## 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)
SONAR 1

**1. Is your project research?**

(●) Yes ( ) No

**2. Select one category from the list below:**

( ) Clinical trial of an investigational medicinal product

( ) Combined trial of an investigational medicinal product and an investigational medical device

( ) Clinical investigation or other study of a 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

- [x] Scotland
- [x] Wales
- [x] 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?**

- [x] IRAS Form
- [ ] Confidentiality Advisory Group (CAG)
- [ ] HM 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

Please describe briefly the involvement of the student(s):
Dr Reshma C Patel is Trainee Lead Investigator on the project and is aiming to complete an MD (Res) at UCL as part of this project. She is supervised by Professor R. Moonesinghe and her secondary supervisor is Dr P Sultan.

**9a. Is the project being undertaken in part fulfilment of a PhD or other doctorate?**

◉ 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)
SONAR 1

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

**REC Name:**
PR committee

**REC Reference Number:**
24/PR/0353

**Submission date:**
15/03/2024

## PART A: Core study information

### 1. ADMINISTRATIVE DETAILS

**A1. Full title of the research:**

Snapshot Obstetric National Anaesthetic Research Project 1 (SONAR-1)

**A2-1. Educational projects**

Name and contact details of student(s):

**Student 1**

| | Title | Forename/Initials | Surname |
|---|---|---|---|
| | Dr | Reshma | Patel |
| Address | University College London Hospital | | |
| | 235 Euston Road | | |
| | Department of Anaesthetics | | |
| Post Code | NW1 2BU | | |
| E-mail | reshma.patel21@nhs.net | | |
| Telephone | | | |
| Fax | | | |

Give details of the educational course or degree for which this research is being undertaken:
Name and level of course/ degree:

MD (Res)

Name of educational establishment:
University College London

Name and contact details of academic supervisor(s):

**Academic supervisor 1**

| | Title | Forename/Initials | Surname |
|---|---|---|---|
| | Professor | Ramani | Moonesinghe |
| Address | University College London | | |
| | Charles Bell House | | |
| | 43-47 Foley Street | | |
| Post Code | W1T 7SG | | |
| E-mail | ramani.moonsinghe@nhs.net | | |
| Telephone | | | |
| Fax | | | |

Please state which academic supervisor(s) has responsibility for which student(s):
*Please click "Save now" before completing this table. This will ensure that all of the student and academic supervisor details are shown correctly.*

| **Student(s)** | **Academic supervisor(s)** |
|---|---|
| **Student 1** Dr Reshma Patel | ☑ Professor Ramani Moonesinghe |

*A copy of a current CV for the student and the academic supervisor (maximum 2 pages of A4) must be submitted with the application.*

**A2-2. Who will act as Chief Investigator for this study?**

- ○ Student
- ◉ Academic supervisor
- ○ Other

**A3-1. Chief Investigator:**

| | Title | Forename/Initials | Surname |
|---|---|---|---|
| | Professor | Ramani | Moonesinghe |
| Post | Professor of Perioperative Medicine, UCL; Honorary Consultant Anaesthetist, UCL Hospitals, London | | |
| Qualifications | BSc. (Hons) FRCP FRCA FFICM MD (Res) | | |
| ORCID ID | 0000 0002 6730 5824 | | |
| Employer | University College London Hospitals NHS Foundation Trust (Department of Anaesthesia and Perioperative Medicine) University College London (Research Department of Targeted Intervention) | | |
| Work Address | University College London | | |
| | Charles Bell House | | |
| | 43-47 Foley Street | | |

| | |
|---|---|
| Post Code | W1T 7SG |
| Work E-mail | ramani.moonesinghe@nhs.net |
| * Personal E-mail | ramani.moonesinghe@nhs.net |
| Work Telephone | 07956620717 |
| * 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 |
|---|---|---|
| Mr | Pushpen | Joshi |

| | |
|---|---|
| Address | UCLH/UCL Joint Research Office UCL (part of the Research Support Centre) |
| | 1st floor Maple House (Suite B) |
| | 124 Tottenham Court Road |
| Post Code | W1T 7DN |
| E-mail | uclh.randd@nhs.net |
| Telephone | 0203 447 5696 |
| 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): | EDGE 129383 |
| Sponsor's/protocol number: | NA |
| Protocol Version: | 1.2 |
| Protocol Date: | 29/08/2023 |
| Funder's reference number (enter the reference number or state not applicable): | WKR0 - 2019 - 0036 |
| Project website: | NA |

**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.*

Approximately 25% of UK pregnancies are delivered by lower segment Caesarean section (LSCS). Most women undergoing LSCS do so under epidural or spinal anaesthetic, collectively known as neuraxial anaesthesia (NA). These are injections in the back which are intended to numb the abdomen and pelvis, while the patient remains awake. This study aims to understand the experiences of women undergoing LSCS, and specifically to understand the how often patients may feel intraoperative pain, dissatisfaction and distress.

The initial pilot study will take place at University College London Hospitals for a 4 week enrolment period to ensure any problems or issues with a multicentre study are minimised. All patients undergoing caesarean section which start with neuraxial anaesthesia (awake) during that 4 week period will be provided with a participant information leaflet about the study. These patients will have routine data recorded on a proforma by the anaesthetist responsible for their care. This data will include some information about the patient, the surgery, the anaesthetic and the maternal and fetal outcome.

After surgery and initial recovery is completed, these patients will then be approached to consent for participation in the study. Consenting patients will then be approached to complete two questionnaires - one within 24 hours (+/- 6 hours) of surgery (in person or by phone if discharged from hospital), and one 6 weeks later (+/- 3 days) (by phone). The first questionnaire will ask about women's experiences of the procedure and their short-term recovery. For women who felt pain or discomfort during their procedure, we will ask about how effective additional pain relief was, and explore how communication was with the anaesthetist and broader obstetric team. The 6 week (+/- 3 days) questionnaire will ask about symptoms of postnatal depression and post-traumatic stress.

The study findings will be used to guide future research looking at interventions to reduce the number of women affected by intra-operative pain and inadequate anesthesia during caesarean section.

**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.*

Issue 1 - Recruitment and follow up

The overall planned outline for each potential parturient participating in both the single centre feasibility study and the multicentre study is as follows:

Following admission, patient is provided information about the study and given a Patient Information Sheet (PIS) as early as possible within reason. Any member of admitting staff can give the patient a PIS and inform them that the study is occurring within the facility, but any specific patient questions regarding the study should be directed to a local investigator. All available PIS sheets are the same, regardless if they are given in outpatients or on admission to a delivery suite.

In most cases, provision of information regarding SONAR 1 will occur shortly following admission and before delivery. However, in emergencies or for other local logistical reasons, some patients may only receive the PIS after delivery. In this case, local investigators are required to ensure that the patient is given at least one hour to consider the information on the PIS before being approached for consent.

Potential participants should be approached for consent at the earliest feasible post-operative opportunity but not earlier than one hour after provision of the PIS. The post-operative period has been selected as the better time to commence the consent process to reduce the burden on the intra-operative anaesthetist responsible for checking against inclusion/exclusion criteria and completing CRF1. Patients who do not consent should be noted on a local study log. Audit data will be entered into the study database, but there will be no patient identifiable data entered; this data will be used for sensitivity analyses to compare patients who do and do not consent to study participation. We

have chosen a minimum 1-hour timeframe as it is common for patients to move from recovery and post-natal wards and see many other health professionals during the immediate post-natal phase.

Patients who undergo CS under NA and who meet the inclusion criteria should have relevant intraoperative audit data collected on CRF1 by the anaesthetist responsible for the case. Where possible, this should be done intraoperatively or immediately after the case. The patient is then entered on to the study log.

Participants may be informed of and given the study PIS at the earliest feasible opportunity in the perioperative period. For example, it may be reasonable to discuss the study with elective patients prior to their CS, if surgery is planned with NA. It may be reasonable to discuss and deliver the PIS to Category 2 or 3 patients prior to CS if time or the clinical situation/urgency allows. Patients should be consented at the earliest feasible opportunity post-operatively. If patients are too unwell to be included in the study during the immediate post-operative period (e.g. if they have received a large dose of opioids or a GA), we would urge local investigators to use clinical judgement and aim to recruit as soon as possible, ideally within 24 hours (+/- 6 hours) of the CS. Omission of recruitment during the 24-hour (+/- 6 hours) time window does not exclude patients from eligibility, and recruitment can still occur after 24 (+/- 6 hours) hours with a note of the variance to standard recruitment protocol and the reason(s) for this.

Patients who consent should ideally complete CRF2 no later than 24 hours (+/- 6 hours) postoperatively.

Patients should be contacted by telephone at 6 weeks (+/- 3 days) postoperatively for completion of CRF3. Three attempts should be made to contact patients (including a text message and email to check availability before the 3rd attempt). Following this, if no contact is possible after three attempts, these patients are ‘lost to follow up’. Each attempt at contact should be noted on the study log.

Upon completion of CRF3, or following three failed attempts at contact, the patient record is closed, and their data should be uploaded to the central REDCAP™ database.

Issue 2 - Consent

Patients aged 18 or above who undergo CS conducted under NA and meet the inclusion/exclusion criteria will be approached to provide informed consent to participate. Consent should be sought by anyone who has completed the required training to obtain consent according to local R&D guidelines – this may include, for example, clinical staff, research nurses, research midwives or non-clinical research assistants. Potential participants must be given at least one hour to consider the information provided before they are approached for informed consent. The study will be openly advertised to patients and other members of the public through posters on relevant hospital areas.

Issue 3 - Risks, burdens, benefits
We do not consider this observational study to carry any significant risks to participants or investigators. Care of patients will be in line with local site policies and the at the discretion of local anaesthetic, obstetric, and midwifery teams at all times during inpatient stay.

It is possible that the study may follow-up patients who are at increased risk of post-natal depression and anxiety. A systemic review by Anderson et al.22. Found that, within the obstetric population, the two most important risk factors for the development of post-traumatic stress disorder (PTSD) were ‘subjective distress in labour’ and ‘obstetrical emergencies’. By nature of the specific cohort of patients being studied in SONAR 1, those who either experience pain as a consequence of inadequate NA and/or who undergo an emergency CS are at increased risk.

Our research team has a wide breadth of experience of seeking post-operative patient reported outcomes. Our CI has led research where patient feedback has been sought after surgery in over 35,000 patients across the UK, often on multiple occasions up to a year after the initial procedure. Dr O Carroll has experience on the ObsQoR project, where a quality of recovery tool was developed specifically in the post-operative obstetric population, in both the elective and emergent settings.

During our engagement with patient representatives and PPI groups, we have received feedback on this particular issue. In addition, we consulted recent papers by Lawton et al, and Hallowell et al. These authors conducted qualitative research during an observational study and wrote of their experiences of recruitment and consenting during emergencies in the peripartum setting. We have used these important findings, and our team experience to inform our protocol and our Standard Operating Procedures. (SOPs).

We will have the opportunity to discuss the project and its workings with Local Investigators. We will be clear in describing and discussing this potential risk with Local Investigators, with a view to ensuring they are informed and

aware of any potential distress that may be caused. Based on team experience, and findings from Lawton and Hallowell et al, we will, amongst other issues, ensure we emphasise:

Making a clear distinction between research and clinical care.

Consent is expedited by simplified verbal and written consent, and the importance of the PIS, and the opportunity to ask questions when given the PIS on admission.

Lawton et al showed that when given the choice, virtually all patients prefer to be contacted by phone, and we encourage this over other methods.

Lawton et al showed that taking part in interviews meant that patients felt as though their psychological health is also being looked after, and we are keen that this is reflected in follow up rates,

Patients valued revisiting information given antenatally in the early post-partum period, and thus visiting in recovery, and the 24-hour (+/- 6 hours) visit is key.

That even if patients feel satisfied with the consent process at the time of recruitment, their perspectives may subsequently change, highlighting the importance of following patients up post-trial, especially those identified as having negative experiences. We are keen that this is reflected in take up of the 6-week (+/- 3 days) follow-up trial.

As such, enrolled patients could potentially be identified as suffering from PTSD or anxiety earlier than conventional community-based methods during follow-up questioning. Local care teams at participating hospitals (or wherever is clinically most appropriate) will maintain responsibility for management and follow-up of clinical problems, including inadequate NA, that are identified through structured follow-up as part of the study; indeed, this will become increasingly key should the study become larger and be run in other centres.

Should a participant score more than 11 on the EPDS, more than 30 on the PCL-5 PTSD checklist, or more than 10 on the GAD7 then they will be informed as such via a letter. This letter will encourage them to contact their GP or health visitor for further guidance. It will include a list of available resources for both urgent mental health help and specific resources for post-partum depression. A letter will also be sent to their GP to inform them that their patient has met these scoring thresholds. The letters are available in the study documents.

Issue 4 - Confidentiality

All investigators and study staff will be expected to comply with the requirements of the Data Protection Act 2018 with regard to the collection, storage, processing and disclosure of personal information and will uphold the Act’s core principles.

Data will be collected on all patients who meet the inclusion criteria and who consent to the study (as detailed in Sections 4 and 5). Nominated staff that will be responsible for data collection and postoperative follow-up. No patient data will leave the UK, and all data analysis will be performed by the study group that is based in the UK. All CRFs are included as Appendices.

At a local level, completed paper CRFs for the patient study will be held in a secure location accessible only to the local PI and any named members of the site study team, in accordance with Good Clinical Practice (GCP) guidelines and local information and research governance frameworks. Information from the paper CRF will then be entered on to a central online database via a secure web-based portal.

The perioperative anaesthetic providers will complete CRF1 for each patient that meets the inclusion criteria. Patient Identifiable data (name, hospital number) will be on CRF1 in order to link the patient and her subsequent questionnaires, but no PID will leave the hospital or be made available to the central team. The information will comprise questions regarding patient risk factors, type of anaesthesia, surgical process data, and subjective and objective assessment of pain. Where a patient is handed over between anaesthetists, the most senior anaesthetist

present at the end of surgery will be asked to review the responses to the questionnaire and amend if necessary.

For follow-up at 6 weeks (+/- 3 days), local investigators will ask patients during completion of CRF2 for contact details and a preferred day/time to call. Patients will be asked to complete CRF3 via telephone at 6 weeks (+/- 3 days) post-discharge from hospital, and this should be made clear when completing CRF2 and gaining contact details from the participant. Ideally, CRF3 will be completed via telephone within 6 weeks (+/- 3 days) of the participant's procedure.

In accordance with a locally determined schedule, completed CRF responses will be taken directly to a secure location accessible by the local PI or designated members of the local investigative team who will then enter data from the paper form for upload on to the central study database. Data will be entered electronically via a secure, encrypted connection onto an online portal hosted by University College London. The software used for data capture will be REDCap™ (Research Electronic Data Capture – http://www.project-redcap.org), a secure web application for building and managing online surveys and databases. Access to the REDCap™ data entry system will be protected by a username and password created during the local investigator registration process.

No PID will be transferred from the local site to the central investigative team. An anonymised dataset will be uploaded on to the centralised study database via UCL's REDCAP™ web-based portal hosted on secure UCL servers. No PID from the hospital CRF paperwork will be uploaded to REDCapTM. REDCapTM will create a unique ID, not based on PID for central team logs. Local investigators will have access to enter and edit data from their own hospital only. Functionality of the CRFs and study database will be assessed as one of the objectives of this pilot study.

In order to facilitate follow-up of patients at six weeks, (+/- 3 days), the participant's name, contact details and relevant previous study questionnaire responses will be only shared within the site of recruitment and only between designated members of the local investigative team (which may include Clinical Trial Assistants/Research Nurses). PID will not be shared between recruitment sites, nor with the central investigative team. PID will be held only for the minimal necessary period. Once the 6-week (+/- 3 days) follow-up is complete, the site will destroy paper records after 3 months. The electronic study data will be securely deleted after a specified time point (10 years after the end of the study).

The study is compliant with the requirements of the General Data Protection Regulation (2016/679) and the Data Protection Act (2018). All investigators and study site staff will comply with the requirements of the General Data Protection Regulation (2016/679) with regards to the collection, storage, processing, and disclosure of personal information, and will uphold the Act's core principles. UCL is the data controller; the UCL Data Protection Officer is Alex Potts (a.potts@ucl.ac.uk, data-protection@ucl.ac.uk) The data processors will be the investigators of the study. These individuals are all based at one or more of the following institutions.

• University College London Hospitals NHS Foundation Trust

• University College London (Department of Applied Health Research)

The central team will have no access to personal data.

## 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.*

To evaluate the relationship between hospital level, patient, anaesthetic and obstetric risk factors, and short- and longer-term outcomes following caesarean delivery using neuraxial anaesthesia.

To evaluate the relationship between hospital level, patient, anaesthetic and obstetric risk factors and the incidence of intraoperative pain following caesarean delivery using neuraxial anaesthesia.

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

RQ1: What is the impact of intraoperative pain during CD on short term (within 24 hours (+/- 6 hours)) patient recovery and satisfaction? (GAD7, Maternal Comfort and Satisfaction scores)

RQ2: What is the impact of intraoperative pain during CD on longer term (6-week (+/- 3 days)) patient reported outcome measures? (EPDS, GAD7, and PCL-5 scores)

RQ3 What is the relationship between intraoperative pain during CD and postpartum psychological morbidity?

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

Neuraxial anaesthesia (an injection into the bottom of the back, and awake and painfree during surgery)(NA) is the ideal method of anaesthesia for caesarean sections. However, NA is not always successful and how often inadequate NA occurs varies widely and depends on factors such as: urgency of surgery, type of NA (spinal versus epidural), and surgical approach - as well as other patient factors.
The incidence of unanticipated pain during caesarean sections remains unknown. Learning about the scale of this problem is the first step in improving national standards. What also remains unclear is how this complication of NA affects patients in the weeks and months following delivery.
There have been no large scale studies within the past decade evaluating how often inadequate NA occurs, and no studies which consider contemporary obstetric anaesthesia practices and techniques.
Evaluation of the effects of intraoperative pain on subsequent maternal outcomes is required in order to aid and inform clinician decision making in these challenging clinical scenarios.

In this study we aim to determine the failure rate of inadequate neuraxial anaesthesia in contemporary obstetric anaesthesia practice using a multicentre approach in the UK. SONAR 1 will collect and collate data on how pain during caesarean sections is managed, aiming to understand the scale of the problem, and how successfully anaesthetists are addressing these issues. We will also collect patient-reported data in the short and medium term after the birth, in order to understand the longer-term impact of inadequate NA and failure of NA in our new parent population.

**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.*

SONAR-1 is a study of obstetric patients undergoing caesarean sections (CS) in participating hospitals to understand how common intra-operative pain and inadequate neuraxial anaesthesia (NA)(where the patient is made numb, but is not asleep) is.

Data will be collected on all patients meeting the inclusion criteria in our participating UK hospital, UCLH, during the 4 week study period.(where we aim to recruit at least 100 patients). If the pilot study is felt to be feasible, we plan to roll the study out to more hospitals, to get a feel of the scale of this problem in the whole country.

Abbreviation

Throughout this summary the abbreviation NA is used. This stands for Neuraxial Anaesthesia. This is a collective term used to mean either:

- an injection into the bottom of the back, which leaves the recipient awake and pain-free during surgery. This is known as a spinal.

- an injection in the bottom of the back, which is done to place a catheter through which pain medication can be given. This is known as an epidural. If an anaesthetist gives specific additional medication through the epidural, then the epidural can be used to keep a patient comfortable during a caesarean section (CS).

NA is the ideal mode of anaesthesia used for caesarean sections but is not always possible for medical reasons. In these cases, a general anaesthetic (GA) is used. This is sometimes referred to as ‘going off to sleep’.

Introduction

We do not have very good information about how well neuraxial anaesthesia during caesarean section performs, nor how intraoperative pain should be managed, or what the outcomes are for patients who experience pain during awake caesarean sections.

The aim of SONAR-1 is to:

Estimate how often NA fails and intraoperative pain is experienced during caesarean section

To use patient centred tools to assess the impact on patients who experience pain during caesarean section

Who will we involve?

Every adult patient who has a caesarean section, including if the caesarean section is planned or unplanned (an urgent or emergency case), at any time of day or night, and is done awake using NA.

Data Collection

There will be 3 points of data collection.

Form 1 will be completed by the responsible anaesthetist for the case. It will collect basic anaesthetic, obstetric, and surgical information. There will be nothing on Form 1 that is not already routinely collected by hospitals for all caesarean sections.

Form 2 will be filled in by the researcher together with the patient between 18 and 30 hours after the caesarean. It will consist of questions regarding their experience of the caesarean section, any intraoperative pain or discomfort they may have experienced, and their satisfaction with the anaesthetic care, and their quality of the recovery. It is estimated that this will take about 10-15 mins.

Form 3 will be filled in by a researcher who calls the patient approx. 6 weeks after the caesarean section. The form will consist of questionnaires to help identify the impact to those who have had any negative experiences, compared to those who did not. These are validated questionnaires that are used to identify Post-Traumatic Stress, Anxiety, and Post-Natal Depression. This will probably take about 10-15 mins.

Should a patient score above a specific threshold on these Form 3 questionnaires, they will receive a letter informing them, with a list of resources. Their GP will also be informed by letter.

The results of this study will help us to better understand and manage pain during caesarean section, but also have better information when consenting patients for caesarean section and discussing risks.

Study schedule

Patient is given a Patient Information Sheet about the surgery as early as possible within reason. This might be in a clinic, or a delivery suite, or a consultant-led labour ward. If there are any study-specific questions, these will be answered by a researcher on site. In urgent or emergency cases, this may occur after the baby is born.

Patients are approached to be consented into the study as the earliest opportunity after the caesarean section within reason. This will likely be in the recovery area.

If the patient has been given the Patient Information Sheet after the baby is born, then they will be given at least one hour to consider the information before being approached for consent.

Form 1 will have already been completed by the anaesthetist, and as it solely obstetric, anaesthetic and surgical data that is routinely collected, consent is not required.

All patients who consent will be entered into the study log, so that they can be followed up at 24 hours and 6 weeks. Patients who do not consent are also entered into the study log kept on site, but only so that researchers know how many people do not wish to consent. They will not then be contacted by the researchers.

Only researchers who have undergone confidentiality and research method training will have access to the study log.

Patients who do consent will complete Form 2 with a researcher no later than 24 hours (+/- 6 hours) after the caesarean section.

Patients will then be contacted by telephone using a number they provide whilst completing Form 2 at 6 weeks (+/- 3 days) following the caesarean section. Three attempts will be made to contact the patients, but appropriate judgement will be used as it is not always possible to find time to speak on the phone in the newborn period. We anticipate that Form 3 will take 15 mins to complete. Researchers will be led by the patients as to when might be a good time for us to call.

All the information from all the forms are entered into a study database, and there is no identifiable patient information on that database. It is specifically encrypted so that no one can be identified from the looking at the database.

Withdrawal

Participants are free to withdraw from the study at any time and without reason. This will be recorded in the study log only to prevent unnecessary follow up.

If they withdraw before recruitment is complete, their data will be removed from the study log and not used for analysis. If withdrawal is after the study closes, it will not be possible to remove their data as analysis will have started. This will be made clear on the study Information Sheet.

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

*Give details of involvement, or if none please justify the absence of involvement.*

The themes of this study were prompted by Ms. Susanna Stanford's personal experience of neuraxial failure, as published in the International Journal of Obstetrics and Gynaecology. This paper highlights the paramount importance of communication between patient and anaesthetic provider. Following the lessons learned from Ms. Stanford's experiences, it is prudent to explore patient and structural risk factors of inadequacy of NA, as well as the impact on patients and their families.

We have sought PPI from community-based parent groups in North London, comprised of people who have had a baby at UCLH or their partner hospitals within the last year, (From Jan 1st 2022 onward) and have had our protocols, patient information leaflets, patient information posters, consent forms and CRFs reviewed by the group. They have also reviewed the letters that would be sent to the patient and GP were patients to score highly in screening tools of postpartum depression and postpartum post traumatic stress disorder.
In addition, we sought feedback from Ms Stanford, who has reviewed the study documents. Ms Stanford and the PPI group have provided valuable feedback and changes to the study documents.

## 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
- [x] 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
- [x] Reproductive Health and Childbirth
- [ ] Respiratory
- [ ] Skin
- [ ] Stroke

| | |
|---|---|
| Gender: | Female participants only |
| Lower age limit: 18 | Years |
| Upper age limit: 65 | Years |

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

-Aged 18 years or above

-Gestation beyond 32/40 weeks

-Receiving NA (spinal, labour epidural extended for surgical anaesthesia or combined spinal epidural)

-Receiving any scheduled or unscheduled CS of any category.

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

Patient refusal

Patients who are unable to provide informed consent

Other modes of delivery (e.g., instrumental delivery)

De novo GA as an anaesthetic method

## 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 |
|---|---|---|---|---|
| Seeking informed consent | 1 | 0 | 15 mins | To be completed by the local research team within 24 hours of completion of obstetric surgery. |

| | | | | |
|---|---|---|---|---|
| Theatre Data Collection Form (CRF1) | 1 | 1 | 15 mins | To be completed by the perioperative anaesthetic team at, or around the time of the obstetric theatre procedure conducted under NA |
| Patient Case Report Form (Questionnaire CRF2) | 1 | 0 | 15 mins | To be completed by a patient who has given consent within 24 hours (+/- 6 hours)of their procedure |
| Patient Case Report Form (Questionnaire CRF3) | 1 | 0 | 15mins | To be completed by a patient who has given consent within 6 weeks (+/- 3 days)of their procedure |

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

Based on CS rates we aim to recruit over a set 4 week study period for the pilot study. UCLH has approximately 20 elective CS a week, and a similar number of non-elective sections. Thus we aim to recruit approx. 100 patients. We aim to collect postoperative outcome data at 24 (+/- 6) hours (short-term) and 6 weeks (+/- 3 days) (medium-term) postoperatively. Thus, we anticipate an approximate 11-week duration of enrolment and follow-up, allowing additional time for participants to provide data.

**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.*

This study involves the use of data so there are risks associated with breaches in confidence or failure to maintain data security. To minimise this risk patient identifiable information collected via paper-based case report forms (CRFs) will be securely and confidentially held (as would be expected of patients' medical notes) and with due attention to Good Clinical Practice (GCP), the Data Protection Act (DPA) 1998 and General Data Protection (GDPR) at each local study site.
Data will be transcribed by local investigators onto an electronic CRF held on a secure online database. Paper-based CRFs will be stored securely by local investigators for 3 months after the study recruitment window ends before being destroyed confidentially.
All investigators for each local study site will be expected to act in full compliance with GCP, GDPR, the DPA 1998 and the Research Governance Framework for Health and Social Care (2005).

We do not consider this observational study to carry any significant clinical risks to participants or investigators. Care of patients will be in line with local site policies and the at the discretion of local anaesthetic, obstetric, and midwifery teams at all times during inpatient stay.

It is possible that the study may follow-up patients who are at increased risk of post-natal depression and anxiety. A systemic review by Anderson et al. found that, within the obstetric population, the two most important risk factors for the development of post-traumatic stress disorder (PTSD) were ‘subjective distress in labour’ and ‘obstetrical emergencies’. By nature of the specific cohort of patients being studied in SONAR 1, those who either experience pain as a consequence of inadequate NA and/or who undergo an emergency CS are at increased risk. As such, enrolled patients could potentially be identified as suffering from PTSD or anxiety earlier than conventional community-based methods during follow-up questioning. Local care teams at participating hospitals (or wherever is clinically most appropriate) will maintain responsibility for management and follow-up of clinical problems, including inadequate NA, that are identified through structured follow-up as part of the study; indeed, this will become increasingly key should the study become larger and be run in other centres. Should a participant score more than 11 on the EPDS, more than 10 on GAD7, or more than 30 on the PCL-5 PTSD checklist then they will be informed as such via a letter. This letter will encourage them to contact their GP or health visitor for further guidance. It will include a list of available resources for both urgent mental health help and specific resources for post-partum depression. A letter will also be sent to their GP to inform them that their patient has met these scoring thresholds. The letters are available in the study documents.

**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

*If Yes, please give details of procedures in place to deal with these issues:*

We are asking about patients mental wellbeing at a time after their delivery which can be emotive. In particular, we

are screening for mental health conditions of postpartum depression, anxiety, and postpartum Posttraumatic stress disorder (PTSD). We acknowledge that these may be sensitive or upsetting experiences. In order to counter this, we will ensure that patients understand before consenting to the study we will be asking questions about their mental health, that taking part in this study is entirely voluntary and remind them of the procedure to withdraw from the study, if they wish to. The research team at each site will undergo specific training in how to complete the CRF with the patients and ensure they follow a set script. In addition, if the patient does score highly with the screening tools used for postpartum depression and/ or PTSD, we will inform them, both at the time and in writing afterwards, and also inform their GP. We will give them a list of mental health resources available to aid them.

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

Participation in this study will not directly benefit the participants during their hospital stay. However, we hope that the information gained from conducting this study will improve the care delivered in hospitals in the future, thus potentially affording prospective benefits to the participants themselves, or their friends and family if they need to undergo caesarean section under NA.

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

None.

## 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).*

Hospital Recruitment

The lead clinician for obstetric anaesthetic services will be contacted for agreement to participate. At the confirmed site, there will be a principal investigator (PI) and a trainee lead investigator will be nominated to oversee a local investigative team who will facilitate delivery of the study on the maternity unit.

Participant recruitment

All patients who undergo a CS will be recorded on the local site screen log.

Eligibility will be assessed based on the inclusion/exclusion criteria (as per Section 2.2).

All patients who meet the eligibility criteria in participating hospitals will have intraoperative data collected on CRF1 by the responsible anaesthetist for the CS.

Patients will then also be approached for participation in the Patient Study (CRF2 and CRF3) after their surgery. It may be more appropriate for a member of the local investigative team who was not the responsible intraoperative anaesthetist to approach the patient, and this is acceptable also.

As there can often be time pressures on labour wards, it may not be possible for CRF1 to be completed at the time of surgery. Local investigators will be responsible for completing the patient's data retrospectively by accessing patient notes.

Thus, for feasibility assessment and the STROBE flowchart, the site log will inform us of:

Number of patients screened

Number of patients eligible

Number of patients consented

Number of patients who complete CRF2 and CRF3

**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:*
All patients who have a caesarean section conducted using a neuraxial anaesthetic technique during the study period in the participating hospitals will be screened for eligibility. If they are >18 years of age and able to provide informed consent they are eligible for the study.

**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.*

All investigators and study staff will be expected to comply with the requirements of the Data Protection Act 2018 with regard to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles.

Data will be collected on all patients who meet the inclusion criteria and who consent to the study (as detailed in Sections 4 and 5). Nominated staff that will be responsible for data collection and postoperative follow-up. No patient data will leave the UK, and all data analysis will be performed by the study group that is based in the UK. All CRFs are included as Appendices.

At a local level, completed paper CRFs for the patient study will be held in a secure location accessible only to the local PI and any named members of the site study team, in accordance with Good Clinical Practice (GCP) guidelines and local information and research governance frameworks. Information from the paper CRF will then be entered on to a central online database via a secure web-based portal.

Perioperative anaesthetic providers will complete CRF1 for each patient that meets the inclusion criteria. Patient Identifiable data (name, hospital number) will be on CRF1 in order to link the patient and her subsequent questionnaires, but no PID will leave the hospital or be made available to the central team. The information will comprise questions regarding patient risk factors, type of anaesthesia, surgical process data, and subjective and objective assessment of pain. Where a patient is handed over between anaesthetists, the most senior anaesthetist present at the end of surgery will be asked to review the responses to the questionnaire and amend if necessary.

For follow-up at 6 weeks (+/- 3 days), local investigators will ask patients during completion of CRF2 for contact details and a preferred day/time to call. Patients will be asked to complete CRF3 via telephone at 6 weeks (+/- 3 days) post-discharge from hospital, and this should be made clear when completing CRF2 and gaining contact details from the participant. Ideally, CRF3 will be completed via telephone within 6 weeks (+/- 3 days) of the participant's procedure.

In accordance with a locally determined schedule, completed CRF responses will be taken directly to a secure

location accessible by the local PI or designated members of the local investigative team who will then enter data from the paper form for upload on to the central study database. Data will be entered electronically via a secure, encrypted connection onto an online portal hosted by University College London. The software used for data capture will be REDCap™ (Research Electronic Data Capture – http://www.project-redcap.org), a secure web application for building and managing online surveys and databases. Access to the REDCap™ data entry system will be protected by a username and password created during the local investigator registration process.

No PID will be transferred from the local site to the central investigative team. An anonymised dataset will be uploaded on to the centralised study database via UCL's REDCAP™ web-based portal hosted on secure UCL servers. No PID from the hospital CRF paperwork will be uploaded to REDCapTM. REDCapTM will create a unique ID, not based on PID for central team logs. Local investigators will have access to enter and edit data from their own hospital only. Functionality of the CRFs and study database will be assessed as one of the objectives of this pilot study.

In order to facilitate follow-up of patients at six weeks, (+/- 3 days), the participant's name, contact details and relevant previous study questionnaire responses will be only shared within the site of recruitment and only between designated members of the local investigative team (which may include Clinical Trial Assistants/Research Nurses). PID will not be shared between recruitment sites, nor with the central investigative team. PID will be held only for the minimal necessary period. Once the 6-week (+/- 3 days) follow-up is complete, the site will destroy paper records after 3 months. The electronic study data will be securely deleted after a specified time point (20 years after the end of the study).

The study is compliant with the requirements of the General Data Protection Regulation (2016/679) and the Data Protection Act (2018). All investigators and study site staff will comply with the requirements of the General Data Protection Regulation (2016/679) with regards to the collection, storage, processing, and disclosure of personal information, and will uphold the Act's core principles. UCL is the data controller; the UCL Data Protection Officer is Alex Potts (a.potts@ucl.ac.uk, data-protection@ucl.ac.uk) The data processors will be the investigators of the study. These individuals are all based at one or more of the following institutions.

• University College London Hospitals NHS Foundation Trust (Surgical Outcomes Research Centre)

• University College London (Department of Applied Health Research)

The central team will have no access to personal data.

**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?**

CRF1: Intraoperative audit data

Patients who meet the eligibility criteria will be informed about the study by any member of clinical staff following admission to labour ward/birth centre and given a PIS. During this time, they will also have the opportunity to ask questions about the study. Where not possible to provide the PIS preoperatively, participants should be approached at the earliest post-operative opportunity and consented no earlier than 1-hour post-administration of the PIS. CRF1 will be completed by the responsible anaesthetist during the operative period. As this comprises routinely collected audit

data, this aspect of the study does not require patient consent.

CRF2: 24-hour (+/- 6 hours) Patient Study

Patients may be approached for consent following transfer to their postoperative destination as soon as appropriate. This may include recovery, and observational bay, labour ward, or on the postnatal ward. For those who agree to participate, a patient consent form should be completed. This is then followed by completion of CRF2 no later than 24 hours (+/- 6 hours) following the CS for consenting participants. For example, opportunity could be made of the postoperative anaesthetic follow-up visit to complete CRF2 where possible. During this time, local investigators will also obtain suitable contact details from each participant to facilitate completion of CRF3 at 6 weeks (+/- 3 days) post-procedure following hospital discharge.

In all the above cases, consenting patients will be recorded on to a local site study log. Those who decline consent will also be recorded on this log to ensure that they are not followed-up. This logging will be for the purpose of reporting results according to STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidance.

CRF3: 6-week Patient Study

In all the above cases, for consenting patients, CRF3 will be completed at 6 weeks following CS (+/- 3 days). In most cases, patients will have been discharged from hospital. An interval of 3 days either side of 6 weeks has been selected in order to provide maximum opportunity to select an appropriate time for the patient's convenience. Local investigators will be tasked with completing CRF3 via telephone using contact details obtained during inpatient follow-up.

**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.*

Patients aged 18 or above who undergo CS conducted under NA and meet with the inclusion/exclusion criteria will be approached to provide informed consent to participate. Consent should be sought by anyone who has completed the required training to obtain consent according to local R&D guidelines – this may include, for example, clinical staff, research nurses, research midwives or non-clinical research assistants. Potential participants must be given at least one hour to consider the information provided before they are approached for informed consent. The study will be openly advertised to patients and other members of the public through posters on hospital wards.

*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?**

Patients will have the PIS available to them on admission, and will have the time between admission and any necessary CS to consider the information. 1 hour will be given between providing PIS and approach for consent. We have chosen this timeframe as it is common for patients to move from recovery and postnatal wards and see many other health professionals during the immediate postnatal phase. It is much more likely that patients will be able to see and speak to their anaesthetist consenting them for the study whilst in the recovery area.

**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)*

Patients who cannot provide informed consent will be excluded. Where required, we will make use of Language Line, which is available in clinical areas in order to ensure participants are fully consented adequately.

**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?**

We will ensure that the consent form and patient information sheet are translated into Welsh.

**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:*

In the extremely unlikely event that a patient has lost capacity to consent to the study at the 6-0week postpartum phone call, we would not proceed with the questionnaire, and cease the follow up at that point. In order to ensure maternal and neonatal safety, we would seek to explore the extent of the capacity loss and inform their direct care team where appropriate.

## 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
- ☑ 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
- ☑ 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
- [ ] University computers
- [ ] Private company computers
- [ ] Laptop computers

*Further details:*
Members of the research team at each hospital site will be required to access medical records to identify patient participants, obtain clinical information pertinent to the study dataset and to complete follow up. In order to complete CRF2, the completing member of the research team will need to ensure the patient has already completed the consenting and enrollment process into the study.

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

The completed paper Case Report Forms (CRFs) will be stored securely and confidentially at each site in line with local information governance guidelines. Each hospital will store study data in locked cabinets in locked rooms. These will not leave the local NHS organisation at any stage. Once data has been transcribed onto the secure online study database, all data stored electronically will be password protected.

**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.*

All investigators and study staff will be expected to comply with the requirements of the Data Protection Act 2018 with regard to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles.

Data will be collected on all patients who meet the inclusion criteria and who consent to the study. Nominated staff that will be responsible for data collection and postoperative follow-up. No patient data will leave the UK, and all data analysis will be performed by the study group that is based in the UK.

At a local level, completed paper CRFs for the patient study will be held in a secure location accessible only to the local PI and any named members of the site study team, in accordance with Good Clinical Practice (GCP) guidelines and local information and research governance frameworks. Information from the paper CRF will then be entered on to a central online database via a secure web-based portal.

Perioperative anaesthetic providers will complete CRF1 for each patient that meets the inclusion criteria. Patient Identifiable data (name, hospital number) will be on CRF1 in order to link the patient and her subsequent questionnaires, but no PID will leave the hospital or be made available to the central team. The information will comprise questions regarding patient risk factors, type of anaesthesia, surgical process data, and subjective and objective assessment of pain. Where a patient is handed over between anaesthetists, the most senior anaesthetist present at the end of surgery will be asked to review the responses to the questionnaire and amend if necessary.

For follow-up at 6 weeks (+/- 3 days), local investigators will ask patients during completion of CRF2 for contact details and a preferred day/time to call. Patients will be asked to complete CRF3 via telephone at 6 weeks (+/- 3 days) post-discharge from hospital, and this should be made clear when completing CRF2 and gaining contact details from the participant. Ideally, CRF3 will be completed via telephone within 6 weeks (+/- 3 days) of the participant's procedure.

In accordance with a locally determined schedule, completed CRF responses will be taken directly to a secure location accessible by the local PI or designated members of the local investigative team who will then enter data from the paper form for upload on to the central study database. Data will be entered electronically via a secure, encrypted connection onto an online portal hosted by University College London. The software used for data capture will be REDCap™ (Research Electronic Data Capture – http://www.project-redcap.org), a secure web application for building and managing online surveys and databases. Access to the REDCap™ data entry system will be protected by a username and password created during the local investigator registration process.

No patient identifiable data (PID) will be transferred from the local site to the central investigative team. An anonymised dataset will be uploaded on to the centralised study database via UCL's REDCAP™ web-based portal hosted on

secure UCL servers. No PID from the hospital CRF paperwork will be uploaded to REDCapTM. REDCapTM will create a unique ID, not based on PID for central team logs. Local investigators will have access to enter and edit data from their own hospital only. Functionality of the CRFs and study database will be assessed as one of the objectives of this pilot study.

In order to facilitate follow-up of patients at 6 weeks, (+/- 3 days), the participant's name, contact details and relevant previous study questionnaire responses will be only shared within the site of recruitment and only between designated members of the local investigative team (which may include Clinical Trial Assistants/Research Nurses). PID will not be shared between recruitment sites, nor with the central investigative team. PID will be held only for the minimal necessary period. Once 6 week (+/- 3 days) follow-up is complete, the site will destroy paper records after 3 months. The electronic study data will be securely deleted after a specified time point (10 years after the end of the study).

Email address information maybe gathered in the optional portion on the consent form to allow participant to receive a summary of the results of the study. The email addresses will not use used for any other purpose. It must remain at the local site only; no email address should be sent to the central study team. The collected email addresses should be kept in the secure location, along with the telephone contact details that will facilitate the 6-week follow-up data collection, the email addresses only on the optional part of the consent form, and not the CRFs, as the CRFs remain entirely anonymous.

The study is compliant with the requirements of the General Data Protection Regulation (2016/679) and the Data Protection Act (2018). All investigators and study site staff will comply with the requirements of the General Data Protection Regulation (2016/679) with regards to the collection, storage, processing, and disclosure of personal information, and will uphold the Act's core principles. UCL is the data controller; the UCL Data Protection Officer is Alex Potts (a.potts@ucl.ac.uk, data-protection@ucl.ac.uk) The data processors will be the investigators of the study. These individuals are all based at one or more of the following institutions.
• University College London Hospitals NHS Foundation Trust (Surgical Outcomes Research Centre)
• University College London (Department of Applied Health Research)

The central team will have no access to personal data.

**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.*

Local clinical teams and researchers will have access to participants' personal data during the study, limited to individuals with a formal governance role with the Trust (i.e. substantive or honorary contract).

## 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?**

Data will be anonymised on entering into a secure online database. Anonymised data will be analysed at the Division of Surgery and Interventional Science, UCL.

Analyses will be conducted by members of the study team:
- Prof SR Moonesinghe
- Dr James O Carroll
- Dr Reshma Patel (Trainee Lead)
- Dr Justin Kua (Trainee Investigator)
- Dr Bo Hou (Applied Health Statistical support)

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

| | Title | Forename/Initials | Surname |
|---|---|---|---|
| | Professor | S. R. | Moonesinghe |
| Post | Professor and Head of Centre for Perioperative Medicine, UCL; Honorary Consultant in Anaesthesia, UCLH; Director NIAA Health Services Research Centre | | |

| | |
|---|---|
| Qualifications | BSc. (Hons) MBBS FRCP FRCA FFICM MD(Res) |
| Work Address | Division of Surgery, University College London Charles Bell House 43-45 Foley Street, London<br>University College London Hospitals NHS Foundation Trust (Department of Anaesthesia and Perioperativ |
| Post Code | W1W 7TS |
| Work Email | ramani.moonesinghe@ucl.ac.uk |
| Work Telephone | 07956620717 |
| 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: 10
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.*

The study master file will be kept at UCL for the period stipulated in the protocol and in line with all relevant legal and statutory requirements. Local PIs at each participating site must agree to archive his/her respective site's study documents for 3 months and in line with all relevant legal and statutory requirements. Following this period, documents can be securely destroyed.

## 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 plan to register the study with www.clinicaltrials.gov a publically-accessible registry which accepts observational research studies. (www.clinicaltrials.gov)

*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:*

- [x] Peer reviewed scientific journals
- [x] Internal report
- [x] Conference presentation
- [x] Publication on website
- [x] 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)

Dissemination to professional stakeholders will include engagement with professional bodies and colleges; dissemination to patient and public will be informed by our PPIE team and supported through the NIHR Central London Patient Safey Research Collaboration

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

We will not be publishing dis-aggregated patient level data.

**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.*
Information will be provided in the patient information sheet describing how they will be able to register with the study website so that they can be informed of the findings of the study when they are available. Patients will be informed of the results by it being publicised widely via the OAA, peer review publications etc.

## 5. Scientific and Statistical Review

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

- [x] 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:*
The study has been developed in conjunction with subject matter experts representing the Health Services Research Centre at the Royal College of Anaesthetists (research expertise), and the Obstetric Anaesthetic Association (clinical experience).
We underwent peer review during a grant application process - the application was reviewed by three independent external assessors. As a result the full sum of £54.011 was awarded by the NIAA Small Research Grant Award scheme in June 2019.

*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
- [x] Review by educational supervisor
- [x] 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 |
|---|---|---|---|
| | Professor | S. R. | Moonesinghe |
| Department | Professor and Head of Centre for Perioperative Medicine, UCL; Honorary Consultant in Anaesthesia, UCLH; Director NIAA Health Services Research Centre | | |

| | |
|---|---|
| Institution | University College London |
| Work Address | Division of Surgery, University College London |
| | Charles Bell House |
| | 43-45 Foley Street |
| Post Code | W1W 7ST |
| Telephone | |
| Fax | |
| Mobile | 07956620717 |
| E-mail | ramani.moonesinghe@ucl.ac.uk |


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

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

- patient-reported pain during caesarean section

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

- patient satisfaction
- Patient Reported Outcome Measures - The Obstetric Quality of Recovery(OBsQoR),Maternal Comfort, EPDS for Post Partum Depression survey, GAD7 for Generalised Anxiety Disorder, and PCL-5 Post Traumatic Stress checklist.

**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: | 1500 |
| Total international sample size (including UK): | 1500 |
| Total in European Economic Area: | 1500 |

*Further details:*
For the pilot study We plan to collect data from UCLH for a 4 week study period. UCLH has approximately 20 elective CS a week, and a similar number of non-elective sections. Thus we aim to recruit approx. 100 patients. The subsequent multicentre study will take place over approx two weeks (during a two month time period), aiming to recruit approximately 1500 patients.

**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 initial pilot feasibility study does not including a formal sample size calculation. However we will aim to recruit 100 patients to draw conclusions with regards to feasibility and follow-up rates for the multicentre study. This will facilitate us to calculate a more definitive sample size.
Currently for the multicentre component of the study the sample size is calculated for detection of intraoperative pain, which was estimated to be 15% with a 95% confidence interval and a margin of error of +/-3%. This gives a single centre total of 545 patients recruited. However since there are will be multiple centres in the study, a design effect has been used to account for between site variation and within site clustering. The design effect is 1+ICC*(n-1) and n is the number of subjects per cluster. If there is no empirical data of ICC we could use 2 as the design effect. So the n is 545*2 giving a total sample size of approximately 900 patients, and up to 10% will have incomplete data within their CRFs. At 6 weeks we anticipate approximately 70% of patients will be followed up, this therefore gives a total sample size of 1500 patients.

**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.**

Analysis of patient studies will be predominantly based on providing descriptive epidemiology of the incidence of inadequate NA and how it is managed. The descriptive epidemiology of decision making with regards to analgesia supplementation, and augmentation or conversion of the NA will described. Inferential statistics (regression modelling) will be used to understand modifiable and non-modifiable risk factors for inadequate NA and patient-centred adverse outcomes measured in the Patient Study CRFs, and to understand the relationships between patient and structural risk factors, care processes, short-term and longer-term outcomes. Any free-text responses will be analysed thematically.

## 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 |
|---|---|---|---|
| | Dr | James | O'Carroll |
| Post | Consultant Anaesthetist, University College London Hospital, London, NW1 2BU | | |
| Qualifications | MBBS FRCA | | |
| | Dr Sultan has experience of conducting observational studies at UCLH, and provides distant clinical context and support. No patient or study data will be going to the USA, and this collaborator will only educationally supervise Trainee Lead Investigator. | | |
| Employer | University College Hospital NHS Foundation Trust | | |
| Work Address | 235 Euston Road | | |
| | London | | |
| Post Code | NW1 2BU | | |
| Telephone | | | |
| Fax | | | |
| Mobile | | | |
| Work Email | james.ocarroll@nhs.net | | |

| | Title | Forename/Initials | Surname |
|---|---|---|---|
| | Dr | Reshma | Patel |
| Post | Consultant Anaesthetist, Research fellow | | |
| Qualifications | MBBcH, FRCA | | |
| Employer | University College London Hospitals NHS Foundation Trust (Department of Anaesthesia and Perioperative Medicine) University College London (Research Department of Targeted Intervention) | | |
| Work Address | 235 Euston Road | | |
| | London | | |
| Post Code | NW1 2BU | | |
| Telephone | | | |
| Fax | | | |
| Mobile | 07719404626 | | |
| Work Email | reshma.patel21@nhs.net | | |

| | Title | Forename/Initials | Surname |
|---|---|---|---|
| | Dr | Bo | Hou |
| Post | Senior Research Fellow in Applied Health Statistics | | |
| Qualifications | BsC, MsC, PhD | | |

| | |
|---|---|
| Employer | NIHR Central London Patient Safety Research Collaboration (CL PSRC) and the UCL Division of Surgery and Interventional Science |
| Work Address | Centre for Perioperative Medicine, University College London, Charles Bell House, 43-47 Foley Street |
| Post Code | W1T 7SG |
| Telephone | |
| Fax | |
| Mobile | |
| Work Email | b.hou@ucl.ac.uk |

| Title | Forename/Initials | Surname |
|---|---|---|
| Dr | Nuala | Lucas |

| | |
|---|---|
| Post | Consultant Anaesthetist |
| Qualifications | |
| Employer | London North West University Healthcare NHS Trust |
| Work Address | Northwick Park Hospital<br>Watford Road Harrow Middlesex |
| Post Code | HA1 3UJ |
| Telephone | 020 8864 3232 |
| Fax | |
| Mobile | |
| Work Email | nuala.lucas@nhs.net |

| Title | Forename/Initials | Surname |
|---|---|---|
| Ms | Susanna | Stanford |

| | |
|---|---|
| Post | Patient, Patient Safety Advocate |
| Qualifications | |
| Employer | |
| Work Address | Northumberland |
| Post Code | |
| Telephone | |
| Fax | |
| Mobile | |
| Work Email | susanna@susannastanford.com |

| Title | Forename/Initials | Surname |
|---|---|---|
| Dr | Pervez | Sultan |

| | |
|---|---|
| Post | Consultant Anaesthetist, Associate Professor Aanesthesia |
| Qualifications | MBChB, MD (res) FRCA |
| Employer | Stanford University School of Medicine, Department of Anesthesiology, Perioperative and Pain Medicine |
| Work Address | Dept of Anesthesia 300 Pasteur Dr Rm H3586 MC 5640<br>California |
| Post Code | CA 94305 |
| Telephone | 650) 723-4000 |

| | |
|---|---|
| Fax | |
| Mobile | |
| Work Email | psultan@stanford.edu |

| Title | Forename/Initials | Surname |
|---|---|---|
| Professor | Brendan | Carvalho |

| | |
|---|---|
| Post | Professor of Anesthesiology, Perioperative and Pain Medicine (Adult MSD) |
| Qualifications | MBBCh, FRCA |
| Employer | Stanford University School of Medicine, Department of Anesthesiology, Perioperative and Pain Medicine |
| Work Address | Dept of Anesthesia 300 Pasteur Dr Rm H3586 MC 5640<br>California |
| Post Code | CA 94305 |
| Telephone | |
| Fax | |
| Mobile | |
| Work Email | carvalb@stanford.edu |

| Title | Forename/Initials | Surname |
|---|---|---|
| Ms | Samantha Jane | Hill |

| | |
|---|---|
| Post | Patient |
| Qualifications | |
| Employer | |
| Work Address | |
| Post Code | |
| Telephone | |
| Fax | |
| Mobile | |
| Work Email | samanthajane_hill@hotmail.com |

## 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 | UCL |
| Given name | Pushpsen |
| Family name | Joshi |
| Address | UCL/UCLH Joint Research Office (part of the Research Support Centre), 1st Floor Maple House Suite B |
| Town/city | 149 Tottenham Court Road, London |
| Post code | W1T 7DN |
| Country | United Kingdom |
| Telephone | 0203 447 5696 |
| Fax | |
| E-mail | uclh.randd@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:

**Please give details of funding applications.**

| | |
|---|---|
| Organisation | Obstetric Anaesthetic Association |
| Address | 21 Portland Place<br>London |
| Post Code | W1B 1PY |
| Telephone | 02076318883 |
| Fax | 02076314352 |
| Mobile | |
| Email | secretariat@oaa-anaes.ac.uk |

Funding Application Status: ◉ Secured ◯ In progress

Amount: £54 011

Duration
Years:
Months:

*If applicable, please specify the programme/ funding stream:*

What is the funding stream/ programme for this research project?
NIAA/OAA Large Project Grant

| | |
|---|---|
| Organisation | NIHR Central London Patient Safety Research Collaboration |
| Address | University College London Hospital<br>235 Euston Road |
| Post Code | NW1 2BU |
| Telephone | |
| Fax | |
| Mobile | |
| Email | cl-psrc@ucl.ac.uk |

Funding Application Status: ◉ Secured ◯ In progress

Amount: in kind

Duration
Years:
Months:

*If applicable, please specify the programme/ funding stream:*

What is the funding stream/ programme for this research project?
in kind funding (statistical support, project leadership, dissemination)

**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 |
|---|---|---|---|
| | Mr | Novin | Fard |
| Organisation | UCLH/UCL Joint Research Office, part of the Research Directorate | | |
| Address | 4th Floor, West | | |
| | 250 Euston Road | | |
| | London | | |
| Post Code | NW1 2PG | | |
| Work Email | Uclh.randd@nhs.net | | |
| Telephone | 020 3447 9825 | | |
| 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 Thames

*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: 01/07/2024
Planned end date: 01/10/2025
Total duration:
Years: 1 Months: 3 Days: 1

**A71-1. Is this study?**

○ Single centre
◉ Multicentre

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

- [x] England
- [x] Scotland
- [x] Wales
- [x] Northern Ireland
- [ ] Other countries in European Economic Area

Total UK sites in study 15

**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 | 10 |
| ☐ NHS organisations in Wales | 1 |
| ☐ NHS organisations in Scotland | 1 |
| ☐ HSC organisations in Northern Ireland | 3 |
| ☐ 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: | 15 |

**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 project team, chaired by the CI, plan to oversee and deliver the day-to-day organisation of the study.

The study team will also report to the R&D office at UCL.

## 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 management of the research will be covered by UCL insurance for negligent harm.

*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)

UCL insurance provides cover for negligent harm arising from the design of the research

*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)

NHS Indemnity will apply for UK NHS hospitals.

UCL holds insurance against patient claims for any harm caused by their participation in this clinical study. Participants may be able to claim compensation if they can prove that UCL has been negligent. However, as the main source of data for this clinical study is obtained from participating hospital sites, each site must continue to uphold a duty of care to patients enrolled into SONAR 1. UCL does not accept liability for any breach in the hospital's duty of care or any negligence on the part of hospital employees. This applies whether the hospital is an NHS Trust or otherwise.

*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<br>( ) Non-NHS/HSC Site | Forename: James<br>Middle name:<br>Family name: O'Carroll<br>Email: james.ocarroll@nhs.net<br>Qualification (MD...): MBBS FRCA<br>Country: United Kingdom |

| | |
|---|---|
| Organisation name | UNIVERSITY COLLEGE LONDON HOSPITALS NHS FOUNDATION TRUST |
| Address | 250 EUSTON ROAD |
| | LONDON |
| Post Code | NW1 2PG |
| Country | ENGLAND |

## 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 Suneetha Ramani Moonesinghe on 22/05/2024 15:49.

| | |
|---|---|
| Job Title/Post: | Consultant |
| Organisation: | UCL |
| Email: | ramani.moonesinghe@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 Mr Pushpsen Joshi on 22/05/2024 17:12.

| | |
|---|---|
| Job Title/Post: | Research Governance Manager |
| Organisation: | University College London |
| Email: | pushpsen.joshi1@nhs.net |

**D3. Declaration for student projects by academic supervisor(s)**

1. I have read and approved both the research proposal and this application. I am satisfied that the scientific content of the research is satisfactory for an educational qualification at this level.

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

3. I take responsibility for ensuring that this study is conducted in accordance with the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research, in conjunction with clinical supervisors as appropriate.

4. I take responsibility for ensuring that the applicant is up to date and complies with the requirements of the law and relevant guidelines relating to security and confidentiality of patient and other personal data, in conjunction with clinical supervisors as appropriate.

**Academic supervisor 1**

This section was signed electronically by Dr Suneetha Ramani Moonesinghe on 22/05/2024 15:50.

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|---|---|
| Job Title/Post: | Professor |
| Organisation: | UCL |
| Email: | ramani.moonesinghe@nhs.net |