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)
Remote rehabilitation after ICU (iRehab)

1. Is your project research?

(●) Yes ( ) No

2. Select one category from the list below:

( ) Clinical trial of an investigational medicinal product

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

( ) Clinical investigation or other study of a medical device

(●) Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice

( ) Basic science study involving procedures with human participants

( ) Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology

( ) Study involving qualitative methods only

( ) Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)

( ) Study limited to working with data (specific project only)

( ) Research tissue bank

( ) Research database

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

( ) Other study

2a. Will the study involve the use of any medical device without a UKCA/CE UKNI/CE Mark, or a UKCA/CE UKNI/CE marked device which has been modified or will be used outside its intended purposes?

( ) Yes (●) No

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

a) Does the study involve the use of any ionising radiation? ( ) Yes (●) No

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

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

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

- [x] England
- [x] Scotland
- [x] Wales
- [x] Northern Ireland

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

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

4. Which applications do you require?

- [x] IRAS Form
- [ ] Confidentiality Advisory Group (CAG)
- [ ] Her Majesty's Prison and Probation Service (HMPPS)

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

◉ Yes ○ No

5c. You have indicated that your study has sites located in England. For the research sites located in England, do you wish for the study to be considered for NIHR Clinical Research Network (CRN) support and inclusion in the NIHR Clinical Research Network (CRN) Portfolio? Please see information button for further details

◉ Yes ○ No

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

○ Yes ◉ No

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

○ Yes ◉ No

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

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

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○ 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

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Integrated Research Application System
Application Form for Other clinical trial or investigation

IRAS Form (project information)

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

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

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

Short title and version number: (maximum 70 characters - this will be inserted as header on all forms)
Remote rehabilitation after ICU (iRehab)

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:

Remote multicomponent rehabilitation compared to standard care for survivors of critical illness after hospital discharge: a randomised controlled assessor-blind clinical and cost-effectiveness trial with internal pilot (iRehab).

A3-1. Chief Investigator:

	Title	Forename/Initials	Surname
	Dr	Brenda	O'Neill
Post	Senior Lecturer in Physiotherapy		
Qualifications	PhD, MCSP		
ORCID ID	0000 0002 6471 1413		
Employer	Ulster University		
Work Address	Shore Road Newtownabbey County Antrim		
Post Code	BT37 OQB		
Work E-mail	b.oneill@ulster.ac.uk		
* Personal E-mail			
Work Telephone	028 9036 8812		
* Personal Telephone/Mobile			

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Fax

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

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

	Title	Forename/Initials	Surname
	Mr	Nick	Curry
Address	Head of Research Governance		
	Ulster University		
	Shore Rd, Newtownabbey		
Post Code	BT37OQB		
E-mail	n.curry@ulster.ac.uk		
Telephone	02895365123		
Fax			

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

Applicant's/organisation's own reference number, e.g. R & D (if available):	22/0029
Sponsor's/protocol number:	22/0029
Protocol Version:	V1.0
Protocol Date:	01/04/2022
Funder's reference number (enter the reference number or state not applicable):	132871
Project website:	www.warwick.ac.uk/irehab

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

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

Additional reference number(s):

Ref.Number Description	Reference Number

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

○ Yes ◉ No

Please give brief details and reference numbers.

2. OVERVIEW OF THE RESEARCH

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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.*

We need to find out if a rehabilitation programme will help patients following intensive care who are discharged from hospital.

The objective of this trial is to investigate, in survivors of critical illness following discharge from hospital after an Intensive Care Unit (ICU) admission, the effects of a six-week remote multicomponent rehabilitation intervention compared to standard care on health-related quality of life at eight weeks post-randomisation.

The intervention group will receive a six-week remote rehabilitation programme. The intervention can be delivered over video or telephone. It includes: 1) weekly individual appointment with a member of the iRehab team; 2) home-based exercise sessions; 3) weekly online peer support session. The control group will receive standard care and will not be required to undertake a rehabilitation programme.

We will compare the quality of life, physical strength, and emotional wellbeing of the patients who take part in the rehabilitation programme with the patients who do not. We will also ask patients about their tiredness, views about illness, and anxiety levels. This information will be collected when participants join the study, at eight weeks and at 6 months by researchers not involved in the rehabilitation. The primary outcome is health-related Quality of Life: EQ-5D-5L at eight weeks. Additionally, we will be looking at value for money.

At the end of the trial, we will share our findings with other ICUs, clinicians, researchers, and patient groups to help improve patient care.

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

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

The trial will be conducted in full conformance with the principles of the Declaration of Helsinki and to Good Clinical Practice (GCP) guidelines. It will also comply with all applicable UK legislation and University of Warwick Standard Operating Procedures (SOPs). All data will be stored securely and held in accordance with the Data Protection Act 2018.

Trial participants will be enrolled via two routes of entry, either via a participating NHS site or by self-referral. Before approaching potential trial participants, each site will have an agreement between the relevant NHS Trust and the Sponsor and written confirmation has been received by Warwick Clinical Trials Unit (WCTU).

All direct approaches to potential participants made by sites will be from clinical care teams and all individual data will be held within NHS sites until participants have registered their interest in participating and provided their consent. We will ensure that trial recruitment staff are trained in GCP and consent procedures.

Relevant data will be entered directly by both site staff and participants into a secure online database provided by WCTU, although in some instances, data may be entered into the database by WCTU staff during baseline/follow-up video/telephone calls with trial participants. These data will be considered as source data for the trial.

Participants who are not fluent in written English will be eligible but must have a family member or friend present to translate trial materials.

The trial will be delivered remotely facilitated by online platforms; when participants are not able to access a computer we will use a telephone with support provided from the iRehab team to undertake the study procedures. The intervention is an individually tailored, multi-component intervention delivered remotely to trial participants by an iRehab trained intervention team. Local trial champions will be identified at each recruitment site to support the study, and if needed to assist with identifying local services should patients care need to be escalated to these.

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Exercise carries a very small risk of complications. All participants will be assessed for any underlying health conditions or severe complications that would prevent them from taking part in the trial. Participants will be excluded from the trial at the eligibility stage where exercise is clearly contraindicated, as assessed by the site staff. A further assessment will be undertaken by the iRehab team, through discussion with the patient about their current health, at the time of the initial online intervention assessment. Any additionally identified contra-indications at this stage will result in withdrawal from the trial. The iRehab team will advise on an exercise regime appropriate for each participant's ability. All participants will be advised to have another person nearby for the initial exercise sessions. We will encourage this wherever possible. Nevertheless, safety data and deaths will be closely monitored in all trial participants and these data presented to the DMC regularly. A robust safety reporting procedure will be in place to ensure participant safety and well-being are protected.

3. PURPOSE AND DESIGN OF THE RESEARCH

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

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

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

The overall aim of this trial is to investigate, in survivors of critical illness following discharge from hospital after an Intensive Care Units (ICU) admission, the effects of a six-week remote multicomponent rehabilitation intervention compared to standard care on health-related quality of life at eight weeks post-randomisation.

The main objective is to investigate the effects of a six-week remote multicomponent rehabilitation intervention compared to standard care on physical function, illness perceptions, fatigue, anxiety, depression, and adverse events at eight weeks post-randomisation.

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

Further trial objectives are:
To investigate longer term effects of a six-week remote multicomponent rehabilitation programme compared to standard care on health-related quality of life, physical function, illness perceptions, fatigue, anxiety, and depression at six months post-randomisation.
To determine explanatory factors influencing outcomes via an embedded process evaluation.
And
To evaluate the cost-effectiveness of the multicomponent rehabilitation intervention compared to standard care over six months follow-up.

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

The UK Intensive Care National Audit and Research Centre, described approximately 172,000 admissions to critical care units in England, Wales, and Northern Ireland, with approximately 129,000 patients surviving critical illness discharged from acute hospitals over one year (April 2019 to March 2020).The consequences of critical illness are substantial and multifactorial, and often encompass physical deconditioning, respiratory and swallowing problems, reduced activities of daily living, cognitive and mental health impairments, fatigue, and declines in health-related quality of life (HRQoL). In the UK, one in four patients recovering from critical illness experience an unplanned hospital readmission within 90 days of discharge, substantially higher rates of readmission than hospitalised patients without an ICU stay. At a societal level, nearly half of ICU survivors fail to return to work after 12 months, with UK data highlighting the increase in social care support required. Therefore there is an urgent need to intervene to improve the long term health of patients discharged home after intensive care. Identifying ways to support people returning home after a stay in ICU has been ranked a key priority for research by patients, their families, and researchers.
Guidance has recommended remote rehabilitation as standard of care for critically ill survivors following COVID-19. There is no evidence to support the delivery of remote rehabilitation to the broader population of survivors of critical illness, despite its use and anecdotal evidence of acceptability across many disease populations. This study will provide evidence on whether remote rehabilitation is clinically and cost-effective for survivors following critical illness post-ICU care. This trial will provide high quality evidence regarding the effectiveness of remote rehabilitation on health-related outcomes and whether rehabilitation should be implemented more widely across the NHS, or withdrawn if there is no evidence of improved outcomes for patients.

National Institute for Health and Care Excellence (NICE) guidance currently advises that the recovery pathway following critical illness should include regular assessment of physical and non-physical morbidity, goal-setting, multi-professional rehabilitation input according to individualised needs, and transition of information between care delivery stages. However, this practice has either been applied poorly or not at all following hospital discharge, and rehabilitation services post-critical illness in the UK are ad hoc, geographically inconsistent, and variable in terms of structure, content, and format of delivery. A survey of 242 UK hospitals conducted in 2020 found that few responding hospitals offered a post-discharge physical rehabilitation programme (31/176, 18%).
Exercise programmes can aid physical recovery in patients with chronic obstructive pulmonary disease, chronic fatigue, and congestive heart failure. Our Cochrane systematic review found that evidence for the effectiveness of post-hospital discharge rehabilitation interventions for survivors of critical illness was inconclusive. Nonetheless, findings from qualitative studies suggest that the patient experience of participating in rehabilitation programmes is markedly positive across domains of health, wellbeing, and perceived rate and quality of recovery. This suggests that the primary indicator of clinical effectiveness for these complex, multifactorial interventions may lie not only in objective markers of physical symptoms, but in measures reflecting broader aspects of quality of life. Patient needs after critical illness are multifaceted and we found that patients specifically re-enforced the need for multicomponent rehabilitation as well as a more individualised approach.

There is evidence to support the rehabilitation of critically ill patients within ICU, but a paucity of literature to support rehabilitation following discharge from ICU and hospital. Of the four Cochrane systematic reviews that explore rehabilitation after critical illness, there are no trials that address remote rehabilitation or technology enhanced care for post-hospital discharge rehabilitation in survivors of critical illness. No such trials are currently registered. Technology-enabled care has been shown to be effective and accessible for delivery of rehabilitation in other illnesses and settings e.g. cardiac rehabilitation, balance rehabilitation in older people, chronic obstructive pulmonary disease but this needs to be tested in people after critical illness before widespread implementation in the NHS. We also need feasible methods and alternative approaches to provide rehabilitation to patients during ongoing pandemic restrictions. Our proposed intervention includes strategies to improve recovery, collectively delivered in an efficient format for ease of user-accessibility in a modern health service. The active intervention will be delivered remotely and accommodates accessibility issues, including ethnic diversity as well as being acceptable for those from more deprived socioeconomic areas. Therefore, it provides a real opportunity to scale a rehabilitation service to be available to everyone in the UK who could benefit, irrespective of geographic location, ethnicity or income.

In summary, this trial provides an opportunity to deliver a definitive trial for the pragmatic evaluation of a remote multicomponent rehabilitation programme targeting survivors of critical illness following discharge from the ICU in whom post-hospital morbidity is substantial. This trial will be the first to systematically test a technology-driven remote approach to evaluate the clinical and cost-effectiveness of a rehabilitation intervention in patients recovering from critical illness after ICU care.

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.*

A pragmatic, randomised (allocation ratio 1: 1.17), controlled, assessor blind, multi-centre trial with internal pilot and embedded process evaluation.

Patients will be identified via two routes:
1. NHS sites
Hospital teams will screen hospital data and identify potential participants for contact by either approaching people before discharge or by phone call/mail. Sites will provide/send potential participants an invitation letter, consent form and Participant Information Leaflet.

If a person would like to participate, their initial eligibility will be checked by a suitably trained member of the hospital research team listed on the study delegation log. The research team member will ensure the potential participant has read the participant information sheet (PIS), understands what is involved with the study, is willing to be randomised and has had the chance to answer and discuss any questions before proceeding to consent. Consent to join the trial will be usually be taken, by telephone or video call, once the participant has returned home. Consent will be taken by an appropriately delegated member of the research team.

If consent is obtained, staff will complete the participant registration information on the WCTU database. This information will include the patient's first name, surname, address, post code, telephone number(s), email address, next of kin contact details, GP name and GP address. The participant will be sent a link via email/text to complete baseline questions directly onto the WCTU database. Where participants do not have a computer, they will be able to complete these via a phone call with a WCTU member of staff. The same WCTU staff member will arrange a sit-to-stand test with the participant and collect any further missing baseline data if required. In exceptional circumstances patients can complete a paper based questionnaire and send this through to WCTU. The participant will then be randomised into the trial by the online system.

2. Self Referral
The trial will be promoted though local media/social media, relevant charities and on the trial website. People who are interested can contact the trial team at WCTU and the lead NHS site will be notified of them wishing to take part. The patient's hospital discharge letter will be used to confirm any registration/eligibility data. The steps above will then be followed.

428 participants will be randomised to the iRehab intervention or standard care on a 1.17:1 basis using a computer-generated randomisation sequence, performed by a minimisation algorithm stratified by (i) hospital site and (ii) duration of invasive mechanical ventilation (≤7 days : >7 days).

Standard care:
People in this group will be provided with the information and care that is currently given to patients who have been in intensive care. They will not be required to undertake a rehabilitation programme. If case level mental health disorder (HADS scale) is identified from questionnaires, participants will be referred to their GP for treatment/advice.

iRehab intervention (six-weeks):
This is delivered to the participants' homes using computers or by telephone. The rehabilitation intervention has three parts:
1. Weekly online individual 1:1 appointments
Weekly one-to-one remote needs assessment will identify what is important to the participant and help the trial team to guide the programme to best suit their recovery. They will have six, weekly appointments with an iRehab specialist lasting up to one hour each. They will help them to plan ways to exercise/do physical activity and manage their symptoms during the week ahead. They will be supported to manage any psychological symptoms, e.g. anxiety or low mood, by undertaking specific strategies that we can teach them.
2. Weekly online exercise sessions
The participant will have the opportunity to attend at least one additional exercise session during the week, as well as their weekly 1:1 session. They can join a live session, access recorded sessions or use their exercise manual (provided to them by the trial team) to follow the exercise programme. Where possible groups of participants can do the live sessions. We will help them plan which option suits their needs and we will include this in their plan for the week ahead.
3. Weekly online peer support sessions (iRehab Café)
The participant will also have the opportunity to attend a weekly online group-based support session (iRehab café). This will provide them with an opportunity to meet with other people who have been in ICU, share and discuss challenges, and share strategies that have helped with aspects of recovery. These sessions will be facilitated by a member of the iRehab team.
Rehabilitation participants will be provided with an iRehab participant manual(s) which includes tips that can help with recovery after being in intensive care. There will be a copy of the exercise programme with pictures and words to guide how to do these. There will also be information about the support sessions, and space to record the dates and times of their appointments.
We will record some or all of the participants online appointments, exercise sessions and support sessions to check the quality of our research team’s delivery. This is for quality control purposes and to provide the iRehab team with an understanding of the topics and issues that generate discussion in the sessions.

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Outcomes will be assessed at baseline pre-randomisation, eight weeks and six months (post randomisation). The primary outcome is health-related quality of life, measured using the EQ-5D-5L at eight weeks post-randomisation. Data will be collected directly from trial participants using online data collection.

At the end of the trial, qualitative interviews will allow in-depth exploration of the acceptability of trial and the trial intervention. A separate PIS will be given to patients who have previously consented to being approached about the interviews, and a separate consent will be taken. Members of the iRehab team will also be approached about the interviews and consent will be taken.

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

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

Give details of involvement, or if none please justify the absence of involvement.
We have partnered with PPI members including former ICU patients during the development and refinement of this proposal. PPI collaborators will continue to be involved at every stage of the project.
We have set up a PAG and support for all PPI members in the PAG will be offered to help with understanding of study and study procedures, and to optimise opportunity for meaningful input. Furthermore, PPI membership have been appointed to the TSC and they will have a pivotal role in steering the conduct of the trial; and they will link back into the PAG also.

Examples of active contribution by the Patient Advisory Group will include informing best practice guidance on lay language to explain the trial to patients and relatives when identifying patients for the study, preparing materials including recruitment materials to optimise equity of access, advising on how the approach to delivery of the intervention needs to be refined at individual level to be cognisant of specific circumstances. Our PAG have reviewed and inputted to the Participant Information Sheets, Consent Forms, Invite Letter, and Participant Manuals attached to this application.
Our PAG will be given the opportunity to engage in trial publicity and the dissemination of findings through appropriate channels i.e. social media, lay conferences, public engagement events, service provider events, newsletter articles. Their input will help ensure findings are presented in a format that is accessible to a wide audience. All activity will be appropriately reimbursed at INVOLVE rates, for which there is adequate provision in the grant application.

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

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- [x] Generic Health Relevance
- [ ] Infection
- [ ] Inflammatory and Immune System
- [ ] Injuries and Accidents
- [ ] Mental Health
- [ ] Metabolic and Endocrine
- [ ] Musculoskeletal
- [ ] Neurological
- [ ] Oral and Gastrointestinal
- [ ] Paediatrics
- [ ] Renal and Urogenital
- [ ] Reproductive Health and Childbirth
- [ ] Respiratory
- [ ] Skin
- [ ] Stroke

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

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

1. Aged ≥ 18 years
2. Received invasive mechanical ventilation for 48 hours or longer
3. Are within 12 weeks following discharge home from hospital at time of consent
4. Understands spoken English or has family member/friend/other present to translate trial materials
5. Able to participate in the intervention and with trial procedures (e.g. using equipment such as telephone)

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

1. Declined consent or unable to provide consent.
2. Previous randomisation into the present trial.
3. Participating in another rehabilitation or self-management support trial
4. Contra-indication to exercise
5. Severe mental health problems that preclude participation in a group intervention
6. Discharged to a rehabilitation unit, or care home with/without nursing care
7. Pregnancy
8. Prisoners

RESEARCH PROCEDURES, RISKS AND BENEFITS

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

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

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

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Intervention or procedure	1	2	3	4
Informed Consent	1	0	15 mins	Consent to join the trial will be usually be taken, by telephone or video call, once the participant has returned home. Consent will be taken by the Principal Investigator or delegated to an appropriately trained member of the hospital research team.
Questionnaires - Including EQ-5D-5L, BIPQ, FACIT-F, HADS, Health and Social Care use	3	0	30 mins	Performed by participant at home via trial database or by video/telephone by independent Research Fellow at WCTU.
Sit-to-stand test	3	0	10 mins	Performed by video/telephone by independent Research Fellow at WCTU.
Qualitative interviews - participants	1	0	30-45 mins	These will be completed by a designated research team member based at Queens University Belfast, who is not involved in the delivery of the intervention. A sub-group of participants who consent to this will be interviewed to explore their views about participating in the trial and/or intervention(~n=25 intervention group, ~n=25 control).
Qualitative interviews - staff	1		20-30	These will be completed by a designated research team member based at Queens University Belfast, who is not involved in the delivery of the intervention. The iRehab team delivering the intervention (n=3) and a sample of study champions (from participating sites) will be interviewed to explore their views about the acceptability of the intervention and the trial process
Informed consent - Qualitative interviews	1	0	15 mins	Consent to join the trial will usually be taken, by telephone or video call. Consent will be taken by a member of the research team who will be delegated and appropriately trained.

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

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

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

Intervention or procedure	1	2	3	4
Weekly iRehab session(s): (i) 1:1 support session including needs assessment, exercise/physical activity, and action planning	6+	0	60-120	Remote home based intervention. Delivered by iRehab intervention team member. The intervention team will be trained to deliver the intervention and will be supported by a multidisciplinary team including Speech & Language Therapy, Occupational Therapy, Physiotherapy, Dietetics, and the study's designated clinical Psychologist. Participants will be expected to engage with the intervention at least once per week. Participants may also complete unsupervised exercise and/or activities aligned to their weekly action plan (which they will have prepared during the weekly 1:1 session).
(ii) live group exercise session or independent exercise session	0-6	0	30-40	Participants will have the opportunity to attend a group based online class once per week or complete an independent exercise session.
(iii) peer support	0-	0	30-	Participants will have the opportunity to attend a group based peer support group

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group (iRehab cafe)	6	60	once per week.

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

○ Yes ◉ No

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

6 months following randomisation

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

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

Completion of the 3 outcome assessment sessions and the 6 week iRehab intervention (for those in the intervention group) will take place outside usual clinical
management and therefore may be an inconvenience for the patient. Any potential burden is minimised by providing the trial using remote delivery to the participants home. Anyone who is unable to complete the outcome measures online can complete them with the researcher via video/telephone (in this case they will be provided with a paper reference copy of the outcome measures to help follow along with the questionnaires).

Exercise or physical activity carries a very small risk of complications. All participants will be assessed at screening for any underlying health conditions or severe complications that would result in them being ineligible for the trial. A further assessment will be undertaken by the iRehab intervention team, through discussion and assessment with the patient about their current health and symptoms. Any additionally identified contra-indications at this stage will result in withdrawal from the trial.

Anyone in the intervention group who is unable to use a computer to access the weekly online intervention sessions will receive their session by telephone supported by the trial participant intervention manuals[study Tablets or telephones can be provided on loan if required]. During the intervention the iRehab specialist will advise on an exercise or physical activity regime appropriate for each participant's ability. All intervention sessions will be led by iRehab staff trained in assessment, prescription and delivery of exercise for clinical populations. All participants will be advised to have another person nearby for the exercise sessions. We will encourage this wherever possible. The instructions for undertaking exercise or physical activity will include appropriate warnings regarding when to stop exercise e.g. chest pain, faintness, dizziness and a contact telephone number. Patients will also be advised to contact their GP in such circumstances. Participants will have the opportunity to identify and discuss any issues with the iRehab specialist at their weekly 1:1 sessions. They may also contact the iRehab team or the study team via email or telephone with any further queries.

The intervention team will receive bespoke training, either face-to-face or online training, to deliver the iRehab intervention. This will include a detailed intervention manual for the intervention team, supporting materials for trial participants, presentations, rehearsals, and interactive problem solving via case studies prior to delivering the intervention. We will include certification of the intervention team to deliver the intervention and they will be supported with frequent and ongoing mentorship throughout the study as well as training updates. This support will include case reviews and problem solving with the iRehab MDT [including Speech & Language Therapy, Occupational Therapy, Physiotherapy, Dietetics, and clinical Psychologist].

Quality control measures will ensure delivery of all study procedures and of the intervention to a high standard.

There is a small chance that a participant might become upset during the delivery of the questionnaires, interviews, or intervention. However, the researchers and intervention team will be trained to provide appropriate support and assistance if needed.

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

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◉ Yes ○ No

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

There is a small chance that a participant might become upset during the delivery of the questionnaires, interviews, or intervention. However, the researchers and intervention team will be trained to provide appropriate support and assistance if needed.

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

The rehabilitation intervention may improve quality of life, physical strength and endurance, fatigue levels, self-efficacy, emotional well-being, and clinical status. If this study shows that the intervention is clinically effective and cost effective, then it will provide useful information which will inform the development of services for patients after critical illness.

The intervention includes strategies to improve recovery, collectively delivered in an efficient format for ease of user-accessibility in a modern health service. The active intervention will be delivered remotely and accommodates accessibility issues. It provides a real opportunity to scale a rehabilitation service to be available to everyone in the UK who could benefit, irrespective of geographic location, ethnicity or income.

It also has the potential to reduce the demand on health and social services more widely and improve economic productivity.

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

At the end of the intervention patients in the intervention group will receive a short consultation to set goals relating to continuing exercise or physical activity at home. Participants will be able to retain the trial participant manuals containing instructions on exercise and symptom management for their own continued self directed use and reference.

Other than this, there will be no further provision for continuation of the intervention or study procedures for either group.

The intervention materials including the participant manuals and iRehab intervention team manuals and training slides will be made available for use by NHS sites for the future delivery of remote rehabilitation for this population.

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

We do not anticipate any risks to the researchers, all members of the research team will be trained to deliver this study.

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).*

Clinical care teams at each NHS site will screen hospital data and identify potential participants for contact in hospital, by mail or phone call. Eligible people may be identified through patient electronic databases at each of the trial sites, referrals or while attending follow-up clinics. Hospital electronic registers/databases will be used to identity people by date of hospital discharge post-ICU care.

The trial will also be promoted though local media/social media, relevant charities and on the trial website. People who meet the criteria following hospital discharge will be able to self-refer. Self-referred patients will be directed to the lead NHS site and follow the same process as described for those recruited from NHS site.

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

(●) Yes ( ) No

Please give details below:
Potential participants will be identified by clinical teams at each NHS site involved in the trial. Sites will provide potential participants an invitation letter and a copy of the consent form and PIL. If patients are interested in taking part in the trial, appropriately trained staff will take consent and enter registration/eligibility data directly onto the WCTU online database. Participants will be sent a link to access the baseline questionnaires, or they will be supported to complete these by telephone, if preferred. [For telephone completion, the participant will have a reference copy of the questionnaires to follow, and when the independent WCTU Research Fellow makes contact, they will record the participants response and enter it onto the study database]. The WCTU Research Fellow will then ask participants to complete a sit-to-stand test and then the participant will be randomised into the trial.

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

All participant identification will be undertaken by trained NHS clinical research staff within the hospital facility at each site, using approved clinical systems, databases and medical notes. All staff will abide by existing NHS and GDPR regulations. Identifiable personal information of patients will be transferred from the Hospital sites to the trial team via a secure online database programmed by WCTU, and only after consent has been obtained.

Disclosure of confidential information will only be considered if there is an issue which may jeopardise the safety of the participant or another person, according to WCTU SOPs (WCTU SOP 15 part 1) and the UK regulatory framework. There is no reason to expect this situation to occur in this trial more than any other.

Where possible, TNOs will be used in place of any PID.

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

(●) Yes ( ) No

A27-5. Has prior consent been obtained or will it be obtained for access to identifiable personal information?

(●) Yes ( ) No

If Yes, please give details below.
This is described in full detail in the patient information sheet and consent is specifically requested from participants for this on the consent form.

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

(●) Yes ( ) No

If Yes, please give details of how and where publicity will be conducted, and enclose copy of all advertising material (with version numbers and dates).
The trial will be promoted though local media/social media (including a trial Twitter account), relevant charities and on the trial website. People who meet the criteria following hospital discharge will be able to self-refer; in this case their randomisation will be allocated to a participating hospital site.

Eligibility for self-referred patients will need to be confirmed via hospital clinical or research teams with permission provided by the potential participants to source this confirmation.

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

Identification and approach procedure:
1. Identification and first approach of potential participants will be via clinical care teams at hospital sites or via self-referral.
2. Hospital sites will provide/send potential participants an invitation letter, consent form and PIL. Self referrals will be sent an invitation letter, consent form and PIL by email/post.
3. Interested potential participants will be provided with opportunity to ask questions and have these answered prior to consent. They will complete the consent form either in person at the hospital site or via telephone/video call.
4. A copy of the signed consent form will be given to the participant or sent to the participant via email or post and a copy will be sent to their GP and consultant at their treating hospital.
5. The participant will be directed to complete the baseline questionnaire. Once the consent form, registration details, sit-to-stand test and baseline questionnaire have been completed by the participant they will be formally enrolled in the study.

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

(●) Yes ( ) No

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

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

Consent process:
1. If a person would like to participate in the trial, their initial eligibility will be checked by a suitably trained member of the hospital research team listed on the study delegation log. The research team member will ensure the potential participant has read the patient information sheet (PIS), understands what is involved with the study, is willing to be randomised and has had the chance to answer and discuss any questions before proceeding to consent.
2. Consent to join the trial will be taken in person e.g. if the potential participant is attending a hospital clinic; in most other cases consent will usually be taken, by telephone or video call, once the participant has returned home. Consent will be taken by an appropriately trained member of the research team as per the delegation log. They will talk through each line of the consent form with the participant. The participant will be given as much time as they need to consider the trial and provide consent. The consent forms will then be completed via telephone/video call by the research staff on behalf of the participant.
3. If consent is obtained, staff will complete the participant registration information on the WCTU database.
4. A copy of the fully signed consent will be sent to the participant and a copy will be sent to their GP and treating hospital.
5. The participant will be directed to complete the baseline questionnaire. Once the consent form, registration details, sit-to-stand test and baseline questionnaire have been completed by the participant will be formally enrolled in the study.

Responsibility: The PI will retain overall responsibility for informed consent and will ensure that any person with delegated responsibility to participate in the informed consent process, is duly authorised, trained, qualified and competent.

When confirming consent for those unable to read English, a friend or family member of the patient or an NHS translator will be present to confirm correct explanation.

New information: Any new information that arises during the trial that may affect participants' willingness to take part will be reviewed by the TSC; if necessary this will be communicated to all participants. A revised consent form will be completed if necessary.

Decline/withdrawal: People who have entered the study will still have the option to withdraw before treatment starts (i.e. between baseline assessment and the beginning of the intervention/control), if for any reason they change their mind. While we will attempt to explore the reason(s) for withdrawal, the right of a potential participant to refuse participation without giving reasons will be respected and recorded on the screening log. The participant will remain free to withdraw at any time without giving reasons and without prejudice to any further treatment, and will be provided with a contact point where he/she may obtain further information about the trial.

Participants will be asked to consent (or not) to being contacted around three months after they have entered the trial to share their views and experiences of the intervention and control. A separate PIS will be provided. Telephone/video

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verbal consent will be taken and documented prior to the interview taking place. Participant interviews will be completed online.
Members of the iRehab team will also be approached about the interviews and consent will be taken following the same process as with the patients.

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

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

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

(●) Yes ( ) No

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

The potential participant will be allowed up to around 10 weeks from initial contact with the researcher in order to consider the trial and decide whether to take part. This amount of time will be determined by when the participant is first contacted and time since hospital discharge.

Timing and appropriateness of obtaining consent will be closely monitored by the Trial Management Group (TMG) and reviewed by the independent Trial Steering Committee (TSC).

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

(●) Yes
( ) No
( ) Not Known

If Yes, please give details and justify their inclusion. If Not Known, what steps will you take to find out?

Recruitment to this study for patients already participating in other studies will be considered on a case by case basis, however patients already participating on another active rehabilitation or self-management support trial will not be eligible. Patients on observational trials mirroring clinical care will be enrolled. If patients are on other interventional trials, they will only be approached about the current study if enrolment will not impact the outcome of either trial and if the burden on the patient is not significant.
Co-enrolment will be monitored by the Trial Management Group (TMG) and reviewed by the independent Trial Steering Committee (TSC).

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

Participants must be able to understand spoken English or have a family member/friend/other present to translate trial materials and must be able to participate in the intervention and with trial procedures (e.g. using equipment such as telephone).

During the internal pilot of this trial we will include collection of information about the population including language, ethnicity and socioeconomic status which is often not reported in studies. This will enable us to plan for the use of translated materials and interpreters in the main trial, as well as the identification of optimal strategies to ensure reach to all members of the potential participant community and stakeholders for the main trial.

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

The trial team will liaise with Health and Care Research Wales and the local Health Board, who is responsible for providing translations of patient information sheets and consent forms where required.

A34. What arrangements will you make to ensure participants receive any information that becomes available during

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the course of the research that may be relevant to their continued participation?

Any new information that arises during the trial that may affect participants' willingness to take part will be communicated to all participants. If deemed necessary, the participant will be contacted by the relevant researcher and asked whether they still wish to continue participating in the trial. If required a revised PIS and consent form will be made available and the participant may be asked to read, consider and re-sign the consent form.

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

- ○ The participant and all identifiable data or tissue collected would be withdrawn from the study. Data or tissue which is not identifiable to the research team may be retained.
- ◉ The participant would be withdrawn from the study. Identifiable data or tissue already collected with consent would be retained and used in the study. No further data or tissue would be collected or any other research procedures carried out on or in relation to the participant.
- ○ The participant would continue to be included in the study.
- ○ Not applicable – informed consent will not be sought from any participants in this research.
- ○ Not applicable – it is not practicable for the research team to monitor capacity and continued capacity will be assumed.

Further details:

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

CONFIDENTIALITY

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

Storage and use of personal data during the study

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

- ☑ Access to medical records by those outside the direct healthcare team
- ☑ Access to social care records by those outside the direct social care team
- ☑ Electronic transfer by magnetic or optical media, email or computer networks
- ☑ Sharing of personal data with other organisations
- ☐ Export of personal data outside the EEA
- ☑ Use of personal addresses, postcodes, faxes, emails or telephone numbers
- ☑ Publication of direct quotations from respondents
- ☐ Publication of data that might allow identification of individuals
- ☑ Use of audio/visual recording devices
- ☑ Storage of personal data on any of the following:
  - ☑ Manual files (includes paper or film)
  - ☑ NHS computers
  - ☐ Social Care Service computers
  - ☐ Home or other personal computers
  - ☑ University computers

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☐ Private company computers

☑ Laptop computers

Further details:
All information will be entered onto a secure online database, set up by the University of Warwick Clinical Trials Unit, that only authorised personnel will have access to. Case Report Forms and the Trial Master File will be kept securely in accordance to University of Warwick's Clinical Trials Unit SOPs and only authorised personnel will have access. Direct quotations may be published during the dissemination of the research findings - these will be anonymised at all times.
Audio/visual recording will be used to monitor quality and provide the iRehab team with an understanding of topics and areas for discussion. No personal data will be published in this process and the study consent form will include a section relating to this.
Qualitative interviews will be recorded and transcribed - both the recording and transcription will be fully anonymised.
All electronic devices will be password protected as per NHS Trust policies and WCTU SOPs and as per GDPR.
Contact details will be shared with a third party text messaging service in order for participants to be contacted about the trial. Participants who are randomised to the iRehab intervention arm will also be asked to register an account with a third party online video platform using their name and email address if they agree to the terms and conditions. This will enable the participants to access the intervention content. Participants will be asked to complete brief questionnaire polls via the online system before and after each supervised group exercise session. This will allow the iRehab team to collect information on adverse events. Information on data sharing with other organisations is detailed in the PIL and Consent Form.

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

Personal data collected during the trial will be handled and stored in accordance with GDPR and Data Protection Act 2018.
Handling of personal data will be clearly documented in the participant information sheet and consent obtained.
Disclosure of confidential information will only be considered if there is an issue which may jeopardise the safety of the participant or another person, according to Warwick Standard Operating Procedures and the UK regulatory framework. There is no reason to expect this situation to occur in this trial more than any other.
The database will be developed by the Programming Team at WCTU and all specifications (i.e. database variables, validation checks, screens) will be agreed between the programmer and appropriate trial staff including the trial statistician.
All essential documentation and trial records will be stored at WCTU in conformance with the applicable regulatory requirements and access to stored information (paper and electronic) will be restricted to authorised personnel.
Electronic data will be stored on password protected university or NHS computers.

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

All data will be pseudo-anonymised after the collection of the baseline demographic data for each participant. Confidentiality will be strictly maintained and names or addresses will not be disclosed to anyone other than the staff involved in running the trial. All electronic participant-identifiable information will be held on a secure, password protected database accessible only to essential personnel. Paper forms with participant-identifiable information will be held in secure, locked filing cabinets within a restricted area of WCTU. Participants will be identified by a participant number only on the paper forms. Direct access to source data/documents will be available for trial-related monitoring or audit by Warwick CTU for internal audit, regulatory authorities or ethics committees. The principal investigator will arrange for retention of trial records on site in accordance with GCP and local Trust's policies.
Disclosure of confidential information will only be considered if there is an issue which may jeopardise the safety of the participant or another person, according to WCTU SOPs (WCTU SOP 15 part 1) and the UK regulatory framework. There is no reason to expect this situation to occur in this trial more than any other

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

Participants will be asked to consent to providing the trial management team with their contact details to enable follow-up questionnaires to be sent to them either electronically or via post.
The majority of data will be received directly from participants who will enter their data into the online trial database. Site staff will also have access to the online database and will provide eligibility, registration and consent information.

After collection of the baseline data for each participant and following randomisation all data will be pseudo-

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anonymised where possible. Confidentiality will be strictly maintained and names, addresses or personal identifiable information will not be disclosed to anyone other than the staff involved in running the trial. All electronic participant-identifiable information will be held on a secure, password-protected database accessible only to essential personnel. Paper forms will be held in secure, locked filing cabinets within restricted areas. Participants will be identified by a participant number only on the paper forms. Direct access to source data (online trial database) will be available for trial-related processes, monitoring or audit by WCTU for internal audit or regulatory authorities. The PI must arrange for retention of trial records on site in accordance with GCP and local Trust's policies.
Direct access to source data/documents will be required for trial-related processes and monitoring. For quality assurance, the data and results will be statistically checked. A full data management plan will be produced by the trial manager and statistician to outline the data monitoring checks required.
Requests for data sharing will be managed in accordance with University of Warwick/WCTU policy on data sharing. The datasets generated during and/or analysed during the current study are/will be available upon request. The publication of a trial protocol, trial results and trial data will be in line with the NIHR standard terms and will follow WCTU SOPs

Storage and use of data after the end of the study

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

Data analysis will be undertaken by the University of Warwick Clinical Trials Unit Statistical Team.

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

	Title	Forename/Initials	Surname
	Dr	Brenda	O'Neill
Post	Senior Lecturer in Physiotherapy		
Qualifications	PhD, MCSP		
Work Address	Shore Road		
	Newtownabbey		
	County Antrim		
Post Code	BT37 OQB		
Work Email	b.oneill@ulster.ac.uk		
Work Telephone	02890368812		
Fax			

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

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

If longer than 12 months, please justify:
According to University of Warwick policy and data regulations pseudonymised data will be kept for up to 10 years.

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

Years: 10
Months: 0

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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.*

As per NHS Trust policy, once the trial has come to an end and the analysis has taken place, trial documentation will be held for approximately 10 years.

All essential documentation and trial records will be stored at WCTU in conformance with the applicable regulatory requirements and access to stored information (paper and electronic) will be restricted to authorised personnel. All data will be stored in a designated storage facility within the WCTU. Electronic data will be stored on password protected university computers.

INCENTIVES AND PAYMENTS

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

○ Yes ◉ No

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

○ Yes ◉ No

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

○ Yes ◉ No

NOTIFICATION OF OTHER PROFESSIONALS

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

◉ Yes ○ No

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

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

◉ Yes ○ No

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

PUBLICATION AND DISSEMINATION

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

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

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◉ Yes ○ No

Please give details, or justify if not registering the research.
ISRCTN
University of Warwick website

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?

Identifiable data will not be used during the analysis of trial data. The data will be pseudonymised to facilitate the analysis of the data and no identifiable data will be published, only anonymised data.

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

If there will be no arrangements in place to inform participants please justify this.
Warwick CTU, with Ulster University and partners from our Patient Advisory Group (PAG), will jointly lead on strategies for knowledge dissemination and engagement within the NHS and wider public. Our PAG will help ensure findings are presented in a format that is accessible to a wide audience. All organisations will work together to ensure that clinically important findings are disseminated and, by working collaboratively, we will help facilitate the adoption of such outcomes within the NHS to enhance patient care.

Towards the end of the trial, we will host a joint investigator and participant event to release and promote key trial findings. The results of the trial will be made available once the final report is complete. Key findings will be posted on the trial and institutional websites, and participants will be able to request a copy of the results through contacting the local study team.

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

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☐ 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 trial will be reviewed by the HRA

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
	Prof Ranjit Lall
Department	Warwick Clinical Trials Unit
Institution	University of Warwick
Work Address	Warwick Clinical Trials Unit, Warwick Medical School University of Warwick Coventry
Post Code	CV4 7AL
Telephone	02476574650
Fax	
Mobile	
E-mail	R.Lall@warwick.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?

Health-related quality of life
Health-related quality of life will be measured using the Euroqol EQ-5D-5L Health Utility score. It is a validated, generic HRQoL measure consisting of five dimensions, each with five levels. Each combination of answers can be converted into a health utility score. It has good test-retest reliability, is simple to use, and gives a single preference-based index value for health status that can be used for cost- effectiveness analysis.

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

30 second sit to stand test - This will be used to assess physical function by encompassing participants leg strength and endurance.

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Brief Illness Perception Questionnaire - This will assess illness perception by measuring patients' cognitive and emotional representations of their illness using a ten-point Likert scale.
Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scale - This will assess fatigue. The questionnaire asks patients to rate their level of fatigue during their usual daily activities over the past week using on a four point Likert scale.
Hospital Anxiety and Depression Scale (HADS) - This will be used to measure anxiety and depression.

Safety - We will collect data on serious adverse events.
Healthcare and social care utilisation questionnaire.

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: 428
Total international sample size (including UK): 428
Total in European Economic Area:

Further details:
We aim to recruit 428 participants, who will be randomised to standard care or the iRehab intervention on a 1:1.17. This equates to 197 patients in the control arm and 231 participants in the intervention arm.

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

The total sample size for iRehab will be 428 participants. Using our primary outcome of EQ-5D-5L utility score, our target difference is 0.08 with a standard deviation of 0.2 (i.e. effect size=0.4). If we assume that there are on average six therapists for the intervention delivery and a clustering effect will exist (ICC=0.01) and allowing for 30% loss to follow up (LTFU), a total of 428 (control: 197 and intervention: 231) participants will be required. This uses the Morbeek's formulation and an unequal randomisation of the ratio of 1: 1.17. A difference of 0.08 on the primary outcome is a justifiable clinical effect. We will endeavour to minimise losses to follow-up. If we achieve a 15% loss to follow-up, we will be able to detect a smaller effect size (up to 0.37) at 90% power.

A61. Will participants be allocated to groups at random?

(●) Yes ( ) No

If yes, please give details of the intended method of randomisation:
We aim to recruit 428 participants, who will be randomised to the iRehab intervention or standard care only on a 1.17:1 basis using a computer-generated randomisation sequence, performed by minimisation and stratified by hospital site and duration of invasive mechanical ventilation.
Participants will be randomised strictly sequentially at trial level, as participants are eligible for randomisation.

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.

A detailed statistical analysis plan will be written and approved by the Data Monitoring Committee (DMC).

The main statistical analysis will be based on intention-to-treat. Data will be summarised and reported in accordance with CONSORT guidelines for RCTs. The impact of compliance on outcomes will be assessed using a CACE (complier average causal effect) analysis or other appropriate approach.

Baseline data will be summarised by treatment arm, using means, standard deviations, medians, interquartile ranges for continuous variables and frequencies and proportions for categorical variables. Screening data will be summarised descriptively between the randomised patients, those ineligible and those eligible but not consented. A CONSORT diagram will be presented to show the patient flow throughout the trial.

The primary outcome will be summarised using means, standard deviations, medians and interquartile ranges. Linear regression will be used to estimate the treatment effect with 95% confidence interval, with and without adjustment for important patient-level covariates and site effect, by intention-to-treat. The impact of compliance will be assessed using CACE (complier average causal effect) analysis or other appropriate approach.

Secondary outcomes will be summarised using means, standard deviations, medians and interquartile ranges. Linear regression will be used to estimate the treatment effect with 95% confidence interval, with and without adjustment for important patient-level covariates and site effect.

Subgroup analysis which are specified apriori include (a) duration of mechanical ventilation and (b) age. The primary outcome will be examined in relation to these subgroups using an interaction in the model with treatment and sub-group effect.

The frequency and timing of the interim analysis will be reviewed and agreed by the DMC. Detailed stopping rules will be developed and specified in the SAP. The interim analysis will be conducted by trial statistician(s). The DMC will review unblinded interim data and make their decision to terminate the trial early based on the statistical evidence or safety concerns. Trial team will remain blinded during the trial unless necessary.

A prospective within-trial economic evaluation, adhering to NICE Reference Case recommendations will compare intervention with standard care. Healthcare resource use data will include in-patient and community care health service contacts during the six-month follow-up period, collected via trial CRFs and costed using the most recently available published reference costs. Generic health-related QoL will be assessed at baseline, eight weeks and six months using the EQ-5D-5L, with responses converted to health status scores using the NICE-recommended UK value set
and sensitivity analyses conducted using alternative tariffs if this is likely to be useful for decision- making. Patient-level QALY estimates will be calculated using the trapezoidal rule. Every effort will be made to minimize missingness, but if appropriate, a suitable method such as multiple imputation will be used to account for missingness. Bootstrapped bivariate regression will estimate and visualize incremental cost-effectiveness ratios (ICERs), acceptability curves (CEACs) and net monetary benefit (NMB). If findings are non-convergent at six months, we will explore the sensitivity of cost-effectiveness to extrapolation of costs and benefits beyond the trial time horizon, via a suitable decision model or parametric survival analysis model. Value of information analysis (VOI) will be conducted to explore the sensitivity of health economic recommendations to additional research. Sensitivity analyses will also explore the impact of broadening the decision perspective beyond the NICE reference case to include indirect costs such as the impact on productivity. Additional secondary cost-effectiveness analyses will also explore the unit cost of any achieved reductions in fatigue or anxiety/depression resulting from the intervention.

Qualitative data analysis:
Interview transcripts will be analysed using framework analysis. While each component of the process evaluation will be undertaken and analysed separately, the findings will be triangulated to integrate the qualitative findings and the trial outcomes, and we will explore the mechanistic pathways for any treatment effects.

6. MANAGEMENT OF THE RESEARCH

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

	Title	Forename/Initials	Surname
	Prof	Danny	McAuley
Post	Professor and Consultant in Intensive Care Medicine		
Qualifications	MD, Diploma in Intensive Care Medicine, Fellow in Medicine		
Employer	The Queen's University Belfast		
Work Address	Wellcome-Wolfson Institute for Experimental Medicine		
	Queen's University		
	Belfast		
Post Code	BT9 7BL		
Telephone	028 90635794		
Fax			
Mobile			
Work Email	d.f.mcauley@qub.ac.uk		

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	Title	Forename/Initials	Surname
	Prof	Judy	Bradley
Post	Director of Clinical Research Facility		
Qualifications	PhD		
Employer	The Queen's University Belfast		
Work Address	Wellcome-Wolfson Institute for Experimental Medicine Queen's University Belfast		
Post Code	BT9 7BL		
Telephone	028 95047973		
Fax			
Mobile			
Work Email	Judy.Bradley@qub.ac.uk		

	Title	Forename/Initials	Surname
	Prof	Julie	Bruce
Post	Professorial Fellow		
Qualifications	PhD		
Employer	University of Warwick		
Work Address	Warwick Clinical Trials Unit Warwick Medical School, University of Warwick Coventry		
Post Code	CV4 7AL		
Telephone			
Fax			
Mobile			
Work Email	julie.bruce@warwick.ac.uk		

	Title	Forename/Initials	Surname
	Dr	Bronwen	Connolly
Post	Senior Lecturer		
Qualifications	PhD		
Employer	Queen's University, Belfast		
Work Address	Wellcome-Wolfson Institute for Experimental Medicine Queen's University Belfast		
Post Code	BT9 7BL		
Telephone			
Fax			
Mobile			
Work Email	b.connolly@qub.ac.uk		

	Title	Forename/Initials	Surname
	Prof	Martin	Underwood
Post	Professor of Primary Care Research		
Qualifications	PhD, MRCP		
Employer	University of Warwick		
Work Address	Warwick Clinical Trials Unit Warwick Medical School, University of Warwick Coventry		

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Post Code	CV4 7AL
Telephone	
Fax	
Mobile	
Work Email	m.underwood@warwick.ac.uk

Title	Forename/Initials	Surname
Prof	Paul	Dark

Post	Chair in Critical Care Medicine
Qualifications	PhD, FRCS
Employer	University of Manchester
Work Address	Ellen Wilkinson Building Oxford Road Manchester
Post Code	M15 6JA
Telephone	
Fax	
Mobile	
Work Email	paul.m.dark@manchester.ac.uk

Title	Forename/Initials	Surname
Prof	Kamlesh	Khunti

Post	Professor of Primary Care Diabetes & Vascular Medicine
Qualifications	FRCGP, FRCP, MD, PhD
Employer	University of Leicester
Work Address	University of Leicester, Leicester General Hospital Gwendolen Road Leicester
Post Code	LE5 4PW
Telephone	
Fax	
Mobile	
Work Email	kk22@le.ac.uk

Title	Forename/Initials	Surname
Prof	Gavin	Perkins

Post	Professor in Critical Care Medicine
Qualifications	MD
Employer	University of Warwick
Work Address	Warwick Clinical Trials Unit Warwick Medical School, University of Warwick Coventry
Post Code	CV4 7AL
Telephone	
Fax	
Mobile	
Work Email	g.d.perkins@warwick.ac.uk

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	Title	Forename/Initials	Surname
	Prof	Nigel	Hart
Post	Clinical Professor		
Qualifications	Doctorate Medicine, Fellow		
Employer	Queen's University, Belfast		
Work Address	School of Medicine, Dentistry and Biomedical Sciences Queen's University Belfast		
Post Code	BT9 7BL		
Telephone			
Fax			
Mobile			
Work Email	n.hart@qub.ac.uk		

	Title	Forename/Initials	Surname
	Dr	Andrew	Willis
Post	Research Associate		
Qualifications	PhD		
Employer	University of Leicester		
Work Address	University of Leicester, Leicester General Hospital Gwendolen Road Leicester		
Post Code	LE5 4PW		
Telephone			
Fax			
Mobile			
Work Email	Aw187@le.ac.uk		

	Title	Forename/Initials	Surname
	Dr	Rachel	Clarke
Post	Clinical Psychologist		
Qualifications			
Employer	University Hospitals Plymouth NHS		
Work Address	The Therapy Collective 6 Ermington Terrace Plymouth		
Post Code	PL4 6QG		
Telephone			
Fax			
Mobile			
Work Email			

	Title	Forename/Initials	Surname
	Mrs	Eileen	Wright
Post	PPI Member		
Qualifications			
Employer			
Work Address			

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Post Code	
Telephone	
Fax	
Mobile	
Work Email	

Title	Forename/Initials	Surname
Prof	Ranjit	Lall

Post	Professor of Clinical Trials and Biostatistics
Qualifications	PhD
Employer	University of Warwick
Work Address	Warwick Clinical Trials Unit Warwick Medical School, University of Warwick Coventry
Post Code	CV4 7AL
Telephone	
Fax	
Mobile	
Work Email	R.Lall@warwick.ac.uk

Title	Forename/Initials	Surname
Dr	Chen	Ji

Post	Senior Research Fellow - Statistics
Qualifications	PhD
Employer	University of Warwick
Work Address	Warwick Clinical Trials Unit Warwick Medical School, University of Warwick Coventry
Post Code	CV4 7AL
Telephone	
Fax	
Mobile	
Work Email	C.Ji.3@warwick.ac.uk

Title	Forename/Initials	Surname
Prof	Jason	Madan

Post	Professor of Health Economics
Qualifications	PhD
Employer	University of Warwick
Work Address	Warwick Clinical Trials Unit Warwick Medical School, University of Warwick Coventry
Post Code	CV4 7AL
Telephone	
Fax	
Mobile	
Work Email	j.j.madan@warwick.ac.uk

A64. Details of research sponsor(s)

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A64-1. Sponsor

Lead Sponsor

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

Commercial status: Non-Commercial

If Other, please specify:

Contact person

Name of organisation	Ulster University
Given name	Nick
Family name	Curry
Address	Ulster University, Shore Road
Town/city	Newtownabbey, Co Antrim
Post code	BT37 0QB
Country	United Kingdom
Telephone	028 9036 8812
Fax	
E-mail	N.Curry@ulster.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	

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A65. Has external funding for the research been secured?

Please tick at least one check box.

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

What type of research project is this?

- (•) Standalone project
- ( ) Project that is part of a programme grant
- ( ) Project that is part of a Centre grant
- ( ) Project that is part of a fellowship/ personal award/ research training award
- ( ) Other

Other – please state:

Please give details of funding applications.

Organisation	National Institute for Health Research
Address	Evaluation, Trials and Studies Coordinating Centre, University of Southampton
	Alpha House, Enterprise Rd
	Chilworth, Southampton
Post Code	SO17 1BJ
Telephone	02380597501
Fax	
Mobile	
Email	netspostawardsetup@nihr.ac.uk

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

Amount: £1,582,568.69

Duration

Years: 3

Months: 0

If applicable, please specify the programme/ funding stream:

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

Health Technology Assessment

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?

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◯ Yes ◉ No

Please provide a copy of the unfavourable opinion letter(s). You should explain in your answer to question A6-2 how the reasons for the unfavourable opinion have been addressed in this application.

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

	Title	Forename/Initials	Surname
	Ms	Alison	Murphy
Organisation	Belfast health and Social Care Trust		
Address	Research & Development Office Room 2010, 2nd Floor King Edward Building Royal Hospitals Site		
	Grosvenor Road		
	Belfast		
Post Code	BT12 6BA		
Work Email	Alison.Murphy@belfasttrust.hscni.net		
Telephone	028 9063 6366		
Fax			
Mobile			

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

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

Planned start date: 01/01/2022
Planned end date: 31/12/2024
Total duration:
Years: 2 Months: 11 Days: 31

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 30

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*

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give approximate numbers if known:

☑ NHS organisations in England	20
☑ NHS organisations in Wales	3
☑ NHS organisations in Scotland	5
☑ HSC organisations in Northern Ireland	2
☐ GP practices in England	
☐ GP practices in Wales	
☐ GP practices in Scotland	
☐ GP practices in Northern Ireland	
☐ Joint health and social care agencies (eg community mental health teams)	
☐ Local authorities	
☐ Phase 1 trial units	
☐ Prison establishments	
☐ Probation areas	
☐ Independent (private or voluntary sector) organisations	
☐ Educational establishments	
☐ Independent research units	
☐ Other (give details)	
Total UK sites in study:	30

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

◉ Yes ○ No

A73-2. If yes, will any of these organisations be NHS organisations?

○ Yes ◉ No

If yes, details should be given in Part C.

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

The study will be monitored by Ulster University and by the Quality Assurance team at Warwick Clinical Trials Unit as representatives of the trial management team, to ensure that the study is being conducted as per protocol, adhering to Research Governance and GCP. The approach to, and extent of, monitoring will be specified in a trial monitoring plan determined by the risk assessment undertaken prior to the start of the study. A Trial Monitoring Plan will be developed and agreed by the Trial Management Group (TMG) and Trial Steering Committee (TSC) based on the trial risk assessment, including on-site monitoring if applicable. Processes to be considered in the monitoring plan will include participant enrolment, consent, eligibility, and allocation to trial groups; adherence to trial interventions and policies to protect participants, including reporting of harm and completeness, accuracy, and timeliness of data collection. This plan will be available from the trial coordination centre and will also be lodged with the Sponsor. Whilst the monitors work alongside the CI and trial team (WCTU), they will act independently in this role. Sites persistently late in reporting SAEs, receipt of multiple late/poorly completed CRFs, or evidence from CRFs that the trial protocols and procedures are not being adhered to (as assessed by the CI or the TMG) may be considered triggers for on-site monitoring visits. The sponsor will ensure investigator(s) and/or institutions will permit trial-related monitoring, audits and REC review, providing direct access to source data/documents as required. Monitoring will be performed by exploring the trial dataset or performing central monitoring procedures and/or site visits, as defined in the trial

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monitoring plan.
Recruitment sites are obliged to assist the sponsor in monitoring the study. These may include hosting site visits, providing information for remote monitoring, or putting procedures in place to monitor the study internally.

A75-1. What arrangements will be made to review interim safety and efficacy data from the trial? Will a formal data monitoring committee or equivalent body be convened?

The Data Monitoring Committee (DMC) will be established in line with the charter set by Warwick Clinical Trials Unit and will be independently chaired and established in accordance with the principles of Good Clinical Practice and Warwick Clinical Trials Unit Standard Operating Procedures (SOPs). All Serious Adverse Events (SAEs) will be entered onto the Serious Adverse Event reporting form within 24 hours of the Investigator/research team becoming aware of them. Once received, causality and expectedness will be confirmed by the Chief Investigator. SAEs that are deemed to be unexpected and possibly related to the trial interventions will be notified to the Research Ethics Committee (REC) and Sponsor within 15 days. All such events will be reported to the Trial Management Group at their next meeting. Experience suggests that the nature of trial design is such that there is unlikely to be sufficient data available to make decisions regarding efficacy prior to the end of the recruitment phase of the study. This will in part be determined by the study recruitment patterns, which will be routinely monitored by DMEC, therefore they may decide that a narrow window of opportunity does exist to assess treatment efficacy. If so, they are at liberty under the DMEC charter to make recommendations and suggestions to the Trial Management and Steering Committees at end stage of the study.

If a formal DMC is to be convened, please forward details of the membership and standard operating procedures to the Research Ethics Committee when available. The REC should also be notified of DMC recommendations and receive summary reports of interim analyses.

A75-2. What are the criteria for electively stopping the trial or other research prematurely?

The trial will be stopped prematurely if:
• Mandated by the Ethics Committee
• Following recommendations from the Data Monitoring Committee (DMC)
• Funding for the trial ceases
The Research Ethics Committee will be notified in writing within 90 days when the trial has been concluded or within 15 days if terminated early.

A76. Insurance/ indemnity to meet potential legal liabilities

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

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

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

☐ NHS indemnity scheme will apply (NHS sponsors only)

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

The University of Warwick and Ulster University has Public Liability and Clinical Trials insurance cover in place to cover its own legal liabilities arising from the Study, including for any harm caused to participants by the design of the research protocol.

Please enclose a copy of relevant documents.

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

Note: Where researchers with substantive NHS employment contracts have designed the research, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For other protocol

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authors (e.g. company employees, university members), please describe the arrangements and provide evidence.

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

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

The University of Warwick and Ulster University has Public Liability and Clinical Trials insurance cover in place to cover its own legal liabilities arising from the Study, including for any harm caused to participants by the design of the research protocol.

Please enclose a copy of relevant documents.

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

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

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

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

NHS indemnity (via participating NHS sites) covers NHS staff, medical academic staff with honorary contracts, and those conducting the trial. NHS bodies carry this risk themselves or spread it through the Clinical Negligence Scheme for Trusts, which provides unlimited cover for this risk.
The University of Warwick and Ulster University has Public Liability and Clinical Trials insurance cover in place to cover its own legal liabilities arising from the Study, including for any harm caused to participants by the design of the research protocol.

Please enclose a copy of relevant documents.

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

○ Yes ◉ No

Please enclose a copy of relevant documents.

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

○ Yes ◉ No ○ Not sure

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PART C: Overview of research sites

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

Investigator identifier	Research site		Investigator Name	
IN1	(●) NHS/HSC Site ( ) Non-NHS/HSC Site		Forename Middle name Family name Email	Danny McAuley d.f.mcauley@qub.ac.uk
	Organisation name	Belfast Health & Social Care Trust	Qualification (MD...)	MD
	Address	Knockbracken Healthcare Park Saintfield Road BELFAST COUNTY ANTRIM	Country	United Kingdom
	Post Code	BT8 8BH		
	Country	NORTHERN IRELAND		
IN2	(●) NHS/HSC Site ( ) Non-NHS/HSC Site		Forename Middle name Family name Email	Ema Swingwood Ema.Swingwood@uwe.ac.uk
	Organisation name	UNIVERSITY HOSPITALS BRISTOL AND WESTON NHS FOUNDATION TRUST	Qualification (MD...)	PhD
	Address	TRUST HEADQUARTERS MARLBOROUGH STREET BRISTOL	Country	United Kingdom
	Post Code	BS1 3NU		
	Country	ENGLAND		

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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. I understand that the main REC or its operational managers may share information in this application or supporting documentation with the Medicines and Healthcare products Regulatory Agency (MHRA) where it is relevant to the Agency's statutory responsibilities.

13. 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.

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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 Brenda O'Neill on 04/04/2022 15:10.

Job Title/Post:	Senior Lecturer in Physiotherapy
Organisation:	Ulster University
Email:	b.oneill@ulster.ac.uk

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D2. Declaration by the sponsor's representative

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

I confirm that:

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

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

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

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

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

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

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

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

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

This section was signed electronically by Ms Elaine Bell on 04/04/2022 15:12.

Job Title/Post:	Research Governance Officer
Organisation:	Ulster University
Email:	e.bell2@ulster.ac.uk

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