Full title: A multi-centre, single arm feasibility study of a complex intervention to improve Recovery after an Episode of Delirium in adults over 65 years: the RecoverED study

Short title: A feasibility study to improve Recovery after an Episode of Delirium: the RecoverED study

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This protocol describes work package 2 (WP2) of the above programme grant. The full programme includes four inter-related work packages:

WP 1 – Design of the complex intervention

WP 2 – Single arm feasibility study to test the acceptability of the intervention and an embedded process evaluation to inform iterative revisions of the intervention (this study)

WP 3 – A definitive randomised controlled trial to evaluate the effectiveness and cost-effectiveness of the intervention compared to usual care, with an embedded process evaluation

WP 4 – Implementation of the intervention

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the trial in compliance with the approved protocol and will adhere to GCP guidelines, the Sponsor's (and any other relevant) SOPs, and other regulatory requirements as amended.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies and serious breaches of GCP from the study as planned in this protocol will be explained.

For and on behalf of the Trial Sponsor:

Signature: Date:
..../...../.....

Name (please print):

.....

Position:
.....

Chief Investigator:

Signature: Date:
..../...../.....

Name: (please print):

.....

(Optional)

Statistician:

Signature: Date:
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Position:
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ii. LIST OF ABBREVIATIONS

ADL	Activities of daily living
AE	Adverse event
APACHE II	Acute physiology and chronic health evaluation II
AUC	Area under the curve
BAME	Black, Asian and minority ethnic
CAPA	Corrective and preventative action
CEA	Cost effectiveness analysis
CI	Chief investigator
CRF	Case report form
CTIMP	Clinical trial of investigational medicinal product
CTU	Clinical trials unit
DAD	Disability assessment for dementia
DECIDE	Delirium and cognitive impact in dementia study
DEMQOL	Dementia quality of life
DMP	Data management plan
DSM-5	Diagnostic and statistical manual of mental disorders 5th edition
EDC	Electronic data capture
ExeCTU	Exeter clinical trials unit
GCP	Good clinical practice
GDS-4	Geriatric depression scale 4 item
GP	General practitioner
HRA	Health research authority
HRQL	Health related quality of life
HSV	Health state values
HTTPS	Hyper text transfer protocol secure
I-AGeD	Informant assessment of geriatric delirium
ICECAP-A	ICEpop capability measure for adults
ICECAP-O	ICEpop capability measure for older people
ICER	incremental cost-effectiveness ratio
ICH	International conference on harmonisation of technical requirements for registration of pharmaceuticals for human use.
ICMJE	International committee of medical journal editors
IQCODE	Informant questionnaire on cognitive decline in the elderly
ISO	International organization for standardization

ISRCTN	International standard randomised controlled trials number
ISRUM	Items for a standardised resource use measure
MDAS	Memorial delirium assessment scale
Mini-ACE	Mini-Addenbrooke's cognitive examination
MRC	Medical research council
NICE	National institute for health and care excellence
NIHR	National institute for health and care research
NHS	National health service
OSLA	Observational scale of level of arousal
OT	Occupational therapist
PGfAR	Programme grants for applied research
PI	Principal investigator
PIS	Participant information sheet
PPI	Patient and public involvement
PSC	Programme steering committee
PT	Physiotherapist
QALY	Quality adjusted life years
RCT	Randomised controlled trial
R&D	Research and development
RDS	Relational database service
REC	Research ethics committee
RSW	Rehabilitation support worker
RUQ	Resource use questionnaire
RUSAE	Related unexpected serious adverse event
SAE	Serious adverse event
SAP	Statistical analysis plan
SMG	Study management group
SOP	Standard operating procedure
TMF	Trial master file
TLS	Transport layer security
TUG	Timed up and go
USM	Urgent safety measure
WALY	Wellbeing adjusted life years
WP	Work package

ZBI-12	Zarit burden interview-12 item

iii. STUDY SUMMARY

Table 1 Study summary

Study Title	A multi-centre, single arm feasibility study of a rehabilitation programme to improve Recovery after an Episode of Delirium in adults over 65 years: the RecoverED feasibility study	
Internal ref. no. (or short title)	RecoverED Feasibility Study	
Clinical Phase	III	
Study Design	Feasibility, single arm, complex intervention with a process evaluation	
Participants	Male and female adults aged over 65 years old diagnosed with delirium during acute hospital admission	
Planned Sample Size	60 patient and carer participant pairs	
Treatment duration	6 - 12 weeks	
Follow up duration	6 months	
Planned Study Period	10-month set-up, 6 months recruitment, 6 months follow-up, 4 months analysis and intervention refinement (26 months total)	
	Objectives	Outcome Measures
Feasibility study	The primary objective is to conduct a feasibility study of the rehabilitation intervention in older adults who have had delirium to determine if it is acceptable to patients and their carers and if it is possible to test the effectiveness and cost-effectiveness of the intervention in a future definitive randomised controlled trial (RCT).	1. The number of people with delirium identified on hospital wards 2. The proportion (and number) of people with delirium who meet the eligibility criteria 3. The proportion of eligible people with delirium who agree to participate in the study 4. The proportion of carers who agree to participate in the study 5. The proportion of participating people with delirium who start the intervention 6. The proportion of participating people who complete ≥60% of the intervention sessions

		7. The proportion of participating people with delirium who remain in the study until final follow-up at 6 months 8. The proportion of people with delirium providing valid outcome data for each primary and secondary outcome measure (described below) at 3 and 6 month follow ups 9. The acceptability of the intervention assessed during the process evaluation 10. The estimated standard deviation and six month follow-up rate for the proposed primary outcome, in order to either verify or inform revision of the proposed sample size calculation for the definitive RCT
Intervention	A rehabilitation programme delivered in participants' homes. The programme consists of physical activities, cognitive rehabilitation activities such as personal care tasks/leisure activities, and talking therapy sessions. The rehabilitation programme will be manualised and delivered by trained healthcare professionals with the assistance of an unpaid carer who is taking part in the study with the patient participant. The programme content, frequency and total number of sessions will undergo iterative revision during the feasibility study.	
Process evaluation	A sample of 15 – 20 patient/carer participants and 20 – 24 healthcare professionals will be interviewed to explore their views on the intervention.	
Stop/Go criteria for progression to RCT (WP3)	Definite Go ('green light'): • ≥ 25% of eligible participants consenting (or consultee agreeing) to feasibility study • ≥ 70% participants attend ≥ 60% of sessions as planned • Retention of ≥ 60% of recruited participants for key outcome data at 6 months • Evidence from the process evaluation that the intervention can be delivered with fidelity and that it is acceptable to participants and professionals.	

	Definite Stop ('red light'): • < 10% of eligible participants consenting to feasibility trial • < 30% participants attend ≥ 60% of sessions as planned • Retention of < 50% of consented participants for provision of key outcome data at 6 months • Evidence from the process evaluation that the intervention cannot be delivered with fidelity and that it is not acceptable to participants and professionals Intermediate targets will be defined as amber and will be reviewed by the programme steering committee and funder.

iv. FUNDING AND SUPPORT IN KIND

The NIHR PGfAR is providing full financial support for the research costs of this study. No organisations are providing support in kind.

v. ROLE OF TRIAL SPONSOR AND FUNDER

The Royal Devon University Healthcare NHS Foundation Trust is the sponsor for this study. The sponsor has had input into the design of the study but overall responsibility for the design lies with the chief investigators (LA, LC). The sponsor is responsible for authorising the initial submission to the research ethics committee (REC) and health research authority (HRA) and subsequent amendments, ensuring appropriate agreements and indemnity arrangements are in place, overseeing the conduct of the study and ensuring it adheres to the principles of good clinical practice (GCP) and the UK Policy Framework for Health and Social Care Research and for archiving at the end of the study. The sponsor is not responsible for and has no involvement in the data analysis or interpretation, or for writing manuscripts.

The NIHR as funder is responsible for providing funds to cover the agreed research costs as part of a programme grant. The funder is not responsible for and has no involvement in data analysis or interpretation, or for writing manuscripts.

vi. ROLES AND RESPONSIBILITIES OF TRIAL MANAGEMENT COMMITEES/GROUPS & INDIVIDUALS

Programme Steering Committee

The programme steering committee (PSC) will be composed of an independent chairperson with expert knowledge in the subject area and a minimum of two additional independent professional members and a minimum of one independent lay representative. The chief investigators and lead statistician will join the PSC as non-independent members.

The trial manager and representatives of the sponsor and the funder will be invited to attend PSC meetings as observers but will not be voting members.

The roles and responsibilities of the PSC are documented in the PSC charter, available upon request to the trial manager. The PSC will fulfil the roles of a trial steering committee and data monitoring committee for this study.

Study Management Group

The study management group (SMG) will be composed of the chief investigators, programme collaborators, the statisticians, qualitative researchers, health economist, co-applicants at regional sites, patient and public involvement (PPI) lead, a lay representative, the programme manager and trial manager.

The SMG will write the protocol, statistical analysis plan (SAP) and participant-facing materials, obtain relevant approvals from an NHS research ethics committee (REC) and the Health Research Authority (HRA), coordinate with NHS Trusts to set up sites and ensure the study is conducted according to the principles of GCP and the UK Policy Framework for Health and Social Care. The SMG will meet quarterly to monitor safety, key performance indicators and discuss and resolve emerging issues. A sub-set of the SMG will meet at least monthly to manage the day-to-day running of the study.

Members of the SMG will analyse the data, interpret the analyses, write reports to the funder and write and submit manuscripts to peer-reviewed journals.

Patient and Public Involvement Group

A Patient and Public Involvement (PPI) group, led by RL of “Innovations in Dementia”, will inform the development of participant-facing materials, resource use questionnaires and the intervention. The

PPI group will provide ongoing support for the duration of the study and will co-produce lay summaries of the results and advise on public dissemination.

vii. KEY WORDS:	Delirium, dementia, feasibility, rehabilitation, complex intervention

Background

Delirium is a neurocognitive disorder common in older people. The primary feature is disturbance in attention and awareness, accompanied by impairments in cognition and changes in behaviour. It arises as a direct physiological consequence of another medical condition, and has an acute onset and fluctuating course [1]. Delirium is associated with poor outcomes: increased length of stay in hospital, hospital-acquired complications, distress, poor functional recovery and increased mortality [2-7]. Cognitive and functional deficits can persist for months after an episode of delirium and some patients may never recover, with 21% having persistent delirium at 6 months [8].

Prior dementia is the strongest risk factor for delirium, and delirium causes a worsening of the cognitive trajectory in dementia [9, 10]. 20% of people admitted to hospital and 45% of those with known dementia admitted to hospital have delirium [11, 12]. Previous research has addressed prevention of delirium in hospitals and care homes, and there are guidelines on short-term treatment of delirium during admission [13, 14]. However, no studies have addressed the problem of longer-term recovery after delirium. The recent NICE guideline for dementia identified an important question in this area: “What are the most clinically and cost-effective non-pharmacological interventions for helping the long-term recovery of people with delirium superimposed on dementia?” [15]. We aim to address this question for the first time. The recovery of people with delirium who do not have a prior diagnosis of dementia was outside the scope of the NICE guideline, but we also plan to explore whether people who do not have prior dementia could also benefit from the newly developed intervention.

Delirium was initially thought of as transient, but several studies have shown it is often persistent [16-20]. In a systematic review delirium was persistent in 44% of older patients at 1 month, 26% at 3 months and 21% at 6 months after onset of delirium [8]. When considering people who have some delirium symptoms but not a full delirium syndrome, persistence is higher still [4, 21, 22]. After hospital discharge, Levkoff et al found that 87% of 91 patients had some delirium symptoms at 3 months and 68% at 6 months, and McCusker found delirium symptoms persisting up to 12 months in one third of patients both with and without dementia [16, 23]. The adverse outcomes of delirium include functional decline and lead to an increased need for support [24].

Despite evidence of persisting symptoms, little is currently known about the support needs of people with delirium and their carers, or what support these individuals receive after discharge. In one study, families expressed a need for more extensive information about delirium and how they could help the patient [25]. Studies which have shown a decrease in activities of daily living (ADL) after delirium suggest that patients have ongoing care needs which may be ameliorated by rehabilitation [2, 20]. People with cognitive impairment or dementia are often not referred for rehabilitation due to a perception that they do not have “rehabilitation potential”; however, rehabilitation interventions can be readily applied to people with cognitive impairment and are effective [26, 27]. We have undertaken a realist review to examine current evidence for, and theory underpinning, interventions to help people recover after delirium [28]. In the first stage of the review, we found four trials of interventions which aimed to help people recover after delirium. They included interventions such as a nurse case manager, cognitively stimulating activities for people with delirium superimposed on dementia, being read a story or poem based on patient’s interests, and a ‘hospital in the home’ delirium pathway including carer information and support, a patient management plan and multidisciplinary intervention [29-32]. Results of these trials showed mixed evidence of effectiveness.

The second stage of our realist review broadened the inclusion criteria to include research in related fields and identified 46 additional papers, which provided further theory as to how an intervention might improve recovery after delirium. We have developed a programme theory which consists of three interdependent recovery domains and four recovery facilitators. Recovery domains are: 1) support for physical recovery through structured physical activity programmes; 2) support for cognitive recovery through cognitively stimulating activities; 3) support for emotional recovery through talking with skilled helpers. Recovery facilitators are: 1) involvement and support of carers; 2) tailoring intervention to individual needs, preferences and abilities; 3) quality and continuity in relationships of care; 4) enabling socialisation and positive expressions of self.

Under work package 1 we used the principles of the MRC guidance on developing and evaluating complex interventions to undertake initial development work required to produce a suitable intervention for this clinical problem [15, 33, 34]. We have subsequently developed a non-pharmacological rehabilitation intervention which has been presented to an expert panel. We have manualised the intervention, specified staffing needs, and developed a training programme for therapy staff. In the current feasibility study (work package 2) we will perform iterative revision of the intervention.

If the feasibility progression criteria are met, we will undertake a separate definitive randomised controlled trial (RCT) to test the clinical and cost-effectiveness of the intervention in comparison with usual care (work package 3; not included in this protocol).

2. Rationale

Delirium incidence is strongly associated with age and, in an ageing population, it is thus a growing problem. The costs of delirium to patients, carers, the health/social care services supporting them and wider society are high, with total inpatient costs attributable to delirium ranging from £12,575 to £49,689 per patient-episode [35]. If people require discharge to institutional care after an episode of delirium then there are additional costs for social care as well as healthcare costs. Whilst delirium prevention interventions are cost-effective, up to 30% of older people who are admitted to hospital already have delirium at the time of admission and, at best, only 30% of cases that develop in hospital can be prevented [5, 36]. The treatment of delirium and its consequence is thus a major unmet medical need. It is currently unknown whether interventions to improve recovery after delirium would be cost effective, but it is likely that they will be as people who recover poorly after delirium are likely to require an increased level of care or institutionalisation [5].

Dementia is also a growing problem in our ageing society and delirium is associated with subsequent dementia in general medical inpatients, post hip surgery/hip fracture and in population studies [3, 21, 37, 38]. Delirium is also associated with worsening of the course of previously diagnosed dementia [9, 10, 39]. If we can improve recovery after delirium, it may be possible both to prevent the decline which occurs after delirium in those with dementia and reduce incidence of new onset dementia after delirium.

Assessment and management of risk

3. The participant population are older adults who have been diagnosed with delirium, with or without a previous diagnosis of dementia, during an admission to an acute hospital. Participants may be vulnerable and could lack the capacity to provide informed consent to take part in the study. The impact of delirium and any co-morbidities on participants is heterogeneous so individual risk will vary, e.g., some participants may have greater cognitive impairment but with minimal impairment to physical functioning, whereas other participants may have higher levels of cognitive function but have impaired physical function.

The intervention as a package is novel (although many of the individual elements are not novel) and will be tested for the first time in this study so there is no direct evidence to support a risk/benefit analysis. A full risk assessment will be completed prior to commencing recruitment and maintained as a living document throughout the study. The intervention was carefully designed with a panel of experts and members of a PPI group based on published evidence from previous trials and other studies of treatment for delirium. The intervention has been designed to be sufficiently flexible as to be suitable for people across the range of cognitive and functional ability.

The intervention is a rehabilitation programme involving structured physical activity, cognitively stimulating activities and talking therapy, plus usual care. All of these activities are currently used in the care of older people and are low risk, although they have not been used together in this specific context. Usual care for delirium post-hospital discharge is not well established but could involve a home assessment visit or referral to primary or community care services. If the hospital admission was for a physical injury such as hip fracture, the patient might be offered physiotherapy. The intervention is designed to be compatible with usual care so that additional burden is not placed on participants.

3.1. Potential risks

Patient participants may be considered to be vulnerable due to delirium and dementia and may lack the capacity to understand what the study involves and give informed consent.

Physical activity in our participant population could lead to injury and potential re-admission to an acute hospital.

The intervention takes place in the participant's home where emergency medical assistance may not be immediately available, e.g., to manage falls and other medical problems.

Cognitive stimulation and/or talking therapy could cause emotional distress.

The intervention has the potential to put a greater burden on patient and carer participants than usual care alone (i.e., if not taking part in the study).

There is a risk of COVID-19 infection from home visits from healthcare professionals who wouldn't otherwise be visiting the home.

3.2. Potential benefits

Structured physical activity rehabilitation could lead to improved physical functioning and independence with daily activities such as getting out of bed.

Cognitive stimulation and/or talking therapy may lead to quicker recovery from delirium and can be cathartic.

Having the intervention at home provides greater convenience to patients and carers, i.e., there will not be any requirement to travel to additional community or hospital appointments as a result of taking part in the study. Participants will have the option of completing follow-up visits at the acute hospital or at home, depending on their preference and abilities.

Inclusion of carers in the intervention could lead to long term benefits for both patients and carers as a result of having a greater understanding of their condition and the rehabilitation activities.

3.3. **Mitigation of risk**

Potential patient and carer participants will be fully informed of the risks and potential benefits before deciding whether to take part in the study, and will be required to provide informed consent before undertaking any research activity. Patients who lack capacity to provide informed consent will not be recruited into the study without obtaining a positive opinion from a consultee (in England) or consent from a relative/welfare guardian (in Scotland).

In collaboration with our PPI group we have designed participant information sheets that are accessible to patients with delirium and dementia, including a short summary cover sheet.

Patients who are unable to communicate verbally due to advanced dementia or aphasia will be excluded from the study as they are unlikely to benefit from the intervention.

All participants must have an unpaid carer such as a family member or friend who normally spends at least one hour a week with the participant to be eligible to take part. The carer will have an integral role in supporting the patient participant with the intervention.

Expert healthcare professionals, including a physiotherapist, occupational therapist and clinical psychologist will deliver comprehensive training to rehabilitation support workers (RSW) who will deliver the intervention in the participant's home under the supervision of a physiotherapist and occupational therapist. RSWs will be provided with a comprehensive manual describing the intervention procedures.

The intervention will be tailored to the individual based on an initial assessment of physical and cognitive function. Activities will be graded so that they remain challenging enough to encourage interest, motivation and improvement, without being so challenging that they are overwhelming and discourage participation.

To minimise participant burden the intervention dose and frequency has been carefully selected by a panel of experts and members of the PPI group to increase the chances of effectiveness without over-burdening or over-stretching the participant and carer. During the intervention period, we will undertake iterative revision of the intervention and update the manual following periodic focus group sessions with the therapists and feedback from qualitative interviews with participants and health and social care professionals.

To further minimise patient participant burden, if a participant is receiving rehabilitation as part of usual care, the RSW will review the care package and choose activities from the intervention manual that complement rather than replicate the usual care activity.

The research team have considerable expertise in working with the patient population involved in this study in both a clinical and a research capacity and will undertake the study in full compliance with the Mental Capacity Act 2005, the Adults with Incapacity (Scotland) Act 2000, the opinion of an NHS REC and the UK policy framework for health and social care research.

Each NHS Trusts' infection control policy and government guidelines will be followed at all times to minimise the risk of COVID-19 infection. Our patient population are likely to already receive home care as part of standard care, or have regular visits to healthcare settings so the risk of catching COVID-19 will never be zero but we will minimise the risk as much as possible.

Objectives and outcome measures

4.1. Primary objective

The aim of the study is to test the feasibility of conducting a research study of the intervention.

4. Objective A: the primary objective is to conduct a feasibility study of the rehabilitation intervention in older adults who have had delirium to determine if the intervention is acceptable to patients and their carers.

4.2. Secondary objectives

Objective B: to examine the acceptability of the intervention for people with protected characteristics via a process evaluation.

Objective C: to test the ability to collect the data required to address the primary and secondary outcomes for the definitive randomised controlled trial (RCT).

Objective D: to test the cost-effectiveness framework for the definitive RCT.

Objective E: to perform iterative refinement of the intervention for the definitive RCT.

4.3. Feasibility outcome measures

The following feasibility outcomes will be assessed:

1. The number of people with delirium identified on hospital wards
2. The proportion (and number) of people with delirium who meet the eligibility criteria
3. The proportion of eligible people with delirium who agree to participate in the study*
4. The proportion of carers who agree to participate in the study
5. The proportion of participating people with delirium who start the intervention
6. The proportion of participating people who complete ≥60% of the intervention sessions*
7. The proportion of participating people with delirium who remain in the study until final follow-up at 6 months*
8. The proportion of people with delirium providing valid outcome data for each primary and secondary outcome measure (described below) at 3 and 6 month follow ups
9. The acceptability of the intervention assessed during the process evaluation*
10. The estimated standard deviation and six month follow-up rate for the proposed primary outcome, in order to either verify or inform revision of the proposed sample size calculation for the definitive RCT

The above described feasibility outcomes will also be considered separately for those with and without dementia. See Table 2 for a list of objectives matched with feasibility outcomes.

*Feasibility outcomes marked with an asterisk will be used to determine if the study meets the stop/go criteria for the definitive RCT (see section 4.4).

4.4. Progression criteria

Definite Go ('green light'):

- ≥ 25% of eligible participants consenting (or consultee agreeing) to feasibility study
- ≥ 70% participants attend ≥ 60% of sessions as planned
- Retention of ≥ 60% of recruited participants for key outcome data at 6 months
- Evidence from the process evaluation that the intervention can be delivered with fidelity and that it is acceptable to participants and professionals.

Definite Stop ('red light'):

- < 10% of eligible participants consenting to feasibility trial
- < 30% participants attend ≥ 60% of sessions as planned
- Retention of < 50% of consented participants for provision of key outcome data at 6 months
- Evidence from the process evaluation that the intervention cannot be delivered with fidelity and that it is not acceptable to participants and professionals

Intermediate targets will be defined as amber and will be reviewed by the PSC and funder.

Table 2 Feasibility objectives matched to outcomes

Feasibility objectives	Outcome Measures	Timepoint(s) of evaluation of this outcome measure
Primary Objective		
Objective A: the primary objective is to conduct a feasibility study of the rehabilitation intervention in older adults who have had delirium to determine if the intervention is acceptable to patients and their carers.	The proportion of eligible people with delirium who agree to participate in the study The proportion of carers who agree to participate in the study The acceptability of the intervention assessed during the process evaluation The accuracy of the sample size calculation for the definitive RCT	Recruitment Recruitment Post-intervention Throughout
Secondary Objectives		
Objective B: to examine the acceptability of the intervention for people with protected characteristics via a process evaluation	The acceptability of the intervention assessed during the process evaluation	Post-intervention
Objective C: to test the ability to collect the data required to address the primary and secondary outcomes for the definitive randomised controlled trial (RCT)	The number of people with delirium identified on hospital wards The proportion (and number) of people with delirium who meet the eligibility criteria The proportion of participating people with delirium who start the intervention The proportion of participating people who complete ≥60% of the intervention sessions The proportion of participating people with delirium who remain in the study until final follow-up at 6 months* The proportion of people with delirium providing valid outcome data for each primary and secondary outcome measure (described below) at 3 and 6 month follow ups The estimated standard deviation and six month follow-up rate for the proposed primary	Recruitment Recruitment 3 months 3 months 6 months 3 months and 6 months 6 months

Feasibility objectives	Outcome Measures	Timepoint(s) of evaluation of this outcome measure
	outcome, in order to either verify or inform revision of the proposed sample size calculation for the definitive RCT	
Objective D: to test the cost effectiveness framework for the definitive RCT	The proportion of people with delirium providing valid outcome data for each primary and secondary outcome measure (described below) at 3 and 6 month follow ups	3 months and 6 months
Objective E: to perform iterative refinement of the intervention for the definitive RCT	The acceptability of the intervention assessed during the process evaluation	Post-intervention

4.5. Planned outcomes for a definitive RCT

We plan to measure the outcomes described in Table 3 in a separate definitive RCT (work package 3; described in a separate protocol). The outcome data will be collected in this single arm feasibility study to test if the data can be collected but it will be presented descriptively only. It is possible that the outcomes will change as part of iterative revision of the study prior to undertaking the definitive RCT.

Table 3 Planned future RCT outcomes

Measure	Description	Time point
Primary		
Activities of daily living (ADL) assessed with the Disability Assessment for Dementia (DAD) [40]	The DAD is an informant-rated questionnaire or structured interview consisting of 40 binary items regarding the subject's involvement in ADL. Seventeen items address basic ADL (hygiene, dressing, continence, and eating), and 23 items relate to instrumental ADL (meal preparation, telephoning, going on an outing, finance and correspondence, medications, and leisure and housework). Items can be categorised as part of initiation, planning and organization, and effective performance subscales, with the total score used most frequently, as is proposed as the primary outcome. Non-applicable items (e.g., those that a patient did not participate in even before the onset of their illness) are excluded from scoring, with the final scores being converted to a percentage. Scores thus have a potential range from 0 to 100%, with higher percentage scores representing greater competence in ADL. This outcome measure covers ADLs which are of importance to older people and it has been recommended for use in dementia trials. We have chosen this outcome because we expect that participants without dementia will still have cognitive deficits and an ADL scale for dementia will be most sensitive to change in this group.	Baseline, 6 months
Secondary		
Activities of daily living (ADL) assessed with the Disability Assessment for Dementia (DAD)	As described above for primary outcome	Baseline, 3 months
Mobility	Assessed using the Timed Up and Go (TUG). Patient participants stand up and walk 3 metres, turn around and walk back. The time taken to complete it is recorded. The test is scored as time in seconds.	Baseline 3 months 6 months
Delirium persistence or recurrence according to DSM-5 criteria	The assessment of delirium will be based on the protocol we have previously published for the Delirium and Cognitive Impact in Dementia	Baseline, 3 months,

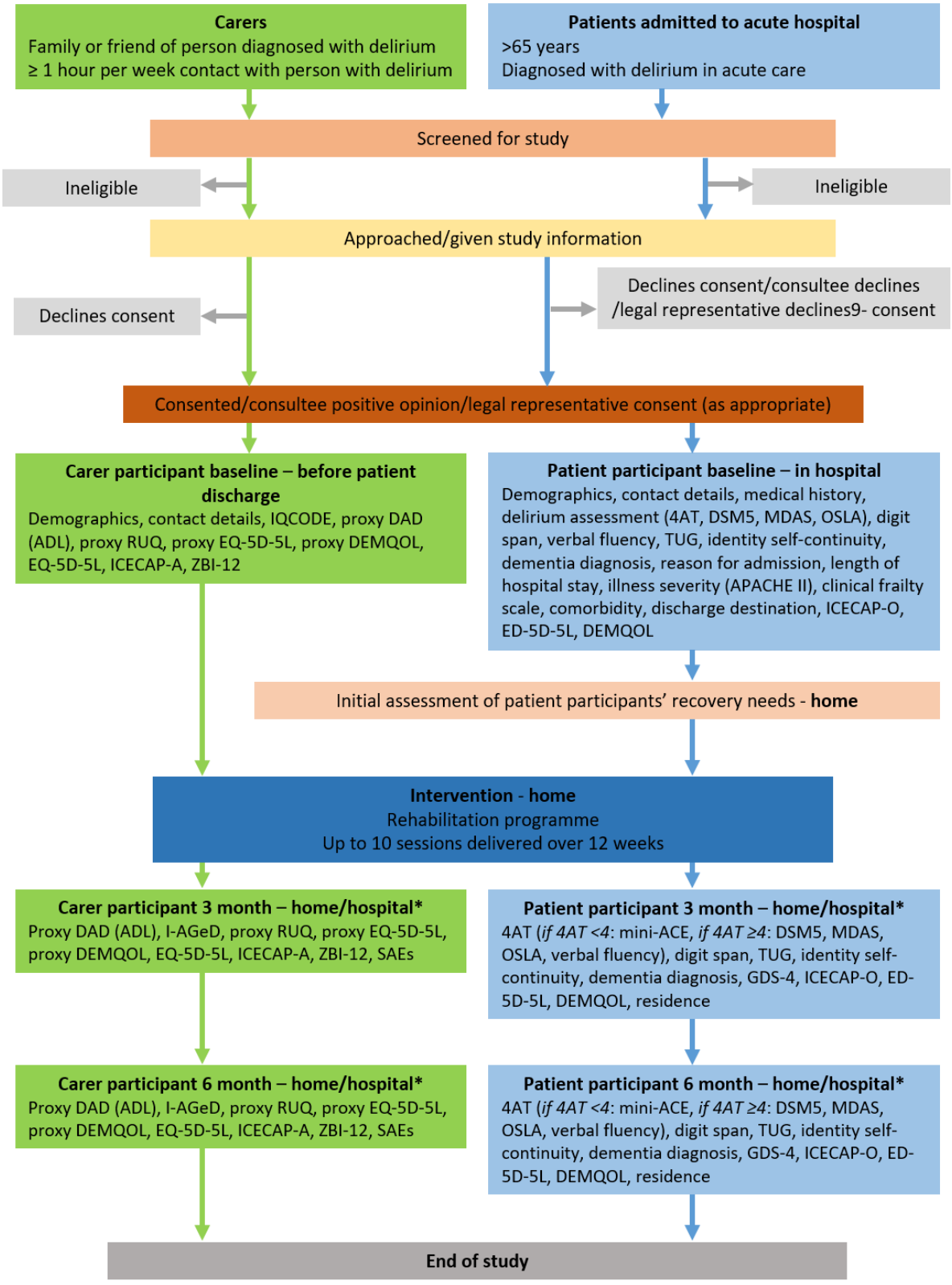
	(DECIDE) study in which diagnosis is made according to DSM5 criteria [41], with some additional enhancements including use of the Informant Assessment of Geriatric Delirium scale (I-AGeD) [42].	6 months
Attention	Assessment of attention using number of months of the year backwards. Participants will be asked to recite the months of the year backwards from December to June, and given a score ranging from 0-7 representing number of months successfully recited before failure. A score of 7 indicates completely correct recital	Baseline, 3 months, 6 months
Observational Scale of level of Arousal (OSLA) [43]	The OSLA is a four-item scale (scored 0-15) which was developed to assess level of arousal in people with delirium.	Baseline, 3 months, 6 months
Cognition assessed with mini ACE (Mini-ACE) [44]	The Mini-ACE consists of 5 items and has a maximum score of 30.	Baseline, 3 months, 6 months
Verbal fluency	Verbal fluency will be assessed using the 'Animals' assessment from the mini-ACE assessment. The assessment is scored as the correct number of animals stated in 1 minute.	Baseline? 3 months, 6 months
Identity self-continuity	Single item question to assess how the patient participant feels about themselves. Scored on a Likert scale (Strongly disagree/disagree/neither agree nor disagree/agree/strongly agree)	Baseline, 3 months, 6 months
Verbal short term and working memory	This will be assessed with the Digit span test (Forward Digit Span and Reverse Digit Span). This is a verbal task, with stimuli presented auditorily. Participants repeat a sequence of numbers in forward or reverse order. The length of digit span repeated correctly will be scored 0-9 for forward and 0-8 backward with score given for the best length of sequence achieved, .	Baseline, 3 months, 6 months
Mood assessed with the Geriatric Depression Scale-4 (GDS-4) [45]	The 4 binary item scale will be used which has been validated in older people and people with dementia. The items will be summed to form a total score with potential range of 0-4.	3 months, 6 months
Wellbeing assessed with the ICEpop CAPability measure for Older people (ICECAP-O) [46]	This is a measure of capability in older people for use in economic evaluation, and explicitly recognised by the National Institute for Health and Care Excellence (NICE) for use in cost-effectiveness analyses of interventions with a social care element [41]. Unlike most measures used in economic evaluations, the ICECAP-O focuses on wellbeing defined in a broader sense than health. The measure covers attributes of wellbeing that were found to be important to older people in the UK. ICECAP-O comprises five attributes (the lay terms are in brackets): Attachment (love and	Baseline, 3 months, 6 months

	friendship); Security (thinking about the future without concern); Role (doing things that make you feel valued); Enjoyment (enjoyment and pleasure); Control (independence). Responses to the ICECAP-O are converted to a single index value, which represents a quantitative measure of capability wellbeing, using a published and validated algorithm [46]. These wellbeing values, which are suitable for the estimation of wellbeing-adjusted life years (WALYs) for use in economic evaluation, range from zero for the lowest level of wellbeing described by the ICECAP-O to 1 for the highest.	
Residence category	Record of whether the patient participant is living in their own home, living with family, assisted living/warden supported, care home without nursing, care home with nursing or other residence type	3 months, 6 months
Patient health-related quality of life (HRQL) assessed with the EQ-5D-5L and EQ-5D-5L proxy [47]	If the participant has capacity and has provided informed consent they will complete the EQ-5D-5L. In addition, the carer will assess the patient's HRQL using the Proxy version 2 of the EQ-5D-5L. This descriptive system comprises five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 levels: no problems, slight problems, moderate problems, severe problems and extreme problems. The person is asked to indicate his/her health state by ticking the box next to the most appropriate statement in each of the five dimensions. Participant responses to the EQ-5D-5L will be converted to health state values (HSVs) using the approach recommended by the National Institute for Health and Care Excellence (NICE) at the time of data analysis [48]. These HSVs, which range from -0.594 to 1 on a scale where 1 corresponds to full/perfect health and zero is equivalent to being dead, provide the "quality weights" required for the calculation of quality-adjusted life-years (QALYs).	Baseline, 3 months, 6 months
Patient HRQL assessed with the DEMQOL and DEMQOL-Proxy [49]	This is a measure of HRQL in dementia that is appropriate for use at all stages of dementia severity. There are two versions of DEMQOL: a 28-item (score range 28 to 112, higher scores indicate better QOL) interviewer-administered questionnaire that is self-reported by the person with dementia (DEMQOL) and a 31-item (score range 31 to 124; higher scores indicate better HRQL) interviewer-administered questionnaire that is proxy-reported by a caregiver (DEMQOL-Proxy). Patient participants will completed the DEMQOL if they have capacity and have provided informed consent and carers will complete the DEMQOL-Proxy. Participant responses to the DEMQOL and the DEMQOL-Proxy will also be used to provide	Baseline, 3 months, 6 months

	DEMQOL-U and DEMQOL-proxy-U values, which are suitable for use in economic evaluation.	
Carer burden assessed with the Zarit burden interview 12 (ZBI-12) [50]	The 12-item (rated 0-4) version of the Zarit Burden Interview is the instrument most consistently used in dementia caregiving research. Summation of the items with a total score range 0-48.	Baseline, 3 months, 6 months
Carer quality of life assessed with the EQ-5D-5L	The NICE reference case for methods of health technology appraisal states that all direct health effects should be considered, "whether for patients, or when relevant, for carers" [51]. Therefore, carers participating in this study will be asked to report their own HRQOL, using the EQ-5D-5L, as described above.	Baseline, 3 months, 6 months
Carer wellbeing assessed with the ICEpop CAPability measure for Adults (ICECAP-A) [52]	This instrument was designed using the same conceptual basis and methods as the ICECAP-O, in order to provide a measure of capability wellbeing in adults aged over 18 years. As with the ICECAP-O, this measure is recognised by NICE for use in cost-effectiveness analyses of interventions with a social care element [41].	Baseline, 3 months, 6 months
Resource use assessed with a bespoke questionnaire	Data on the use of health, social care and wider resources will be collected via a proxy Resource Use Questionnaire (RUQ), which will be designed specifically for this study. The RUQ will be informed by the 'CORE Items for a Standardised Resource Use Measure (ISRUM)' [53] and the Database of Instruments for Resource Use Measurement [54], and will be designed in collaboration with the PPI group.	Baseline, 3 months, 6 months

5.

Study schema



*Location depends on participant preference and abilities, and the capacity of the research team.

Figure 1 Study schema

Study design

The study is a multi-centre, single arm feasibility study of a rehabilitation programme intervention with an embedded qualitative process evaluation. Patient participants (people with delirium with or without dementia) and carer participants (unpaid family members or friends of patient participants) will be recruited in pairs. All participant pairs will be offered the intervention, with follow-up assessments conducted at 3-months and 6-months post-discharge home. No long-term follow-up is planned.

6.

The study is designed to test the feasibility of conducting a definitive multi-centre RCT of the effectiveness and cost-effectiveness of the intervention compared to usual care. The study will inform the feasibility of identifying potential participants, recruiting patient and carer participant pairs, uptake and acceptability of the intervention, retention of participants until the final follow-up at 6 months and data collection.

Participants and professionals providing care to patient participants will be recruited to the embedded qualitative process evaluation which will inform iterative revision of the intervention during the feasibility study and assess acceptability of the intervention.

The study will assess a proposed economic evaluation framework which would be implemented in a future definitive RCT to measure cost effectiveness.

6.1. Study setting

The study will recruit patients from six acute NHS hospital Trusts in the UK that provide care for older people with delirium. Additional sites will be added if required. Participants will be recruited and baseline data collected prior to discharge of the patient from hospital for their index admission. The intervention will take place in participants' private homes. Follow-up will take place either in the participants' home or at the acute Trust, depending on participant preference and abilities, and the capacity of the research delivery team at the Trust.

Some participating acute NHS Trust sites also provide the community therapy services to deliver the intervention and follow-up in participants' homes ('all research activities' site). Some acute NHS Trusts do not directly provide community therapy services. In these instances, participants will be recruited and baseline and follow-up data collected by the acute NHS Trust ('recruitment and follow-up' site) and the intervention will be delivered by a community Trust ('intervention only' site).

6.2. Participant eligibility criteria

Participants are patients who have been admitted to a participating acute NHS Trust and have a clinical diagnosis of delirium for at least 48 hours. Patients with delirium for less than 48 hours will be screened again after 48 hours from the onset of delirium have passed. Patients with delirium either with or without dementia will be screened for suitability to take part in the study. Carers will be screened and recruited to the study as a pair with the patient participant.

Carers are defined as a close family member or friend who receive no financial reimbursement for the care they provide to the patient participant. If a patient has multiple carers then the patient and carers will decide themselves who is best suited to be the carer participant.

See section 7.10 for details of professional participants who will be invited to take part in the embedded qualitative process evaluation.

6.2.1. Inclusion criteria patient participants

1. Aged over 65 years;
2. Admitted to an acute hospital;
3. Clinical diagnosis of delirium lasting for more than 48 hours;
4. Expected to be living in a private dwelling after discharge from hospital or immediate care (a period of 4 weeks of intermediate care will be allowed before discharge home);
5. Has a carer who is willing to assist with completion of outcomes (see section 6.2 for carer definition);
6. Has the capacity to provide informed consent to participate, OR, has a consultee who is able to give an opinion on the participation of the person with delirium (in England), OR, has a relative/welfare guardian who is able to give informed consent on behalf of the person with delirium (in Scotland).

6.2.2. Exclusion criteria patient participants

1. Diagnosis of delirium cannot be confirmed during patient's hospital visit;
2. Unable to communicate verbally due to advanced dementia or aphasia;
3. Carer declines participation in the study;
4. Undergoing end of life care;
5. Participating in another intervention study

6.2.3. Inclusion criteria carer participants

1. Family member or friend of the person with delirium who is going to take part in the study;
2. In contact with patient participant for at least one hour per week;
3. Able to communicate in English sufficiently well to complete the proxy outcome measures;
4. Has capacity to provide informed consent.

6.2.4. Exclusion criteria carer participants

There are no exclusion criteria for carer participants.

Trial procedures

7.1. Recruitment

7.1.1. Participant Identification

7. Patient participants will be identified from hospital records by a clinical researcher embedded within the clinical team, who will hold substantive or honorary contracts with the NHS Trust. Where it is not possible to embed a researcher in the clinical team a member of the clinical team will ask the patient or carer if they can be approached by a clinical researcher. Potential participants will be in-patients primarily on older people's medical wards, general medical wards and trauma and orthopaedics wards. Patients aged over 65 years with a clinical diagnosis of delirium identified as part of standard care will be screened for the study.

Potentially eligible patient participants will be asked to provide details of a friend or family member who may be approached to become carer participants. If the patient participant lacks capacity to understand that they are being approached about a research study, contact details for carers will be provided to the researcher by the clinical care team. The clinical care team will contact the carer initially to request permission for their contact details to be shared with the researcher.

7.1.2. Screening

Patients will be screened for delirium as part of standard care using a suitable well-established method such as the Confusion Assessment Method or the 4AT [55]. All patients aged over 65 years who screen positive for delirium will be discussed with the clinical care team by the clinical researcher to establish whether a clinical diagnosis of delirium has been made and for how long. The eligibility of people with delirium will initially be assessed through discussion with the clinical care team to screen out participants who are clearly ineligible (≤65 years of age, care home residents, are receiving palliative care). Potentially eligible patients will have been assessed by the clinical care team to confirm a diagnosis of delirium. The detailed assessment for delirium is conducted as part of good practice as recommended by NICE for people who screen positive for delirium [14].

Patients who have not been delirious for 48 hours at the time of initial delirium screening will be reassessed after 48 hours of diagnosis to confirm persistent delirium. Review of the persistence of delirium is a standard part of clinical care.

Patients who are unable to communicate verbally due to advanced dementia or aphasia, or who do not have an appropriate carer will be screened out by the researcher by interaction with the patient and clinical care team.

Carers will be screened on the basis that the patient they care for is otherwise eligible to participate pending the willingness of a carer to take part in the study with them. Carers must be able to communicate sufficiently well in English so as to complete the proxy primary outcome measure which is validated in the English language. This will be established by discussion with the carer and the patients' clinical care team.

A screening form will be completed for all patients who screen positive for delirium as part of standard care and are aged over 65 years old. Screening forms will record anonymised patient demographic data (age, sex, ethnicity) so as the patient population can be described, eligibility, whether or not eligible patients were approached, whether the approach was by proxy, and if the patient (direct or by proxy) and carer consented. Reasons for ineligibility and declining consent will be recorded where applicable. Personal identifiable data will not be recorded on screening forms, instead a unique screening number will be assigned.

7.2. **Payment**

No payments will be made to patient or carer participants for their participation in the study. Patient and carer participants will be reimbursed travel and parking expenses for follow-up visits which take place at the acute Trust hospital.

Healthcare professionals will not receive any payment for taking part in the qualitative process evaluation study.

7.3. **Consent**

All participants will be required to give informed consent, either directly or in accordance with relevant legislation for conducting research with patients who lack the capacity to provide informed consent.

The study will recruit both patients who have the capacity to provide informed consent and patients who lack capacity to provide informed consent. This protocol respects and adheres to The Mental Capacity Act 2005 and the Adults with Incapacity (Scotland) Act 2000. Recruitment of patients who lack capacity to provide informed consent is justified as the intervention is designed for people with delirium, a condition which impacts on a person's mental capacity. As delirium is a condition which presents in many forms, some patients will be less severely affected than others meaning some may have capacity to understand and retain information about participating in the research while others may not.

We aim to be inclusive in recruiting to this study. Funding is available to provide translation services where required. Further, if any patients or carers struggle with reading, which is not uncommon in people with delirium and dementia, the participant materials can be read out to them by a member of the research team or a family member/friend as appropriate.

7.3.1. **Consent for patient participants**

All potential participants, irrespective of their mental capacity, will be provided with written information about the study in the form of a participant information sheet. The information sheet will contain a simplified summary cover page giving brief details of the study, with an invitation to read the full study details if interested. However, the written materials are just one part of the information delivery. The conversation had between the patient, family members and research staff are of significant importance.

Patients will be assumed to have the capacity to make a decision about participation until it is determined by an experienced researcher/healthcare professional that they do not have capacity.

The researcher will determine that the patient is able to:

- understand the purpose and nature of the research
- understand what the research involves, its benefits (or lack of benefits), risks and burdens
- understand the alternatives to taking part
- be able to retain the information long enough to make an effective decision
- be able to make a free choice
- be capable of making this particular decision at the time it needs to be made (though their capacity may fluctuate, and they may be capable of making some decisions but not others depending on their complexity)

If a patient has capacity to provide informed consent to take part in the study, the researcher will discuss the study with them in full and answer any questions they may have. The patient will be given as much time as they need to consider the study and discuss it with their family and/or friends. If they are willing to take part the researcher will provide the patient with a paper consent form and discuss each of the consent statements with them so as they are fully aware of what they are agreeing to. If the patient still agrees to take part they will be asked to sign the consent form and the recruiting researcher will countersign the consent form. The patient will be given a copy of the signed consent form to keep, a copy will be filed in the patients' medical notes and a copy will be filed in the investigator site file.

If a patient is deemed to lack the mental capacity to make a decision about participation in the study, the researcher will talk them through the study to provide a level of information appropriate to the patient where applicable. The researcher will then contact an appropriate personal consultee/legal representative (the appropriate proxy will be identified according to legislation in England or Scotland) to inform them of the study and provide them with the appropriate participant information sheet. Participant information sheets for consultees/legal representatives will be provided either face-to-face (if able to attend the hospital in person) or by email or post if they are not able to attend the hospital in person, depending on their preference. A member of the clinical care team will make initial contact with the consultee/legal representative to seek permission to share their contact details with the researcher (if the researcher is not part of the clinical care team). After receipt of the information sheet the researcher will discuss the study with the consultee/legal representative in full either face to face or over telephone or video call, depending on preference and whether they are able to attend the hospital in person.

Consultees/legal representatives (if appropriate) will be given as much time as they need to consider the study, ask questions to the researcher, other members of the care team and family and friends before deciding whether or not they think the patient would wish to take part.

If a patient or consultee/legal representative has not reached a decision prior to hospital discharge they will be categorised as 'no decision given'.

Written informed consent will be obtained by the researcher from all patient participants who have the capacity to give consent. For patients who lack capacity to give informed consent, a written account will be taken of any verbal or non-verbal communication that determines their willingness to participate. An opinion on the patients' wishes to participate will be obtained from a personal consultee in writing if in person, or by electronic consent (eConsent; REDCap Academic (see section 10.1) or postal consent depending on the consultees' preferences.

For patients recruited in Scotland who lack capacity, written informed consent will be obtained from a relative/welfare guardian in person or by electronic consent (eConsent) or postal consent depending on the consultees' preferences.

If a participant who enrols in the study through a consultee/legal representative appears distressed by taking part in the study they will be withdrawn with no prejudice to their care.

7.3.2. Change in capacity to consent during the trial

If during the 6-month study period a patient participant regains capacity to give informed consent, a researcher will give or send the participant a participant information sheet and consent form, with a covering letter to explain that they were enrolled in the study and what stage they are at. The researcher will discuss the study with them either face-to-face or by telephone/video call. Written informed consent (either face to face or postal consent) will be obtained from the participant to affirm their willingness to continue in the study, or the participant will be withdrawn from the study upon their request. This may be obtained on paper if face to face, or by eConsent or postal consent, depending on the participants' preference.

In England, if a patient participant who had capacity upon enrolment loses capacity during the study, the researcher will approach a consultee/legal representative for advice on whether the patient participant would wish to continue in the study. The outcome will be documented on a case report form. In Scotland, the patient participants original consent to participate will be upheld and they will continue in the study unless their carer or other close relative or friend raises and objection. If the participant who lacks capacity appears distressed by their continued participation they will be withdrawn.

If possible, where a participant has withdrawn consent for the intervention, the assessments at 3- and 6-months will still be conducted unless the participant, carer or a healthcare professional specifically requests they be withdrawn from the assessments (see section 7.12).

7.3.3. Consent for carers

Eligible carers will be provided with a carer participant information sheet either face-to-face in hospital, or by email or post (depending on preference) if the carer is not able to attend the hospital (e.g., due to COVID-19 restrictions). The researcher will discuss the study with the carer face-to-face or by telephone/video call and will answer any questions, giving the carer as much time as they need to consider participating in the study. If a suitable carer cannot be identified or is not willing to consent to the study the patient participant will not be eligible and consent will not be sought.

Carer participants will provide written informed consent if in person, or by eConsent or postal consent (depending on preference) if unable to attend the hospital.

It is essential that carer participants have mental capacity throughout the study due to the proxy data collection requirements. If a carer participant loses mental capacity during the study, they will be withdrawn in full and a replacement carer will be sought. If a replacement carer cannot be identified or one is not willing to consent to participate, the patient participant will be withdrawn from the study.

7.3.4. Additional consent considerations

Consent will be sought from patients and carers for participation in the embedded qualitative process evaluation. Participation in the process evaluation is optional and declining participation will not affect a participant's ability to take part in the main intervention study.

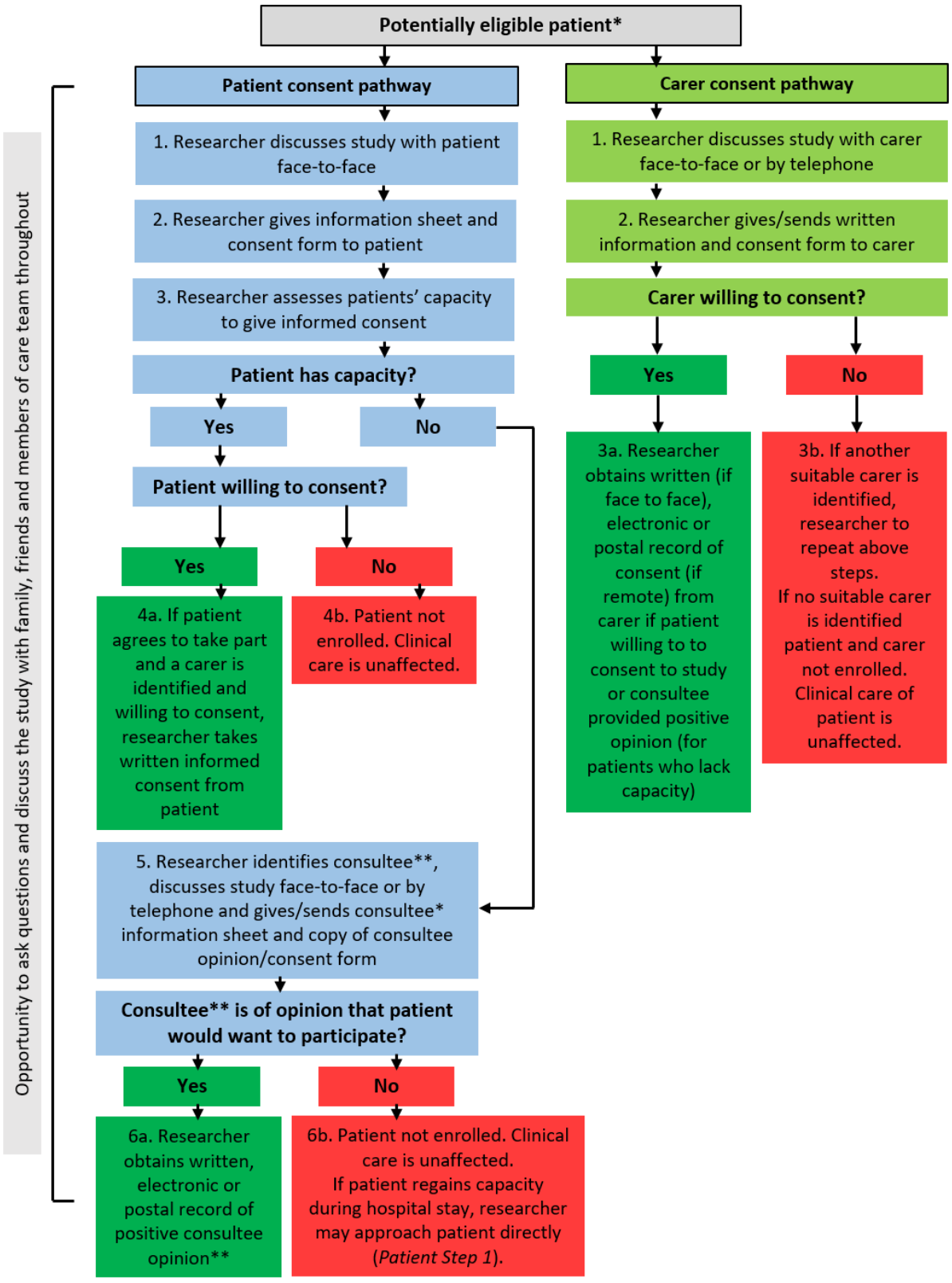
To assess fidelity to the intervention, a sample of 15-20 intervention sessions will be audio-recorded. Consent will be sought from patient and carer participants for this. Audio-recording of intervention sessions is optional and declining consent will not affect a participant's ability to take part in the main intervention or the process evaluation. Both the patient and carer participant must consent to audio-recording of an intervention session. If one member of the patient/carer pair does not consent then they will not be selected for audio-recording of an intervention session (see section 7.6).

Carer participants may also be the personal consultee/legal representative for the patient participant.

When discussing the study with patients, researchers will follow COVID-19 infection control measures according to NHS Trust guidelines. COVID-19 positive patients will not be excluded from the study but consent and the baseline research assessment will not take place until the patient is no longer infectious.

Signed original consent/declaration of opinion forms will be filed at sites according to local Trust policy.

See Figure 2 for a summary of the patient and carer consent pathways.



* Potentially eligible as patient only eligible if eligible carer identified and willing to participate
**Consultee applies to England only. In Scotland the study will be discussed with a nearest relative/welfare guardian who, if willing, will give proxy-consent for the patient to take part in the study

Figure 2 Patient and carer consent pathway

7.4. Baseline assessments and data collection

Baseline data collection and assessments will be undertaken or supported by a clinical researcher (e.g. research nurse or equivalent) who is appropriately trained and authorised to work on the study.

Baseline assessments will be conducted as soon as possible after the patient and carer pair have consented to take part in the study and while the patient is still admitted to the acute hospital. Allowance will be made for patient fatigue following recruitment so if necessary the researcher will return to the bedside after a suitable break.

Assessments and participant-reported outcome measures will be undertaken as shown in Figure 1 and Table 6. The researcher will also support the patient and carer participants to complete self-completed paper questionnaires. Medical history (from medical records), demographics and contact details and preferences will be collected prior to discharge from hospital.

7.5. Intervention

The RecoverED intervention is a manual of rehabilitation activities designed to support recovery from delirium at home. The manual will be used by community rehabilitation staff (physiotherapists (PT), occupational therapists (OT) and RSW)) to design a patient-centred rehabilitation programme for each patient-carer participant pair. The intervention recovery domains and example of intervention activities are shown in Table 4. The intervention will be delivered in the patient participants' home.

Table 4 Intervention domains and example activities

The intervention covers five recovery domains:	Example intervention activities
1. Cognitive	Orientation activities – completing a diary Challenging cognition in function – focus on personalised ADL activities
2. Physical	Personalised physical activity programme. Integration of physical activity into ADL activities
3. Emotional	Delirium education Active listening Phone call to carer to offer support / coaching
4. Physiological/functional	Nutrition and hydration education Fatigue management – principles of pacing activities Washing and dressing practice
5. Social	Regular contact with carer, friends and family Weekly RecoverED intervention sessions -confidence building through activities Identifying barriers to engagement in social activities Signposting to local and relevant groups

Detailed information on rehabilitation activities to support recovery with each domain is provided in the RecoverED intervention manual.

Upon discharge from the acute hospital, the patient may be admitted to either an intermediate care setting (e.g. a care home or community hospital) or a home-based virtual ward for a period of up to four weeks before starting the intervention. If intermediate care continues beyond four weeks the patient and carer participant pair will be withdrawn from the study.

The research team (PI, research nurse or equivalent) should monitor the patients' discharge status, including discharge from intermediate care/virtual ward and notify the community care team who will deliver the intervention when the patient has been fully discharged home. If the intervention will be delivered by a different Trust to the acute Trust, a referral should be made by the acute Trust research team so as the community Trust can review relevant information in the medical notes and initiate the intervention.

The intervention will be initiated with a home assessment visit from a community PT or OT (or equivalent depending on how community rehabilitation is provided by the Trust). The home assessment visit should take place within 2 weeks from discharge from hospital. If this time window is exceeded, the home assessment should still go ahead as soon as possible and a protocol deviation will be recorded. The home assessment visit will take up to 90 minutes and will include:

- assessing the usual care package the patient is already receiving
- assessing the safety of the home environment
- a functional and mobility assessment
- signposting to relevant NHS or local authority services
- reviewing medication and referring to the patients GP if specified medications of concern are identified (therapists will be provided with a list of medications to indicate when GP referral is required)
- providing participants with a recovery record including delirium information sheet
- discussion regards goals and a brief summary of the intervention

A proforma will be completed by the PT/OT at the home assessment visit to record the patient participants' current abilities, impairments and personal goals so as the intervention can be tailored to their individual needs. The chosen interventions will be discussed and agreed with the patient and carer ensuring they are both informed regards the structure of the intervention programme. Both the patient and the carer participants should be present at the home assessment visit.

The PT/OT will review the proforma with a RSW to plan the details of the intervention sessions around the patient participants' needs and goals. The RSW will deliver up to 10 home intervention sessions over 12 weeks post the home assessment visit. As the intervention is patient-centred, some participants may require fewer sessions. The frequency of the 10 sessions will be determined by the PT/OT and RSW depending on the participants' needs. Each intervention session will take up to 60 minutes but will be tailored around the individual to account for different abilities and fatigue (e.g. some sessions may take less time). The activities planned for each intervention session will be purposefully selected from the intervention manual. The carer should be present at intervention sessions but, pragmatically this may not always be possible so sessions are permitted to proceed without the carer participant if it is safe to do so.

See Table 5 for a summary of the intervention delivery.

Participants' will be provided with a paper-based recovery record to keep for the duration of the study. The recovery record will be used by the RSW and the participants to plan and record activities and keep a time line of their progress. Use of the record by participants between sessions will be optional. The record will not be collected by the research team or used in the data analysis for the study.

Approximately half way through the intervention period, the PT/OT may accompany the RSW during an intervention session to review the patient participant's progress and discuss their goals with the patient and their carer to see if any changes to the planned intervention are required.

The PT and/or OT and RSW will manage any safe guarding issues identified at the visits according to their NHS Trust policy. If a participant is found to be unwell during a visit, or in communication with the participants, standard NHS procedure will be followed and emergency support will be sought if necessary. Participant safety will always be prioritised over providing the intervention.

If a patient is re-admitted to hospital during the 12-week intervention period they will remain on the same intervention timeline, e.g. if a patient is admitted to hospital for two weeks, the 12-week intervention period will not be extended by two weeks. Planning and/or re-arranging intervention sessions will be managed pragmatically, with the safety and wellbeing of the patient participant being prioritised. If a participant-pair are unable to complete any or all of the intervention for any reason, including re-admission to hospital or severe acute illness, they will be retained in the study for follow-up unless they specifically opt to withdraw.

7.5.1. **Intervention training and support**

The core study team OT and PT will deliver a comprehensive intervention training package to the OTs, PTs and RSWs who will be delivering the intervention (the intervention delivery team). The training will be delivered flexibly online. To accommodate for differing learning styles a training booklet and resources, including the intervention manual, will be shared with individuals beforehand to allow for prior reading. Training sessions will be recorded and made available to the intervention delivery team at the site.

Intervention delivery review sessions will be offered to the intervention delivery teams on a 6-weekly basis (allowing flexibility for leave and seasonal holidays). Review sessions will be provided by the core study team OT, PT and qualitative researcher.

The initial intervention training package will take approximately eight hours. Depending on the individual site capacity and preference, it may be delivered over one session or multiple shorter sessions. The intervention review sessions will take approximately eight cumulative hours per site over the course of the intervention delivery period. Throughout the study the core OT, PT and members of the SMG will be available to the intervention delivery teams for ad-hoc support. This supervision will be specific to the study and is in addition to usual clinical supervision delivered in the workplace. We will deliver appropriate training to new staff who come on board during the study as required.

Table 5 Intervention delivery summary

Patient discharged home (including from virtual ward)					
What	**Where**	**Who**	**When**	**Number**	**Activities**
Initial home assessment	Patients' home	PT or OT (or equivalent)	Within 2 weeks of discharge	1	• assessing the usual care package the patient is already receiving • assessing the safety of the home environment • a functional and mobility assessment • signposting to relevant NHS or local authority services • reviewing medication and referring to the patients GP if specified medications of concern are identified (therapists will be provided with a list of medications to indicate when GP referral is required) • providing participants with a recovery record including delirium information sheet • discussion regards goals and a brief summary of the intervention
Rehabilitation session	Patients' home	RSW	Over 12 weeks post-home assessment. Session frequency determined by patient need.	Up to 10	See intervention manual for details. Activities to be planned by PT/OT and RSW to meet the individual patient/carer needs.
Midway review	Patients' home	PT or OT and RSW	Approximately half way through the	1 (to be incorporated into one of the	Review of goals with patient and carer participants.

			intervention period	rehabilitation sessions	

7.6. Intervention fidelity

Healthcare support workers delivering the intervention will complete a case report form (CRF) at each intervention session to document the activities undertaken by the participant, any issues with completing the session and the time spent undertaking the intervention.

In addition, a purposive sample of 15-20 intervention sessions will be audio-recorded by the healthcare support worker using an encrypted audio-recorder. We will aim to include intervention sessions across all sites in the sampling. We will aim to record sessions from patient participants both with and without dementia and across a range of different intervention activities (i.e. a sample of physical activity, cognitive activities and talking therapy sessions). As this is a feasibility study, the qualitative research team will develop the purposive sampling method as part of the study and may revise it during the study. The qualitative researchers will notify the healthcare support workers when an intervention session should be recorded.

All potential participants will be informed of the option to audio-record intervention sessions in the participant information sheet and in discussions with the researcher during recruitment. Informed consent will be obtained from the patient and carer participants at the time they consent to the main study. Healthcare support workers will be given a short information sheet and consent form via DocuSign to obtain informed consent to audio-record intervention sessions that they deliver. The healthcare support worker will verbally re-affirm the patient and carer participants' consent at the start of the session prior to starting the recording and document the confirmation on the CRF. If either member of the patient/carer participant declines consent to audio-recording of an intervention session, their session will not be recorded.

To protect the confidentiality of other people in the household who are at home but not taking part in the study, the healthcare support worker will advise the patient or carer participants to notify other people in the home of the audio-recording and request that they do not enter the room during the session. If a person does enter the room who has not consented to be audio-recorded, the healthcare support worker will pause the recording and let them know that recording is taking place and only resume recording once the person has left the room.

The healthcare support worker will upload the recording to a secure area of their NHS computer at the earliest opportunity and upload it via secure file transfer to the University of Exeter where it will be stored in a secure SharePoint folder with restricted access. Once receipt has been confirmed by the qualitative research team member and the file checked, the healthcare support worker will be instructed to delete the audio-recording from their computer and the audio-recorder. Audio-recordings of intervention sessions will not be transcribed. The recordings will be used to assess the fidelity of the intervention delivery against a fidelity checklist to ensure treatment fidelity and assess the intervention approach (i.e. to check that it is person-centred). The fidelity checklist will include items such as 'was there a discussion about personal rehabilitation goals'. The audio-recordings will be used to assess the delivery of the intervention by the healthcare support worker, and not to assess whether the participant did the intervention correctly. The audio-recordings will be retained until the analysis is complete at the end of the study, after which point they will be securely deleted. The fidelity checklist data will be entered directly into a secure electronic data capture (EDC) system (REDCap Academic).

7.7. Follow-up

The follow-up schedule will begin from the date of discharge home. Discharge home is defined as being discharged to a private home which could be the patients' own home or that of a family member. If a patient participant is sent home to be cared for on a virtual ward, the follow-up schedule will start from the date the patient is discharged from the virtual ward.

Before organising a follow-up visit, the research nurse (or equivalent) should conduct a check of the records for both the patient and the carer participant to identify any deaths. If the patient is found to have died, it must be reported as a serious adverse event (SAE) following the process in Section 8 and a change in participation status CRF must be completed to withdraw the carer participant from the study. The carer participant should be contacted to let them know they are being withdrawn and ascertain preferences on receiving study newsletters and a copy of the study results (it should not be assumed that the surviving participant would not want to receive the results of the study). If the carer participant is found to have died a change of participation status CRF should be completed for the carer (but should not be reported as an SAE). The research nurse (or equivalent) should contact the patient participant to determine whether they wish to continue with the study. If they do wish to continue, an alternative carer participant must be identified and consented prior to undertaking any study-related activities (see Section 7.12). If the patient participant does not wish to continue, or an alternative carer cannot be identified/consented, a change of participation CRF should be completed to withdraw the patient participant.

The research nurse (or equivalent) from the participating site will contact the patient or carer participant (based on best judgement and capacity of the patient participant or prior agreement of who will be the main point of contact) to organise a convenient time and date and location (participants' home or the acute hospital Trust) for the follow-up visit. Contact will be made using the standard Trust procedure for booking research visits. The research nurse (or equivalent) will remind the patient or carer participant (whoever the primary contact is) of the visit prior to attending the home. Verbal confirmation of continued consent will be obtained prior to data collection.

Before or shortly after the visit, the research nurse (or equivalent) will check the patients' medical records for details of reportable serious adverse events and report them as described in section 8.2.

A research nurse (or equivalent) will either visit the patient and carer participant pair in their home, or arrange for them to attend the hospital 3 months and 6 months post-discharge to conduct the assessments shown in Table 6, support the collection of participant-reported outcome data and ask the patient and the carer if the patient has experienced any reportable SAEs.

The allowed visit window for follow-up visits is ± 2 weeks for both 3 and 6 month follow-ups.

The research nurse (or equivalent) and participants will complete pseudonymised paper CRFs and questionnaires which the research nurse (or equivalent) will return to the hospital (if visit conducted in participants' home) for data entry into the EDC system.

Research nurses (or equivalent) will be expected to follow their local Trust policy on lone working. If safe-guarding issues are identified at any time, the research nurse (or equivalent) should follow their local Trust policy in reporting and providing immediate assistance where necessary, e.g. phoning the patients' GP.

7.8. Data collection

Data collection will include all the items detailed in Table 6. Anonymised screening data including age, sex, ethnicity, eligibility and reason for declining consent (if applicable) will be collected on all patients who are aged >65 years old and screen positive for delirium during hospital admission as part of standard care. Screening forms will be completed at the hospital site and filed at the site in the local investigator site file or according to local Trust policy.

Data will be collected on all consented participants from medical records on to a paper CRF, by researchers completing paper assessment CRFs and by patient and carer participants completing paper questionnaires (Table 6). Baseline data will be collected at the hospital sites and filed in participant CRF folders. Data will be transcribed into a secure web-based EDC system (REDCap; see section 10.1) by the researcher at the acute Trust.

Source data will be the original occurrence of the data item.

During intervention sessions in participants' homes, data will be collected on to paper CRFs to record planned and actual intervention activities. Pseudonymised intervention data CRFs will be posted to Exeter CTU for data entry into the EDC system. Paper records will be filed in a locked filing cabinet in a room with controlled access.

Patient and carer participants will complete the follow-up assessments either in the patients' home or at the acute hospital Trust with the assistance of a researcher (research nurse or equivalent). Assessments will be in the form of paper questionnaires completed by the patient and the carer, and CRFs that the researcher will complete. Pseudonymised paper forms completed in the home will be transported back to the hospital site by the researcher and entered into the EDC system.

Serious adverse event data will be obtained from medical records and entered directly into the EDC system.

Personal identifiable information will not be collected on the paper questionnaires or CRFs (with the exception of the CRF recording contact details and preferences), instead questionnaires and CRFs will be pseudonymised with the participant's unique ID code and initials.

Audio-recorded data will be collected from interviews for the process evaluation and the sample of intervention sessions. Process evaluation interview recordings will be transcribed by a third party provider based in the UK (Victoria Pink) and both files (the audio and the text transcription) will be stored securely at the University of Exeter. Audio-recordings of intervention sessions will not be transcribed. Audio files will be stored securely at the University of Exeter.

Personal identifiable data (name, NHS number (patient only) address, and email address) will be collected from consented patient and carer participants on to a paper CRF and entered into a separate area of the EDC system, with access restricted to only authorised members of the University of Exeter research team who need to use the data. This data will be used to send regular participant newsletters (optional), the end of study results summary (optional), conduct monitoring and for the qualitative researchers to contact participants who have consented to be contacted about an interview. Recruiting NHS Trusts will also use the information to securely refer the participants to other NHS service providers involved in delivery of the study if applicable to the site.

7.9. Study assessments

Table 6 Data collection and schedule of assessments

		Enrolment	Baseline	Intervention	Follow-up	
		Patient in hospital		Patient at home/hospital		
No.	TIMEPOINT	$-t_1$	t_0	t_1. t_{14}	$3m^5$	$6m^5$
	ENROLMENT:					
1	***Clinical delirium diagnosis[1]*** *(P)*	X				
2	***Eligibility screen*** *(P, C)*	X				
3	***Demographics***	X[2] *(P)*	X*(C)*			
4	***Informed consent[3]*** *(P, C)*	X				
5	***Contact details*** *(P, C)*		X			
6	***Medical history (Inc. dementia diagnosis)*** *(M)*		X			
7	***Reason for admission*** *(M)*		X			
8	***Length of hospital stay*** *(M)*		X			
9	***Clinical frailty scale*** *(P/M)*		X			
10	***Charlson comorbidity index*** *(M)*		X			
11	***Illness severity (APACHE II)*** *(M)*		X			
12	***Discharge destination*** *(P)*		X			
	INTERVENTION:					
13	***Rehabilitation intervention[4]*** *(P, C)*			X		
	DETAILED DELIRIUM ASSESSMENT:					
14	***4-AT***		X		X	X
15	***DSM-5*** *(P)*		X		X[5]	X[5]

16	***OSLA*** *(P)*		X		X[5]	X[5]
17	***MDAS*** *(P)*		X		X[5]	X[5]
	ASSESSMENTS /PROMS:					
18	***Mini-ACE*** *(P)*				X[6]	X[6]
19	***Digit span*** *(P)*		X		X	X
20	***Proxy DAD (ADL)*** *(C)*		X		X	X
21	***Proxy DEMQOL*** *(C)*		X		X	X
22	***Proxy RUQ*** *(C)*		X		X	X
23	***DEMQOL*** *(P)*		X		X	X
24	***Identity self-continuity*** *(P)*		X		X	X
25	***Verbal fluency*** *(P)*		X		X[7]	X[7]
26	***Timed up and go (TUG)*** *(P)*		X		X	X
27	***Patient EQ-5D-5L*** *(P)*		X		X	X
28	***Carer EQ-5D-5L*** *(C)*		X		X	X
29	***Patient ICECAP-O*** *(P)*		X		X	X
30	***GDS-4*** *(P)*				X	X
31	***Proxy EQ-5D-5L*** *(C)*		X		X	X
32	***Proxy-IQCODE*** *(C)*		X			
33	***Carer ICECAP-A*** *(C)*		X		X	X
34	***Zarit Burden Interview-12 (C)***		X		X	X
35	***I-AGeD*** *(C)*				X	X
36	***Residence*** *(P)*				X	X
37	***Serious adverse events*** *(M)*		→			

	QUALITATIVE RESEARCH:					
38	***Interview*** *(P, C)*			X[8]		
39	***Intervention audio-recording*** *(P, C)*			X[9]		

[1]Standard care
[2]Anonymised data prior to consent
[3]Informed consent or proxy equivalent as appropriate to England or Scotland regulations
[4]Includes initial home assessment within 2 weeks of discharge home. Delivered in participant's private home with a support worker, dose up to 10 sessions across 12 weeks after the initial home assessment
[5]Completed only if evidence of persistent delirium if 4AT score ≥4 at visit
[6]Mini-ACE completed only if 4AT score <4 at follow-up visit
[7]Completed as standalone item if mini-ACE not completed at visit (see footnote 6 above)
[8]One-off interview to be conducted face-to-face-, online or by telephone with a sample of 15-20 participants/patient-carer pairs and 20-24 healthcare professionals shortly after the end of the intervention.
[9]A sample of 15-20 intervention sessions will be audio-recorded to assess fidelity of the delivery of the intervention.
P = patient, C = carer, M = medical records, 3m = 3-month follow-up, 6m = 6-month follow-up, $t_{(week)}$ = time point in weeks

Participant-reported outcome measure booklets will include the following content. The type of content should be made clear to the patient and carer when collecting the data so as they understand what kind of data is going to be collected and the reason for it.

Patient reported outcome booklet

EQ-5D-5L: this is a 5-item measure of general health and wellbeing. The domains include Mobility, Self-Care, Usual Activities, Pain/Discomfort and Anxiety/Depression.

ICE-CAP-O: this is a measure of quality of life. The sections include Love and Friendship, Thinking about the Future, Doing things that make you feel valued, Enjoyment and pleasure and Independence.

GDS-4: this is a short 4-question questionnaire on life satisfaction and feeling afraid or happy.

Carer-reported outcome booklet

Proxy EQ-5D-5L: as above but the carer completes the questionnaire based on how they believe the patient feels.

IQCODE: this is a questionnaire that the carer completes about the patients' memory and their ability to make everyday decisions just before their admission to hospital compared to 10 years ago.

I-AGeD: this questionnaire asks the carer about things they've noticed with regard to the patients' memory and attentiveness over the last few days.

EQ-5D-5L: as above, but with the questions asked of the carer themselves.

ICE-CAP-A: this is a measure of the carers quality of life. The sections include Feeling settled and secure, Love, friendship and support, Being independent, Achievement and progress and Enjoyment and pleasure.

Zarit Burden Inventory-12: this questionnaire asks for the carers views on caring for another person. Some of the questions are of a sensitive nature. The carer participant must be assured that their answers will be confidential and not shared with the patient participant.

Interviewer-led outcome booklet

DAD-ADL: this is a proxy-reported measure of the patient participants' ability to carry out every day activities (e.g. hygiene, dressing, meal preparation).

Proxy DEMQOL: this questionnaire asks for the carers view on the patient participants' feelings, memory and everyday life.

Resource use questionnaire: this questionnaire is for the collection of data on number and type of healthcare visits and the use of social care and community organisations.

DEMQOL (patient): this questionnaire asks for the patient participants' view of their own feelings, memory and everyday life.

Identity self-continuity: this is a single question measure of how well the patient participant feels like their self.

Patient and carer participants should be advised to keep their answers confidential from each other unless they expressly wish to share them as some of the content could be sensitive.

7.10. Embedded qualitative process evaluation

Patient and carer participants and professionals will be invited to take part in an embedded qualitative process evaluation (interview study). All patient and carer participants will be eligible to take part. Professionals will be eligible if they are providing care to participants in the study and have the capacity to provide informed consent. Professionals could include occupational therapists, physiotherapists, rehabilitation support workers, clinical psychologists, social workers, social care staff and service managers.

Patient and carer participants will give informed consent for the interview study at the time of consenting to the main feasibility study. They will still be able to participate in the main study even if they decline participation in the interview study. Professionals will be sent a participant information sheet and informed consent form electronically using DocuSign provided through the University of Exeter. Consent will be verbally reaffirmed just before the interview is conducted

In-depth, semi-structured, face-to-face, online or telephone qualitative interviews will be conducted with 15-20 participant/participant-carer pairs. Semi-structured online or telephone interviews will be conducted with 20-24 professionals in three participating sites. Participant/carer interviews will be conducted shortly after the intervention to avoid Hawthorne effects. Participants will be purposively sampled to include those with and without a dementia diagnosis, individuals living in both rural/urban areas and areas with a range of socioeconomic profiles, and those from black, Asian and minority ethnic (BAME) backgrounds. Professionals will be sampled to include the range of roles involved in planning and delivery of services. This will include those working across the boundaries of health and social care, and also commissioners and managers in order to inform the potential scalability of the intervention.

Interviews will be conducted by a research associate/fellow appropriately trained in working with vulnerable adults. Interview topic guides developed by the research team and approved by an NHS research ethics committee will be used to guide the interviews. Interviews will be recorded using an encrypted audio digital recorder. Participants will be interviewed once for up to 60 minutes, with breaks if necessary.

Interviews will explore acceptability, participant responses to the intervention, views about the optimal dose of the intervention, and contextual factors affecting the intervention, in order to refine the programme theory developed previously and to inform the design for the definitive RCT. Interviews with professionals will also collect data on implementation, to include the following aspects: diversity of population reached by the intervention (reach); factors affecting fidelity of delivery; delivery of the intervention at the interface with social care; organisational and contextual factors affecting services in the different sites; and potential scalability of the intervention [56]. Reach and dose will also be monitored through trial records, and fidelity of delivery will be measured through audio recordings of 15-20 intervention sessions using a fidelity checklist.

Interviews will be fully transcribed, either by a member of University of Exeter staff or an approved transcription company, and uploaded to NVivo 20. The transcription company will have a data sharing agreement, to ensure the confidentiality of data provided by participants and to ensure any data or transcripts are transferred between the company and University of Exeter securely.

Qualitative data will be analysed using a combined realist analysis and thematic analysis approach, with QSR Nvivo 20. It will draw on theoretical perspectives such as normalisation process theory,

boundary work theory or negotiated order theory, depending on the development of themes. The findings will also be compared between participants with and without a dementia diagnosis, considering whether the interventions are relevant and acceptable to people in each group and whether the primary outcome is relevant to people without dementia and across a range of socioeconomic profiles, and those from BAME backgrounds. The intervention, study population and trial procedures will be refined by the research team following review of the findings from WP2, including the process evaluation, and the manuals will be revised as necessary.

A subset of quantitative data (e.g. previous or new dementia diagnosis) will be analysed using descriptive statistics. Qualitative and quantitative process evaluation findings will be integrated using a triangulation strategy [57]. The suitability of the intervention for people without dementia will be explored to determine whether to include people without dementia in the definitive trial. PPI panel members will be invited to contribute to process evaluation data analysis during discussions of themes and/or data triangulation.

Each participant will be assigned a unique ID code and interview transcripts will be pseudonymised prior to analysis. Data will be stored on password protected secure University of Exeter servers and accessed only by authorised members of the research team. Data will be archived for a period of 5 years after the end of the study. After 5 years the data will be fully anonymised and retained indefinitely for future ethically approved research.

7.11. Economic evaluation

This feasibility study will be used to test the methods for a subsequent, policy-relevant, cost-effectiveness analysis (CEA) of the rehabilitation intervention, compared to usual care. This future economic evaluation will be undertaken alongside the definitive RCT and will: (i) establish the resources required to provide the intervention, (ii) estimate intervention costs, and (iii) conduct a full CEA. The intervention costing and CEA, based on within-trial data collection, will be undertaken against a primary perspective of the NHS/Social Care, with participant and broader societal perspectives considered in sensitivity analyses. The future CEA will synthesise cost and outcome data to present an incremental cost-effectiveness ratio (ICER) for the primary economic endpoint of policy relevance (cost per quality-adjusted life-year [QALY]).

For the purposes of the feasibility study, the economic analysis will describe mean incremental costs and mean incremental effects, presenting disaggregated costs and consequences in a tabular format. Methods will be trialled for capturing: i) the resources required to deliver the intervention; ii) health, social and wider care service resource use; iii) health economic outcomes relating to health-related quality of life and capability wellbeing.

7.11.1. Intervention resource use

The resources required to deliver the intervention will be assessed via participant-level case-records, and discussion with the intervention developers and providers. This is expected to include staff time (e.g., OT, PT, RSW), travel, training, supervision and materials. Staff time will be documented in terms

of per-participant contact and non-contact time, and any additional time required for delivery of the intervention.

Nationally recognised UK unit costs for health and social care services will be applied to this resource use data [58]. Where national costs are not available, costs will be identified in consultation with the intervention developers and providers. The mean cost per participant of the intervention will be estimated.

7.11.2. Health, social care and wider resource use

Data on the use of health, social care and wider resources will be collected via a proxy Resource Use Questionnaire (RUQ) bespoke for this population. The RUQ will be designed in collaboration with the PPI group, and areas of social care service and resource use and own expenses will be specifically explored. Items from the 'CORE Items for a Standardized Resource Use Measure (ISRUM)' will be included in the RUQ, which will also draw on measures in the Database of Instruments for Resource Use Measurement for this/related populations [53, 54]. The questionnaire will be completed by participating carers at baseline and 3-month and 6-month follow-ups. Recall at 3 and 6 months will be considered with the PPI group, who will advise on the design of questions to aid recall, maximise response rates, and minimise missing data.

The feasibility study will provide the opportunity to test the RUQ, to explore the extent of missing data, and to modify it as required. Descriptive statistics (mean, standard deviation, range) will be provided for each category of resource use (primary care, secondary care, social care, other services, patient out-of-pocket expenses, carer out-of-pocket expenses, etc) and for each perspective (NHS/social care, societal).

7.11.3. Health economic outcomes

The intended primary economic outcome measure for this study is the EQ-5D-5L [47]. This is a generic measure of HRQL, which is recommended by NICE for use in health technology assessments to estimate the cost-per-QALY of interventions and to inform healthcare policy decisions across the NHS. Patient participants who have capacity and have provided informed consent will be asked to complete the EQ-5D-5L at baseline and at 3-month and 6-month follow-ups. Participating carers will also be asked to complete the EQ-5D-5L Proxy Version 2, on behalf of the patient, at these time-points [59]. This version of the EQ-5D-5L asks carers to rate how they (the proxy) think the patient would rate their own HRQL if the patient were able to communicate it.

HSVs will be derived from responses to the EQ-5D-5L and the EQ-5D-5L Proxy Version 2 using the approach recommended by NICE at the time of data analysis. As of January 2022, the NICE position statement recommends mapping between EQ-5D-5L responses and the published UK health state value set for EQ-5D-3L (an earlier, three-level version of the EQ-5D instrument), using an approved algorithm [48, 60, 61]. Descriptive statistics will be presented for HSVs at each assessment point (mean, standard deviation, range) and for QALYs over the six-month follow-up period, calculated using the standard area-under-the-curve (AUC) approach.

Of relevance to this study are three limitations of the standard approach to economic evaluation, which uses generic measures to gather data on the HRQL experienced by patients [51]: (i) generic measures may not capture all aspects of HRQL that are important to specific patient groups, including people living with dementia [62]; (ii) interventions may have impacts on broader aspects of wellbeing beyond HRQL [63]; and (iii) interventions may have important "spill over effects" on informal carers and other family members [64]. Each of these factors may result in some of the effects of an intervention being omitted, potentially resulting in an incomplete estimate of cost-effectiveness. The feasibility study will be used to assess whether these limitations could be addressed via sensitivity analyses, which would be undertaken in a future full economic evaluation alongside a definitive RCT, in the following ways:

(i) We will assess the feasibility of collecting data from the DEMQOL and DEMQOL-proxy in order to provide a dementia-specific measure of patient HRQL that is suitable for use in economic evaluation. This will involve deriving HSVs from patient and carer responses to the DEMQOL and DEMQOL-proxy using two published and validated indices, the "DEMQOL-U" and "DEMQOL-proxy-U", which have been developed in order to provide HSVs for use in assessing the cost-effectiveness of interventions for people living with dementia [62]. Descriptive statistics will be presented for dementia-specific HSVs at each assessment point (mean, standard deviation, range) and for QALYs over the six-month follow-up period, calculated using the standard AUC approach.

(ii) We will assess the feasibility of collecting data from the ICECAP-O, in order to provide a measure of patient wellbeing that is suitable for use in economic evaluation. This will involve deriving wellbeing values from patient and proxy carer responses to the ICECAP-O using a published and validated index, which was developed in order to enable the cost-effectiveness of health and social care interventions to be assessed in terms of their impact on the wellbeing of older patients or care recipients, beyond the usual remit of HRQL measures [46]. Descriptive statistics will be presented for wellbeing values at each assessment point (mean, standard deviation, range) and for WALYs over the six-month follow-up period, calculated using the standard AUC approach.

(iii) We will assess the feasibility of collecting self-reported data from informal carers using the EQ-5D-5L and the ICECAP-A, in order to derive HSVs and wellbeing values for carers. Carer HSVs will be derived from responses to the standard UK version of the EQ-5D-5L using the approach recommended by NICE at the time of data analysis, as described above. Carer wellbeing values will be derived from the ICECAP-A using a published and validated index similar to that for the ICECAP-O [65]. Descriptive statistics will be presented for carer HSVs and wellbeing values at each assessment point (mean, standard deviation, range) and for QALYs and WALYs over the six-month follow-up period, calculated using the standard AUC approach. Consideration will be given to proposed methods for the incorporation of carer effects alongside patient effects in economic evaluation [64, 66].

7.12. Withdrawal and change of participation status

Participants have the right to withdraw at any time during the study without prejudice to their care. In addition, a patient participant may be withdrawn in good faith at the request of a carer or healthcare professional if they feel it is within the best interest of the patient, e.g., if a patient participant shows signs of distress from participating in the study. Participant pairs will also be withdrawn by a healthcare professional if prior to their discharge from their acute admission, their circumstances change and the patient will no longer be discharged to a private dwelling and will instead be discharged to a residential/nursing home on a long-term basis (an interim stay of up to 4 weeks in intermediate care will be permitted).

Patient participants will be able to flexibly change their participation in the study by selectively ceasing any or all of the following aspects:

- The intervention
- One or both follow-up assessments
- Passive data collection from medical records (except where required for reporting of serious adverse events)
- The embedded qualitative process evaluation (interview study), if applicable
- Audio-recording of an intervention session, if applicable

Patient participants who withdraw consent to the intervention prior to collection of baseline data will be fully withdrawn from the study and no further data will be collected. In this event their carer pair will also be fully withdrawn.

Any withdrawal or change of participation status will be documented in the individual CRF.

If a patient participant withdraws from the intervention and follow-up, passive data collection from medical records will continue unless expressly requested to stop by the patient (or their carer/consultee in the event that the patient lacks capacity). Follow-up data will continue to be collected from the carer if they are still willing to participate without the patient. In the event the carer wishes to continue, the withdrawn patient participant will be asked if they are willing to allow their carer to complete the proxy-reported outcome measures. If the patient does not agree, the carer will only be asked to completed the carer-reported outcome measures and will not complete any proxy-reported outcome measures.

If a carer participant withdraws from the study at any stage and the patient participant wishes to continue with the study, another eligible carer will be sought for consent to participate and they will continue in the study in place of the original carer. Only one carer participant can take part with the patient at any one time so if a carer withdraws from the intervention or follow-up they will be fully withdrawn and a new carer participant will be sought.

If one of the patient/carer pair did not consent to, or withdraws consent from the process evaluation (interview study), but the other member of the patient/carer pair did consent, the non-consenting/withdrawn individual will be asked if they agree to the consenting individual discussing them during their interview. If the non-consenting/withdrawn individual does not agree, the consenting individual will not be interviewed.

If both the patient and carer pair had initially consented to audio-recording of an intervention session and then one of the pair withdraws consent from that aspect of the study, audio-recording of an intervention session will not take place, even if the other party still consents.

Allowing flexibility in participation status will protect the rights and wellbeing of the participants while maximising the opportunity to collect important outcome data and limit research waste.

All data collected up to the point of withdrawal will be retained and used in the analysis, including audio-recordings and transcriptions.

If a participant becomes uncontactable and stops engaging with the study they will be deemed ‘lost to follow-up’. Passive data collection will continue until the participant expressly indicates they wish to withdraw.

All participants who withdraw or change their participation, or who are lost to follow-up, will still have the option to receive information about the study, including newsletters and end of study results unless they opt not to receive them.

Healthcare professionals can withdraw from the process evaluation or opt out of audio-recording and intervention session at any time prior to the interview/audio-recording taking place by notifying the qualitative researcher at the University of Exeter.

7.13. End of trial

The study will end once the last 6 month follow-up assessment is complete, all data have been recorded in the study database, the data have been cleaned and the database locked. A declaration of end of study form will be submitted to the NHS REC who awarded the favourable opinion within 90 days of the end of study.

If the study is terminated early, the study will end on the date the Sponsor formally declares the study terminated in writing. The main NHS REC will be notified of early termination within 15 days of the Sponsor deciding to end the study.

Safety

8.1. Definitions

Term	Definition
Adverse Event (AE)	Any unintentional, unfavourable clinical sign or symptom, or any new illness or disease or the deterioration of existing disease or illness.
Serious Adverse Event (SAE)	A serious adverse event is any untoward medical occurrence that: • results in death • is life-threatening • requires inpatient hospitalisation or prolongation of existing hospitalisation • results in persistent or significant disability/incapacity Other 'important medical events' may also be considered serious if they jeopardise the participant or require an intervention to prevent one of the above consequences. NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.
Related and Unexpected SAE (RUSAE)	A related and unexpected SAE is an event with is related to the intervention; and 'unexpected' – that is, the type of event is not listed in the protocol as an expected occurrence.

8.2. Recording and reporting of AEs, SAEs, AND RUSAEs

This is a low risk intervention study in an older population who are expected to experience acute illness resulting in hospitalisation, development of new medical conditions and deterioration of existing medical conditions. To reduce excessive unnecessary data collection and burden on hospital staff, and reduce the amount of sensitive patient data that is collected for research purposes, we are taking a risk-proportionate approach to the collection and reporting of safety data. We will only be recording and reporting safety data for the patient participants.

Adverse events (AE)

Non-serious AEs will not be recorded or reported for the study. The justification for this is safety of the intervention is not an outcome measure, the intervention is very low risk (as identified with a risk assessment) and the individual components of the intervention are not novel in this patient population.

Serious adverse events (SAE)

All deaths (from any cause) and hospitalisations due to falls, fractures or musculoskeletal injury will be recorded. Other SAEs will not be recorded or reported. Only SAEs that are categorised as related to the intervention will be subject to expedited reporting. See Figure 3 for the safety reporting pathway.

Causality of reportable SAEs will be assessed by the site PI (or authorised delegate). All SAEs which are possibly, probably or definitely related to the intervention will be categorised as 'related'. If the PI or delegate is unable to assign causality within 24 hours of the site becoming aware of the event, the SAE will be treated cautiously and subjected to expedited reporting.

Related unexpected serious adverse events (RUSAE)

Death is an unexpected event. Deaths related to the intervention will be categorised as RUSAEs and subjected to expedited reporting as shown in Figure 3.

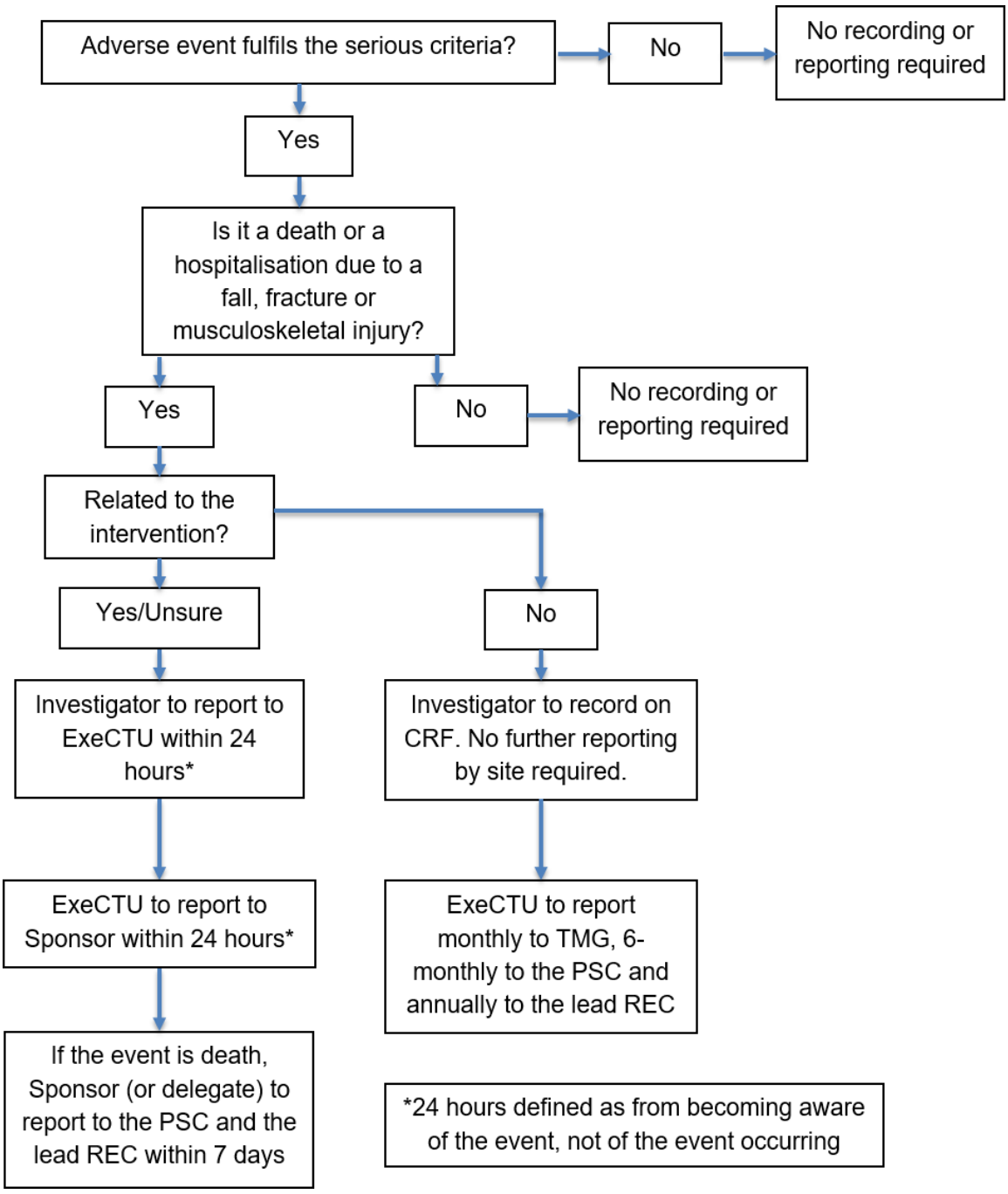


Figure 3 Safety reporting flow diagram

8.3. Responsibilities

Authorised members of the site research team will review the patient participants' medical records before each 3-month and 6-month follow-up time-point (even if the visit does not go ahead, e.g. due to withdrawal from follow-up or re-hospitalisation) and record all events that are reportable SAEs in the study EDC system. Research nurses (or equivalent) conducting follow-up visits will also ask participants if the patient has had a reportable SAE.

Principal investigators (PI) or their authorised delegates will be responsible for using medical judgement in assigning severity and causality of the event. PIs (or delegate) will be responsible for recording SAEs in line with the reporting requirements in Figure 3 and entering the data into the study EDC system. PIs (or delegate) are responsible for signing off reportable SAEs within the EDC system. This will be a role-restricted task that only authorised users of the EDC can complete.

The chief investigator (CI) or their authorised delegate will review a line listing of SAEs on a monthly basis. RUSAEs will be reviewed within 24 hours. The CI (or delegate) will confirm their agreement or disagreement with the PIs decision on causality. The CI will not downgrade any decisions made by the PI, but may upgrade them. Any disagreements will be discussed between the CI, the PI and the Sponsor. The responsibility for final decision making lies with the Sponsor.

The PSC will periodically review SAE data to determine patterns and trends of events, or to identify safety issues, which would not be apparent on an individual case basis.

8.4. Notification of deaths

All deaths will be recorded in the study EDC system. Cause of death will be recorded. Deaths related to the intervention (RUSAEs) will be will be onward reported to the PSC and the lead REC within 7 days of the Sponsor being made aware of the event.

8.5. Pregnancy reporting

Pregnancy is considered very unlikely due to the lower age limit for inclusion being 65 years. If a participant becomes pregnant during their participation in the trial it will not be recorded or reported.

There are no special considerations for children born to, or the partners of, male participants.

8.6. Urgent safety measures

A decision to implement an urgent safety measure (USM) can be made by the Sponsor, CI, PI and/or PSC in the event of identifying an immediate risk to participant safety.

USMs implemented by PIs at sites must be notified to the CI within 24 hours. The CI must notify the Sponsor within 24 hours of being made aware of an USM.

If the CI and the Sponsor consider the USM to affect all participants, all PIs must be informed of the USM.

A protocol amendment will be submitted to the HRA and REC at the earliest opportunity (and within three days) following implementation of the USM. If the USM requires a temporary halt to the study, this will be notified by an amendment.

8.7. Annual report to the REC

An annual report will be submitted to the NHS REC who issued the favourable opinion using the appropriate form provided by the Health Research Authority. As the study will receive a favourable opinion from two RECs (one in England and one in Scotland), the annual report will be provided to the lead REC in England only.

9. Statistics and data analysis

A separate Statistical Analysis Plan (SAP) will be produced by the trial statistician and the lead statistician in collaboration with the SMG. The SAP will be finalised and signed off by the statisticians, the co-CIs and the independent statistician before the database is locked following completion of data collection.

9.1. Sample size calculation

As a single arm feasibility study, the aim of the trial is not to determine the effectiveness of the intervention, but rather to estimate key feasibility parameters to inform the design of a subsequent definitive randomised trial. As a result, no formal power calculation has been undertaken to determine the required sample size. Instead, the aim will be to recruit a total of sixty participants to the study. If the value of key feasibility parameters, such as the follow-up rate and the percentage of participants attending at least 60% of the intervention sessions, is 70%, a total of sixty participants will allow estimation with a 95% confidence interval of 57% to 81%.

9.2. Planned recruitment rate

The study aims to recruit 60 patient participant and carer pairs across 6 acute NHS Trusts in 6 months. Sites will be asked to recruit 10 patient-carer participant pairs each at a rate of 1.7 – 2 per month.

On average we anticipate 60% of screened patients to be eligible, and 60% of eligible patients to consent to participate. On this basis, we will need to screen approximately 185 patients, of which 111 would be eligible and 67 would consent to participate. This would allow for a 10% withdrawal rate for participants whose circumstances change between baseline and discharge from hospital and are not discharged to a private home.

9.3. Statistical analysis

9.3.1. Summary of baseline data and flow of participants

Participant- and carer- level baseline demographic and outcome data will be summarised. Specifically, continuous data will be reported as means and standard deviations, or as medians and interquartile ranges if the data appear skewed. Categorical data will be reported using numbers and percentages. A CONSORT flow diagram will be produced to illustrate the flow of participants through the trial. Specifically, the number of participants approached, eligible, consented and recruited, and assessed at baseline, three months and six months will be illustrated, along with the number of participants withdrawn or lost to follow-up between each data collection time point. The reasons for ineligibility, eligible participants not being recruited, as well as the reasons for withdrawal where available, will also be presented. In order to participate in the trial, both the patient and their carer need to be eligible and willing to consent. As a result, we will also present the ineligibility and unwillingness to participate figures broken down by patient and carer.

9.3.2. Feasibility Outcomes

The feasibility outcomes to be reported as part of this study are:

- The number of people with delirium identified on hospital wards
- The proportion (and number) of people with delirium who meet the eligibility criteria
- The proportion of eligible people with delirium who agree to participate in the study
- The proportion of carers who agree to participate in the study
- The proportion of participating people with delirium who start the intervention
- The proportion of participating people who complete ≥60% of the intervention sessions
- The proportion of participating people with delirium who remain in the study until final follow-up at 6 months
- The proportion of people with delirium providing valid outcome data for each primary and secondary outcome measure at 3 and 6 month follow ups

- The acceptability of the intervention assessed during the process evaluation (assessed using qualitative data)
- The estimated standard deviation and six month follow-up rate for the proposed primary outcome, in order to either verify or inform revision of the proposed sample size calculation for the definitive RCT

Each of the feasibility outcomes will be presented alongside 95% confidence intervals overall (with the exception of the acceptability process evaluation outcome), and separately for participants with and without dementia.

9.3.3. Proposed outcomes for a definitive trial

Part of the purpose of this feasibility study is to assess the completion of the primary and secondary outcomes proposed for the definitive trial. Whilst no inferential analysis or hypothesis testing of any of the outcomes will be undertaken, summary statistics for each outcome at baseline, three months and six months will be presented.

Details of the methods used to derive each of the outcomes will be provided in the SAP.

9.4. Subgroup analyses

As a feasibility study, no inferential subgroup analyses will be undertaken. However, it is of interest to explore the feasibility outcomes separately for participants with dementia and for those without. As a result, each of the feasibility outcomes, as well as the summary statistics for each outcome measure, will be presented overall and according to the presence or absence of dementia.

9.5. Adjusted analysis

Not applicable as this as there will be no inferential analyses

9.6. Interim analysis and criteria for the premature termination of the trial

There are no planned interim analyses or criteria for early termination of the trial.

9.7. Participant population

Summary statistics will be computed for all participants who provide data, regardless of their adherence to or compliance with the intervention.

Adverse event data will be summarised overall and according to whether or not the participant received any “dose” of the intervention (the As Treated population).

9.8. Procedure(s) to account for missing or spurious data

There are no plans to impute missing data before calculation of the summary statistics for any of the proposed outcomes. However, if individual items within an outcome are missing, these may be imputed in line with instrument-specific published guidance or scoring instructions. Further detail will be provided in the SAP.

The degree of missing data for each outcome at each time point will be reported in order to inform the design of a subsequent definitive trial.

Data management

10.1. Data collection tools and source document identification

10.

Data will be collected onto paper CRFs and entered into a secure online study EDC system, with the exception of SAE data which will be recorded directly into the EDC system (source data will be medical records).

In addition to CRFs, transcriptions of audio-recorded material will be saved as source data.

Where data are available from medical records (e.g. demographics, dementia diagnosis) the medical records will be the source data. For all data which are captured directly on a CRF as the first ever recording of the data (e.g. participant-reported outcome measures) the CRF is the source data. Refer to Table 6 Data collection and Assessments for details of data collection and its source.

CRFs will be designed by Exeter Clinical Trials Unit to capture accurate, legible, complete and attributable data. Each CRF will capture the date of completion and name of person completing it. The EDC system forms will be designed to mirror the paper CRFs and maintain a full audit trail of the users entering and amending data. The eCRF will be validated to query data discrepancies and missing data and maintain an audit trail of any data changes.

Investigators at participating sites will retain the paper CRFs and other source documents and transfer data to Exeter Clinical Trials Unit by entering the data into the EDC system.

Screening, consent and baseline data will be completed during the inpatient stay at the participating acute NHS Trust where participants are recruited. Paper CRFs will be stored in a secure area at the Trust and the data transcribed into the EDC system.

The intervention monitoring CRFs and 3- and 6-month outcome measure CRFs will be completed in participants' homes (or at the hospital in the case of follow-up CRFs). CRFs will be pseudonymised to protect the identity of the participants. Paper CRFs completed at 3- and 6-month visits will be transferred to the participating site by the research nurse (or equivalent) where the data will be transcribed into the EDC system. Paper intervention CRFs will be stored securely at the relevant Trust premises and posted to Exeter CTU at the end of the intervention period for data entry into the EDC by an authorised member of the research team.

A separate EDC project will be used to store personal identifiable data (i.e. names, addresses, email addresses, telephone numbers) that will be separate from the research data. Personal data will be collected to facilitate the sharing of newsletters and study results and monitoring of consent forms by

the Exeter CTU trial team and assist with retention and follow-up activities. Access to the contact details will be restricted to individuals authorised by the chief investigator.

All EDC system users will require individual log-in credentials and authorisation from an approved member of the trial management team before access is granted. The EDC system will incorporate role restriction such that individual users will only be able to access and enter or edit data as their individual permissions allow.

The Exeter CTU trial management team will run regular reports for missing data and remind sites at least monthly to enter data that is expected and document any reasons for missing data.

Healthcare professional consent forms will be signed using DocuSign provided by the University of Exeter. The qualitative researcher will have a DocuSign account with secure individual log in credentials that are not shared with other members of the study team. Completed consent forms will be downloaded and saved on a secure server with restricted access. All documents will be deleted immediately from download folders and computer recycle bins.

10.2. Data handling and record keeping

A data management plan (DMP) will be implemented prior to starting recruitment and will be updated throughout the study as appropriate. Working instructions will be provided to the central study team, site teams and intervention delivery teams on record keeping and data entry processes. Electronic systems will be validated, tested and documented before starting recruitment. The DMP and validation documents will be available upon request to the Exeter CTU.

10.3. Access to Data

Access to data held at participating sites will be restricted to those holding a substantive or honorary contract for the Trust or a research passport and who have a relevant purpose to access the data. Access will be granted to authorised representatives from the Royal Devon University Healthcare NHS Foundation Trust as the Sponsor, as well as representatives from the University of Exeter for the purposes of auditing and monitoring the study. Participants will be asked to consent to representatives of the Sponsor or the University of Exeter accessing their data that is relevant to their participation in the study.

Audio-recordings of interviews and intervention sessions will be transcribed and stored on password-protected secure University of Exeter servers accessed only by authorised members of the study team.

Data entered into the EDC system will be accessed by authorised members of the study team at participating sites and at Exeter CTU. Access will be restricted with individual log-in credentials and site and role restriction applied so as individuals can only access data appropriate to their location and role.

10.4. Archiving

The trial master file and EDC system data will be archived following the Exeter Clinical Trials Unit standard operating procedure following authorisation from the Sponsor.

Participating sites will be responsible for archiving their investigator site files, including paper CRFs and consent forms, following their local NHS Trust archiving procedure. Sites will be required to notify the Sponsor of their archiving arrangements.

Study documents will be archived for 5 years after the end of the study. After 5 years, all personal identifiable data will be securely destroyed upon authorisation from the Sponsor. The anonymised dataset will be stored indefinitely for the purposes of future ethically approved research.

Monitoring, Audit & Inspection

11. A detailed monitoring plan will be agreed between the CI, Exeter Clinical Trials Unit and the Sponsor. The monitoring plan will be based on the risk assessment that will be reviewed periodically and in response to amendments to the study protocol.

Monitoring will be conducted by a combination of remote and central monitoring, led by the Exeter Clinical Trials Unit. On-site monitoring will be conducted if one or more triggers are met, as detailed in the monitoring plan, or if concerns are raised by an individual with knowledge of the study.

Sites will be expected to cooperate with remote and onsite monitoring procedures by provision of copies of requested documents in a timely manner and the completion of self-audit checklists. In the case of triggered on-site monitoring visits, sites will be expected to provide a space for the monitor(s) to work on the Trust premises and provide access to all documents requested in the notification of monitoring visit letter. The PI or a delegated member of the study team must be available during on-site monitoring visits. The Exeter Clinical Trials Unit will provide sites with sufficient notice to prepare for a monitoring visit.

The Sponsor and/or regulatory authorities may audit or inspect any aspect of the study, including on-site visits, at any time during the study.

A separate data monitoring committee will not be convened for this study. The PSC will fulfil the role of a data monitoring committee and will review data completeness, data quality and accumulating safety data at agreed intervals throughout the study.

12. A copy of the monitoring plan and risk assessment is available upon request to Exeter Clinical Trials Unit.

Ethical and regulatory considerations

12.1. Research Ethics Committee (REC) review & reports

As a non-CTIMP study involving adults who lack capacity to consent recruiting participants in England and Scotland, the study protocol and supporting documents will be reviewed by both an independent

NHS REC in England and by the Scotland A REC in Scotland. Recruitment will only commence in either country following the issue of a favourable opinion letter in the respective country.

The study will also receive approval from the HRA prior to commencing recruitment.

Details of the favourable opinion of the RECs and the HRA will be added to this protocol as part of the next protocol amendment.

The chief investigator will report to the REC annually and will follow HRA guidance on notifying the REC of the end of the trial and submission of the final report.

12.2. Peer review

This study was reviewed by a panel of independent experts and lay representatives as part of the competitive funding application to the NIHR.

12.3. Public and Patient Involvement

A PPI panel were involved in the identifying the area of research and advising on the design of the intervention during the funding application stage.

Our collaborator, Rachael Litherland, oversees PPI on the study and has convened a group of people with lived experienced of delirium and dementia, including carers, who have given input on the participant facing materials, intervention design, health resource use questionnaire and the study logo. A member of the PPI group joined the expert panel as part of work package 1 to further plan the intervention. Two PPI representatives will be invited to join the trial management group and an independent lay representative sits on the PSC.

The PPI group will meet regularly throughout the study to advise the research team of study conduct and at the end of the study they will be involved in interpreting and disseminating the results. Insights from the PPI group will be essential for iterative revision of the study prior to undertaking the definitive RCT as part of work package 3. The research team will regularly feedback progress with the study to the PPI group, including specific information on how their input has informed decision making.

12.4. Regulatory Compliance

Recruitment will commence at participating sites once the local NHS R&D department has confirmed capacity and capability to deliver the study and signed a model non-commercial agreement with the Sponsor.

The latest HRA guidance will be followed at all times with regard to notification and implementation of amendments at sites.

12.5. Protocol compliance

All staff undertaking research activities outlined in the protocol will be trained prior to commencing work on the trial.

The CRFs and EDC system will be designed to assist in adherence to the protocol by guiding study personnel through the assessments and data collection, as well as reminding staff when follow-ups

are due. The EDC system will also be validated to minimise protocol deviations, e.g. blocking off access to baseline and follow-up form groups if a patient does not meet the eligibility criteria.

Exeter CTU will conduct regular central monitoring of key data items, including consent details and follow-up adherence to identify protocol deviations. Study personnel will be trained to notify the trial manager in the event of a protocol deviation or suspected or actual serious breach. A deviation log will be maintained by Exeter CTU and reviewed regularly by the CI and the Sponsor. Recurrent deviations will be discussed with the study management group and PSC, as appropriate. We will work with study personnel to identify the cause of the deviations and put in place steps to mitigate them, as appropriate.

Rehabilitation support workers will complete a CRF for intervention sessions to record the planned and actual intervention activities undertaken, and any issues arising which prevented the intervention from taking place.

Protocol compliance will be reported at the end of the trial.

12.6. Notification of Serious Breaches to GCP and/or the protocol

A serious breach is a breach that is likely to affect:

(a) the safety or physical or mental integrity of the participants of the study; or

(b) the scientific value of the study

Serious breaches may be identified through routine or triggered monitoring, inspection by the regulatory authorities, by chance or by direct report to Exeter CTU and/or the Sponsor by a member of the study team or other party.

All suspected serious breaches will be notified to the Sponsor by a member of the Exeter CTU study team following Exeter CTU standard operating procedure. Research sites may notify Exeter CTU in the first instance who will onward report the suspected breach to the Sponsor.

The suspected breach will be logged on the Exeter CTU quality management system. The Sponsor representative will decide if the event constitutes a serious breach. The sponsor will report serious breaches to the REC within 7 days of becoming aware as per the SOP for Research Ethics Committees.

In the event of a serious breach, the Sponsor, Exeter CTU and the individuals involved will work together to agree and implement a corrective and preventative action (CAPA) plan, and follow up on the plan at agreed intervals to ensure effective implementation.

12.7. Data protection and patient confidentiality

This study will be conducted in a way that protects the rights and dignity of the participants. We will adhere to the Data Protection Act 2018 when collecting, storing and reporting data. Study data will be reported anonymously so that it will not be possible to identify any individual taking part in the study.

Each participant will be assigned a unique ID number. Personal identifiable data will be collected and stored separately to research data and will only be accessible to authorised members of the research team. Personal data will only be used for reasons relevant to the research as outlined in the

participant information sheets and will be stored for 5 years after the end of the study before being destroyed.

Data will be managed by the UKCRC registered Exeter Clinical Trials Unit (ExeCTU) following UK General Data Protection Regulation. Data will be collected and stored in accordance with the Data Protection Act 2018 and ICH GCP E6 R2. Access to the EDC system (REDCap Academic) web interface will be over Hyper Text Transfer Protocol Secure (HTTPS) / Transport Layer Security (TLS) version 1.2 as a minimum and it will be ensured that web traffic to and from the REDCap server is encrypted. We will host REDCap Academic in Amazon Webservices (AWS). Amazon Relational Database Service (RDS) will be encrypted. Amazon RDS encrypted database instances use the industry standard AES-256 encryption algorithm to encrypt the data on the server that hosts the Amazon RDS database instances. The AWS global infrastructure is designed and managed according to security best practices as well as a variety of security compliance standards. AWS provides on-demand access to security and compliance reports and select online agreements through AWS Artefact. Standards include ISO 27001 and ISO 9001.

Only principal investigators or their authorised delegates who are suitably qualified and trained will access the patients' medical notes to gather the required information for the study. Investigators will hold substantive or honorary contracts with the NHS Trust at which the patient is recruited and will therefore be bound by the confidentiality clauses that all NHS staff adhere to. Referrals made to other NHS service providers will be made using only nhs.net to nhs.net email.

Data collected at sites on paper such as participant contact information and consent forms (conforming to local policies on infection control), will be stored and archived at site. Data collected on paper in participants' homes during intervention and follow-up sessions will be pseudonymised with the unique participant ID number to protect the identity of the participant.

Audio-recordings of interviews and intervention sessions will be initially stored on an encrypted audio-recording device and then transferred to a secure area on University of Exeter servers accessible only to authorised members or the research team. Every effort will be made not to identify participants in the audio-recordings but this is not always possible due to the nature of the work. A third party transcription service, Victoria Pink, will be used to transcribe the audio-recordings. A data sharing and confidentiality agreement is in place between Victoria Pink and the University of Exeter. Transcriptions will be anonymised such that individuals cannot be identified, and saved on a secure University of Exeter server.

The data controller for the study is the Sponsor, the Royal Devon University Hospitals NHS Foundation Trust.

12.8. Financial and other competing interests

The chief investigator and co-chief investigator do not have any competing interests. Members of the PSC will complete conflict of interest forms declaring any competing interests that will be filed in the work package 2 trial master file (TMF). Independent members of the PSC are approved by the funder as being independent of the study. PIs will be provided with a PI declaration form as part of the model non-commercial agreement in which competing interests will be identified.

12.9. Indemnity

This is an NHS-sponsored research trial. If an individual suffers negligent harm as a result of participating in the trial, NHS indemnity covers NHS staff and those people responsible for conducting the trial who have honorary contracts with the relevant NHS Trust. In the case of non-negligent harm, the NHS is unable to agree in advance to pay compensation, but an ex-gratia payment may be considered in the event of a claim. Any harm arising from the design of the research is covered by the University of Exeter insurance policy. There are no arrangements for the Sponsor to pay compensation in the event of harm to research participants where no legal liability arises.

12.10. Amendments

All substantial amendments and relevant non-substantial amendments will be discussed by the SMG and with the PPI group if appropriate. The chief investigator will be responsible for the final decision on making an amendment to the protocol. The approval of the PSC chairperson will be sought for substantial amendments to the protocol in advance of submitting them to the REC and/or HRA, and if necessary, a meeting of the PSC will be convened to discuss the amendment. The funder representative will be notified of relevant substantial amendments in advance of submission, and a full list of all substantial and non-substantial amendments will be provided as part of regular funder reports.

The Sponsor will decide if an amendment is substantial or non-substantial following HRA guidance.

All amendments will be submitted to the NHS REC that issued a favourable opinion (if appropriate) and the HRA following the appropriate HRA amendment process in place at the time of submission. Amendments will be communicated by the trial manager to R&D departments, PIs and research teams at participating sites as soon as possible upon receipt of approval to do so from the HRA.

The chief investigator or delegate will inform the trial registry of changes to the study.

An amendment log will be maintained by the trial manager and filed in the TMF. The protocol version history will be recorded in an appendix to the protocol. Research sites will be provided with an updated document version control list where applicable following an amendment.

12.11. Post trial care

The study will end for a participant after the 6 month assessment data collection is complete. After this point, patient participants will continue to receive standard NHS care with no special arrangements made in relation to the study.

12.12. Access to the final trial dataset

We will store anonymised research data and outputs in the University of Exeter's Open Research Exeter repository (https://ore.exeter.ac.uk/repository/) in order to facilitate open access to, and the impact of, our research. All future research proposals must obtain the appropriate ethical and regulatory approvals.

Dissemination policy

13.1. Dissemination policy

13 The results of the trial will be disseminated regardless of outcome. We aim to publish the findings in peer reviewed scientific and clinical journals and via presentations at local, national and international meetings. We aim to publish the results in an open access journal within 24 months of study completion, in line with NIHR guidelines. Outcome papers will adhere to CONSORT guidelines. We will work with the PPI group to provide a lay-accessible summary of the results to all study participants. Participants will be asked to provide their contact method preferences so that they receive the results in a format of their choice (i.e. hardcopy by post or digital copy by email). Participants will not be provided with copies of their individual data, due to the nature of the study the data collected would not be relevant to their continued care. Clinical data recorded in medical records irrespective of their taking part in the research will be available to participants through normal processes for accessing medical records.

The results will be posted on the publicly available registry (ISRCTN). A summary of the results will be submitted to the HRA within 12 months of the end of the study in line with HRA guidelines.

The study protocol will be published in a peer-reviewed journal before the end of the recruitment stage and will be publicly available on the NIHR Journals Library at the end of the study.

13.2. Authorship eligibility guidelines and any intended use of professional writers

We will follow the International Committee of Medical Journal Editors (ICMJE) authorship criteria for outcome papers:

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

An authorship plan will be agreed prior to the drafting of outcome papers. We do not plan to engage the use of professional writers for this study.

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Appendices

15.1. Appendix 1 – Amendment History

15.

Amendment No.	Protocol version no.	Protocol date	Author(s) of changes	Details of changes made
N/A	2.0	10 October 2022	Abby O'Connell	Revised initial submission pre-favourable opinion. 7.3.2 and 7.3.3 added detail on the process for participants who lose capacity during the study. 7.7 added a paragraph on completing death checks ahead of follow-up visits. 7.9 added details of the individual participant-reported outcome measures and the need to allow participants to complete them confidentially.
SA5	3.0	26 January 2023	Abby O'Connell	Title page: added ISRCTN number Key contacts: Updated trial statistician from Ben Jones to James Connors. 4.5 Table 3 corrected scoring for the digit span assessment. 7.5 and 7.5.1 inserted details of the midway therapist review during the intervention delivery. Other minor corrections made throughout.