The PreOperative Management of Patients Awaiting Anterior Cruciate Ligament Reconstruction: a mixed-methods study	
The POP-ACLR Study	
Version and Date of Protocol:	v1.2 10/Aug/2022
Sponsor:	University Hospitals of Derby and Burton NHS Foundation Trust
Chief Investigator:	Hayley Carter
Local Study Reference:	UHDB/2020/022
IRAS Number:	315154
ISRCTN/ ClinicalTrials.gov number:	This study will be registered with ISRCTN.
Funder(s):	This study is funded by a National Institute for Health Research (NIHR) Clinical Doctoral Research Fellowship.
This protocol has regard for the HRA guidance	

Confidentiality Statement

This document contains confidential information that must not be disclosed to anyone other than the Sponsor, the Investigator Team, host NHS Trust, regulatory authorities, and members of the Research Ethics Committee.

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirement.
I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor.
I also confirm that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

Protocol version 1.2, 10.08.2022 authorisation signatures:

Chief Investigator:

Signature: Hayley Carter Digitally signed by Hayley Carter Date: 2022.08.10 11:35:03 +01'00'

Date: 10/08/2022

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Sponsor:	University Hospitals of Derby & Burton NHS Foundation Trust Royal Derby Hospital Uttoxeter Road Derby, DE22 3NE 01332 724639 UHDB.sponsor@nhs.net
Funder(s):	Hayley Carter, Clinical Doctoral Research Fellow, NIHR302104, is funded by Health Education England (HEE) / NIHR for this research project.

STUDY SUMMARY

Study Title:	**The POP-ACLR Study - The PreOperative Management of Patients Awaiting Anterior Cruciate Ligament Reconstruction: a mixed-methods study**
Local Study Reference:	UHDB/2020/022
Study Design:	A mixed-methods sequential exploratory design: Phase 1: Qualitative semi-structured individual interviews Phase 2: Nominal group technique consensus method
Study Participants:	Phase 1: Adults with an anterior cruciate ligament (ACL) rupture awaiting surgical intervention (anterior cruciate ligament reconstruction [ACLR]) Phase 2: Healthcare professionals with a special interest/expertise in ACL injuries, musculoskeletal outpatient therapy managers and patient representatives
Planned Number of Sites:	1
Planned Sample Size:	Phase 1: up to 36 participants (12 participants at three interview time points) Phase 2: up to 12 participants
Participant Involvement	Phase 1: One interview per participant lasting approximately 60 minutes Phase 2: (a) Reading of pre-meeting material/voting on preliminary ideas (approximately 30 minutes) (b) Participation in a single face-to-face meetings lasting up to 7.5 hours or in a series of shorter online meetings of approximately 2-3 hours
Follow Up Duration:	Phase 1: no follow-up required as each participant will be interviewed once Phase 2: all meetings/communication regarding the consensus meetings will take place over a 4 month period
Planned Start Date:	Phase 1 planned start date: 1st August 2022 Phase 2 planned start date: 1st April 2023
Planned Recruitment End Date:	Phase 1: 31st December 2022 Phase 2: 31st May 2023
Planned Study End Date:	Phase 1: 31st March 2023 Phase 2: 30th September 2023
Research Question/ Aims:	Phase 1: To understand patients' lived experiences of the treatment pathway following a diagnosis of an ACL rupture and agreed surgical management with an ACLR Phase 2: To work with patients and stakeholders to develop a novel prehabilitation intervention for patients awaiting ACLR

FUNDING AND SUPPORT IN KIND

Funder(s)	**Financial and Non-Financial Support Given**
Hayley Carter, Clinical Doctoral Research Fellow, NIHR302104, is funded by Health Education England (HEE) / NIHR for this research project.	Research cost in full and salary costs as follows: Chief Investigator 1 WTE for 36 months
	Academic supervisory and mentor support from Professor Pip Logan, Dr Fiona Moffatt, Dr Paul Leighton, Dr Benjamin Smith, Professor David Beard and Professor Kate Webster.

ROLES & RESPONSIBILITIES

Sponsor

The Sponsor, University Hospitals of Derby & Burton NHS Foundation Trust, take on overall responsibility for appropriate arrangements being in place to set up, run and report the research project. The sponsor is not providing funds for this study, but has taken on responsibility for ensuring finances are in place to support the research.

Funder

This study is funded by a National Institute for Health Research (NIHR) Clinical Doctoral Research Fellowship. It is a contractual requirement that copies of all of project outputs are checked by the NIHR Academy (academy@nihr.ac.uk) a minimum of three working days before publication or presentation.

Study Management Committees

Trial Management Group (TMG)

The trial management group will meet monthly to oversee the day-to-day management of the trial, including all aspects of the conduct of the trial. Any problems with study conduct will be raised and addressed during TMG meetings.

Members: Hayley Carter, Pip Logan, Fiona Moffatt, Paul Leighton and Ben Smith.

Trial Steering Committee (TSC)

The trial steering committee will oversee and supervise the progress of the trial and ensure that it is being conducted according to the protocol and the applicable regulations. The TSC will meet every six months or more/less frequently if circumstances dictate during the study.

Members: Hayley Carter, Pip Logan, Fiona Moffatt, Paul Leighton, Ben Smith, Kate Threapleton (sponsor representative), Michelle Slack (outpatient therapy manager) and Charlotte Dodsley and Josh McCallion (patient representatives).

Patient and Public Involvement and Engagement (PPIE) Group

Two patient representatives (named above) will be part of the TSC meeting every six months. There will also be regular meetings, every three months, with the wider PPIE group for updates on progress of the study and for advice from a patient and stakeholders' perspective. Any concerns raised will be addressed in the following TMG meeting. The PPIE group will also aid with the dissemination of the results from phase 1 and 2 to lay audiences and healthcare professionals by supporting press releases, social media posts and website content.

Protocol Contributors

A number of protocol contributors have been involved in the development of this protocol, these include: Hayley Carter, Pip Logan, Fiona Moffatt, Paul Leighton, Benjamin Smith, Kate Webster, David Beard, Kate Threapleton (sponsor representative), Charlotte Dodsley and Josh McCallion (patient representatives). Protocol contributors are responsible for inputting into the design of the study, ensuring that it is designed transparently and efficiently.

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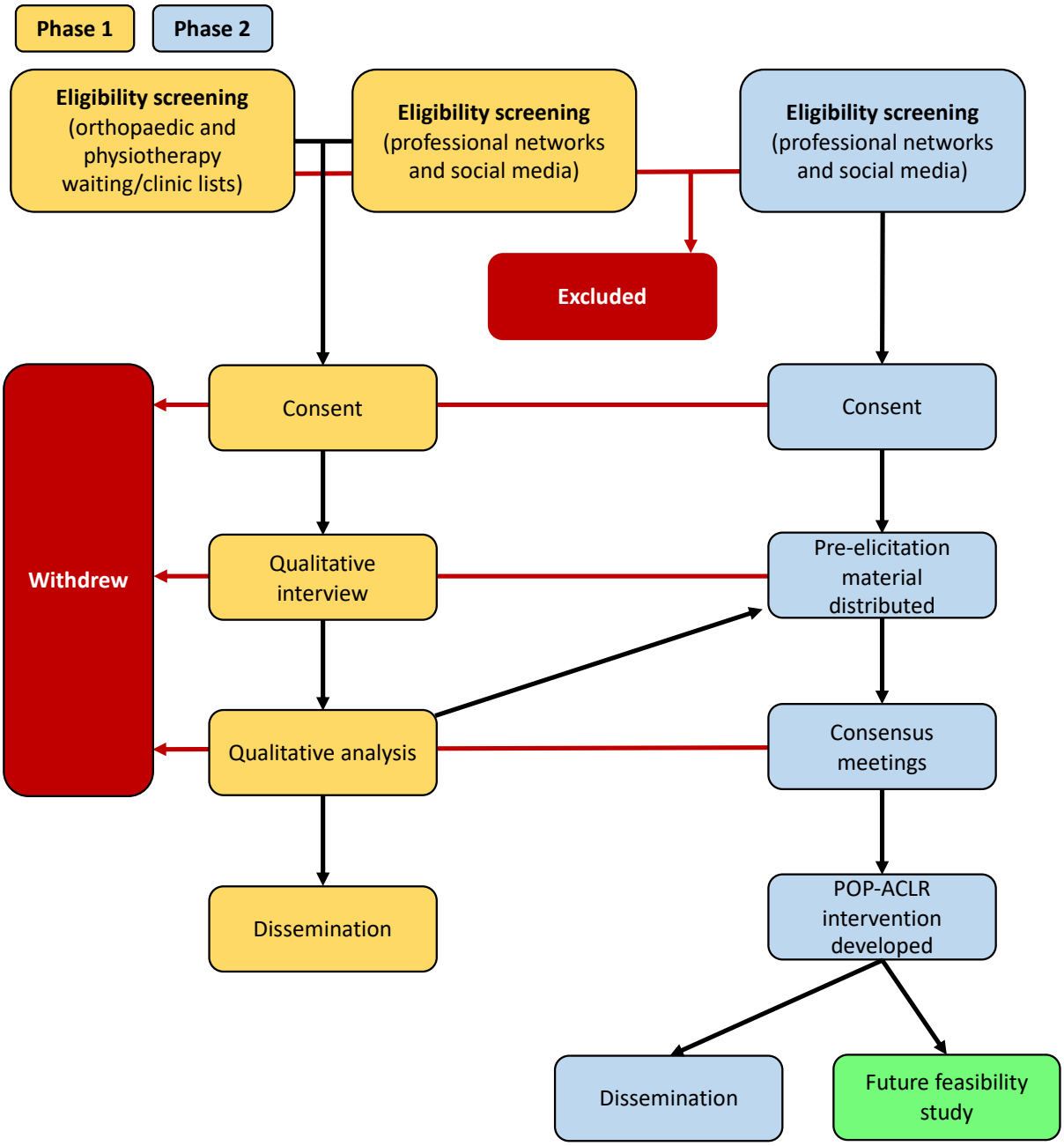
LIST OF ABBREVIATIONS

ACL	Anterior Cruciate Ligament
ACLR	Anterior Cruciate Ligament Reconstruction
AE	Adverse Event
ATOCP	Association of Trauma and Orthopaedic Chartered Physiotherapists
BASK	British Association for Surgery of the Knee
BOA	British Orthopaedic Association
CI	Chief Investigator
CRF	Case Report Form
DMEC	Data Monitoring and Ethics Committee
GCP	Good Clinical Practice
GMP	Good Manufacturing Practice
ICF	Informed Consent Form
ICH	International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use.
ISF	Investigator Site File
ISRCTN	International Standard Randomised Controlled Trials
NHS R&D	National Health Service Research & Development
PI	Principal Investigator
PIC	Participant Identification Centre
PIS	Participant Information Sheet
QA	Quality Assurance
QC	Quality Control
RCT	Randomised Control Trial
REC	Research Ethics Committee
SAE	Serious Adverse Event
SDV	Source Data Verification
SOP	Standard Operating Procedure
TMG	Trial Management Group
TSC	Trial Steering Committee
TMF	Trial Master File
UHDB	University Hospitals of Derby and Burton NHS Foundation Trust

STUDY FLOW CHART: mixed-methods sequential exploratory design



STUDY TIMELINE: starting from 1st April 2022

	Year 1 2022/23												Year 2 2023					
	Apr	May	Jun	Jul	Aug	Sept	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sept
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Planning																		
Phase 1	12 months																	
Submit & await ethical approval																		
Recruitment																		
Interviews																		
Qualitative analysis																		
Phase 2													6 months					
Recruitment																		
Distribution of pre-elicitation material																		
Consensus meetings																		
POP-ACLR intervention finalised																		
Trial management group																		
Trial steering committee																		
PPIE meetings																		
Write up																		
Dissemination																		

STUDY PROTOCOL

1. BACKGROUND

The anterior cruciate ligament (ACL) is the most commonly injured ligament in the knee with an estimated 200,000 injuries occurring each year in the US (UK data unavailable).[1] Surgery is currently standard treatment for this injury and aims to help patients return to work and preinjury levels of physical activity.[2,3] There are an estimated 14,000 surgeries performed each year in England.[4]

Prior to COVID-19, waiting times for anterior cruciate ligament reconstruction (ACLR) were between 4 and 12 months,[1] however this has increased in the past two years due to the cancellation of elective procedures during the COVID-19 pandemic.[5] Whilst awaiting surgery, preoperative rehabilitation (also termed 'prehabilitation') has been identified as an important component to help patients prepare, both physically and mentally, for surgery and postoperative rehabilitation.[6–8] However, current practice for this stage is varied and it is unknown what proportion of patients receive prehabilitation.[9]

Patients have high expectations of ACL surgery[10] and most set a goal of returning to work and their preinjury level of sport/activity.[11–13] However, this outcome is frequently documented to be sub-optimal with only 24% returning to preinjury levels of activity at 1 year.[14] Despite the high prevalence of ACL injuries amongst the physically active population, the qualitative evidence base accounting in-depth experiences remains limited. No study to date has looked to understand: (1) patients' lived experiences of ACL injury, rehabilitation and returning to physical activity following ACLR (2) sources and consistency of healthcare advice prior to surgery and (3) patients' involvement in, and views of prehabilitation. This remains an important gap in the evidence base.

ACL injuries, surgery and rehabilitation are costly to the NHS, costing upwards of £63 million each year.[1] With a lack of clinical guidelines or standard treatment pathway to inform clinicians, the effectiveness of care provided by the NHS during the lengthy preoperative period is questionable. Ensuring the patient journey is successful is therefore hugely important. Optimising treatment prior to ACLR could improve patient outcomes and ensure greater value for money.

2. RATIONALE

There are no established guidelines to inform the preoperative management of patients awaiting ACLR and currently, there is a lack of evidence demonstrating its effectiveness.[15] A recent systematic review found only three, low quality, randomised controlled trials which explored treatment effectiveness.[15] The results concluded that prehabilitation including strength, balance and perturbation training, when compared to no prehabilitation, offers small benefits (established through effect size calculations) to quadriceps strength and single leg hop distance (a commonly used postoperative functional test) three months after ACLR.

In addition, there are currently no prehabilitation programmes that include psychological elements and no studies evaluating the effect of prehabilitation on psychosocial outcomes; paradoxically, these are key components highlighted in the literature to predict postoperative outcomes and influence return to preinjury levels of activity.[2,16–18] It has further been highlighted that an individual's response

to injury, surgery and rehabilitation is an important consideration in ACL treatment and that the role of psychological factors has been undervalued.[17,19–24]

At present, the evidence does not provide consensus for clinical practice. The evidence gaps support the need to explore patients experiences further and develop an intervention that is implementable within an NHS setting to support patients prior to ACLR.

3. OBJECTIVES AND OUTCOME MEASURES/ ENDPOINTS

3.1. Objectives

Aim

This research aims to:

(1) Understand patients' lived experiences of the treatment pathway following a diagnosis of an ACL rupture and agreed surgical management.
(2) Develop a prehabilitation intervention for use with patients awaiting anterior cruciate ligament reconstruction (ACLR).

This project underpins future work for a study that will understand feasibility, acceptability and tolerability of the prehabilitation intervention with respect to participants and clinicians in an NHS setting.

Objectives

Phase 1:

1. To interview approximately 36 participants at three time points:
    (1) 12 participants up to 3 months before surgery
    (2) 12 participants 3 months after surgery
    (3) 12 participants 12 months after surgery
2. To explore patients' lived experiences of ACL injury, rehabilitation and returning to physical activity following ACLR
3. To explore patients' involvement in and views of prehabilitation
4. To understand patients' sources and consistency of healthcare advice prior to surgery

Phase 2:

1. To develop a prehabilitation intervention for use with patient awaiting ACLR using the nominal group technique

3.2. Outcome

Phase 1: lived experiences of the treatment pathway following a diagnosis of an ACL rupture and agreed surgical management

Phase 2: development of a novel intervention for use with patients awaiting ACLR to be implemented into clinical practice as part of a feasibility study

4. STUDY DESIGN

A mixed-methods sequential exploratory design utilising semi-structured qualitative interviews and nominal group technique consensus method.

5. STUDY SETTING

Both phases will be run at the Florence Nightingale Community Hospital within the University Hospitals of Derby and Burton NHS Foundation Trust (UHDB).

Phase 1: interviews will be carried out at the hospital, virtually or at a location preferred by the participant.

Phase 2: consensus meetings will take place in-person or virtually dependent upon participants geographical location range and preference.

6. ELIGIBILITY CRITERIA

6.1. Inclusion Criteria

Phase 1:

(1) ≥ 18-years-old

(2) Patient who is awaiting or has previously had an ACLR in the NHS

Phase 2:

(1) ≥ 18-years-old

(2) Participants will be in one of the following categories:

(a) Healthcare professional in the NHS with a special interest/expertise in treating ACL injuries (must have treated a patient prior to or post ACLR within the last 2 years)

(b) Therapy manager of an NHS musculoskeletal outpatient therapy department

(c) Patient who is awaiting or has previously had an ACLR in the NHS

6.2. Exclusion Criteria

Phase 1:

(1) Concomitant injuries requiring surgical intervention that will significantly alter the postoperative rehabilitation protocol e.g. meniscal repair requiring a non-weight bearing period

(2) Previous knee surgery to the affected limb

(3) Co-existing injuries requiring surgical intervention impacting on the individual's participation in pre- or post-operative rehabilitation

(4) Pregnancy

Phase 2:

(1) Anyone with a recognised conflict of interest

7. STUDY PROCEDURES

7.1. Recruitment

7.1.1. Patient Identification

Phase 1: Patients will be purposively sampled to obtain a varied sample in relation to patient characteristics, physical activity (running, cutting/pivoting sports, level of physical activity participation) and those who received prehabilitation or not. The sampling framework will be responsive to data emerging from previous interviews to allow for further exploration of points of interest. It is anticipated that the characteristics of participants at the three different time point will not be identical, and will complement each other aiming for a wide variety in patient characteristics.

The recruitment of patients has been discussed with surgeons and physiotherapists at UHDB. The surgeon's secretary will provide a list of patients awaiting surgery and orthopaedic postoperative clinical review to the physiotherapy team. The physiotherapy team will also identify appropriate patients on their clinical caseload. A member of the physiotherapy team will contact patients regarding the study to confirm eligibility, provide study information if appropriate and gain consent for the researcher to make contact to discuss the study. If a participant interested in the study does not read or speak English, relevant study material will be translated into their preferred language and communicated with facilitation of a translator. This will be arranged following normal procedures of the in-house translation service in the Physiotherapy Department at the University Hospitals of Derby and Burton NHS Foundation Trust.

The researcher will also advertise the study to potential participants through posters in physiotherapy and orthopaedic clinics and to colleagues through professional and special interest networks (such as Association of Trauma and Orthopaedic Chartered Physiotherapists [ATOCP], British Association for Surgery of the Knee [BASK] and British Orthopaedic Association [BOA]) via a letter/email and/or poster, to allow potential participants to contact the researcher directly. These networks will also be asked to share the material to promote the study on their social media platforms.

Phase 2: participants will be recruited via professional and special interest networks (ATOCP, BASK, BOA) via a letter/email and/or poster. These networks will also be asked to share the material to promote the study on their social media platforms. There will be at least one therapist and therapy manager recruited from UHDB, as this will be the primary site for feasibility testing of the intervention in a future study.

A social media account for the study (Twitter: @POP_ACLR) will also advertise the recruitment material for phase 1 and 2.

7.1.2. Screening

Phase 1: eligibility screening will take place on initial identification/contact with potential participants. If deemed eligible they will be provided with the participant information sheet (PIS) and consent form. No further screening will be completed.

Phase 2: eligibility screening will take place by potential participants on response to study advertisement. On making contact with the research team, eligibility will be confirmed prior to gaining consent for participation. No further screening will be necessary.

7.2. Consent

Patients meeting the eligibility criteria for phase 1 and 2, will be invited to participate in the study and provided with the participant information sheets and consent documents relevant to the phase of the study. This will include contact information for the CI to give participants the opportunity to ask further questions if needed. Consent will be gained as per Good Clinical Practice guidelines. This will include an explanation of the study purpose, what participation in the study involves including its benefits, risks, burdens and rights to withdraw at any time.

Informed consent must be obtained prior to the participant undergoing procedures that are specifically for the purposes of the study.

The Chief Investigator (CI) retains overall responsibility for the informed consent of participants and must ensure that any person delegated responsibility to participate in the informed consent process is duly authorised, trained and competent according to the REC approved protocol and applicable guidelines and regulations.

7.3. Withdrawal Criteria

Participants will be free to withdraw at any time from phase 1 or 2 without this affecting their future care (applicable to patients in phase 1 and 2). Participants will be made aware (via the information sheet and consent form) that should they withdraw, the data collected to the point of withdrawal may not be able to be erased and may still be used in the final analysis due to blinding of data.

7.4. End of Study

The end of study will be defined as when all data has been received and queries resolved. The CI will notify the Sponsor, participating sites and REC within 90 days of the end of study. The clinical study report will be written within 12 months of the end of study.

8. DATA HANDLING

8.1. System and Compliance

Data will be collected using a mix of paper and electronic methods. Where possible a patient ID number will be used rather than identifiable information. Data from paper forms will be transcribed into an electronic database in Microsoft Word or Excel stored on OneDrive. Microsoft OneDrive is an ISO 27001 information security management compliant service that allows secure and controlled sharing of data amongst the research team. Data will also be backed up to secure servers at UHDB. Paper hard copies will be stored in the relevant Investigator Site Files. Study documentation will be stored securely (i.e. cupboards, shelves or filing cabinets with restricted access e.g. within a locked office) in the Physiotherapy Department at Florence Nightingale Community Hospital to maintain participant confidentiality and study data integrity.

Qualitative data will be organised and managed using NVivo software. Audio recordings and transcriptions will be stored on OneDrive and backed up to secure servers at UHDB. An NHS-approved third-party transcription service will be used that complies with data security regulations. Audio recordings will be uploaded to OneDrive and deleted from the original recording device. Recordings kept on OneDrive will be archived as outlined in section 8.5.

8.2. Source Data

Data	Source	Location of Original
Consent (qualitative)	ACL-POP Qualitative Consent Form	Trial site for paper copies / OneDrive for electronic copies
Consent (consensus meetings)	ACL-POP Consensus Consent Form	Trial site for paper copies / OneDrive for electronic copies
Field notes	CI notes from interviews and consensus meetings	Trial site for paper copies / OneDrive for electronic copies
Interview recordings	Audio dictation files	OneDrive
Interview transcripts	Word documents	OneDrive
Consensus meeting recordings	Audio dictation files	OneDrive
Consensus meetings voting (quantitative)	Word documents	OneDrive

8.3. Data Workflow

The CI will maintain the electronic study files. This will be hosted on OneDrive and backed up to secure servers at UHDB

8.4. Data Access and Security

The CI will control access to the electronic database. Direct access will be granted to authorised representatives from the Sponsor, host institution and the regulatory authorities to permit study-related monitoring, audits and inspections.

8.5. Archiving

At the end of the study, following completion of the end of study report, UHDB will securely archive all centrally held study related documentation for a minimum of 5 years. At the end of the defined archive period arrangements for confidential destruction will be made. It is the responsibility of the CI to ensure that data and all essential documents relating to the study are retained securely for a minimum of 5 years after the end of study, and in accordance with national legislation. All archived documents must continue to be available for inspection by appropriate authorities upon request.

9. STATISTICS AND DATA ANALYSIS

9.1. Sample Size

Phase 1: up to 36 participants will be recruited
Phase 2: up to 12 participants will be recruited

9.2. Data Analysis

9.2.1. Summary of Baseline Data and Flow of Patients

Descriptive statistics will be presented to summarize baseline variables of participants. The categorical variables (e.g. gender, ethnicity) will be reported with frequencies & percentages.

9.2.2. Outcome Analysis

Phase 1: qualitative data analysis
An inductive approach will be used to allow flexibility to generate data that reflects the experiences of participants. The CI will keep a reflexive journal to document initial thoughts after each interview and on initial reading of the transcripts. Data familiarisation will be established by reading and re-reading transcripts to allow for data immersion and generation of preliminary ideas. The CI will be responsible for coding the dataset with a sample (25%) of the scripts peer-coded by another member of the supervisory team. Codes will then be compared and grouped into themes and sub-themes. The derived themes and sub-themes will be discussed during academic supervisory and TMG meetings. Only those involved in coding the dataset will have access to the raw data. Only samples of scripts will be taken to TMG meetings which will remain anonymous. Themes will then be reviewed to ensure they accurately represent the raw and coded data.

The results of phase 1 will contribute to the design of the intervention using an adapted nominal group technique. This will involve the use of a 'pre-elicitation technique'[25] where participants will be provided with a summary of the themes generated from the interviews prior to the first consensus meeting to help inform their ideas and decision making process. This may also include preliminary voting on key intervention components to be discussed at the first meeting.

Phase 2: nominal group technique
Consensus group meetings will be held with healthcare professionals with a special interest/expertise in ACL injuries (e.g. physiotherapists, occupational therapists, surgeons), physiotherapy managers and patient representatives to discuss and agree the key components of the prehabilitation intervention.

Consensus group meetings will take place in a single, face-to-face meeting (lasting up to a full day of 7.5 hours) or in a series of shorter online meetings – based on participants preference. They will aim to gain consensus about key components of the intervention for patients who have been diagnosed with an ACL rupture and listed for surgery. Components may include (1) referral guidance for orthopaedic colleagues (including timeline and reasonings for a referral to physiotherapy), (2) aims and content of physiotherapy sessions, (3) outcome measures to be used and (4) patient education.

Participants will rank ideas pertaining to each intervention component, it is common amongst the literature that five ideas are ranked [26–28] with the larger number reflecting greater importance. In line with consensus recommendations,[29,30] the threshold will be set at ≥70%. If consensus cannot be reached, points of contention will be discussed at TMG meetings. Components of the intervention will

be finalised with the patient representatives and presented to the patient and stakeholder group at informal coffee mornings.

Data analysis for both phases will be performed by the CI with supervision and checking by the academic supervisory team.

9.3. Subgroup Analyses

Subgroup analysis will be considered in phase 1 to compare codes, themes and sub-themes between participants who:

(1) received treatment at UHDB and those treated outside of the Trust (if recruited)
(2) engaged in prehabilitation and those who didn't
(3) were interviewed at the three different time points

9.4. Criteria for the Premature Termination of the Study

The Sponsor may suspend or prematurely terminate either the entire study for significant reasons that must be documented (e.g. an unacceptable risk to participants or serious repeated deviations from the protocol/ regulations). If this occurs the Sponsor shall justify its decision in writing and will promptly inform any relevant parties (i.e. participants, investigators REC, regulatory bodies).

10. MONITORING, AUDIT & INSPECTION

The Investigator(s) must ensure that source documents and other documentation for this study are made available to study monitors, the REC or regulatory authority inspectors. Authorised representatives of the Sponsor may visit the participating sites to conduct audits/ inspections. No further monitoring above this is planned.

11. ETHICAL AND REGULATORY CONSIDERATIONS

11.1. Assessment and Management of Risk

The main risks associated with participation in the qualitative interviews is the potential to elicit feelings of anxiety and distress when discussing personal experiences, confusion of the research process with a therapeutic encounter and the identification of need for further help. The interviewer is a trained physiotherapist with four years' experience treating this patient group. They have the appropriate training and knowledge to discuss any potential negative experiences mentioned in the interview and to signpost the participants to appropriate departments/organisations should they deem it necessary. They are trained in Safeguarding Level 3, with an awareness of appropriate procedures to follow. The CI will be responsible for assessing and managing risk, reporting this to the TMG and TSC as appropriate.

There are no known risks to participation in phase 2.

11.2. Peer review

This study has been peer reviewed as part of the NIHR Clinical Doctoral Research Fellowship application process.

11.3. Public and Patient Involvement

A PPIE group was formed prior to the application for funding to assist with the project design. The patient representatives and wider PPIE group will continue to be involved in:

- TSC meetings
- Reviewing patient/public facing information
- Reviewing project timelines and discussing/interpreting early results
- Dissemination

11.4. Research Ethics Committee (REC) & Regulatory Considerations

The study will be conducted in compliance with the approved protocol and the Declaration of Helsinki. The protocol and all related documentation (e.g. informed consent form, participant information sheet, questionnaires) have been reviewed and received approval by a Research Ethics Committee (REC). The investigator will not begin any participant activities until approval from the HRA and REC has been obtained and documented. All documentation and correspondence must be retained in the trial master file/investigator site file. Substantial amendments that require HRA and REC (where applicable) review will not be implemented until the HRA and REC grants a favourable opinion (with the exception of those necessary to reduce immediate risk to participants).

It is the responsibility of the CI to ensure that an annual progress report (APR) is submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, annually until the study is declared ended. The CI is also responsible for notifying the REC of the end of study (see Section 6.9) within 90 days. Within one year of the end of study, the CI will submit a final report with the results, including any publications/abstracts to the REC.

Before any site can enroll a patient into the study confirmation of capacity must be sought from the site's research and development (R&D) department. In addition for any amendment that will potentially affect the site's permission, the research team must confirm with the site's R&D department that permission is ongoing (Section 11.10).

11.5. Protocol Compliance / Non-compliance Reporting

The chief investigator is responsible for ensuring that the study is conducted in accordance with the procedures described in this protocol. Prospective, planned deviations and/or waivers to the protocol are not acceptable, however accidental protocol deviations (non-compliances) may happen and as such these must be recorded. Non-compliances should be recorded in the CRF and/or a non-compliance log kept in the ISF. All non-compliances should be reviewed and assessed by the PI (or appropriately delegated individual) to determine if they meet the criteria of a "serious breach" (Section 12.6). Non-compliances which are found to frequently recur are not acceptable, will require immediate action, and could potentially be classified as a serious breach.

11.6. Notification of Serious Breaches to GCP and/or the Protocol

A "serious breach" is a departure from the protocol, Sponsor procedures (i.e. SOPs), or regulatory requirements which is likely to effect to a significant degree –

(a) The safety or physical or mental integrity of the subjects of the study; or
(b) The scientific value of the study.

If the PI (or delegate) is unsure if a non-compliance meets these criteria, they should consult the Sponsor for further guidance.

If a serious breach is identified the investigator should notify the Sponsor immediately (i.e. within 1 working day) using the 'Non-CTIMP Notification of a Serious Breach' form. The report will be reviewed by the Sponsor and CI, and where appropriate, the Sponsor will notify the REC within 7 calendar days of being made aware of the breach.

11.7. Data Protection and Patient Confidentiality

The study will be conducted in accordance with the Data Protection Act 2018. The investigator must ensure that participant's anonymity is maintained throughout the study and following completion of the study. Participants will be identified on all study specific documents (except for the informed consent form and enrolment log) only by the participants study specific identifier (and initials if deemed necessary). This identifier will be recorded on documents and the database. The Investigator Site File will hold an enrolment log detailing the study specific identifier alongside the names of all participants enrolled in the study.

All documents will be stored securely with access restricted to study staff and authorised personnel.

Hayley Carter (CI) will act as the custodian of the data generated in the study.

11.8. Financial and Other Competing Interests for the Chief Investigator, Principal Investigators at Each Site and Committee Members for the Overall Study Management

Hayley Carter, Clinical Doctoral Research Fellow, NIHR302104, is funded by Health Education England (HEE) / NIHR for this research project. The views expressed are those of the author(s) and not necessarily those of the NIHR, NHS or the UK Department of Health and Social Care.

11.9. Indemnity

As UHDB is acting as the research Sponsor for this study, NHS indemnity applies. NHS indemnity provides cover for legal liabilities where the NHS has a duty of care. Non-negligent harm is not covered by the NHS indemnity scheme. UHDB, therefore, cannot agree in advance to pay compensation in these circumstances. In exceptional circumstances an ex-gratia payment may be offered.

11.10. Amendments

If changes to the study are required these must be discussed with the Sponsor, who is responsible for deciding if an amendment is required and if it should be deemed substantial or non-substantial. Substantial amendments will be submitted to the relevant regulatory bodies (REC, HRA) for review and approval. The amendments will only be implemented after approval and a favourable opinion has been obtained. Non-substantial amendments will be submitted to the HRA for their approval/ acknowledgment. Amendments will not be implemented until all relevant approvals are in place.

11.11. Access to Final Study Dataset

Access to the final study dataset will be limited to the research team and sponsor.

12. DISSEMINATION POLICY

12.1. Dissemination Policy

Data will be disseminated in the following ways:

- Publication in peer-reviewed open-access journals
- Presentation of national/international physiotherapy and orthopaedic conferences such as those run by Chartered Society of Physiotherapy (Physiotherapy UK), British Orthopaedic Association (BOA) and British Association for Surgery of the Knee (BASK)
- Newsletter for participants/public contributors
- In-service training sessions at the University Hospitals of Derby and Burton NHS Foundation Trust
- Social media and trial website

12.2. Authorship Eligibility Guidelines and any Intended Use of Professional Writers

It is expected that any first drafts of publications for academic journals and the final study report will be authored by the named co-investigators. Final authorship shall be in accordance with the International Committee of Journal Medical Editors (ICJME) guidance.[31]

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14. APPENDICES

14.1. Appendix 2 – Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made
0	V1.0	31 May 2022	Hayley Carter	Initial document
1	v1.1	20 July 2022	Hayley Carter	Further detail added regarding risk management, destruction and transcription of interview recordings
2	v1.2	10 Aug 2022	Hayley Carter	Pre-operative interview window extended from 2 weeks before surgery to 3 months before surgery