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)
FraiLTI Study: Frailty in Chronic Limb Threatening Ischaemia

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. 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
☐ Confidentiality Advisory Group (CAG)
☐ Her Majesty's Prison and Probation Service (HMPPS)

Most research projects require review by a REC within the UK Health Departments' Research Ethics Service. Is your study exempt from REC review?

○ Yes ◉ No

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 Research administering questionnaires/interviews for quantitative analysis or mixed methodology 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)
FraiLTI Study: Frailty in Chronic Limb Threatening Ischaemia

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

REC Name:

REC Reference Number: **Submission date:**

PART A: Core study information

1. ADMINISTRATIVE DETAILS

A1. Full title of the research:

A Multicentre Prospective observational study to investigate the prevalence and short-term impact of frailty in chronic limb threatening ischaemia (CLTI)

A3-1. Chief Investigator:

	Title	Forename/Initials	Surname
	Mr	Sandip	Nandhra
Post	NIHR Academic Clinical Lecturer		
Qualifications	MBBS, PGCME, MD, FHEA, FRCS		
ORCID ID	0000 0002 6036 5760		
Employer	NIHR		
Work Address	Northern Vascular Centre Level 4, Freeman Hospital Newcastle		
Post Code	NE77DN		
Work E-mail	Sandip.nandhra@nhs.net		
* Personal E-mail	sjnandhra@gmail.com		
Work Telephone	07905356903		

* Personal Telephone/Mobile 07905356903

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
		Laura	Frisby
Address	Newcastle Joint Research Office ntre		
	Level1, Regent Point, Regent Farm Road		
Post Code	NE3 3HD		
E-mail	nuth.nuthsponsorship@nhs.net		
Telephone	0191 2825959		
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):	09683
Sponsor's/protocol number:	1
Protocol Version:	1.8
Protocol Date:	01/05/2021
Funder's reference number (enter the reference number or state not applicable):	NIHR BRC
Project website:	

Additional reference number(s):

Ref.Number Description	Reference Number

Registration of research studies is encouraged wherever possible. You may be able to register your study through your NHS organisation or a register run by a medical research charity, or publish your protocol through an open access publisher. If you have registered your study please give details in the "Additional reference number(s)" section.

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.*

This is an observational study. Patients with vascular problems affecting the blood supply to their legs that results in constant pain or ulceration are a particular priority. Their limbs are at risk. Frailty is a condition of deconditioning, weakness, more general function and health, it typically affects older people. There is some evidence that frailty may lead to worse outcomes such as survival and complications in other areas of surgery.

Lower limb vascular disease termed chronic limb threatening ischaemia (CLTI) is a high risk condition, with patients having multiple associated health problems. It is not known whether these patients are frail, or weakened in the same way as older people. In addition at present we are not sure if the same risks that affect other frail patients apply in this group for vascular patients.

the multiple co-existing conditions are also associated with adverse outcomes in heart failure patients. The contribution of mulit-morbidity to outcome is poorly evaluated and understood in vascular care. This study presents the unique opportunity to evaluate these in high risk CLTI patients.

The FraiLTI study has been designed to observe patients with CLTI, assess and record their frailty scores by means of a grip strength assessment and then to use assessment calculations. These patients will then undergo their routine care. At 90 days the study will observe if there has been any adverse outcomes such as death, limb-loss and whether this is associated with frailty in any way. Patients will receive no intervention in the study context and this study will not interfere with routine care.

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.

This is an observational study that will not Impact on the planned routine care. There will be some baseline assessments using grip strength and one additional questionnaire but these will not Impact on the care received and are of little or no 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.*

Identify the prevalence of frailty, sarcopenia and multi-morbidity (multiple long term condtions) among chronic limb threatening limb ischaemia (CLTI) patients using standardised assessments/

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

To understand if frailty, sarcopenia and multi-morbidity are associated with:
1)Major-lower limb amputation rate at 3 months (limb-loss or amputation)
2)Survival at 3 months (who is alive at the three month timepoint)
3)Re-interventions (repeat surgery or procedures)
4)Length of hospital stay
5)Discharge home
6) re-admissions and re-intervention (who is re-admitted to hospital or needs further admission and procedures)

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

FraiLTI (Frailty in chronic Limb Threatening Ischaemia) is a UK first, multi-centre prospective observational study evaluating the impact of frailty, sarcopenia and multi-morbidity on outcomes following vascular intervention for Chronic limb threatening ischaemia (CLTI). CLTI is a patient-led JLA priority for vascular research, as outcomes may be worse in those with multi-morbidity and potentially frailty.

Frailty, traditionally defined as an age-related multi-system decline leaves patients vulnerable to stressors such as illness, trauma or surgery. Some surgical specialties have identified that the presence of frailty is associated with inferior clinical outcomes for example, patients with frailty under-going major colorectal surgery had a worse survival and a longer stay in the intensive care unit.
A key component of frailty is sarcopenia - skeletal muscle dysfunciton that develops over a period of time and typically affects older patients leading to reduced strength and muscle mass. Some evidence exists that sarcopenia alone leads to worse survival following endovascular surgery and following elective joint replacement. The association of frailty and the interaction with sarcopenia is not fully understood nor is the the interaction within high risk CLTI patients.

Multiple long-term conditions (multimorbidity) is also an important factor potentially affecting outcomes. Most work to date in vascular surgery has focussed on cardiometabolic comorbidities, and there is a need to examine the impact of multimorbidity including conditions outwith the central cardiovascular system. Our preliminary retrospective work has identified that both anaemia and sarcopenia (publication accepted 2021) are adversely associated with survival and limb loss following revascularization surgery for CLTI. Older patients undergoing aneurysm surgery may well be at greater risk of adverse outcome, but many patients with CLTI are relatively young and fall under the radar before proceeding to in-hospital intervention or major surgery to attempt to save limb. Multimorbidity has been shown to reduce cardiovascular quality of life and worse survival in related populations such as those with heart failure patients.

It is postulated that CLTI patients with frailty and/or multi-morbidity, may be associated with worse outcomes, potentially independent of age. FraiLTI has been developed to assess the nationwide scale of the problem and and to develop a platform on which to build future intervention studies to mitigate the impact of frailty, sarcopenia and multimorbidity in this group of patients

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.*

All patients admitted with chronic limb threatening ischaemia (CLTI) to a dedicated vascular centre will be invited to participate. Confirmation of CLTI diagnosis will be made by the admitting vascular specialist. These will then be screened according to the inclusion and exclusion criteria. Patients meeting the below inclusion criteria will be invited to participate in the FraiLTI study.

Patients will undergo their routine care in the hospital.

On admission, patients will be first notified about the study by a member of the clinical team. If potential participants are interested and would like more information verbal consent for their details to be shared with the FraiLTI (local site

academic or clinical academic team).

At this point a member of the FraiLTI study team (on the delegation log and meeting GCP etc) will approach the patient to provide the details of the study, PIS etc.

After a period of typically 24 hours a study team member will consent the patient formally for participation.

Routine data will be collected that is already part of the admission process (no new blood tests or scans).

In addition the EQ5D Quality of Life assessment will be made at baseline.

Two functional assessments will be made: Grip strength and sit/stand test. This will provide data on frailty.

Thereafter if the patients undergo a CT (as per their routine care - no additional imaging) these will be used to measure muscle area.

After this patients will then continue on their routine care journey.

On discharge, their admission length, surgical procedure and outcomes will be recorded.

At 90 days patients will be reviewed electronically to record and adverse outcomes in line with the follow-up data.

Patients will be invited to complete a EQ5D Quality of life assessment over the telephone.

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

Give details of involvement, or if none please justify the absence of involvement.
We performed a 12 patient PPI exercise. Patients were able to participate in the functional assessments. there were some challenges to the walk test which has been removed from the assessment bundle as a result of patient feedback. The baseline QOL and assessments were acceptable to all patients. Patients were happy to be contacted at 90 days and felt that this was a reassuring extra contact with the hospital. Patients agreed that understand who is most at risk of death, limb-loss or other complications is important.

A patient representative has been included in the study design, documentation development and attends the study steering group meetings.

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
- [x] 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: 100	Years

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

All adults over 18, able to consent and participate with ongoing assessments
All chronic limb-threatening ischaemia patients with specifically:
- Tissue loss
- Rest-pain

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

Admissions for non CLTI
Unable to agree to assessments or participate in study assessments
Pregnant women
Under 18

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
Screening patients and initial contact/recruitment	1	0	20	review of admissions, liaison with clinical team. Conducted by the study RN or PI.
Consent	1	0	15	Consent to participate by the CI/PI or Research nurse team. At baseline within 24hours of admission.
Grip Strength	1	0	10	One of grip strength assessment, yes of three, performed by the PI/CI or RN.
sit to stand test	1	0	5	assessment of ability to sit to stand as a functional assessment. by the CI/PI or RN
QOL EQ5D	2	0	10	A baseline and final over the telephone EQ5D tool will be used CI/PI/RN
Nottingham Extended ADL Scale	2	0	10	In person at baseline and over the telephone at 90days.

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

90 days for follow-up.

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.

We expect that there won't be any burden placed on the participants.

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?

The information from this trial will be useful to improve the overall quality of care that we will provide for future patients diagnosed with chronic limb threatening ischaemia. The results are likely to improve care not only in the local area, but also nationally.
As an observational study there Weill be no direct benefit to the participants

The participants themselves are unlikely to have a particular benefit as this is a observational study in nature.

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

There would be no significant disadvantages or risks in taking part in the study. All the data collected will be anonymised.

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).

Potential eligible patients admitted to the clinical service will be signposted to the study team. In some instances the study team on the delegation log will also be part of the clinical team. This is a pragmatic multi-centre study.
Some centers will have completely separate academic study teams, in which case the clinical team will notify the patient of the study and the alert the academic team. At this point the study team (on the delegation log) will then meet with the patinet and share the information, PIS, discuss the attributes. After a period of thinking time in the order of 24hours minimum the patients will then be invited to participate formally by means of the consent process.

In order to ensure as many eligible patients are identified as possible it is likely that members of the clinical team will be the vector for alerting the study team. In some cases this will be the same individual(s).

All participating sites have a mechanism of similar format to screen new admissions or referrals.

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:

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?

Ward/ acute admission:
A member of the clinical care team will signpost the patient with respect to the sutdy. In some cases this individual may well be a member of the study team. In other setup this individual will notify the research/study team to then continue the contact. No data will be shared unless the clinical team have discussed this first.

After this A member of the research team with GCP will approach the potential participant. This will be once the acute or critical care has been administered.

Out-Patients: Participants will be approached in the clinic after their consultation by a clinical team member. Thereafter a study team member will continue the process of participation enrollment.

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.

We will be consenting eligible participants in a face to face manner.

After initial contact and signpost by the clinical team has been conducted and a patient or participant has suggested that they may be interested a member of the study team will then attend for review.

Once the information has been shared, the PIS has been left and the patient has had 24 hours of review time, the study team member will re-approach to formally consnet in person and using the CF enclosed.

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

patients have to be about to perform these assessments an complete the QOL

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?

24hours as a minimum.

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)*

Telephone translation is available as part of routine NHS practice.

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 you plan to retain and make further use of identifiable data/tissue following loss of capacity, you should inform participants about this when seeking their consent initially.

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)*

- [x] 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
- [ ] 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:
  - [ ] Manual files (includes paper or film)
  - [x] NHS computers
  - [ ] Social Care Service computers
  - [ ] Home or other personal computers
  - [ ] University computers
  - [ ] Private company computers
  - [ ] Laptop computers

Further details:
• Personal data will be regarded as strictly confidential
• An NHS computer will be used for all inputting of data onto a database. This will be password protected and have IT security measures offered by the Freeman Hospital IT department.
• No data will leave the study site
• The study will comply with the Data Protection Act 1998 and Caldicott Principles
• All study records and investigator Site Files will be kept at site in a locked filing cabinet with restricted access

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

• Personal data will be regarded as strictly confidential
• An NHS computer will be used for all inputting of data onto a database. This will be password protected and have IT security measures offered by the Freeman Hospital IT department.
• No data will leave the study site
• The study will comply with the Data Protection Act 1998 and Caldicott Principles
• All study records and investigator Site Files will be kept at site in a locked filing cabinet with restricted access

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.*

• Personal data will be regarded as strictly confidential
• An NHS computer will be used for all inputting of data onto a database. This will be password protected and have IT security measures offered by the Freeman Hospital IT department.
• No data will leave the study site
• The study will comply with the Data Protection Act 1998 and Caldicott Principles
• All study records and investigator Site Files will be kept at site in a locked filing cabinet with restricted access

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 research staff only.

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 data will be analysed by the chief investigator, statistician (pending funding approval at Newcastle Univeristy) and participating researchers

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

Title	Forename/Initials	Surname
Mr	Sandip	Nandhra

Post	NIHR Clinical Lecturer
Qualifications	MBBS, PGCME, PGCDI, MD, FHEA, FRCS
Work Address	Level 4, Freeman Hospital Newcastle
Post Code	NE77DN
Work Email	sandip.nandhra@nhs.net
Work Telephone	07905356903
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

If longer than 12 months, please justify:
5 years

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

Years: 5
Months:

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 line with sponsor guidelines, all data will be stored for up to 5 years after the last visit is collected to allow adequate time for review, reappraisal or further research, and to allow any queries or concerns about the data, conduct or conclusions of the study to be resolved.
At the end of the research study, the data collected will be archived at Datatron; the Trust approved off-site archiving facility. The retention period of 5 years is based upon NUTH guidance for non-Ctimp studies.
Any paper documentation, including the master file will be archived in line with local procedures in secure storage provided off site. Access will be restricted by appropriate staff by locking the storage room.
During the consent procedure participants will be informed of this.

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?

◉ Yes ○ No

Please give details, or justify if not registering the research.
We have funding for the publication of the protocol.
We have funding for registration on the ISTRCN website.

Registration of research studies is encouraged wherever possible.
You may be able to register your study through your NHS organisation or a register run by a medical research charity, or publish your protocol through an open access publisher. If you are aware of a suitable register or other method of publication, please give details. If not, you may indicate that no suitable register exists. 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)

The study collaborative includes the Chair NHS England National Clinical Reference Group (CRG) for Vascular Services and this will act as a vector for communication of the results to NHS England and relevant commissioning

bodies

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

No personal identifiable data will be used.

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.
We will distribute and infographc/simple text of the findings in lay language for the participants.

We wil lalso be advertisign this study and its results on the Circulation Foundation website - this is a vascular specific charity.

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
- [x] Review within a multi−centre research group
- [x] Review within the Chief Investigator's institution or host organisation
- [x] 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:
This study has undergone peer review at each of the participating sites by their PI's.

In addition the Vascular and Endovascular Research Network (vascular research collaborative) has reviewed and appropriate changes made. This comprises 14 academic vascular trainees who have a track record in national and global vascular collaborative research. (https://vascular-research.net/)

External peer review was performed by Professor Rob Sayers, University of Leicester British Heart Foundation Cardiovascular Research Centre,
Glenfield General Hospital, Groby Road, Leicester, LE3 9QP, UK.

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
- [x] 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

Department
Institution
Work Address

Post Code
Telephone
Fax
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?

The primary objective is to identify the prevalence of frailty among CLTI patients

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

1)Major cardiovascular events (MACE)
2)Major adverse limb events
3)Survival
4)Re-interventions
5)Length of stay
6)Discharge home

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: 300
Total international sample size (including UK):
Total in European Economic Area:

Further details:
Approximately 30 from each centre over six months

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.*

Although an accurate sample size calculation is not possible without such pilot data, we estimate that a sample size of 200 participants would be sufficient to detect a frailty prevalence of 25% with a precision of +-5% (i.e. 95% CI 20% to 30%). This prevalence is a conservative estimate, based on our local retrospective data for sarcopenia, where the prevalence is approximately 25% of CLTI patients.

We aim to recruit a minimum of 40 patients per centre from a minimum of five centres giving a total of 200 patients in

phase 1.

A61. Will participants be allocated to groups at random?

○ Yes ◉ No

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.

Normally distributed data are presented as mean (SD), and hypothesis testing performed with paired and unpaired t-tests. Non-normally distributed data are presented as median (IQR) values with analysis using Mann-Whitney U test for unrelated samples and Wilcoxon signed rank test (WSR) for paired data. Categorical data will be analysed by means of chi squared ($\chi 2$) or, if necessary, Fisher's exact test.

Statistical analysis will be performed using SPSS version 24 (SPSS, IBM, Chicago, Illinois, USA). A p value of <0.05 will be considered statistically significant for single comparisons. Kaplan-Meier survival curves will be used with log-rank test to compare the overall mortality. Cox Regression analysis will be performed. Hazards ratios (HR) with 95% confidence intervals (CI's) are reported along with p-values. A HR of greater than 1 indicates a shorter time to death and a HR of less than 1 indicates a longer time-to-death. Binary logistic regression analysis will be used to identify associations with complications and multiple variates will be tested. The resultant significant variables will be presented as odds ratios (OR) with 95% CI's. An OR of greater than 1 indicates and increased likelihood of the event occurring.

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
	Professor	Miles	Witham
Post	Professor of trials for Older People		
Qualifications	BM BCh (Oxon) 1995. PhD (Univ of Dundee) 2005. MRCP (UK) 1998. FRCP Edin 2011.		
Employer	AGE research Group, NIHR Newcastle Biomedical Research Centre		
Work Address	Newcastle Biomedical Research Centre 3rd Floor Biomedical Research Building		
Post Code	NE45PL		
Telephone	01912081317		
Fax			
Mobile			
Work Email	miles.witham@ncl.ac.uk		

	Title	Forename/Initials	Surname
	Professor	Gerrard	Stansby
Post	Professor of Vascular Surgery		
Qualifications	MBChB, MD, FRCS		
Employer	Newcastle Upon Tyne Hospitals		
Work Address	Northern Vascular Centre, Level 4, Freeman Hospital		
Post Code	NE7 7DN		

Telephone	01912336161
Fax	
Mobile	
Work Email	gerry.stansby@nhs.net

Title	Forename/Initials	Surname
Dr	Bence Csongor	Baljer

Post	
Qualifications	MBBS, MRes
Employer	Health Education North East
Work Address	Level 4, Freeman Hospital (Ward 8) Newcastle
Post Code	NE77DN
Telephone	01912336161
Fax	
Mobile	
Work Email	bbaljer.80@gmail.com

Title	Forename/Initials	Surname
Dr	Dilraj	Bhullar

Post	Academic Foundation Program
Qualifications	MBChB, MRES
Employer	Health Education North East
Work Address	Level 4, Freeman Hospital (Ward 8) Newcastle
Post Code	NE77DN
Telephone	01912336161
Fax	
Mobile	
Work Email	dilrajbhullar@hotmail.com

Title	Forename/Initials	Surname
Dr	Sarah	Sillito

Post	Vascular academic teaching fellow
Qualifications	MBBS, MRES
Employer	Newcastle Upon Tyne Hospitals Trust
Work Address	Level 4, Freeman Hospital (Ward 8) Newcastle
Post Code	NE77DN
Telephone	01912336161
Fax	
Mobile	
Work Email	sarah.sillito@nhs.net

Title	Forename/Initials	Surname
Mrs	Lauren	Shelmerdine

Post	Vascular Research Fellow
Qualifications	MBBS, MRES, MRCS
Employer	Newcastle University
Work Address	Level 4, Freeman Hospital
Post Code	NE77DN
Telephone	01912336161
Fax	
Mobile	
Work Email	lauren.shelmerdine@nhs.net

Title	Forename/Initials	Surname
Mr	Craig	Nesbitt

Post	Consultant Vascular Surgeon
Qualifications	MBBS, MD, FRCS
Employer	Newcastle Upon Tyne Hospitals Trust
Work Address	Level 4, Freeman Hospital (Ward 8)
	Newcastle
Post Code	NE77DN
Telephone	01912336161
Fax	
Mobile	
Work Email	craig.nesbitt@nhs.net

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	Newcastle Upon Tyne University Hospitals
Given name	Laura

Family name	Frisby
Address	Newcastle Joint Research Office
Town/city	Level1, Regent Point, Regent Farm Road,
Post code	Gosforth, NE3 3
Country	United Kingdom
Telephone	0191 2825959
Fax	
E-mail	nuth.nuthsponsorship@nhs.net

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.

- [x] 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:
NIHR NE BRC grant

Please give details of funding applications.

Organisation	NIHR Newcastle Biomedical Research Centre
Address	NIHR Newcastle Biomedical Research Centre Newcastle Hospitals NHS FT & Newcastle University 3rd Floor, Biomedical Research Building, Campus for Ageing and Vitality, Newcastle
Post Code	NE4 5PL
Telephone	
Fax	
Mobile	
Email	Leanne.Cork@ncl.ac.uk

Funding Application Status: (●) Secured ( ) In progress

Amount: £10,239

Duration
Years:
Months: 10

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
	Laura	Frisby

Organisation	Newcastle Joint Research Office
Address	Level1, Regent Point, Regent Farm Road, Gosforth, NE3 3HD
Post Code	NE3 3HD
Work Email	nuth.nuthsponsorship@nhs.net
Telephone	0191 2825959
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:

North East and North Cumbria

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: 01/06/2021
Planned end date: 01/03/2022
Total duration:
Years: 0 Months: 8 Days: 1

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 12

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	9
☑ NHS organisations in Wales	1
☑ NHS organisations in Scotland	1
☑ HSC organisations in Northern Ireland	1
☐ 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: 12

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 sponsor organization will provide study audit and conduct review.
• This is a low-risk study and major safety issues are not anticipated.
• The study may be subject to inspection and audit by the study sponsor (NUTH).
• This is to ensure that the study is conducted to a high standard in accordance with the protocol, the principles of GCP, relevant regulations, guidelines and with regard to patient safety.

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 Newcastle upon Tyne Hospitals NHS Trust has liability for clinical negligence that harms individuals toward whom they have a duty of care
• NHS Indemnity covers NHS staff conducting the trial for potential liability in respect of harm arising from the conduct of the study.

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 Newcastle upon Tyne Hospitals NHS Trust has liability for clinical negligence that harms individuals toward whom they have a duty of care
• NHS Indemnity covers NHS staff conducting the trial for potential liability in respect of harm arising from the conduct of the study.

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)

• The Newcastle upon Tyne Hospitals NHS Trust has liability for clinical negligence that harms individuals toward whom they have a duty of care
• NHS Indemnity covers NHS staff conducting the trial for potential liability in respect of harm arising from the conduct of the study.

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 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	Dave Bosanquet davebosanquet@hotmail.com
	Organisation name	ANEURIN BEVAN UNIVERSITY LHB	Qualification (MD...)	MBBS, MD, FRCS
	Address	HEADQUARTERS - ST CADOC'S HOSPITAL LODGE ROAD CAERLEON NEWPORT GWENT	Country	United Kingdom
	Post Code	NP18 3XQ		
	Country	WALES		
IN2	◉ NHS/HSC Site ○ Non-NHS/HSC Site		Forename Middle name Family name Email	George smith georgeedsmith@gmail.com
	Organisation name	HULL UNIVERSITY TEACHING HOSPITALS NHS TRUST	Qualification (MD...)	MBBS, MD, FRCS
	Address	HULL ROYAL INFIRMARY ANLABY ROAD HULL	Country	United Kingdom
	Post Code	HU3 2JZ		
	Country	ENGLAND		
IN3	◉ NHS/HSC Site ○ Non-NHS/HSC Site		Forename Middle name Family name Email	Paul Dunlop Paul.Dunlop@chsft.nhs.uk

Organisation name	SOUTH TYNESIDE AND SUNDERLAND NHS FOUNDATION TRUST	Qualification (MD...)	MBBS, MD, FRCS
Address	SUNDERLAND ROYAL HOSPITAL KAYLL ROAD SUNDERLAND	Country	United Kingdom
Post Code	SR4 7TP		
Country	ENGLAND		

IN4

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

		Forename	Tom
		Middle name	
		Family name	Wallace
		Email	tomwallace@doctors.org.uk
Organisation name	LEEDS TEACHING HOSPITALS NHS TRUST	Qualification (MD...)	MBBS, MD, FRCS
Address	ST. JAMES'S UNIVERSITY HOSPITAL BECKETT STREET LEEDS	Country	United Kingdom
Post Code	LS9 7TF		
Country	ENGLAND		

IN5

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

		Forename	Chris
		Middle name	
		Family name	Twine
		Email	christopher.twine@bristol.ac.uk
Organisation name	UNIVERSITY HOSPITALS BRISTOL AND WESTON NHS FOUNDATION TRUST	Qualification (MD...)	MBBS, MD, FRCS
		Country	United Kingdom
Address	TRUST HEADQUARTERS MARLBOROUGH STREET BRISTOL		
Post Code	BS1 3NU		
Country	ENGLAND		

IN6

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

		Forename	Joseph
		Middle name	
		Family name	Shalhoub

			Email	shalhoub.joseph@gmail.com
	Organisation name	IMPERIAL COLLEGE HEALTHCARE NHS TRUST	Qualification (MD...)	MBBS, PhD, FRCS
	Address	THE BAYS ST MARYS HOSPITAL SOUTH WHARF ROAD LONDON	Country	United Kingdom
	Post Code	W2 1BL		
	Country	ENGLAND		

IN7

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

		Forename	Rob
		Middle name	
		Family name	Sayers
		Email	rs152@leicester.ac.uk
Organisation name	UNIVERSITY HOSPITALS OF LEICESTER NHS TRUST	Qualification (MD...)	MBBS, MD, FRCS
Address	LEICESTER ROYAL INFIRMARY INFIRMARY SQUARE LEICESTER	Country	United Kingdom
Post Code	LE1 5WW		
Country	ENGLAND		

IN8

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

		Forename	Maciej
		Middle name	
		Family name	Juszczak
		Email	maciej.juszczak@nhs.net
Organisation name	UNIVERSITY HOSPITALS BIRMINGHAM NHS FOUNDATION TRUST	Qualification (MD...)	MBBS, PhD, FRCS
Address	QUEEN ELIZABETH HOSPITAL MINDELSOHN WAY EDGBASTON BIRMINGHAM WEST MIDLANDS	Country	United Kingdom
Post Code	B15 2GW		
Country	ENGLAND		

IN11

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

Organisation name	THE NEWCASTLE UPON TYNE HOSPITALS NHS FOUNDATION TRUST
Address	FREEMAN HOSPITAL FREEMAN ROAD HIGH HEATON NEWCASTLE UPON TYNE
Post Code	NE7 7DN
Country	ENGLAND

Forename	Sandip
Middle name	
Family name	Nandhra
Email	sandip.nandhra@nhs.net
Qualification (MD...)	MBBS, MD, FRCS
Country	United Kingdom

IN12

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

Organisation name	LIVERPOOL UNIVERSITY HOSPITALS NHS FOUNDATION TRUST
Address	ROYAL LIVERPOOL UNIVERSITY HOSPITAL PRESCOT STREET LIVERPOOL
Post Code	L7 8XP
Country	ENGLAND

Forename	Kaji
Middle name	
Family name	Sritharan
Email	Kaji.Sritharan@liverpoolft.nhs.uk
Qualification (MD...)	MBBS, PhD, FRCS
Country	United Kingdom

IN13

(●) NHS/HSC Site
( ) Non-NHS/HSC Site

Organisation name	NHS Lothian
Address	Waverley Gate 2-4 Waterloo Place Edinburgh Scotland
Post Code	EH1 3EG
Country	SCOTLAND

Forename	Andrew
Middle name	
Family name	Tambyraja
Email	Andrew.Tambyraja@nhslothian.scot.nhs.uk
Qualification (MD...)	MBBS, MD, FRCS
Country	United Kingdom

IN16

(●) NHS/HSC Site

( ) Non-NHS/HSC Site

Forename	Robert
Middle name	
Family name	Blair
Email	rblair520@qub.ac.uk
Organisation name	Belfast Health & Social Care Trust
Qualification (MD...)	MBBS, MRCS
Address	Knockbracken Healthcare Park Saintfield Road BELFAST COUNTY ANTRIM
Country	United Kingdom
Post Code	BT8 8BH
Country	NORTHERN IRELAND

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 Dr Sandip Nandhra on 08/07/2021 08:33.

Job Title/Post:	NIHR Clinical Lecturer
Organisation:	Newcastle University / Northern Vascular Centre, Newcastle, NE7 7DN
Email:	sandip.nandhra@nhs.net

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 Nuth Sponsorship on 08/07/2021 08:52.

Job Title/Post:	Research and Development Officer
Organisation:	The Newcastle upon Tyne Hospitals NHS Foundation Trust
Email:	nuth.nuthsponsorship@nhs.net