

**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)

CLARITY Trial

**1. Is your project research?**

☒ Yes ☐ No

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

- ☐ Ionising Radiation for combined review of clinical trial of an investigational medicinal product
- ☐ Ionising Radiation and Devices form for combined review of 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) Will you be processing identifiable data at any stage of the research (including in the identification of participants)? ☐ Yes ☒ No

b) Please confirm that you will be processing only anonymised or pseudonymised data:

☒ Yes, only anonymised or pseudonymised data ☐ No

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

☒ England

- ☒ Scotland  
☒ Wales  
☒ Northern Ireland

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

- ☒ England  
☐ Scotland  
☐ Wales  
☐ Northern Ireland  
☐ This study does not involve the NHS

**4. Which applications do you require?**

- ☒ IRAS Form  
☐ Confidentiality Advisory Group (CAG)  
☐ 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

**4b. Please confirm the reason(s) why the project does not require review by a REC within the UK Health Departments Research Ethics Service:**

- ☐ Projects limited to the use of samples/data samples provided by a Research Tissue Bank (RTB) with generic ethical approval from a REC, in accordance with the conditions of approval.  
☐ Projects limited to the use of data provided by a Research Database with generic ethical approval from a REC, in accordance with the conditions of approval.  
☒ Research limited to use of previously collected, non-identifiable information  
☐ Research limited to use of previously collected, non-identifiable tissue samples within terms of donor consent  
☐ Research limited to use of acellular material  
☐ Research limited to use of the premises or facilities of care organisations (no involvement of patients/service users as participants)  
☒ Research limited to involvement of staff as participants (no involvement of patients/service users as participants)

**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

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

☐ Yes ☒ No

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

☐ Yes ☒ No

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

☐ Yes ☒ No

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

☐ Yes ☒ No

## Integrated Research Application System

### Application Form for Study limited to working with data (specific project only)

#### 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 familiar to lay reviewers of the application.

**Short title and version number:** (maximum 70 characters - this will be inserted as header on all forms)  
CLARITY Trial

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

**REC Name:**

**REC Reference Number:**

**Submission date:**

## PART A: Core study information

### 1. ADMINISTRATIVE DETAILS

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

CLARITY: An implementation-effectiveness trial of an educational intervention for surgical teams.

#### A3-1. Chief Investigator:

	Title	Forename/Initials	Surname
	Prof	Dion	Morton
Post	Barling Professor of Surgery		
Qualifications	MBChB, FRCS (Eng), MD		
ORCID ID	0000 0001 6784 1689		
Employer	University of Birmingham		
Work Address	Academic Department of Surgery, Heritage Building (Queen Elizabeth Hospital)		
	Room 29, 4th Floor Mindelsohn Way		
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Post Code	B15 2TH		
Work E-mail	Dion.Morton@uhb.nhs.uk		
* Personal E-mail	Dion.Morton@uhb.nhs.uk		
Work Telephone	0		
* Personal Telephone/Mobile	+44 (0)121 697 8390		
Fax	0		

*\* 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
	Dr Birgit Whitman
Address	Head of Research Ethics, Governance & Integrity Birmingham Research Park; University of Birmingham 97 Vincent Drive; Edgbaston; Birmingham
Post Code	B15 2TT
E-mail	researchgovernance@contacts.bham.ac.uk
Telephone	07814650003
Fax	0

**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):	NA
Sponsor's/protocol number:	1
Protocol Version:	1
Protocol Date:	07/01/2024
Funder's reference number (enter the reference number or state not applicable):	NA
Project website:	NA

**Additional reference number(s):**

Ref.Number	Description	Reference Number
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*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.*

Worldwide, appendicitis is the most common emergency treated by surgical teams (1). It is unlikely to resolve without treatment and surgical removal of the appendix is the 'gold standard' management. However, making an accurate diagnosis can be challenging because other conditions share similar symptoms. Consequently, many individuals with suspected appendicitis are unnecessarily hospitalised and operated on. Our prior research in the UK showed that around 60% of patients admitted with suspected appendicitis are later discharged with a different diagnosis and do not receive surgery (2). Furthermore, one in five patients who are admitted and go on to receive surgery are later discovered to have no disease in the appendix. This is an over-treatment rate three times higher than in other European countries. Not only does this create a burden on healthcare resources but importantly exposes patients to unnecessary hospitalisation, pain and risk of complications (3-6).

Although information is available to help surgeons diagnose appendicitis more accurately, it is not always used or easily accessible. To address this problem, our team has collaborated with patients, healthcare experts, and surgical education authorities to develop a tailored education package to help surgical teams to better diagnose appendicitis. The 'CLARITY accurate diagnosis package' is based on best international research and contains three components: an online education module, a checklist, and local implementation strategy. In our study, we plan to implement this package across at least 40 hospital sites in the UK. These centres will be divided into two groups: one group will adopt the package, while the other will continue with standard practices. After 8 weeks of implementation differences will be measured between the groups.

Our research aims to improve the care of individuals with suspected appendicitis and to gain insights into the adoption of this intervention.

- 1) NHS choices. NHS. Available at: <https://digital.nhs.uk/data-and-information/publications/statistical/health-survey-for-england/2019> (Accessed: February 10, 2023).
- 2) Bhangu A. Evaluation of appendicitis risk prediction models in adults with suspected appendicitis. *British Journal of Surgery*. 2019;107(1):73–86. doi:10.1002/bjs.11440
- 3) Fawcner-Corbett D [Internet]. 2020 [cited 2024 Jan 9]. Available from: [https://ora.ox.ac.uk/objects/uuid:7e12d770-a498-43bb-89f9-bc15c41798c7/download\\_file?file\\_format=&safe\\_filename=FawcnerCorbettetalAAM2020.pdf&type\\_of\\_work=Journal+article](https://ora.ox.ac.uk/objects/uuid:7e12d770-a498-43bb-89f9-bc15c41798c7/download_file?file_format=&safe_filename=FawcnerCorbettetalAAM2020.pdf&type_of_work=Journal+article)
- 4) Allaway, M., Eslick, G. and Cox, M., 2018. The Unacceptable Morbidity of Negative Laparoscopic Appendectomy. *World Journal of Surgery*, 43(2), pp.405-414.
- 5) Lee, M., Paavana, T., Mazari, F. and Wilson, T., 2014. The morbidity of negative appendectomy. *The Annals of The Royal College of Surgeons of England*, 96(7), pp.517-520.
- 6) Mock, K., Lu, Y., Friedlander, S., Kim, D. and Lee, S., 2016. Misdiagnosing adult appendicitis: clinical, cost, and socioeconomic implications of negative appendectomy. *The American Journal of Surgery*, 212(6), pp.1076-1082.

**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.*

#### Cluster Randomisation:

The CLARITY Trial employs cluster randomisation as the preferred study design due to the intervention being implemented at the hospital level. The surgical team will undergo educational training, potentially leading to better adherence to best practice recommendations. The intervention's impact is expected to improve the accuracy of standard management pathways.

#### Consent at Hospital Level:

Individual patient consent for the intervention is not deemed necessary as it is implemented at the hospital level and the participants are staff members. Furthermore, the intervention carries minimal risks, with no specific anticipated adverse events. In this pragmatic study, educational e-modules aim to inform and standardise clinical practice, while clinical teams will continue to exercise their judgment for individual patient care. Standard pre- and post-operative care remains unaffected.

#### Standard of Care:

The CLARITY Trial adheres to standard care practices, with no additional research activities beyond routine clinical procedures. Only routinely collected data will be gathered, and patients will not undergo any extra investigations or clinical follow-ups for the main study.

**Fully Anonymised Data:**

The trial prioritises data privacy and security. No sensitive or identifiable patient data will be collected on the REDCap database. Clinical teams will only upload anonymised data, ensuring that the central research team does not have access to patient-identifiable information. All data collected will be fully anonymised for analysis.

**Data Security:** The study acknowledges the risk associated with any breach of confidentiality or data security failure. To mitigate these risks, comprehensive training and support documents will be provided to local collaborators on data capture and reporting. Data will be entered directly onto the secure electronic CLARITY Research Electronic Data Capture (REDCap) database at participating hospital sites. The database will be hosted on the REDCap system managed and maintained by the Birmingham Surgical Trials Consortium (BiSTC), adhering to University of Birmingham policies and GDPR requirements. Each patient dataset will be assigned a unique study number to ensure that no individual can be identified in summary data statistics.

**Low Overall Risk:**

The overall risk of the CLARITY Trial is expected to be quite low and comparable to standard clinical care. The responsibility for patients at sites remains with the clinical organisations, indemnified through their standard arrangements. The intervention is low-risk, aligning with current best clinical practices. Clinical teams will continue to make individualised patient care decisions, ensuring that patients receive what is deemed to be best practice or their usual care, unaffected by the intervention.

### 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)

Cluster randomisation with the cluster being the hospital and the participants being the acute general surgical team.

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

The principal question for the overall trial is:

Can implementation of an evidence based educational intervention, focussed on accurate diagnosis of appendicitis, safely reduce unnecessary admissions to hospital in patients with suspected appendicitis?

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

Other questions the trial is hoping to address are:

- i) To determine whether implementation of the CLARITY evidence based programme can reduce unnecessary surgery and improve patient outcomes.

- ii) To assess the effectiveness of the CLARITY implementation strategy on increasing uptake of the intervention and adherence to evidence-based recommendations in the emergency surgery setting.

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

**Background:**

Acute right iliac fossa (RIF) pain, located in the lower right side of the abdomen, should raise concerns about a condition called appendicitis. Appendicitis is a disease where a small part of the gut called the appendix becomes inflamed. Globally, it is the most common emergency surgical presentation, with England alone recording 61,916 hospital cases of appendicitis in the year 2019-2020.[1] Extrapolating national data from the RIFT Study (2017) we estimate over 160,00 patients are referred for suspected appendicitis annually.[2] People with appendicitis often present with a variety of quite generic symptoms, particularly in the early stages of disease. Prompt and accurate diagnosis is essential for patients to receive the correct treatment.

**What is the problem being addressed?:**

There are many diagnostic approaches to appendicitis and our work has identified the UK to have significant variations in practice.[2] This can lead to patients either receiving surgery they don't need or being kept in the hospital when they could go home. Unnecessary admissions and operations are accompanied with significant risks and costs for the health service. Around 60% of the patients admitted for suspected appendicitis are monitored in a hospital bed and discharged without receiving an intervention.[2] Not only does this signify suboptimal care but it creates a significant burden on the health service. It is believed that education on best practice for appendicitis has the potential to improve diagnostic processes.

Another concern with unnecessary admission is that a proportion of patients —particularly those with longer hospital stays— end up receiving unnecessary surgery.[3] In the UK, 1 out of every 5 people who have surgery for what looks like appendicitis turn out to have a perfectly healthy appendix on microscopic examination after the surgery. This kind of surgery, where they remove a normal appendix, is called a "negative appendectomy." The UK has one of the highest rates of this globally, at 20%, this over-treatment is three times higher than in other European countries.[2] An unnecessary appendectomy carries the same level of complications as surgery for true appendicitis.[5,6] Patients can sustain significant complications including wound infections, port site hernias, pain and unnecessary time away from their usual activities (work / education / caring etc.). This also suggests there are up to 15,000 appendectomies being performed in England annually for patients with a normal appendix. Hence, a large number of patients are being exposed to harm from postoperative complications (7% of women and 23% of men).[2]

**Existing solutions and our proposal:**

Best evidence-based practice recommends the use of clinical prediction scores and targeting of investigations according to individual risk. However, there is a gap in the translation of research into clinical practice. If surgical teams were better supported in decision making, unnecessary admissions and over-treatment of UK patients with suspected appendicitis could be reduced. To date no national approach has been taken to address this issue.

Our proposal follows on from our work on the RIFT Study (2017).[2] This West Midlands Research Collaborative study was the largest international prospective study (including 154 NHS hospitals) of patients with suspected appendicitis. It provided comprehensive evaluation of clinical practice and patient outcomes; validating risk scoring tools for safer patient management. Furthermore, our group has designed an evidence based educational intervention for surgical teams to aid them in their decision making and to hopefully results in harmonisation of practice across the NHS. The overall focus of our package content is on reducing unnecessary admissions, surgical overtreatment and other negative patient outcomes. The package will achieve this by promoting balanced risk management, increasing awareness of the latest evidence-base in diagnostic practice and prioritising effective patient communication.

We are well positioned to deliver this trial as within the last year, our team has successfully completed two cluster randomised controlled surgical trials both using similar methodology. This includes the use of education packages and implementation strategies to increase team work and adoption of best practice recommendations to improve surgical site infections (CHEETAH) and to change decision making in colorectal anastomosis (EAGLE).[6-7]

**Main question and expected benefit:**

Can implementation of an evidence based educational intervention, focussed on accurate diagnosis of appendicitis, safely reduce unnecessary admissions to hospital in patients with suspected appendicitis?

Implementing an intervention to address unnecessary admissions and negative patient outcomes could have a significant positive impact on the quality of patient care. Considering that approximately 160,000 patients are referred with suspected appendicitis in the UK each year, our intervention has the potential to significantly reduce patient harm and to minimise the negative impact on patients. Furthermore, based on the figures above if negative appendectomies were reduced by 30%, NHS England could prevent 3173 unnecessary operations every year (over



9,500 bed days). Patients who receive negative surgery spend more time in hospital than patients with non-perforated appendicitis. (3.3 days vs 1.7 days).[7] Reducing these numbers and unnecessary admissions in patients with an alternate diagnosis could have significant implications on surgical bed-service management, resources and waiting times.

Overall this trial will hopefully inform us on if the surgical culture in the UK around appendicitis can be changed and the impact on outcomes for patients. Secondly and very importantly this trial will help inform whether this style of implementation intervention is successful in encouraging surgical teams to adopt evidence based recommendations. If the latter is true, this opens up significant avenues for future researchers to bring about meaningful change in practice for neighbouring surgical fields and areas of clinical concern.

#### References:

1. NHS choices. NHS. Available at:

<https://digital.nhs.uk/data-and-information/publications/statistical/health-survey-for-england/2019> (Accessed: February 10, 2023).

2. Bhangu, A., 2019. Evaluation of appendicitis risk prediction models in adults with suspected appendicitis. *British Journal of Surgery*, 107(1), pp.73-86

3. Fawcner-Corbett, D. (2020) Rift Study Group on behalf of the West Midlands Research Collaborative ... Available at: [https://ora.ox.ac.uk/objects/uuid:7e12d770-a498-43bb-89f9-bc15c41798c7/download\\_file?file\\_format=&safe\\_filename=FawcnerCorbettetal\\_AAM2020.pdf&type\\_of\\_work=Journal+article](https://ora.ox.ac.uk/objects/uuid:7e12d770-a498-43bb-89f9-bc15c41798c7/download_file?file_format=&safe_filename=FawcnerCorbettetal_AAM2020.pdf&type_of_work=Journal+article) (Accessed: 09 January 2024).

4. Allaway, M., Eslick, G. and Cox, M., 2018. The Unacceptable Morbidity of Negative Laparoscopic Appendectomy. *World Journal of Surgery*, 43(2), pp.405-414.

5. Lee, M., Paavana, T., Mazari, F. and Wilson, T., 2014. The morbidity of negative

6. Soares AS, Garmanova T, Gravante G, Bywater E, Pettitt M, Venn ML, et al. ESCP Safe Anastomosis Programme in colorectal surgery (EAGLE): Study protocol for an international cluster randomised trial of a quality improvement intervention to reduce anastomotic leak following right colectomy. *Colorectal Disease*. 2021;23(10):2761-71.

7. Ademuyiwa AO, Adisa AO, Bhangu A, Brocklehurst P, Chakrabortee S, Ghosh D, et al. Routine sterile glove and instrument change at the time of abdominal wound closure to prevent surgical site infection (Cheetah): A Pragmatic, cluster-randomised trial in seven low-income and middle-income countries. *The Lancet*. 2022;400(10365):1767-76.

**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.*

#### Research question:

Can implementation of an evidence based educational intervention, focussed on accurate diagnosis of appendicitis, safely reduce unnecessary admissions to hospital in patients with suspected appendicitis?

#### Background:

Acute appendicitis is one of the most common surgical emergencies. Over 55,000 operations for appendicitis are performed each year in England. However, a significant proportion of patients with right iliac fossa pain are misdiagnosed and placed on incorrect care pathways. Most of these patients receive unnecessary hospital admissions for monitoring and do not undergo an intervention. While some admissions result in patients receiving a negative appendectomy exposing them to post-operative pain and risks from complications. Furthermore, this leads to delayed treatment for the underlying condition they initially presented to hospital with.

#### Aim:

To improve right iliac fossa care pathways by reducing unnecessary admissions to hospital.

#### Design:

Multicentre, parallel cluster randomised controlled trial with an effectiveness-implementation design. This type of trial combines elements of both implementation and effectiveness research to address the real-world effectiveness of an intervention while also considering how well it can be implemented in practice. Each cluster corresponds to an acute care hospital. Participating sites will be randomised to receive the CLARITY evidence based learning programme on accurate diagnosis of appendicitis (CLARITY EBP) or standard care.

#### Eligibility:

Any UK hospital offering emergency general surgery services, equipped for admitting patients and facilitating follow-up reviews on the ward. Participants include members of the acute surgical team involved in the assessment of patients

with RIF pain and suspected appendicitis. Data from hospital notes will be collected from consecutive patients aged 16 to 39 years old (inclusive) attending hospital with right iliac fossa pain over an 8-week period.

**Intervention:**

The intervention is the CLARITY accurate diagnosis package, which is made up of three components: the evidence based education program (EBP), an implementation checklist (containing prompts) and local implementation strategies (to help build teams and to encourage adoption in the clinical setting). The EBP is considered the main component of our intervention and will be delivered using an electronic learning platform to intervention sites.

**Comparison:**

Routine clinical care (sites without CLARITY accurate diagnosis package).

**Primary Outcome:**

Non-operative admission rate (NOAR) - defined as unnecessary admission.

**Secondary Outcomes:**

Safety (including negative appendectomy and complication rate) and delayed diagnosis, post-op complications and readmissions.

**Sample size:**

40 clusters (20 per arm) of 120 patients would be required to detect a 25% reduction in non-operative admission rate (4800 patients in total, power = 0.90,  $\alpha$  = 0.05).

**Randomisation:** Hospitals will be categorised by bed size (< or >400 beds) and randomised using a 1:1 minimisation algorithm to ensure fairness.

**Follow up:** This will be carried out by reviewing hospital notes 30 days after attendance or admission.

**Analysis:** Intention to treat analysis, per protocol analysis, implementation analysis, sensitivity analysis, and health economics analysis will all be conducted.

**Potential Impact:**

Improved patient care with a reduction in unnecessary admissions and negative appendectomies.

Reduction in healthcare costs by preventing unnecessary surgeries.

More efficient allocation of emergency resources, reducing hospital stays and admissions.

**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?**

- ☒ Design of the research
- ☒ Management of the research
- ☐ Undertaking the research
- ☐ Analysis of results
- ☒ Dissemination of findings
- ☐ None of the above

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

The Patient Advisory Group (PAG) plays an essential role throughout this study. Patients with a lived experience of suspected appendicitis were actively engaged in shaping the study, with a particular focus on co-developing patient-oriented outcomes as well as co-developing the intervention itself. The PAG contributions have been solicited through the use of multiple focus group interviews.

The PAG will also help support development of a communication strategy (including social media), write patient facing documentation and support dissemination of research findings at the end of the trial. Finally, 1 PPI member has been extended in their role and will have active participation in the trial's management and steering group in accordance with the NIHR terms of reference for steering committees. Overall, this group will remain central to the ongoing development of our intervention and management of the trial.

To ensure the CLARITY trial is meeting the UK standards for public involvement, we are committed to adhering to all six standards as laid out by the INVOLVE best practice guideline (2015). Adherence to these standards will ensure

that there is meaningful collaboration with patients and carers, and to ensure collaborators are supported in their role through training and skills development. Finally, we have established a framework for regular communication with our Patient and Public Involvement (PPI) lead and PPI representation at all levels of the study management and oversight. This approach hopefully underscores our commitment to meaningful and sustained engagement with the patient community ensuring their valuable insights continue to shape the progress of this study.

#### 4. RISKS AND ETHICAL ISSUES

#### RESEARCH PARTICIPANTS

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

Select all that apply:

- ☐ Blood
- ☐ Cancer
- ☐ Cardiovascular
- ☐ Congenital Disorders
- ☐ Dementias and Neurodegenerative Diseases
- ☐ Diabetes
- ☐ Ear
- ☐ Eye
- ☐ Generic Health Relevance
- ☐ Infection
- ☐ Inflammatory and Immune System
- ☐ Injuries and Accidents
- ☐ Mental Health
- ☐ Metabolic and Endocrine
- ☐ Musculoskeletal
- ☐ Neurological
- ☒ Oral and Gastrointestinal
- ☐ Paediatrics
- ☐ Renal and Urogenital
- ☐ Reproductive Health and Childbirth
- ☐ Respiratory
- ☐ Skin
- ☐ Stroke

Gender: Male and female participants

Lower age limit: 16 Years

Upper age limit: 39 Years

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

Hospital inclusion criteria

- Any hospital in the UK providing emergency general surgical services
- The ability to schedule patients for a follow up assessment in the surgical admission unit or ambulatory/hot clinic

service

PLEASE NOTE IN QUESTION A15 ABOVE WE HAVE ANSWERED THIS ACCORDING TO THE DATA WE WILL COLLECT, THE PARTICIPANTS ARE THE CLINICAL STAFF BUT IT IS NOT POSSIBLE TO PROVIDE THAT AS AN ANSWER TO QUESTION A15.

The participants of the study are STAFF members, NOT NHS PATIENTS.

Participant inclusion criteria:

- Doctors and clinicians assessing patients with RIF pain, within the acute surgical team
- This includes consultants, specialty doctors, registrars, senior house officers, foundation doctors, surgical nurse practitioner and physicians associates.

Anonymised, routinely collected data will be collected within this study.

The data that will be collected will be from patients who are 16 to 39 year old (inclusive) and old attending hospital with right iliac fossa pain and who are under the care of the general surgery team, including in the emergency department, surgical admissions unit, or paediatrics ward.

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

As the participants in this study are the clinical staff at site NOT NHS patients, we have not specified exclusion criteria for the NHS staff, only inclusion.

the inclusion are:

- Doctors and clinicians assessing patients with RIF pain, within the acute surgical team
- This includes consultants, specialty doctors, registrars, senior house officers, foundation doctors, surgical nurse practitioner and physicians associates.

**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).

The participants are the staff members on the acute general surgical team. They will be identified by the local PI.

The data used within this study will be routinely collected data from patient hospital records.

Data will only be collected on patients aged 16 to 39 years old (inclusive) attending hospital with right iliac fossa pain.

Each participating hospital will decide how best to identify eligible patient data to be included.

As guidance, it is anticipated that patients may be identified from any of the following settings:

- At time of attendance or admission to hospital:  
referrals made to the surgical team, and/or emergency surgical admissions
- During admission:

By the emergency surgical team or research team.

The local research team will formally assess eligibility of the patient against trial inclusion and exclusion criteria. No additional tests or investigations will be required for assessing eligibility.

Patient's whose data will be used within the study will only be accessed by the direct clinical care team. This may include:

1. Any doctor involved in the patients' care (e.g. surgeon in training)
2. Nurse practitioner or research nurse
3. Medical students (these will consequently be checked by other doctors/nurses).

Routinely collected patient data up until 30-days post-discharge will be included in the study.

The research team will have access to anonymised data only.

## 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.

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

Personal data will be stored securely at local sites subject to confidentiality policies and procedures in place at the local NHS Trusts.

All data that will leave the hospital site will be non-identifiable information that will be entered onto the UoB REDCap database.

The REDCap database used for the CLARITY trial is run by the University of Birmingham.  
The security of the study REDCap database system is governed by the policies of the University of Birmingham UK, in accordance with the requirements of the General Data Protection Regulations (GDPR). No sensitive or identifiable data will be collected on the database; the site team will upload only non-identifiable data.

## Storage and use of data after the end of the study

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

The fully anonymised data generated by the study will be held centrally in the University of Birmingham, and be analysed by a Senior Statistician/Epidemiologist, within the clinical trials team at the University of Birmingham.

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

	Title Forename/Initials Surname
	Prof Dion Morton
Post	Barling Professor of Surgery
Qualifications	MBChB, FRCS (Eng), MD
Work Address	Academic Department of Surgery, Heritage Building (Queen Elizabeth Hospital) Room 29, 4th Floor Mindelsohn Way Edgbaston, Birmingham
Post Code	B15 2TH
Work Email	Dion.Morton@uhb.nhs.uk
Work Telephone	+44 (0)121 697 8390
Fax	0

### 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.

Once data collection is complete, the electronic research files will be stored on non-networked computers belonging to the researchers named on the form. Access will be restricted to the researchers themselves. Study data will be

stored within the UoB under controlled conditions, as intermediate storage, until long term offsite data archiving facilities are considered for storage. The BiSTC has standard processes for both hard copy and computer database legacy archiving. Data will be stored and destroyed in accordance with GCP guidelines.

#### INCENTIVES AND PAYMENTS

**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

#### 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 will prospectively register the trial with the ISRCTN registry, the international registry of clinical trials once submitted to Ethics (<https://www.isrctn.com/>).

*Registration of research studies is encouraged wherever possible.*

*You may be able to register your study through your NHS organisation or a register run by a medical research charity, or publish your protocol through an open access publisher. If you are aware of a suitable register or other method of publication, please give details. If not, you may indicate that no suitable register exists. Please ensure that you have entered registry reference number(s) in question A5-1.*

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

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

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

The study data base will only contain anonymised data at the point of entry to the database. The researchers that analyse the data will not have access to any patient identifiable information. Overall, the CLARITY trial will not use identifiable personal data in any report, publication or presentation of the results.

## 5. Scientific and Statistical Review

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

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

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

This study is the natural progression of the previous study delivered in 2017 by the West Midlands Research Collaborative: the RIFT Study (10.1002/bjs.11440). Some 5345 patients across 154 UK hospitals were identified and it was found that in 20 to 30% of appendicectomies performed in the UK, the appendix was subsequently not found to be inflamed on microscopic examination. Therefore, as these people did not have appendicitis, they were subjected to an unnecessary operations which carried the same level of risk and complication rate as necessary operations for appendicitis. People having these unnecessary procedures are subject to pain, risk of complications and receive a procedure which will not treat the cause of their symptoms. In comparison to other European countries, the UK has a threefold increase in the rate of unnecessary operations for appendicitis and therefore resultant sequela. The aim of this randomised control trial is to assess whether the implementation of of an educational intervention on how to diagnose acute appendicitis can effectively reduce unnecessary operations and complications for those with suspected appendicitis in the UK. Leading experts in this field of research are co-applicants/co-investigators on the trial and have contributed to the trial protocol.

Validation of the online training platform:

The evidence based education program has been co-developed and reviewed by the European society of Coloproctology and the West Midlands Deanery Postgraduate School of Surgery. It has been beta-tested by 20 external doctors to ensure clarity of meaning is retained.

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

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

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

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

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

	Title Forename/Initials Surname
	Mr Omar Omar
Department	Birmingham Clinical trials Unit
Institution	Birmingham University
Work Address	Heritage Building, Birmingham,
Post Code	B15 2TT
Telephone	
Fax	
Mobile	
E-mail	o.omar@bham.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?**

Reduction in overnight non-operative admission rate

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

Safety (including negative appendicectomy and complication rate) and delayed diagnosis, post-op complications and readmissions.

**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: 4800

Total international sample size (including UK):

Total in European Economic Area:

*Further details:*

40 clusters (20 per arm) of 120 patients would be required to detect a 25% reduction in non-operative admission rate (4800 patients in total, power = 0.90,  $\alpha$  = 0.05).

**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.**

We determine the expected power for the primary outcome. To detect a 25-percentage point reduction in non-operative admission rate, assuming an intra-cluster correlation (ICC) of 0.06 and an  $\alpha$  of 0.05, 40 clusters (20 per arm) of 120 patients would be required - 4800 patients in total. This sample size would provide a power of 0.90. We have been conservative in these estimates and factored in a cluster size variation of 50%.

Power calculations have allowed for the clustered nature of the design, assuming an exchangeable correlation structure as appropriate in a parallel CRT.[10-11] This has been incorporated in the sample size calculations using the intra-cluster correlation (ICC). The assumed values for these correlations have been guided by correlations for similar outcome in similar settings as well as general patterns in the literature. In particular, the ICC was calculated using data from the RIFT study 2020, which included 154 UK centres.

**A61. Will participants be allocated to groups at random?**

☒ Yes ☐ No

*If yes, please give details of the intended method of randomisation:*

Cluster randomisation will be performed at the hospital level (one hospital is defined as one cluster). The CLARITY



intervention is targeted at healthcare professionals, therefore individual patient-level randomisation would not be appropriate.

A minimisation algorithm will be used at the time of randomisation to ensure the two groups are balanced for size of hospital and other factors which may influence outcomes (i.e. availability of imaging out of hours). In terms of hospital size, we will minimise based on the total number of beds. A large hospital will be deemed to be 400 beds and over, whereas a small hospital is under 400 beds. This is to ensure the numbers of larger or smaller hospitals across the intervention and control groups are balanced for number of patients and other factors including availability of resources (i.e. availability of diagnostic tests).

The randomisation will be performed by a statistician and checked prior to implementation. Centre approvals be checked and finalised before centres are randomised. A minimisation algorithm has been chosen as it allows for sequential allocation of centres as and when they are ready to be randomised. The method will allow for a 1:1 allocation and include a stochastic element to prevent lack of allocation concealment and prevent predictability of upcoming assignment.

**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.**

Statistical analysis for this Trial will be conducted on an intention-to-treat basis i.e. all patients recorded in the database during the scheduled 8-week recruitment periods will be included. We will compile a full statistical analysis plan prior to data analysis. This trial will be reported according to the CONSORT guidelines and the cluster RCT extension.

All analysis will be performed with respect to the clustered nature of the data. Summary data will be tabulated using simple counts and percentages for categorical data. Where continuous data is normally distributed, the mean average will be presented alongside the standard deviation. Where data are not normally distributed, the median average will be presented alongside the 25th and 75th centiles. Given the randomisation we will not formally test differences in the characteristics of people included in the study.

All data will be checked and data quality rules will be implemented to ensure data included in analyses is accurate. Missing covariate data will be fully reported and the reason for missingness established. Where possible centres will be asked to supply the missing data, however, if this is not possible, we will perform multiple imputation when there is a significant amount of missing data (>10%). For missing outcome data, we will perform a best/worst case scenario analysis by imputing missing values with extreme values to assess whether missing outcome data is likely to impact our findings.

For binary outcome measures, we will report the absolute and relative treatment effects, alongside the corresponding 95% confidence intervals. Where an outcome measure is a continuous scale, we will report the mean difference with the corresponding 95% confidence interval. In the primary analysis, we will use mixed effects logistic regression with random cluster (hospital) effects allowing inclusion of baseline risk factors and adjustment for a fixed time effect between time periods. Treatment effects will be estimated using REML and generalised mixed linear models, with relevant small sample corrections. For rare events, we will use methods that maximise the likelihood of model convergence, such as propensity score matching. We will match on pre-specified clinically relevant covariates, including those used within the minimisation algorithm. For matched comparisons we will also present a secondary covariate adjusted analysis.

**Planned subgroup analyses**

Pre-planned exploratory sub-group analyses of the primary outcome will be performed in the following groups:

At cluster (hospital) level:

- Number of beds (<400 versus ≥400 total hospital beds).
- Early adoption (early versus late study entrants).
- Availability of cross sectional imaging and diagnostic tests (Limited blood testing only [only one available from haematology, biochemistry, point of care blood gas testing], comprehensive blood testing [haematology and biochemistry, but no cross sectional imaging], cross sectional imaging available - non-resident radiographer, cross sectional imaging available - resident radiographer).
- Proportion of operating surgeons in each centre completing the online training modules prior to 'post-implementation' data collection (high [≥80%], intermediate [50-79%], low [<50%]).

At patient level:

- Operative approach (open versus laparoscopic).
- Patient age
- Patient sex
- Previous surgery

- Primary operating surgeon experience as reported (trainee versus consultant).

Reverse analysis will also be undertaken to explore what are the characteristics of hospitals with a big change versus no change, and do these differ in respect of cluster characteristics.

## 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 Laura Magill
Post	Senior Lecturer in Clinical Trials
Qualifications	PhD
Employer	Birmingham University
Work Address	Birmingham Clinical Trials Unit Birmingham,
Post Code	B15 2TT
Telephone	07966098477
Fax	0
Mobile	0
Work Email	e.l.magill@bham.ac.uk

	Title Forename/Initials Surname
	Miss Fatima Mansour
Post	Clinical Research Fellow
Qualifications	MBBS5, BSc, MRCS
Employer	University College London
Work Address	9th floor DSIS Pond St, London
Post Code	NW3 2QG
Telephone	
Fax	
Mobile	
Work Email	fatima.mansour@nhs.net

	Title Forename/Initials Surname
	Dr Daoud Chaudhry
Post	Trainee, Head of STARSURG collaborative
Qualifications	MBBS5
Employer	University Hospitals North Midlands
Work Address	
	Stoke-on-Trent
Post Code	ST4 6QG
Telephone	
Fax	

Mobile	
Work Email	daoudchaudhry@gmail.com
	Title Forename/Initials Surname
	Dr Thomas Drake
Post	Clinical Research Fellow
Qualifications	MBChB5 , BSc, PhD
Employer	University of Edinburgh
Work Address	Centre for Medical Informatics, Usher Institute Department of Clinical Surgery
Post Code	
Telephone	
Fax	
Mobile	
Work Email	t.drake@ed.ac.uk

**A64. Details of research sponsor(s)****A64-1. Sponsor****Lead Sponsor**Status: ☐ NHS or HSC care organisation☒ Academic☐ Pharmaceutical industry☐ Medical device industry☐ Local Authority☐ Other social care provider (including voluntary sector or private organisation)☐ OtherCommercial status: ☐ Non-Commercial*If Other, please specify:***Contact person**

Name of organisation University of Birmingham

Given name Birgit

Family name Whitman

Address Head of Research Ethics, Governance and Integrity; Birmingham Research Park

Town/city University of Birmingham; 97 Vincent Drive;

Post code B15 2TT

Country United Kingdom

Telephone 07814650003

Fax 0

E-mail researchgovernance@contacts.bham.ac.uk

**Legal representative for clinical investigation of medical device (studies involving Northern Ireland only)**

*Clinical Investigations of Medical Devices that take place in Northern Ireland must have a legal representative of the sponsor that is based in Northern Ireland or the EU*

**Contact person**

Name of organisation

Given name

Family name

Address

Town/city

Post code

Country

Telephone

Fax

E-mail

**A65. Has external funding for the research been secured?**

*Please tick at least one check box.*

- ☐ Funding secured from one or more funders
- ☐ External funding application to one or more funders in progress
- ☒ No application for external funding will be made

What type of research project is this?

- ☒ Standalone project
- ☐ Project that is part of a programme grant
- ☐ Project that is part of a Centre grant
- ☐ Project that is part of a fellowship/ personal award/ research training award
- ☐ Other

Other – please state:

**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
	Dr Sarah Pountain
Organisation	University Hospitals Birmingham NHS Foundation Trust
Address	Head of Research Governance
	R&D Department; MIDRU, Heartlands Hospital
	Bordesley Green East; Birmingham
Post Code	B9 5SS
Work Email	r&D@uhb.nhs.uk
Telephone	01214243631
Fax	0
Mobile	0

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:**

West Midlands

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

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

Planned start date: 10/06/2024

Planned end date: 09/09/2025

Total duration:

Years: 1 Months: 3 Days: 0

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

- ☐ Single centre
- ☒ Multicentre

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

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

Total UK sites in study

**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:

- |   |    |
|---|----|
| <input checked="" type="checkbox"/> NHS organisations in England                                  | 31 |
| <input checked="" type="checkbox"/> NHS organisations in Wales                                    | 5  |
| <input checked="" type="checkbox"/> NHS organisations in Scotland                                 | 5  |
| <input checked="" type="checkbox"/> HSC organisations in Northern Ireland                         | 5  |
| <input type="checkbox"/> GP practices in England  |    |
| <input type="checkbox"/> GP practices in Wales  |    |
| <input type="checkbox"/> GP practices in Scotland   |    |
| <input type="checkbox"/> GP practices in Northern Ireland   |    |
| <input type="checkbox"/> Joint health and social care agencies (eg community mental health teams) |    |
| <input type="checkbox"/> Local authorities  |    |
| <input type="checkbox"/> Phase 1 trial units  |    |
| <input type="checkbox"/> Prison establishments  |    |
| <input type="checkbox"/> Probation areas  |    |
| <input type="checkbox"/> Independent (private or voluntary sector) organisations                  |    |
| <input type="checkbox"/> Educational establishments   |    |
| <input type="checkbox"/> Independent research units   |    |
| <input type="checkbox"/> Other (give details)   |    |

Total UK sites in study: 46

**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?**

Due to the nature of CLARITY Trial, monitoring will be employed to ensure the credibility of the data. Monitoring will be undertaken centrally and will include, but will not be limited to, monitoring of: protocol adherence; patient selection and minimisation of selection bias; review of data relating to the primary and secondary outcomes. Monitoring will be via data validation and range checks built into the REDCap database used to collect and manage the data; statistical monitoring techniques will be used to compare data from different sites to identify sites that may warrant further investigation, site monitoring and/or support and training. Review by the study oversight committees (SSC, DMOC, SMG) will also include the review of completion of primary and secondary outcomes, adherence to protocol, and selection bias.

The CLARITY study staff from the University of Birmingham will be in regular contact with the site research teams to check on progress and address any queries that they may have. The CLARITY Data Management Committee will check submitted case report forms from the participating hospitals for compliance with the protocol, data consistency and missing data. They will send participating hospitals data queries for missing data or clarification of inconsistencies or discrepancies.

Data Monitoring and Oversight Committee (DMOC) is scheduled to meet prior to the study commencing and at every three months thereafter until the study closes to recruitment. Additional meetings may be called if recruitment is much faster than anticipated and the DMOC may, at their discretion, request to meet more frequently or continue to meet following completion of recruitment. An emergency meeting may also be convened if required. The DMOC will review data completeness, recruitment per-site, recruitment overall, and protocol deviations.

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*

**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	<input checked="" type="radio"/> NHS/HSC Site <input type="radio"/> Non-NHS/HSC Site  Organisation name    UNIVERSITY HOSPITALS BIRMINGHAM NHS FOUNDATION TRUST Address                QUEEN ELIZABETH HOSPITAL MINDELSON WAY EDGBASTON BIRMINGHAM WEST MIDLANDS Post Code                B15 2GW Country                 ENGLAND	Forename                Dion Middle name Family name            Morton Email Qualification (MD...)    MD Country                 United Kingdom
IN3	<input checked="" type="radio"/> NHS/HSC Site <input type="radio"/> Non-NHS/HSC Site  Organisation name    BARTS HEALTH NHS TRUST Address                THE ROYAL LONDON HOSPITAL 80 NEWARK STREET LONDON Post Code                E1 2ES Country                 ENGLAND	Forename                Anna Marie Middle name Family name            minicozzi Email                    annamariaminiocozzi@nhs.net Qualification (MD...)    MD Country                 United Kingdom
IN4	<input checked="" type="radio"/> NHS/HSC Site <input type="radio"/> Non-NHS/HSC Site	Forename                Panna Middle name Family name            Patel Email                    panna.patel@mbht.nhs.uk



	Organisation name	UNIVERSITY HOSPITALS OF MORECAMBE BAY NHS FOUNDATION TRUST	Qualification (MD...)	MD
	Address	WESTMORLAND GENERAL HOSPITAL BURTON ROAD KENDAL	Country	United Kingdom
	Post Code	LA9 7RG		
	Country	ENGLAND		
IN5	<input checked="" type="radio"/> NHS/HSC Site <input type="radio"/> Non-NHS/HSC Site		Forename	Jayesh
			Middle name	
			Family name	Sagar
			Email	Jayesh.sagar@ldh.nhs.uk
	Organisation name	BEDFORDSHIRE HOSPITALS NHS FOUNDATION TRUST	Qualification (MD...)	MD
	Address	LEWSEY ROAD	Country	United Kingdom
		LUTON		
	Post Code	LU4 0DZ		
	Country	ENGLAND		
IN6	<input checked="" type="radio"/> NHS/HSC Site <input type="radio"/> Non-NHS/HSC Site		Forename	Simone
			Middle name	
			Family name	Sebastiani
	Organisation name	HYWEL DDA UNIVERSITY LHB	Email	Simone.Sebastiani@wales.nhs.uk
	Address	CORPORATE OFFICES, YSTWYTH BUILDING HAFAN DERWEN ST DAVIDS PARK, JOBSWELL ROAD CARMARTHEN DYFED	Qualification (MD...)	MD
			Country	United Kingdom
	Post Code	SA31 3BB		
	Country	WALES		
IN7	<input checked="" type="radio"/> NHS/HSC Site <input type="radio"/> Non-NHS/HSC Site		Forename	Athula
			Middle name	
			Family name	Tennakoon
			Email	athula.tennakoon@ulh.nhs.uk

IN8	Organisation name	UNITED LINCOLNSHIRE HOSPITALS NHS TRUST	Qualification (MD...)	MD
	Address	LINCOLN COUNTY HOSPITAL GREETWELL ROAD LINCOLN	Country	United Kingdom
	Post Code	LN2 5QY		
	Country	ENGLAND		
	<input checked="" type="radio"/> NHS/HSC Site		Forename	Chetan
	<input type="radio"/> Non-NHS/HSC Site		Middle name	
			Family name	Parmar
			Email	cparmar@nhs.net
	Organisation name	WHITTINGTON HEALTH NHS TRUST	Qualification (MD...)	MD
	Address	THE WHITTINGTON HOSPITAL MAGDALA AVENUE LONDON	Country	United Kingdom
Post Code	N19 5NF			
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 Professor Dion Morton on 16/05/2024 13:02.

Job Title/Post:            professor of Surgery  
Organisation:            University of Birmingham  
Email:                      Dion.morton@uhb.nhs.uk

**D2. Declaration by the sponsor's representative**

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

I confirm that:

1. This research proposal has been discussed with the Chief Investigator and agreement in principle to sponsor the research is in place.
2. An appropriate process of scientific critique has demonstrated that this research proposal is worthwhile and of high scientific quality.
3. Any necessary indemnity or insurance arrangements, as described in question A76, will be in place before this research starts. Insurance or indemnity policies will be renewed for the duration of the study where necessary.
4. Arrangements will be in place before the study starts for the research team to access resources and support to deliver the research as proposed.
5. Arrangements to allocate responsibilities for the management, monitoring and reporting of the research will be in place before the research starts.
6. The responsibilities of sponsors set out in the UK Policy Framework for Health and Social Care Research will be fulfilled in relation to this research.

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

7. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named in this application. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.
8. Specifically, for submissions to the Research Ethics Committees (RECs) I declare that any and all clinical trials approved by the HRA since 30th September 2013 (as defined on IRAS categories as clinical trials of medicines, devices, combination of medicines and devices or other clinical trials) have been registered on a publically accessible register in compliance with the HRA registration requirements for the UK, or that any deferral granted by the HRA still applies.

This section was signed electronically by Dr Birgit Whitman on 16/05/2024 13:11.

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