in hospital. If the participant is discharged, then the intervention will be stopped. As the intervention is only for 6 days, if the participant remains in hospital past day 6 they would not continue to have the intervention.

A26. What are the potential risks for the researchers themselves? *(if any)*

None. All researchers are trained to use the devices and have completed Good Clinical Practice training.

RECRUITMENT AND INFORMED CONSENT

In this section we ask you to describe the recruitment procedures for the study. Please give separate details for different study groups where appropriate.

A27-1. How will potential participants, records or samples be identified? Who will carry this out and what resources will be used?*For example, identification may involve a disease register, computerised search of GP records, or review of medical records. Indicate whether this will be done by the direct healthcare team or by researchers acting under arrangements with the responsible care organisation(s).*

Adult patients presenting to clinical stroke services to be recruited from centres in UK hospitals

The potential participant will be approached in the hospital setting, a member of the patient's usual care team will approach the patient or their consultee (where a patient lacks capacity to consent) on admission to the respective stroke unit or TIA/stroke clinic. The investigator or their nominee, e.g. from the research team or a member of the participant's usual care team, will inform the participant or their consultee (other individual or other body with appropriate jurisdiction), of all aspects pertaining to participation in the study.

It will be explained to the potential participant that entry into the study is entirely voluntary and that their treatment and care will not be affected by their decision. It will also be explained that they can withdraw at any time without it affecting their care. In the event of their withdrawal it will be explained that data collected so far cannot be erased and we will seek consent to use the data in the final analyses where appropriate.

A27-2. Will the identification of potential participants involve reviewing or screening the identifiable personal information of patients, service users or any other person?

◉ Yes ○ No

Please give details below:
Participants will be admitted to hospital as an emergency admission and once diagnosed with stroke and assessed to fit the trial criteria, will be invited to participate in the trial

A27-3. Describe what measures will be taken to ensure there is no breach of any duty of confidentiality owed to patients, service users or any other person in the process of identifying potential participants.*Indicate what steps have been or will be taken to inform patients and service users of the potential use of their records for this purpose. Describe the arrangements to ensure that the wishes of patients and service users regarding access to their records are respected. Please consult the guidance notes on this topic.*

The screening and consent procedure will require access to the patients medical records when they are admitted to hospital in order to check eligibility for the trial. Only members of the patient's usual care team will have access to the medical records.

A27-4. Will researchers or individuals other than the direct care team have access to identifiable personal information of any potential participants?

○ Yes ◉ No

A28. Will any participants be recruited by publicity through posters, leaflets, adverts or websites?

○ Yes ◉ No

A29. How and by whom will potential participants first be approached?

The trial setting is in secondary care, in acute stroke services across the UK. Participants will be recruited from NIHR Clinical Research Network sites (adoption will be sought from the NIHR Clinical Research Network). These sites have dedicated Local Research Network nurses to facilitate recruitment and follow-up. Participants will be recruited from the acute stroke unit or emergency admissions department. The initial approach will be from a member of the patient's usual care team (which may include investigators). The investigator or their nominee will inform the participant or their consultee of all aspects pertaining to participation in the study.

A30-1. Will you obtain informed consent from or on behalf of research participants?

◉ Yes ○ No

If you will be obtaining consent from adult participants, please give details of who will take consent and how it will be done, with details of any steps to provide information (a written information sheet, videos, or interactive material). Arrangements for adults unable to consent for themselves should be described separately in Part B Section 6, and for children in Part B Section 7.

If you plan to seek informed consent from vulnerable groups, say how you will ensure that consent is voluntary and fully informed.

All participants who are able to will provide written informed consent. The Consent Form will be signed and dated by the participant before they enter the trial. The Investigator (or nominee) will explain the details of the trial and provide a Patient Information Sheet. The Investigator will answer any questions that the participant has concerning study participation. Further information will be provided on request. Potential participants will be given as long as they need to consider whether to consent.

Written informed consent, or consultee opinion from a relative consultee (by phone if not allowed in hospital) or independent physician will be obtained if a patient lacks capacity. A personal consultee will be sought in the first instance and independent physician will only be consulted if a personal consultee cannot be found. Patients with dysphagia typically have severe stroke and so may have parallel cognitive, language problems (aphasia) or wakefulness problems, it is vital that consultee consent may be sought where the patient lacks capacity.

If the participant is unable to write (e.g. in the presence of dominant hand weakness, ataxia or dyspraxia), witnessed verbal consent may be recorded on the consent form. Witnesses may be a relative or member of the usual care team who are not part of the trial.

If you are not obtaining consent, please explain why not.

Please enclose a copy of the information sheet(s) and consent form(s).

A30-2. Will you record informed consent (or advice from consultees) in writing?

◉ Yes ○ No

A31. How long will you allow potential participants to decide whether or not to take part?

Potential participants/consultees will be given as long as they need to consider whether to consent.

A32. Will you recruit any participants who are involved in current research or have recently been involved in any research prior to recruitment?

○ Yes
◉ No
○ Not Known

A33-1. What arrangements have been made for persons who might not adequately understand verbal explanations or written information given in English, or who have special communication needs?*(e.g. translation, use of interpreters)*

If needed, the usual hospital interpreter and translator services will be available to assist with discussion of the trial.

As this is an international trial the patient information sheets will be translated into a limited number of languages.

We will also use pictorial patient information sheets which explain the trial in a simplified way with a combination of pictures and simplified text. This approach has been used in previous trials in patients with acute stroke and/or dysphasia.

A33-2. What arrangements will you make to comply with the principles of the Welsh Language Act in the provision of information to participants in Wales?

If needed, the usual hospital interpreter and translator services will be available to assist with discussion of the trial, the participant information sheets, and consent forms, but the consent forms and information sheets will not be available in Welsh.

A34. What arrangements will you make to ensure participants receive any information that becomes available during the course of the research that may be relevant to their continued participation?

Participants will be provided with information and advice by the local investigator, so that they are able to make an informed choice as to whether to continue their participation in the trial.

A35. What steps would you take if a participant, who has given informed consent, loses capacity to consent during the study? *Tick one option only.*

- ○ The participant and all identifiable data or tissue collected would be withdrawn from the study. Data or tissue which is not identifiable to the research team may be retained.
- ○ The participant would 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.
- ◉ The participant would continue to be included in the study.
- ○ Not applicable – informed consent will not be sought from any participants in this research.
- ○ Not applicable – it is not practicable for the research team to monitor capacity and continued capacity will be assumed.

Further details:

If a participant loses capacity during the study consultee opinion would be sought for any further interventions or follow up.

Please complete Part B, Section 6, giving further information about arrangements for including adults unable to consent for themselves.

CONFIDENTIALITY

In this section, personal data means any data relating to a participant who could potentially be identified. It includes pseudonymised data capable of being linked to a participant through a unique code number.

Storage and use of personal data during the study

A36. Will you be undertaking any of the following activities at any stage (including in the identification of potential participants)?*(Tick as appropriate)*

- ☑ Access to medical records by those outside the direct healthcare team
- ☐ Access to social care records by those outside the direct social care team
- ☑ Electronic transfer by magnetic or optical media, email or computer networks
- ☐ Sharing of personal data with other organisations

- [ ] Export of personal data outside the EEA
- [x] Use of personal addresses, postcodes, faxes, emails or telephone numbers
- [ ] Publication of direct quotations from respondents
- [ ] Publication of data that might allow identification of individuals
- [ ] Use of audio/visual recording devices
- [x] Storage of personal data on any of the following:
  - [x] Manual files (includes paper or film)
  - [x] NHS computers
  - [ ] Social Care Service computers
  - [ ] Home or other personal computers
  - [x] University computers
  - [ ] Private company computers
  - [x] Laptop computers

Further details:
Medical records will be reviewed by trained members of the national coordinating team (delegated this responsibility by the Chief Investigator), in order to verify source data and confirm written informed consent and device accountability.
Individual participant medical information obtained as a result of this trial is considered confidential and disclosure to third parties is prohibited without the participant's permission.
Participant confidentiality is ensured by the use of unique trial identity code allocated at randomisation and used as identifiers on case report forms and other trial documents - in the format - centre number/initials/trial number. Full names appear on consent forms, and names and date of birth will be entered onto the database by sites at randomisation. These allow correct allocation of subsequently entered trial data by the site staff.
Data collection will be via a secure online database with access granted to local investigator teams after appropriate training, with access only via a unique username and password
Names, addresses and telephone numbers will be collected by local investigator teams via a secure online database and used to contact participants for the telephone interviews at day 90. These interviews are carried out by researchers at the University of Nottingham.
Paper files are stored in locked cabinets, in locked offices only accessible by members of the national coordinating team.
NHS and University computers are used to store and analyse data in accordance with local policies and standard operating procedures which comply with the requirements of the Data Protection Act 2018, ICH Good Clinical Practice and the Department of Health Policy Framework for Health and Social Care.

A37. Please describe the physical security arrangements for storage of personal data during the study?

Access is only permitted to investigators who have received training and approval from the chief or principal investigator for the trial. The database has a log of all data entered on the database including corrections made, by whom and time of entry.
Investigators have limited access to the database. They only have access to their site data, which they will have inputted. Data can be printed from the database, by those who have entered it.
The database is locked whilst maintenance takes place with no unauthorised access.
Paper CRF's are locked in a cabinet within a locked room. Only trial staff with approval from the Chief Investigator will have access to the data

A38. How will you ensure the confidentiality of personal data?*Please provide a general statement of the policy and procedures for ensuring confidentiality, e.g. anonymisation or pseudonymisation of data.*

The raw data are only accessible by the trial programmer and kept in an AES encrypted file system. The data are matched with participants in a separate password protected anonymised database using their unique trial code number (centre/initials/trial number).
All trial staff and investigators will endeavour to protect the rights of the trial's participants to privacy and informed consent, and will adhere to the Data Protection Act, 2018. The CRF will only collect the minimum required information for the purposes of the trial. CRFs will be held securely, in a locked room, or locked cupboard or cabinet. Access to the information will be limited to the trial staff and investigators and relevant regulatory authorities (see above). Computer

held data including the trial database will be held securely and password protected. All data will be stored on a secure dedicated web server. Access will be restricted by user identifiers and passwords (encrypted using a one way encryption method).
Information about the trial in the participant's medical records / hospital notes will be treated confidentially in the same way as all other confidential medical information.
Electronic data will be backed up every 24 hours to both local and remote media in encrypted format.

A40. Who will have access to participants' personal data during the study? *Where access is by individuals outside the direct care team, please justify and say whether consent will be sought.*

The consent forms specifically address the need to contact the participant and/or their GP for the day 90 and day 365 telephone interview. At Day 365 NHS Digital/EDRID/central NHS bodies will be contacted to collect death data. The trained members of the national coordinating team (delegated by the chief investigator) will perform the telephone assessments and access the participant's personal contact details in order to do this. The information is held on a secure database and accessible only to the members of the national coordinating team and the local clinical team who entered it.

Storage and use of data after the end of the study

A41. Where will the data generated by the study be analysed and by whom?

The chief investigator will delegate the responsibility for data analysis to a member of the Nottingham stroke trials statistical team at the University of Nottingham.

A42. Who will have control of and act as the custodian for the data generated by the study?

	Title	Forename/Initials	Surname
	Prof	Philip	Bath
Post	Professor of Stroke Medicine		
Qualifications			
Work Address	Stroke Trials Unit, MH&CN		
	D Floor South Block, QMC		
	Nottingham		
Post Code	NG7 2NR		
Work Email	philip.bath@nottingham.ac.uk		
Work Telephone	01158231765		
Fax			

A43. How long will personal data be stored or accessed after the study has ended?

- ○ Less than 3 months
- ○ 3 – 6 months
- ◉ 6 – 12 months
- ○ 12 months – 3 years
- ○ Over 3 years

A44. For how long will you store research data generated by the study?

Years: 7
Months: 0

A45. Please give details of the long term arrangements for storage of research data after the study has ended.*Say where data will be stored, who will have access and the arrangements to ensure security.*

In compliance with the ICH/GCP guidelines, regulations and in accordance with the University of Nottingham Code of Research Conduct and Research Ethics, the Chief or local Principal Investigator will maintain all records and documents regarding the conduct of the study. These will be retained for at least 7 years or for longer if required. If the responsible investigator is no longer able to maintain the study records, a second person will be nominated to take over this responsibility.

The Trial Master File and trial documents held by the Chief Investigator on behalf of the Sponsor shall be finally archived at secure archive facilities at the University of Nottingham. This archive shall include all trial databases and associated meta-data encryption codes.

Personal data will be destroyed after 12 months as it will no longer be necessary to contact a participant.

INCENTIVES AND PAYMENTS

A46. Will research participants receive any payments, reimbursement of expenses or any other benefits or incentives for taking part in this research?

○ Yes ◉ No

A47. Will individual researchers receive any personal payment over and above normal salary, or any other benefits or incentives, for taking part in this research?

○ Yes ◉ No

A48. Does the Chief Investigator or any other investigator/collaborator have any direct personal involvement (e.g. financial, share holding, personal relationship etc.) in the organisations sponsoring or funding the research that may give rise to a possible conflict of interest?

○ Yes ◉ No

NOTIFICATION OF OTHER PROFESSIONALS

A49-1. Will you inform the participants' General Practitioners (and/or any other health or care professional responsible for their care) that they are taking part in the study?

◉ Yes ○ No

If Yes, please enclose a copy of the information sheet/letter for the GP/health professional with a version number and date.

A49-2. Will you seek permission from the research participants to inform their GP or other health/ care professional?

◉ Yes ○ No

It should be made clear in the participant's information sheet if the GP/health professional will be informed.

PUBLICATION AND DISSEMINATION

A50. Will the research be registered on a public database?

The UK Policy Framework for Health and Social Care Research sets out the principle of making information about research publicly available. Furthermore: Article 19 of the World Medical Association Declaration of Helsinki adopted in 2008 states that "every clinical trial must be registered on a publicly accessible database before recruitment of the first subject"; and the International Committee of Medical Journal Editors (ICMJE) will consider a clinical trial for publication only if it has been registered in an appropriate registry. Please see guidance for more information.

◉ Yes ○ No

Please give details, or justify if not registering the research.
The trial will be registered with ISRCTN

Please ensure that you have entered registry reference number(s) in question A5-1.

A51. How do you intend to report and disseminate the results of the study?*Tick as appropriate:*

- ☑ Peer reviewed scientific journals
- ☐ Internal report
- ☑ Conference presentation
- ☐ Publication on website
- ☐ Other publication
- ☑ Submission to regulatory authorities
- ☐ Access to raw data and right to publish freely by all investigators in study or by Independent Steering Committee on behalf of all investigators
- ☐ No plans to report or disseminate the results
- ☐ Other (please specify)

A52. If you will be using identifiable personal data, how will you ensure that anonymity will be maintained when publishing the results?

Not applicable as no identifiable data will be included in any publication

A53. How and when will you inform participants of the study results?

If there will be no arrangements in place to inform participants please justify this.
At the end of the trial the participant will be able receive a summary of the trial results, as per consent form.

5. Scientific and Statistical Review

A54. How has the scientific quality of the research been assessed?*Tick as appropriate:*

- ☑ Independent external review
- ☐ Review within a company
- ☐ Review within a multi−centre research group
- ☑ Review within the Chief Investigator's institution or host organisation
- ☑ Review within the research team
- ☐ Review by educational supervisor
- ☐ Other

Justify and describe the review process and outcome. If the review has been undertaken but not seen by the researcher, give details of the body which has undertaken the review:
Reviewed by funders

For all studies except non-doctoral student research, please enclose a copy of any available scientific critique reports, together with any related correspondence.

For non-doctoral student research, please enclose a copy of the assessment from your educational supervisor/ institution.

A56. How have the statistical aspects of the research been reviewed? *Tick as appropriate:*

- ☐ Review by independent statistician commissioned by funder or sponsor
- ☐ Other review by independent statistician
- ☐ Review by company statistician
- ☑ Review by a statistician within the Chief Investigator's institution
- ☑ Review by a statistician within the research team or multi−centre group
- ☐ Review by educational supervisor
- ☐ Other review by individual with relevant statistical expertise
- ☐ No review necessary as only frequencies and associations will be assessed – details of statistical input not required

In all cases please give details below of the individual responsible for reviewing the statistical aspects. If advice has been provided in confidence, give details of the department and institution concerned.

	Title	Forename/Initials	Surname
	Dr	Trish	Hepburn
Department	Clinical Trials Unit		
Institution	University of Nottingham		
Work Address	Clinical Trials Unit		
	Building 42, University Park		
	Nottingham		
Post Code	NG7 2RD		
Telephone	01158231561		
Fax	01157484092		
Mobile			
E-mail			

Please enclose a copy of any available comments or reports from a statistician.

A57. What is the primary outcome measure for the study?

Primary at day 14
Dysphagia assessed using DSRS, based on bedside clinical assessment/management conducted at days 14±1. Outcome assessment will be assessed by DSRS/FOIS-trained research coordinators, nurses or SLTs who are not involved in treatment.

A58. What are the secondary outcome measures? *(if any)*

Secondary at day 14
DSRS >3, FOIS, EAT-10 and feeding status score (FSS); NGT/PEG in situ; pneumonia; antibiotic use; weight; EQ5D-5L, EQ-VAS (source recorded - patient or proxy).
Note 1: We have included several measures of dysphagia and feeding: DSRS, FOIS, EAT-10 and FSS to triangulate the presence and magnitude of dysphagia and effects on feeding. These will be analysed together using the Wei-Lachin test.

Secondary at discharge/death by hospital assessor blinded to treatment: Length of stay; antibiotic use; swallowing therapy contact time; time to removal of NGT/PEG; admitted to ICU; discharged with PEG; disposition (home, residential home, nursing home, hospital, death).

Secondary at day 90 by central telephone assessor blinded to baseline, treatment and in-hospital data (or by post): DSRS, FOIS, EAT-10, FSS; home time; dependency (modified Rankin Scale 2), disability (Barthel Index), quality of life (EQ-5D5L/EQ-VAS. SWAL-QOL), cognition (TICS 3), mood (Zung 4), disposition.
Note 1: These outcomes are all sensitive to therapeutic change.

Secondary at day 365 – all cause mortality.

Safety: PES has an excellent safety record in previous trials. Participants with PSD, who usually have severe stroke, will have multiple adverse events and SAEs. Hence, we will limit recording to: SAEs over 0-7 days, procedure/device-related (S)AEs over days 0-14; fatal SAEs over days 8-90 days; and all-cause mortality to day 365.

Costs
Health care resource use at discharge and day 90.

A59. What is the sample size for the research? *How many participants/samples/data records do you plan to study in total? If there is more than one group, please give further details below.*

Total UK sample size:	467
Total international sample size (including UK):	800
Total in European Economic Area:	333

Further details:

A60. How was the sample size decided upon? *If a formal sample size calculation was used, indicate how this was done, giving sufficient information to justify and reproduce the calculation.*

The primary outcome, DSRS, will be compared between PES and no PES using multiple linear regression with adjustment for stratification and minimisation variables. The null hypothesis is that PES does not alter DSRS at day 14 in participants with PSD.

Assuming 1:1 randomisation; alpha 5% (two-tailed); power 90%; DSRS difference 1.2 (this target difference lies in the minimal clinically important difference range of 0.3-2.5); standard deviation 5.0; losses 3% (greater than seen in previous PES trials); crossovers 3%; sample rounded up; a sample size of N=800 is needed (PES n=400, control n=400) (assumptions based on pilot trials and STEPS) (using standard t test sample size formula). We and others have shown that adjustment for covariates improves statistical power and so can reduce sample size; however, we have not taken account of this in the above sample size calculation since the relevance of these findings to analysis of DSRS remains unclear. Nevertheless, it is likely that covariate adjustment will improve statistical power so that the final power will probably be greater than assumed here.

Recalculation of sample size: We will investigate our assumptions for the standard deviation of the primary outcome and for the proportion of participants with missing primary outcome data. We will discuss any variation in these parameters with the DMC and TSC and any proposed revision to the target sample size.

A61. Will participants be allocated to groups at random?

(●) Yes ( ) No

If yes, please give details of the intended method of randomisation:
Whilst investigators, participants and their family will be unblinded, outcome assessors will be blinded to treatment. Nevertheless, although PES will not be masked, many participants will have severe stroke and will have a nasogastric tube inserted and so they may be unaware of treatment assignment.

Investigators (medics, research nurses/coordinators, speech therapists) many enrol participants. Randomised treatment assignment will occur when essential baseline data are entered into the trial computer system by investigators. As such, allocation is concealed from investigators up to the time that they have screened, consented and collected and entered baseline data into the trial database.

Maintenance of randomisation codes and procedures for breaking code
Adaptive randomisation will use minimisation so there will be no treatment code lists. The trial computer system will record what treatment each participant is assigned to.

The trial will have a prospective randomised open-label blinded-endpoint (PROBE) design so participants randomised to control will receive standard care. Outcomes will be assessed blinded to treatment assignment.

Investigators who are not involved in outcome assessment can determine, if necessary, what treatment is being received by seeing if they have a PES tube inserted. Masked outcome assessors should never need to unblind themselves.

A62. Please describe the methods of analysis (statistical or other appropriate methods, e.g. for qualitative research) by which the data will be evaluated to meet the study objectives.

Characteristics of randomised participants will be compared between the two trial arms at baseline, using appropriate descriptive statistics: number %, median [interquartile range], mean (standard deviation). Analysis of the primary outcome will be performed by intention-to-treat using multiple linear regression, with adjustment for stratification/minimisation factors (country, age, sex, DSRS, NIHSS, stroke type, circulation/syndrome, time onset to randomisation), and fully specified in the SAP. Secondary outcomes will similarly be compared using multiple linear regression (e.g. Barthel index), ordinal logistic regression (e.g. mRS, FOIS), and Cox proportional hazards regression (e.g. time to NGT/PEG removal, death), again each with adjustment for randomisation factors. Absolute and relative measures of effect and 95% confidence intervals will be presented for each analysis. A worst score will be assigned at day 90 for people who die (e.g. DSRS=13, FOIS=0, mRS=6) to avoid losing participants in analyses and missing a “kill or cure” effect, and to anchor analyses, as we did in ENOS, TARDIS and RIGHT-2.

The trial statistician will perform statistical analyses using code written in the R language. One formal interim analysis will be performed to guide the DMC at the stop-go time-point. The stopping rules for effectiveness are based on the combination of presence of ‘proof beyond a reasonable doubt’ and the likelihood that the results would change clinical practice. The possible DMC recommendations at any assessment are:
1. Stop enrolment if the study is negative: statistical evidence that DSRS or fatal SAE rates are significantly higher in the PES than sham group ($p<0.01$);
2. Stop enrolment if the study is positive: the combination of statistical evidence that DSRS is significantly lower in the PES than sham group “beyond reasonable doubt” (i.e. Haybittle-Peto boundary rule, $p<0.001$) and the overall trial results will lead to a change in clinical practice, e.g. by taking account of delta DSRS and evidence that at least some secondary outcomes are also being benefitted (some of, e.g. FOIS, length of hospital stay, pneumonia, antibiotic use).
3. Continue enrolment if the study is neutral: or if conditions 1 and 2 are not present.
4. Modify study design – if it appears that:
a. Sample size calculation assumptions were incorrect, e.g., if standard deviation exceeds 6.0;
b. Apparent study design aspects will lead to incorrect study conclusions;
c. Specific clinical procedures jeopardise the safe execution of the study.

Formal statistical analyses will be used as “stopping guidelines” rather than absolute rules. In the light of interim data, and other evidence from relevant studies (including updated overviews of relevant randomised controlled trials), the DMC will inform the TSC, if in their view there is proof beyond reasonable doubt that the data indicate that the intervention is either clearly indicated or contra-indicated, either for all or for a particular subgroup of study participants. A decision to inform the TSC will in part be based on statistical considerations. Appropriate criteria for proof beyond reasonable doubt are not specified precisely. A difference of at least 3 standard errors in the primary endpoint may be needed to justify halting, or modifying, the study prematurely. This approach has the practical advantage that the exact number of analyses are of little importance, and so no fixed schedule is proposed. The DMC may also consider supporting evidence from secondary outcomes in their decision making, but the overall guidance remains that the results should be sufficiently convincing to change practice.

6. MANAGEMENT OF THE RESEARCH

A63. Other key investigators/collaborators. *Please include all grant co−applicants, protocol co−authors and other key members of the Chief Investigator’s team, including non-doctoral student researchers.*

	Title	Forename/Initials	Surname
	Prof	Shaheen	Hamdy
Post	Prof of Neurogastroenterology		
Qualifications			
Employer	University of Manchester		

Work Address	CSB, Salford Royal Hospital Salford
Post Code	M6 8HD
Telephone	
Fax	
Mobile	
Work Email	Shaheen.Hamdy@manchester.ac.uk

Title	Forename/Initials	Surname
Dr	Tim	England

Post Qualifications	Consultant Stroke Physician
Employer	University of Nottingham
Work Address	Vascular Medicine, Division of Medical Sciences & GEM, The Medical School, Royal Derby Hospital, Uttoxeter Rd, Derby
Post Code	DE22 3NE
Telephone	01332724668
Fax	
Mobile	
Work Email	timothy.england@nottingham.ac.uk

Title	Forename/Initials	Surname
Prof	Alan	Montgomery

Post Qualifications	Professor of Medical Statistics and Clinical Trials
Employer	University of Nottingham
Work Address	Clinical Trials Unit Building 42, University Park Nottingham
Post Code	NG7 2RD
Telephone	01158231561
Fax	
Mobile	
Work Email	alan.montgomery@nottingham.ac.uk

Title	Forename/Initials	Surname
Prof	Marilyn	James

Post Qualifications	Professor of Health Economics
Employer	University of Nottingham
Work Address	Div of Rehab and Ageing, QMC Derby Road Nottingham
Post Code	NG7 2NR
Telephone	
Fax	
Mobile	
Work Email	marilyn.james@nottingham.ac.uk

	Title	Forename/Initials	Surname
	Prof	Nikola	Sprigg
Post Qualifications	Professor of Stroke medicine		
Employer	University of Nottingham		
Work Address	Stroke Trials Unit, Queens Medical Centre Derby Road Nottingham		
Post Code	NG7 2UH		
Telephone	01158231765		
Fax			
Mobile			
Work Email	nikola.sprigg@nottingham.ac.uk		

	Title	Forename/Initials	Surname
	Prof	Craig	Smith
Post Qualifications	Professor of Stroke Medicine		
Employer	University of Manchester		
Work Address			
Post Code			
Telephone	01612060623		
Fax			
Mobile			
Work Email	craig.smith-2@manchester.ac.uk		

	Title	Forename/Initials	Surname
	Dr	Lisa	Everton
Post Qualifications	Specialist Speech and Language Therapist		
Employer	University of Nottingham		
Work Address	Stroke Trials Unit, Queens Medical Centre Derby Road Nottingham		
Post Code	NG7 2UH		
Telephone	01159709221		
Fax			
Mobile			
Work Email	lisa.everton@nottingham.ac.uk		

A64. Details of research sponsor(s)

A64-1. Sponsor

Lead Sponsor

Status:
- ○ NHS or HSC care organisation
- ◉ Academic
- ○ Pharmaceutical industry
- ○ Medical device industry
- ○ Local Authority
- ○ Other social care provider (including voluntary sector or private organisation)
- ○ Other

Commercial status: Non-Commercial

If Other, please specify:

Contact person

Name of organisation	University of Nottingham
Given name	Angela
Family name	Shone
Address	R&I, East Atrium, Jubilee Conference Centre
Town/city	Triumph Road, Nottingham
Post code	NG8 1DH
Country	United Kingdom
Telephone	01158467906
Fax	
E-mail	sponsor@nottingham.ac.uk

Legal representative for clinical investigation of medical device (studies involving Northern Ireland only)
Clinical Investigations of Medical Devices that take place in Northern Ireland must have a legal representative of the sponsor that is based in Northern Ireland or the EU

Contact person

Name of organisation	
Given name	
Family name	
Address	
Town/city	
Post code	
Country	
Telephone	
Fax	
E-mail	

A65. Has external funding for the research been secured?

Please tick at least one check box.

☑ Funding secured from one or more funders

☐ External funding application to one or more funders in progress

☐ No application for external funding will be made

What type of research project is this?

◉ Standalone project

○ Project that is part of a programme grant

○ Project that is part of a Centre grant

○ Project that is part of a fellowship/ personal award/ research training award

○ Other

Other – please state:

Please give details of funding applications.

Organisation	NIHR
Address	University of Southampton
	Alpha House, Enterprise Road
	Southampton
Post Code	SO16 7NS
Telephone	
Fax	
Mobile	
Email	netspostawardsetup@nihr.ac.uk

Funding Application Status: ◉ Secured ○ In progress

Amount: £1,956,638.49

Duration

Years: 3

Months: 6

If applicable, please specify the programme/ funding stream:

What is the funding stream/ programme for this research project?

A66. Has responsibility for any specific research activities or procedures been delegated to a subcontractor (other than a co-sponsor listed in A64-1) ? *Please give details of subcontractors if applicable.*

○ Yes ◉ No

A67. Has this or a similar application been previously rejected by a Research Ethics Committee in the UK or another country?

○ Yes ◉ No

Please provide a copy of the unfavourable opinion letter(s). You should explain in your answer to question A6-2 how the

reasons for the unfavourable opinion have been addressed in this application.

A68-1. Give details of the lead NHS R&D contact for this research:

	Title	Forename/Initials	Surname
	Ms	Jennifer	Boston
Organisation	Nottingham University Hospitals Trust		
Address	Queens Medical Centre		
	Derby Road		
	Nottingham		
Post Code	NG7 2UH		
Work Email	researchsponsor@nuh.nhs.uk		
Telephone	01159249924		
Fax			
Mobile			

Details can be obtained from the NHS R&D Forum website: http://www.rdforum.nhs.uk

A68-2. Select Local Clinical Research Network for NHS Organisation identified in A68-1:

East Midlands

For more information, please refer to the question specific guidance.

A69-1. How long do you expect the study to last in the UK?

Planned start date: 03/01/2022
Planned end date: 30/06/2025
Total duration:
Years: 3 Months: 5 Days: 28

A71-1. Is this study?

- ○ Single centre
- ◉ Multicentre

A71-2. Where will the research take place? *(Tick as appropriate)*

- ☑ England
- ☑ Scotland
- ☑ Wales
- ☑ Northern Ireland
- ☑ Other countries in European Economic Area

Total UK sites in study 35

Number of sites anticipated in the Community 25

Does this trial involve countries outside the EU?

○ Yes ◉ No

A72. Which organisations in the UK will host the research? *Please indicate the type of organisation by ticking the box and give approximate numbers if known:*

☑ NHS organisations in England	20
☑ NHS organisations in Wales	5
☑ NHS organisations in Scotland	5
☑ HSC organisations in Northern Ireland	5
☐ GP practices in England	
☐ GP practices in Wales	
☐ GP practices in Scotland	
☐ GP practices in Northern Ireland	
☐ Joint health and social care agencies (eg community mental health teams)	
☐ Local authorities	
☐ Phase 1 trial units	
☐ Prison establishments	
☐ Probation areas	
☐ Independent (private or voluntary sector) organisations	
☐ Educational establishments	
☐ Independent research units	
☐ Other (give details)	
Total UK sites in study:	35

A73-1. Will potential participants be identified through any organisations other than the research sites listed above?

○ Yes ◉ No

A74. What arrangements are in place for monitoring and auditing the conduct of the research?

The trial will be overseen by a Trial Steering Committee (TSC) and independent Data Monitoring Committee (DMC) and run by a Trial Management Group (TMG). It will be managed from the International Coordinating Centre (ICC) based in the Nottingham Stroke Trials Unit (STU); the ICC will also manage UK sites whilst National Coordinating Centres (NCC) will manage sites in Austria, Denmark and Germany. Funded trial staff will be based at the ICC; NCCs will use existing local staff, as done in ENOS and TARDIS. NCCs will join the TMC for regular videoconferences to ensure timely recruitment and follow-up, and to address developing problems. Sites will be trained on trial processes by the ICC and NCCs, videos on the website and via the protocol and manual; specific training on PES will be given by Phagenesis and the trial SLT. Specific trial materials (protocol summary, PIS/RIS, consent forms, manual, videos) will be translated into German and Danish. Further details are given below.

Trial Steering Committee
This will lead the trial strategically, reviewing recruitment rate, treatment delivery, data integrity and trial event rates. Any new data emergent from other trials will be discussed for potential impact on PhEAST. The TSC will work according to a charter.

Trial Management Group
This will manage the trial daily and will meet every three weeks. The group will monitor trial accrual, centre

management (with local CRN research nurses/practitioners) and ensure recruitment strategy remains on target. Centres will be regularly contacted in the event of participant attrition. This approach will be mirrored in the National Coordinating Centres in AT, DE and DK.

Independent Data Monitoring Committee
This will review safety as well as the validity and scientific merit of the trial. Unblinded data will be provided by a statistician with no other role in the study and discussed twice yearly. A DMC Charter will be drawn up in line with the Damocles Study Group Guidance.40 The Charter will define the schedule and format of twice yearly meetings (or scheduled as necessary), the method and timing of interim reports and stopping rules:

A76. Insurance/ indemnity to meet potential legal liabilities

***Note:* in this question to NHS indemnity schemes include equivalent schemes provided by Health and Social Care (HSC) in Northern Ireland**

A76-1. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of the sponsor(s) for harm to participants arising from the management of the research? *Please tick box(es) as applicable.*

Note: Where a NHS organisation has agreed to act as sponsor or co-sponsor, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For all other sponsors, please describe the arrangements and provide evidence.

☐ NHS indemnity scheme will apply (NHS sponsors only)

☑ Other insurance or indemnity arrangements will apply (give details below)

The University of Nottingham as research Sponsor indemnifies its staff with both public liability insurance and clinical trials insurance in respect of claims made by research subjects.

Please enclose a copy of relevant documents.

A76-2. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of the sponsor(s) or employer(s) for harm to participants arising from the design of the research? *Please tick box(es) as applicable.*

Note: Where researchers with substantive NHS employment contracts have designed the research, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For other protocol authors (e.g. company employees, university members), please describe the arrangements and provide evidence.

☐ NHS indemnity scheme will apply (protocol authors with NHS contracts only)

☑ Other insurance or indemnity arrangements will apply (give details below)

The University of Nottingham as research Sponsor indemnifies its staff with both public liability insurance and clinical trials insurance in respect of claims made by research subjects.

Please enclose a copy of relevant documents.

A76-3. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of investigators/collaborators arising from harm to participants in the conduct of the research?

Note: Where the participants are NHS patients, indemnity is provided through the NHS schemes or through professional indemnity. Indicate if this applies to the whole study (there is no need to provide documentary evidence). Where non-NHS sites are to be included in the research, including private practices, please describe the arrangements which will be made at these sites and provide evidence.

☑ NHS indemnity scheme or professional indemnity will apply (participants recruited at NHS sites only)

☐ Research includes non-NHS sites (give details of insurance/ indemnity arrangements for these sites below)

Please enclose a copy of relevant documents.

A77. Has the sponsor(s) made arrangements for payment of compensation in the event of harm to the research participants where no legal liability arises?

○ Yes ◉ No

Please enclose a copy of relevant documents.

A78. Could the research lead to the development of a new product/process or the generation of intellectual property?

◉ Yes ○ No ○ Not sure

Part B: Section 2

A. General information

Information in this sub-section will be included in applications to the Research Ethics Committee and NHS R & D offices at the research sites.

1. Is the manufacturer (or other organisation responsible for developing the device) the same organisation named as lead sponsor for this study?

○ Yes ◉ No

If No, please give details of the manufacturer or other organisation responsible for developing the device below:

Organisation	Phagenesis Ltd
Address	Unit 18 Enterprise House Manchester Science Park Manchester
Post Code	M15 6SE
Country	United Kingdom
Telephone	01618204525
Fax	
Mobile	
E-mail	

2. Details of the medical devices to be used in the study

Name of the manufacturer:	Phagenesis Ltd
Manufacturer's trade name for the device:	Phagenesis Phagenyx System
Device identification name and/or number:	
Name:	Phagenyx base station
Number:	EPSBX
Generic name of device and principal intended use(s):	Phagenyx base station - pharangeal electric stimulation to treat dysphagia following stroke
Length of time since device came into use:	15 years
Name of the manufacturer:	Phagenesis Ltd
Manufacturer's trade name for the device:	Phagenesis Phagenyx System
Device identification name and/or number:	
Name:	Phagenyx catheter
Number:	PNX-1000
Generic name of device and principal intended use(s):	Phagenyx catheter - pharangeal electric stimulation to treat dysphagia following stroke
Length of time since device came into use:	15 years

3-1. Further details of the purpose of the study

Does the study involve:

- ○ Investigation of a new medical device
- ○ Investigation of new implantable material
- ○ Use of an existing product outside the terms of its UKCA/CE UKNI/CE marked intended purpose
- ○ Use of a modified product
- ◉ Use of an existing product within its UKCA/CE UKNI/CE marked intended purpose

B. All research other than CTIMPs

In this sub-section, an adult means a person aged 16 or over.

B1. What impairing condition(s) will the participants have?

The study must be connected to this condition or its treatment.

Ischaemic or haemorrhagic anterior or posterior circulation stroke (as diagnosed clinico-radiologically) at a stroke centre, and clinical dysphagia defined as a functional oral intake scale score of 1 (nothing by mouth, feeding by naso-gastric tube [NGT]/percutaneous endoscopic gastrostomy [PEG] tube) or 2 (tube dependent with minimal attempts of food or liquids).

B2. Justify the inclusion of adults unable to consent for themselves. It should be clear why the research could not be carried out as effectively if confined to adults capable of giving consent.

Up to 50% of stroke patients may be incapacitated at the time of the stroke (e.g. due to dysphasia or semi-coma). This is a large and important group of patients who may potentially benefit if the intervention works.

B3. Who in the research team will decide whether or not the participants have the capacity to give consent? What training/experience will they have to enable them to reach this decision?

Someone from the patient's usual care team will assess capacity (which may include the researchers, who are the chief/principle investigator, his consultant colleagues and the specialist stroke nurses). The trial staff are well trained in Stroke Medicine and are trained to assess a patient's capacity based on whether they can: understand the information conveyed, retain this information, weigh the risks against the benefits and come to an informed decision.

B4. Does the research have the potential to benefit participants who are unable to consent for themselves?

◉ Yes ○ No

If Yes, please indicate the nature of this benefit. You may refer back to your answer to Question A24.

The potential benefit would be the same for those participants who can consent for themselves.

B5. Will the research contribute to knowledge of the causes or the treatment or care of persons with the same impairing condition (or a similar condition)?

◉ Yes ○ No

If Yes, please explain how the research will achieve this:

This research is intended to identify a potential new treatment for stroke - the condition that will have caused incapacity.

B6. Will the research involve any foreseeable risk or burden for these participants, or interfere in any way with their freedom of action or privacy?

◉ Yes ○ No

If Yes, please give an assessment below. Highlight any risk, burden or discomfort specific to these participants and say what will be done to minimise it. You may refer back to your answers to Questions A22 and A23.

The Phagenyx® System is a non-signficant risk (NSR) device and its safety profile is well characterized by evidence accumulated from multiple phase II, III and IV clinical studies over a period of 15 years. There are no characteristic device or treatment specific effects that are considered to be serious adverse events. The additional risks associated with the clinical study design are all well understood and can be easily mitigated. None of the protocol-specific assessments are expected to add significant risk over those risks inherent in the care of patients suffering dysphagia in the subacute stroke setting.

Patients participating in this study are expected to be exposed to only marginal incremental risk over standard of

care, and some patients may experience more expedient and more successful outcomes associated with their dysphagia treatment. Hence, the benefits associated with study participation are expected to outweigh any incidental incremental risk.

Questions B7 and B8 apply to any participants recruited in England and Wales.

B7. What arrangements will be made to identify and consult persons able to advise on the presumed wishes and feelings of participants unable to consent for themselves and on their inclusion in the research?

The investigator (or designee) is responsible for performing consent procedures for each patient enrolled in the study. Written informed consent, or personal consultee opinion from a relative (by phone if not allowed in hospital) if patient lacks capacity. Since patients with dysphagia typically have severe stroke and so may have parallel cognitive, language (dysphasia) or wakefulness problems, it is vital that consultee opinion may be sought where the patient lacks capacity. This approach has been used in previous trials in patients with acute stroke and/or dysphagia: STEPS, TARDIS, TICH-2, RIGHT-2, PHAST-TRAC, PHADER.

Please enclose a copy of the written information to be provided to consultees. This should describe their role under section 32 of the Mental Capacity Act and provide information about the research similar to that which might be given to participants able to consent for themselves.

B8. Is it possible that a participant requiring urgent treatment might need to be recruited into research before it is possible to identify and consult a person under B7?

○ Yes ◉ No

If Yes, say whether arrangements will be made instead to seek agreement from a registered medical practitioner and outline these arrangements. Or, if this is also not feasible, outline how decisions will be made on the inclusion of participants and what arrangements will be made to seek consent from the participant (if capacity has been recovered) or advice from a consultee as soon as practicable thereafter.

Question B7-1 applies to any participants recruited in Scotland.

B7-1. What arrangements will be made to identify and seek consent from a guardian or welfare attorney or, if there is no such person, from the participant's nearest relative?

The investigator (or designee) is responsible for performing consent procedures for each patient enrolled in the study. Written informed consent or legal representative consent from a welfare attorney/guardian if one has been appointed(Scottish sites),if not, a nearest relative (by phone if not allowed in hospital) if patient lacks capacity. Since patients with dysphagia typically have severe stroke and so may have parallel cognitive, language (dysphasia) or wakefulness problems, it is vital that legal representative consent may be sought from a welfare guardian/attorney where the patient lacks capacity. This approach has been used in previous trials in patients with acute stroke and/or dysphagia: STEPS, TARDIS, TICH-2, RIGHT-2, PHAST-TRAC, PHADER.7-9,22-24 Participant consent will be sought if the participant regains capacity.

Please enclose a copy of the written information to be provided and the consent form to be used. The information sheet should provide information about the research similar to that which might be given to participants able to consent for themselves.

Questions B7-2 and B8-2 apply to any participants recruited in Northern Ireland.

B7-2. What arrangements will be made to consult a close relative or close friend able to advise on the inclusion of the participant and on their likely wishes?

The investigator (or designee) is responsible for performing consent procedures for each patient enrolled in the study. Written informed consent, or consent from a personal consultee if patient lacks capacity. This may be taken by phone if not allowed in hospital. An independent physician will only be asked if no personal consultee can be contacted. Since patients with dysphagia typically have severe stroke and so may have parallel cognitive, language (dysphasia) or wakefulness problems, it is vital that consultee opinion may be sought where the patient lacks capacity. This approach has been used in previous trials in patients with acute stroke and/or dysphagia: STEPS, TARDIS, TICH-2, RIGHT-2, PHAST-TRAC, PHADER.

B8-2. Is it possible that a participant might need to be treated urgently as part of the research before it is possible to

consult with a close relative or close friend?

◯ Yes ◉ No

If Yes, say whether arrangements will be made instead to seek agreement from a registered medical practitioner and outline these arrangements. Or, if this is also not feasible, outline how decisions will be made on the inclusion of participants.

B9. What arrangements will be made to continue to consult such persons during the course of the research where necessary?

It will be necessary to obtain and store contact details for the consultee/legal representative for this purpose.

B10. What steps will you take, if appropriate, to provide participants who are unable to consent for themselves with information about the research, and to consider their wishes and feelings?

A verbal explanation will be provided in terms suited to the participant's comprehension of the purposes, procedures and potential risks of the study and of their rights as research participants. Pictures and simplified written language will be used here where relevant to facilitate comprehension of information.

B11. Is it possible that the capacity of participants could fluctuate during the research? How would this be handled?

Yes. If the participant regains capacity during the trial then they will be given an information sheet and, should they wish to continue in the trial, sign a consent form. The trial is voluntary and the participants may withdraw at any time without giving reason.

B12-1. What will be the criteria for withdrawal of participants?

The trial is voluntary and the participants may withdraw at any time without giving reason and without it affecting their care. Any decision to withdraw a participant who lacks capacity will be made by the consultee.

If new information becomes available to suggest that the trial is unsafe or there are better alternative treatments, then this information will be conveyed to the patient and withdrawal from the trial will be considered.

B13. Describe what steps will be taken to ensure that nothing is done to which participants appear to object (unless it is to protect them from harm or minimise pain or discomfort).

If the participant appears to object to a procedure in the trial, that procedure can be stopped. All trial staff with direct patient contact are sensitive to the needs of stroke patients and every effort will be made to maintain the participant's comfort. This may include involving their next of kin.

B14. Describe what steps will be taken to ensure that nothing is done which is contrary to any advance decision or statement by the participant?

Permission from the consultee will always be sought. This information should become evident at this point. If information on an advanced decision only becomes available after consent into the trial, the patient can be withdrawn from the trial if appropriate.

PART C: Overview of research sites

Please enter details of the host organisations (Local Authority, NHS or other) in the UK that will be responsible for the research sites. *For further information please refer to guidance.*

Investigator identifier	Research site		Investigator Name	
IN1	◉ NHS/HSC Site ○ Non-NHS/HSC Site		Forename Middle name Family name Email	German Guzman Gutierrez german.guzmangutierrez@nhs.scot
	Organisation name	NHS Grampian	Qualification (MD...)	
	Address	Summerfield House 2 Eday Road ABERDEEN Scotland	Country	
	Post Code	AB15 6RE		
	Country	SCOTLAND		
IN2	◉ NHS/HSC Site ○ Non-NHS/HSC Site		Forename Middle name Family name Email	Louise Shaw louisej.shaw@nhs.net
	Organisation name	ROYAL UNITED HOSPITALS BATH NHS FOUNDATION TRUST	Qualification (MD...)	
	Address	COMBE PARK BATH	Country	
	Post Code	BA1 3NG		
	Country	ENGLAND		
IN3	◉ NHS/HSC Site ○ Non-NHS/HSC Site		Forename Middle name Family name Email	Suzanne Tauro suzanne.tauro@belfasttrust.hscni.net
	Organisation name	Belfast Health & Social Care Trust	Qualification (MD...)	
	Address	Knockbracken Healthcare Park Saintfield Road	Country	

	BELFAST COUNTY ANTRIM
Post Code	BT8 8BH
Country	NORTHERN IRELAND

IN4

- (●) NHS/HSC Site
- ( ) Non-NHS/HSC Site

Forename	Philip
Middle name	
Family name	Clatworthy
Email	philip.clatworthy@nbt.nhs.uk
Qualification (MD...)	
Country	

Organisation name	NORTH BRISTOL NHS TRUST
Address	SOUTHMEAD HOSPITAL SOUTHMEAD ROAD WESTBURY-ON-TRYM BRISTOL
Post Code	BS10 5NB
Country	ENGLAND

IN5

- (●) NHS/HSC Site
- ( ) Non-NHS/HSC Site

Forename	Binu
Middle name	Pushpan
Family name	
Email	b.pushpan@nhs.net
Qualification (MD...)	
Country	

Organisation name	BLACKPOOL TEACHING HOSPITALS NHS FOUNDATION TRUST
Address	VICTORIA HOSPITAL WHINNEY HEYS ROAD BLACKPOOL
Post Code	FY3 8NR
Country	ENGLAND

IN6

- (●) NHS/HSC Site
- ( ) Non-NHS/HSC Site

Forename	Pagadala
Middle name	
Family name	Sridhar
Email	pagadala.sridhar@wales.nhs.uk
Qualification (MD...)	
Country	

Organisation name	HYWEL DDA UNIVERSITY LHB
Address	CORPORATE OFFICES, YSTWYTH BUILDING HAFAN DERWEN

	ST DAVIDS PARK, JOBSWELL ROAD CARMARTHEN DYFED
Post Code	SA31 3BB
Country	WALES

IN7

- (●) NHS/HSC Site
- ( ) Non-NHS/HSC Site

Organisation name	ASHFORD AND ST PETER'S HOSPITALS NHS FOUNDATION TRUST
Address	ST PETERS HOSPITAL GUILDFORD ROAD CHERTSEY
Post Code	KT16 0PZ
Country	ENGLAND

Forename	Giosue
Middle name	
Family name	Gulli
Email	g.gulli@nhs.net
Qualification (MD...)	
Country	

IN8

- (●) NHS/HSC Site
- ( ) Non-NHS/HSC Site

Organisation name	COUNTESS OF CHESTER HOSPITAL NHS FOUNDATION TRUST
Address	COUNTESS OF CHESTER HEALTH PARK LIVERPOOL ROAD CHESTER
Post Code	CH2 1UL
Country	ENGLAND

Forename	Kausik
Middle name	
Family name	Chatterjee
Email	kausikchatterjee@nhs.net
Qualification (MD...)	
Country	

IN9

- (●) NHS/HSC Site
- ( ) Non-NHS/HSC Site

Organisation name	UNIVERSITY HOSPITALS SUSSEX NHS FOUNDATION TRUST
Address	WORTHING HOSPITAL

Forename	Nabarun
Middle name	
Family name	Sengupta
Email	Nabarun.sengupta@nhs.net
Qualification (MD...)	
Country	

	LYNDHURST ROAD
	WORTHING
Post Code	BN11 2DH
Country	ENGLAND

IN10

- (●) NHS/HSC Site
- ( ) Non-NHS/HSC Site

Organisation name	UNIVERSITY HOSPITALS OF DERBY AND BURTON NHS FOUNDATION TRUST
Address	ROYAL DERBY HOSPITAL
	UTTOXETER ROAD
	DERBY
Post Code	DE22 3NE
Country	ENGLAND

Forename	Tim
Middle name	
Family name	England
Email	tim.england@nottingham.ac.uk
Qualification (MD...)	
Country	

IN11

- (●) NHS/HSC Site
- ( ) Non-NHS/HSC Site

Organisation name	DONCASTER AND BASSETLAW TEACHING HOSPITALS NHS FOUNDATION TRUST
Address	DONCASTER ROYAL INFIRMARY
	ARMTHORPE ROAD
	DONCASTER
Post Code	DN2 5LT
Country	ENGLAND

Forename	Dinesh
Middle name	
Family name	Chadha
Email	Dinesh.chadha1@nhs.net
Qualification (MD...)	
Country	

IN12

- (●) NHS/HSC Site
- ( ) Non-NHS/HSC Site

Organisation name	NHS Greater Glasgow and Clyde
Address	J B Russell House

Forename	Keith
Middle name	
Family name	Muir
Email	Keith.muir@glasgow.ac.uk
Qualification (MD...)	
Country	

	Gartnavel Royal Hospital 1055 Great Western Road Glasgow Glasgow Scotland	
Post Code	G12 0XH	
Country	SCOTLAND	

IN13

- (●) NHS/HSC Site
- ( ) Non-NHS/HSC Site

		Forename	Christopher
		Middle name	
		Family name	James
		Email	christopher.james@wales.nhs.uk
Organisation name	HYWEL DDA UNIVERSITY LHB	Qualification (MD...)	
Address	CORPORATE OFFICES, YSTWYTH BUILDING HAFAN DERWEN ST DAVIDS PARK, JOBSWELL ROAD CARMARTHEN DYFED	Country	
Post Code	SA31 3BB		
Country	WALES		

IN14

- (●) NHS/HSC Site
- ( ) Non-NHS/HSC Site

		Forename	Raj
		Middle name	
		Family name	Shekhar
		Email	raj.shekhar@qehkl.nhs.uk
Organisation name	THE QUEEN ELIZABETH HOSPITAL, KING'S LYNN, NHS FOUNDATION TRUST	Qualification (MD...)	
Address	QUEEN ELIZABETH HOSPITAL GAYTON ROAD KING'S LYNN	Country	
Post Code	PE30 4ET		
Country	ENGLAND		

IN15

- (●) NHS/HSC Site
- ( ) Non-NHS/HSC Site

Forename	Senthil
Middle name	

	Organisation name	HYWEL DDA UNIVERSITY LHB	Family name	Kumar
	Address	CORPORATE OFFICES, YSTWYTH BUILDING	Email	Senthil.KumarSubbarayan@wales.nhs.uk
		HAFAN DERWEN	Qualification (MD...)	
		ST DAVIDS PARK, JOBSWELL ROAD CARMARTHEN DYFED	Country	
	Post Code	SA31 3BB		
	Country	WALES		

IN16

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

Organisation name	KING'S COLLEGE HOSPITAL NHS FOUNDATION TRUST	Forename	Maria
Address	DENMARK HILL	Middle name	
	LONDON	Family name	Fitzpatrick
Post Code	SE5 9RS	Email	maria.fitzpatrick@nhs.net
Country	ENGLAND	Qualification (MD...)	
		Country	

IN17

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

Organisation name	KING'S COLLEGE HOSPITAL NHS FOUNDATION TRUST	Forename	Lazlow
Address	DENMARK HILL	Middle name	
	LONDON	Family name	Sztriha
Post Code	SE5 9RS	Email	laszlo.sztriha@nhs.net
Country	ENGLAND	Qualification (MD...)	
		Country	

IN18

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

Forename	Oliver
Middle name	

			Family name	Spooner
			Email	o.spooner@nhs.net
	Organisation name	URGENT TREATMENT CENTRE	Qualification (MD...)	
	Address	C1 GRD FLOOR, SOUTH TOWER	Country	
		ROYAL LONDON HOSPITAL		
		WHITECHAPEL LONDON		
	Post Code	E1 1FR		
	Country	ENGLAND		

IN19

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

		Forename	Youssif
		Middle name	
		Family name	Abousleiman
		Email	Youssif.Abousleiman@stgeorges.nhs.uk
Organisation name	ST GEORGE'S UNIVERSITY HOSPITALS NHS FOUNDATION TRUST	Qualification (MD...)	
Address	ST GEORGE'S HOSPITAL	Country	
	BLACKSHAW ROAD		
	TOOTING LONDON		
Post Code	SW17 0QT		
Country	ENGLAND		

IN20

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

		Forename	Lakshmanan
		Middle name	
		Family name	Sekaran
		Email	lakshmanan.sekaran@ldh.nhs.uk
Organisation name	BEDFORDSHIRE HOSPITALS NHS FOUNDATION TRUST	Qualification (MD...)	
Address	LEWSEY ROAD	Country	
	LUTON		
Post Code	LU4 0DZ		
Country	ENGLAND		

IN22

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

		Forename	Kailash
		Middle name	

			Family name	Krishnan
			Email	kailash.krishnan@nuh.nhs.uk
	Organisation name	NOTTINGHAM UNIVERSITY HOSPITALS NHS TRUST	Qualification (MD...)	
	Address	TRUST HEADQUARTERS QUEENS MEDICAL CENTRE DERBY ROAD NOTTINGHAM	Country	
	Post Code	NG7 2UH		
	Country	ENGLAND		

IN23

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

			Forename	Suzanne
			Middle name	
			Family name	Ragab
			Email	Suzanne.ragab@poole.nhs.uk
	Organisation name	UNIVERSITY HOSPITALS DORSET NHS FOUNDATION TRUST	Qualification (MD...)	
	Address	MANAGEMENT OFFICES POOLE HOSPITAL LONGFLEET ROAD POOLE	Country	
	Post Code	BH15 2JB		
	Country	ENGLAND		

IN24

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

			Forename	Hedley
			Middle name	
			Family name	Emsley
			Email	Hedley.emsley@lthtr.nhs.uk
	Organisation name	LANCASHIRE TEACHING HOSPITALS NHS FOUNDATION TRUST	Qualification (MD...)	
	Address	ROYAL PRESTON HOSPITAL SHAROE GREEN LANE FULWOOD PRESTON	Country	
	Post Code	PR2 9HT		
	Country	ENGLAND		

IN25

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Organisation name	SALFORD ROYAL NHS FOUNDATION TRUST
Address	SALFORD ROYAL STOTT LANE SALFORD GREATER MANCHESTER
Post Code	M6 8HD
Country	ENGLAND

Forename	Natasha
Middle name	
Family name	James
Email	natasha.james2@srft.nhs.uk
Qualification (MD...)	
Country	

IN26

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Organisation name	SHEFFIELD TEACHING HOSPITALS NHS FOUNDATION TRUST
Address	NORTHERN GENERAL HOSPITAL HERRIES ROAD SHEFFIELD
Post Code	S5 7AU
Country	ENGLAND

Forename	Ali
Middle name	
Family name	Ali
Email	Ali.ali9@nhs.net
Qualification (MD...)	
Country	

IN27

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Organisation name	UNIVERSITY HOSPITAL SOUTHAMPTON NHS FOUNDATION TRUST
Address	SOUTHAMPTON GENERAL HOSPITAL TREMONA ROAD SOUTHAMPTON
Post Code	SO16 6YD
Country	ENGLAND

Forename	Richard
Middle name	
Family name	Marigold
Email	james.marigold@uhs.nhs.uk
Qualification (MD...)	
Country	

IN28

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Organisation name	STOCKPORT NHS FOUNDATION TRUST
Address	STEPPING HILL HOSPITAL POPLAR GROVE STOCKPORT
Post Code	SK2 7JE
Country	ENGLAND

Forename	Joseph
Middle name	
Family name	Vassallo
Email	Joseph.vassallo@stockport.nhs.uk
Qualification (MD...)	
Country	

IN29

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Organisation name	UNIVERSITY HOSPITALS OF NORTH MIDLANDS NHS TRUST
Address	NEWCASTLE ROAD STOKE-ON-TRENT
Post Code	ST4 6QG
Country	ENGLAND

Forename	Christine
Middle name	
Family name	Roffe
Email	christine.roffe@uhnm.nhs.uk
Qualification (MD...)	
Country	

IN30

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Organisation name	SOUTH TYNESIDE AND SUNDERLAND NHS FOUNDATION TRUST
Address	SUNDERLAND ROYAL HOSPITAL KAYLL ROAD SUNDERLAND
Post Code	SR4 7TP
Country	ENGLAND

Forename	Naweed
Middle name	
Family name	Sattar
Email	naweed.sattar@chsft.nhs.uk
Qualification (MD...)	
Country	

IN31

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Organisation name	SOMERSET NHS FOUNDATION TRUST
Address	TRUST MANAGEMENT LYDEARD HOUSE MUSGROVE PARK HOSPITAL TAUNTON
Post Code	TA1 5DA
Country	ENGLAND

Forename	Malik
Middle name	
Family name	Hussain
Email	Malik.Hussain@SomersetFT.nhs.uk
Qualification (MD...)	
Country	

IN32

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Organisation name	NHS SOUTHEND CCG
Address	FLOOR 6 CIVIC CENTRE VICTORIA AVENUE SOUTHEND-ON-SEA ESSEX
Post Code	SS2 6EN
Country	ENGLAND

Forename	Paul
Middle name	
Family name	Guyler
Email	paul.guyler@southend.nhs.uk
Qualification (MD...)	
Country	

IN33

◉ NHS/HSC Site
○ Non-NHS/HSC Site

Organisation name	UNIVERSITY HOSPITALS SUSSEX NHS FOUNDATION TRUST
Address	WORTHING HOSPITAL LYNDHURST ROAD WORTHING
Post Code	BN11 2DH
Country	ENGLAND

Forename	Nabarun
Middle name	
Family name	Sengupta
Email	nabarun.sengupta@nhs.net
Qualification (MD...)	
Country	

IN34

- (●) NHS/HSC Site
- ( ) Non-NHS/HSC Site

Organisation name	BETSI CADWALADR UNIVERSITY LHB
Address	EXECUTIVE OFFICES, YSBYTY GWYNEDD PENRHOSGARNEDD BANGOR GWYNEDD
Post Code	LL57 2PW
Country	WALES

Forename	Walee
Middle name	
Family name	Sayed
Email	walee.sayed2@wales.nhs.uk
Qualification (MD...)	
Country	

IN35

- ( ) NHS/HSC Site
- ( ) Non-NHS/HSC Site

Forename	
Middle name	
Family name	
Email	
Qualification (MD...)	
Country	

IN36

- ( ) NHS/HSC Site
- ( ) Non-NHS/HSC Site

Forename	
Middle name	
Family name	
Email	
Qualification (MD...)	
Country	

PART D: Declarations

D1. Declaration by Chief Investigator

1. The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.

2. I undertake to fulfil the responsibilities of the chief investigator for this study as set out in the UK Policy Framework for Health and Social Care Research.

3. I undertake to abide by the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research.

4. If the research is approved I undertake to adhere to the study protocol, the terms of the full application as approved and any conditions set out by review bodies in giving approval.

5. I undertake to notify review bodies of substantial amendments to the protocol or the terms of the approved application, and to seek a favourable opinion from the main REC before implementing the amendment.

6. I undertake to submit annual progress reports setting out the progress of the research, as required by review bodies.

7. I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to security and confidentiality of patient or other personal data, including the need to register when necessary with the appropriate Data Protection Officer. I understand that I am not permitted to disclose identifiable data to third parties unless the disclosure has the consent of the data subject or, in the case of patient data in England and Wales, the disclosure is covered by the terms of an approval under Section 251 of the NHS Act 2006.

8. I understand that research records/data may be subject to inspection by review bodies for audit purposes if required.

9. I understand that any personal data in this application will be held by review bodies and their operational managers and that this will be managed according to the principles established in the Data Protection Act 2018.

10. I understand that the information contained in this application, any supporting documentation and all correspondence with review bodies or their operational managers relating to the application:

    - Will be held by the REC (where applicable) until at least 3 years after the end of the study; and by NHS R&D offices (where the research requires NHS management permission) in accordance with the NHS Code of Practice on Records Management.
    - May be disclosed to the operational managers of review bodies, or the appointing authority for the REC (where applicable), in order to check that the application has been processed correctly or to investigate any complaint.
    - May be seen by auditors appointed to undertake accreditation of RECs (where applicable).
    - Will be subject to the provisions of the Freedom of Information Acts and may be disclosed in response to requests made under the Acts except where statutory exemptions apply.
    - May be sent by email to REC members.

11. I understand that information relating to this research, including the contact details on this application, may be held on national research information systems, and that this will be managed according to the principles established in the Data Protection Act 2018.

12. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the Health Research Authority (HRA) together with the contact point for enquiries named below. Publication will take place no earlier than 3 months after the issue of the ethics committee's final opinion or the withdrawal of the application.

Contact point for publication*(Not applicable for R&D Forms)*

HRA would like to include a contact point with the published summary of the study for those wishing to seek further

information. We would be grateful if you would indicate one of the contact points below.

- ◯ Chief Investigator
- ◯ Sponsor
- ◯ Study co-ordinator
- ◯ Student
- ◯ Other – please give details
- ◯ None

Access to application for training purposes *(Not applicable for R&D Forms)*

Optional – please tick as appropriate:

☐ I would be content for members of other RECs to have access to the information in the application in confidence for training purposes. All personal identifiers and references to sponsors, funders and research units would be removed.

This section was signed electronically by Philip Bath on 04/10/2021 17:13.

Job Title/Post:	Professor of Stroke Medicine
Organisation:	University of Nottingham
Email:	philip.bath@nottingham.ac.uk

D2. Declaration by the sponsor's representative

If there is more than one sponsor, this declaration should be signed on behalf of the co−sponsors by a representative of the lead sponsor named at A64-1.

I confirm that:

1. This research proposal has been discussed with the Chief Investigator and agreement in principle to sponsor the research is in place.

2. An appropriate process of scientific critique has demonstrated that this research proposal is worthwhile and of high scientific quality.

3. Any necessary indemnity or insurance arrangements, as described in question A76, will be in place before this research starts. Insurance or indemnity policies will be renewed for the duration of the study where necessary.

4. Arrangements will be in place before the study starts for the research team to access resources and support to deliver the research as proposed.

5. Arrangements to allocate responsibilities for the management, monitoring and reporting of the research will be in place before the research starts.

6. The responsibilities of sponsors set out in the UK Policy Framework for Health and Social Care Research will be fulfilled in relation to this research.

   Please note: *The declarations below do not form part of the application for approval above. They will not be considered by the Research Ethics Committee.*

7. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named in this application. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

8. Specifically, for submissions to the Research Ethics Committees (RECs) I declare that any and all clinical trials approved by the HRA since 30th September 2013 (as defined on IRAS categories as clinical trials of medicines, devices, combination of medicines and devices or other clinical trials) have been registered on a publically accessible register in compliance with the HRA registration requirements for the UK, or that any deferral granted by the HRA still applies.

This section was signed electronically by Ms Angela Shone on 04/10/2021 15:07.

Job Title/Post:	Head of Research Governance
Organisation:	University of Nottingham
Email:	sponsor@nottingham.ac.uk