Remote STrOke Rehabilitation (ReSTORe): a UK-wide randomised controlled trial

PROTOCOL

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Protocol Amendments

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Substantial amendment 003	13/11/2025	20/11/2025
Substantial amendment 004	07/01/2026	15/01/2026
Non-substantial amendment 012	02/03/2026	03/03/2026

This protocol has regard for current HRA guidance and content.

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STUDY SUMMARY

Study Title	Remote STrOke Rehabilitation (ReSTORe): a UK-wide randomised controlled trial
Short study title	ReSTORe
Clinical Phase	Phase III
Study Design	Multi-centre randomised controlled trial with embedded process evaluation and health economic evaluation

Study Participants	Adults with long-term mild to moderate physical and/or mental health disability after stroke (six to 36 months post-hospital discharge)
Planned sample size	600 people randomly allocated to ReSTORe intervention arm or control arm with allocation ratio 1.08: 1 (ReSTORe intervention arm: 312 and control arm: 288)
Intervention	ReSTORe programme: A 10-week rehabilitation intervention including: 1) a 1-hour, 1:1 online assessment; 2) supervised, live online, home-based, group exercise sessions; 3) live online facilitated group psychosocial and motivational support sessions; 4) signposting to a library of 'on-demand' exercise sessions; 5) a participant workbook.
Control	Best practice usual care: a single online 1:1 appointment with a ReSTORe specialist, including general advice on safe and effective physical activity guided by publicly available Stroke Association information leaflets.
Intervention Duration	Ten weeks
Follow-up Duration	12 months post randomisation
Planned Study Period	01 July 2024 to 31 March 2027
Aim	To run a UK-wide randomised controlled trial (RCT) to test if the 'Remote STrOke Rehabilitation' (ReSTORe) intervention, a supervised, live online, home-based, group physical and mental health rehabilitation programme, can improve health-related quality of life (HRQoL) more than best-practice usual care, for people with long-term mild to moderate physical and/or mental health disability after stroke.
Outcomes	Assessed remotely at baseline pre-randomisation, three, six- and 12- months post-randomisation.
Primary	HRQoL: PROMIS® 29+2 Profile v2.1 (PROPr) measured at six months post-randomisation.
Secondary	**1.** PROMIS 29+2 Profile i. PROPr score (three and 12 months). ii. Sub-scores: depression, fatigue, sleep disturbance, pain interference, physical function, social roles/activities and cognitive function [1, 2]. iii. Sub-scales: anxiety and pain intensity. **2.** PROMIS Neuro-QoL short-form v2.0 - Cognitive Function. [3]. **3.** Health utility: EQ-5D-5L [4]. **4.** Physical Activity: International Physical Activity Questionnaire Short-Form (IPAQ-SF) [5]. **5.** General health: self-report of current overall health compared to baseline. **6.** Health and social care resource use: participant self-report. **7.** Recurrent stroke.

	8. All-cause/cardiovascular mortality. **9.** Adverse events attributable to the trial. **10.** Serious adverse events attributable to the trial. **11.** Simplified Modified Rankin Scale questionnaire (smRSq) score [34]
Pilot Phase	Six-month pilot phase to recruit 200 participants. During months 1 to 3 (from first randomisation), ReSTORe will randomise ~64 participants In months 4 to 6, recruit ~45 participants/month.
Process Evaluation	To explore and contextualise participant and practitioner experience of the study and intervention delivery, barriers, and enablers, to inform interpretation of quantitative interpretation of quantitative data and facilitate wider implementation. Conduct interviews with up to 50 participants and 5 ReSTORe specialists.

LIST OF ABBREVIATIONS/GLOSSARY

Abbreviation	Explanation
AE	Adverse Event
CACE	Compliers Average Causal Effect
CI	Chief Investigator
CAG	Confidentiality Advisory Group
CDMS	Clinical Data Management System
CONSORT	Consolidated *S*tandards *o*f *R*eporting *T*rials
CRF	Case Report Form
CTU	Clinical Trials Unit
DMC	Data Monitoring Committee
GCP	Good Clinical Practice
HADS	Hospital Anxiety and Depression Scale
HRA	Health Research Authority
HRQoL	Health-Related Quality of Life
ICF	Informed Consent Form
IPAQ-SF	International Physical Activity Questionnaire short form
IRAS	Integrated Research Application System
ISRCTN	International Standard Randomised Controlled Trial Number
MRC	Medical Research Council
NHS	NHS
NIHR	National Institute for Health and Care Research
PI	Principal Investigator
PIC	Patient Identification Centre
PIS	Participant Information Sheet
PPI	Patient & Public Involvement
PROMIS	PROMIS – Patient-Reported Outcomes Measurement Information System
PROPr	PROMIS Preference score
QoL	Quality of Life
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
R&D	Research and Development
RRDN	Regional Research Delivery Network
SAE	Serious Adverse Event

SSNAP	Sentinel Stroke National Audit Programme
TMG	Trial Management Group
TSC	Trial Steering Committee
UHCW	University Hospitals Coventry and Warwickshire NHS Trust
UoW	University Of Warwick
UKGDPR	UK General Data Protection Regulation
WCTU	Warwick Clinical Trials Unit

1. BACKGROUND

1.1 Background and rationale

At least one third of long-term stroke survivors living at home experience ongoing (≥6 months) mild to moderate disability including debilitating fatigue, low functional capacity, muscle weakness, anxiety and depression [7]. In the UK this equates to approximately 500,000 people, about a quarter to a third of which are of working age [8]. Health-related quality of life (HRQoL) and societal participation are profoundly affected [9]. Our patient partners identified that, after the period of scheduled contact with health professionals ended (≥6 months), the lack of effective treatments for post-stroke fatigue, low fitness, anxiety, and depression was challenging and frustrating, leading to feelings of helplessness and abandonment. There is a massive unmet need for effective ongoing support in this group.

Out-patient centre-based rehabilitation programmes soon after hospital discharge can result in short-term improvements in fatigue, physical and mental health, and HRQoL after stroke [10], but provision in the UK is patchy. Long-term physical and mental health rehabilitation may also be beneficial but centre-based programmes are not offered due to a lack of evidence, and the cost to the NHS and patients. As a low resource, high capacity alternative, supervised, live online, home-based, group rehabilitation programmes developed and tested during and after the COVID-19 pandemic, have proven feasible and acceptable to people with long-term conditions and to rehabilitation ReSTORe specialist[11]. This approach may benefit people with long-term (≥6 months) mild to moderate physical and/or mental health disability after stroke, but this has not been investigated.

We propose a UK-wide, decentralised, pragmatic trial to test the clinical and cost-effectiveness of an evidence-informed physical and mental health rehabilitation intervention targeted at geographic areas of high disease burden and underserved populations, addressing evidence gaps identified by NHS England's Demand Signalling and the James Lind Alliance Priority Setting Partnership; specifically, 'long-term physical and psychological therapies'; 'community based telerehabilitation'; 'managing mood and fatigue'; 'promoting strength, fitness and recovery'; 'interventions to facilitate improvement in every-day abilities'; 'improve motivation, well-being and engagement'.

1.2 Existing knowledge

Our 2021 systematic review [10] of exercise-based rehabilitation after stroke (n=1,836, 30 studies) found a small to moderate benefit in HRQoL over three to six months (standardised mean difference −0.23 [95% CI, −0.40 to −0.07]) which diminished in the longer-term (>9 months) (SMD −0.11 [95% CI, −0.26 to 0.04]). In the short-term, physical (SMD −0.33 [95% CI, −0.61 to −0.04]) and mental health (SMD −0.29 [95% CI, −0.49 to −0.09]) improved. Dedicated psychosocial and behavioural interventions were rarely delivered alongside exercise despite some evidence of benefit [12], and no programmes were delivered online. A 2023 update of the systematic review did not identify any further trials, and we found no adequately powered RCTs on trial registries.

In our recent REGAIN trial[11] (NIHR 132046; n=585), supervised, live online, home-based, group rehabilitation was clinically effective compared to usual care for improving HRQoL (PROMIS-PROPr; 0.03 [0.01 to 0.05] p=0.015) and fatigue (PROMIS fatigue subscale; 2.5 [1.19 to 3.81] p<0.001) in people with debilitating long-term physical and mental health symptoms after COVID-19 hospital discharge. Home-based supervised rehabilitation programmes can also improve fatigue and HRQoL in other long-term conditions e.g., cancer survivorship and multiple sclerosis [13, 14].

In long-term stroke survivors with mild to moderate physical and/or mental health disability, there is a significant burden of disease that is not addressed by conventional stroke rehabilitation and care pathways [7]. The number of long-term survivors is increasing due to an ageing population and because treatments have led to better survival rates [15]. It is projected that the annual number of strokes in the UK will increase by 60% between 2015 and 2035 and the number of stroke survivors will double [15].

People with severe disability after stroke are commonly supported by long-term holistic health and social care systems [7]. The long-term physical and mental health needs of those with mild to moderate disability, however, may not be appropriately managed, most likely due to the inability of the healthcare system to support demand. A clinically and cost-effective supervised online rehabilitation programme has the low-resource infrastructure and capacity to reach and support large numbers of long-term stroke survivors in the UK, contributing to their ongoing rehabilitation and effective return to societal participation and economic productivity.

In addition to generalised mild to moderate physical and/or mental health disability after stroke, at least one third of long-term stroke survivors have communication impairments such as

aphasia (difficulty understanding spoken language, reading, writing, and speaking) [16]. This can make participation in rehabilitation and clinical trials more difficult and can lead to poorer outcomes compared to stroke survivors without aphasia [17]. People can have multiple communication impairments after stroke that require adaptations to enable them to participate in rehabilitation interventions [18]. As such, this group are typically excluded from research into new interventions, thus potentially worsening the inequity in outcomes [19]. There is a real need to include this group in rehabilitation research.

Rehabilitation delivered online can improve fatigue and HRQoL in clinical populations, but data are not available for long-term stroke survivors. A definitive trial of the clinical and cost effectiveness of remote rehabilitation intervention for long-term stroke survivors with mild to moderate physical and/or mental health disability is needed; the 'Remote STrOke Rehabilitation' (ReSTORe) trial will address this research gap.

1.3 Hypothesis

Research question: Is 'Remote STrOke Rehabilitation' (ReSTORe) superior to best-practice usual care (a single session of advice) for improving HRQoL in people with long-term (≥6 months) mild to moderate physical and/or mental health disability after stroke?

Objectives: To run a definitive RCT testing the clinical and cost-effectiveness of the ReSTORe intervention versus a single session of advice including:

1. Pre-pilot to adapt, refine and test intervention materials, delivery, and practitioner training, and prepare trial set-up.
2. Internal pilot with formative process evaluation to test recruitment and trial procedures.
3. Main trial with embedded process evaluation.

1.4 CONSORT

The study will be reported in line with the CONSORT (*Consolidated Standards of Reporting Trials*) statement [20].

2. STUDY DESIGN

2.1 Study summary and flow diagram

ReSTORe is a multi-centre, RCT testing the clinical and cost-effectiveness of the ReSTORe intervention vs. best practice usual care.

Building on rehabilitation interventions previously developed and tested by our team, we have undertaken a six-month development phase to refine the ReSTORe intervention. An internal pilot recruiting from multiple locations around the UK will confirm recruitment rate and provide provisional data on intervention fidelity, safety, participant compliance and recruitment demographics. We will then run a UK-wide, decentralised, pragmatic RCT, delivered by WCTU with rehabilitation intervention delivered from a single trial hub (UHCW), with an embedded process evaluation and economic analysis.

Population

Adults with long-term mild to moderate physical and/or mental health disability after stroke who are between six- and 36-months post-hospital discharge for stroke.

Procedures

Potential participants will be identified from NHS primary and secondary care database screening, self-referral, and public health and charitable organisations (e.g. Be Part of Research network, Aphasia Alliance, Stroke Association). Invitation letters and flyers (and/or text message) with a link to online information will be sent electronically/via post. Interested recipients will be invited to visit an online portal to complete an eligibility check and expression of interest which will be returned electronically to the WCTU ReSTORe team. Subsequently, potential eligible participants will be asked to complete an online consent form or if required, may be contacted directly by a ReSTORe specialist based at UHCW to confirm eligibility and informed consent. Participants will complete baseline outcome measures online before randomisation. Throughout the recruitment process and trial procedures, people with communication impairments will be assisted by ReSTORe specialists with skills in communication support, using bespoke materials and video-conferencing tools.

Interventions

ReSTORe intervention

A 10-week rehabilitation intervention delivered by trained ReSTORe specialist, including:

1. A 1-hour, 1:1 online assessment
2. Supervised, live online, home-based, group exercise sessions
3. Live online facilitated group psychosocial and motivational support sessions
4. Signposting to a library of ‘on-demand’ exercise sessions
5. A participant workbook

Best-practice usual care

A single online 1:1 appointment with a ReSTORe specialist, including general advice on recommended physical activity guided by the publicly available Stroke Association information leaflets.

Outcomes

Participants will complete outcome measures remotely online before randomisation (baseline), three, six and 12 months. The primary outcome will be HRQoL at six months measured with the Patient-Reported Outcomes Measurement Information System Preference (PROMIS-PROPr) score, derived from the PROMIS 29+2 Profile. Secondary outcomes include PROMIS 29+2 fatigue, cognitive function, anxiety, depression, pain, physical function, sleep, social roles/activities sub-scores/scales; plus physical activity, health utility, health and social care use, all-cause mortality, adverse events and smRSq.

Sample

We will randomise 600 participants to the ReSTORe intervention or best-practice usual care in a ratio of 1.08:1, using a computer-generated randomisation sequence, performed by minimisation, with sex, age (<65 or ≥65 years), and simplified modified Rankin Scale (smRS) score (≤2 or 3-4) as stratification variables.

Analysis

Reported as per CONSORT with intention-to-treat analyses. A partially nested heteroscedastic regression model will estimate the intervention effect (with 95% CIs), adjusted for clinically important variables. Pre-specified, exploratory sub-group analyses will examine the interactions with treatment assignment. Cost-effectiveness will be assessed as incremental cost per QALY estimates and credible intervals, cost-effectiveness acceptability curve and value-of-information analyses.

Timeline (months)

Ethics, set-up, pre-pilot (-3 to 3); internal pilot (4 to 9); recruitment (4 to 18); primary outcome (10 to 24); 12-month follow-up (16 to 30); analysis, dissemination, reporting (31 to 33).

Impact/dissemination

ReSTORe has the potential to change practice nationally and globally. Results will be published in leading journals and presented at scientific meetings. Collaboration with patient partners, charities, national governing bodies, and guideline committees will ensure timely, accessible dissemination.

Intervention development and pre-pilot testing

We have followed MRC guidance for development of complex interventions [21]. Through systematic review of the literature, expert opinion, and stakeholder engagement and consensus meetings, we identified existing intervention components suitable for adaptation and refinement for testing with people recovering from stroke who may have aphasia or cognitive impairment. Data from our systematic review [10], co-designed stroke exercise programme [22], portfolio of existing online rehabilitation interventions[23-25], long-standing stroke service user group and qualitative research [26], and stroke communication work [27-30], provided a strong evidence base with which to develop and refine the ReSTORe intervention.

All intervention components have been feasibility and acceptability tested and piloted, and many definitively tested in multi-centre RCTs in stroke populations or other clinical groups with similar physical and mental health profiles. This provides reassurance that the intervention is both safe and deliverable at scale in long-term stroke survivors with mild to moderate functional disability. Detailed descriptions of our complex intervention development processes for interventions on which ReSTORe is based are available in the published literature[23-25, 31, 32]. During the pre-pilot we will engage further with our patient partners with aphasia and refine the ReSTORe intervention to be suitable for those with communication impairments.

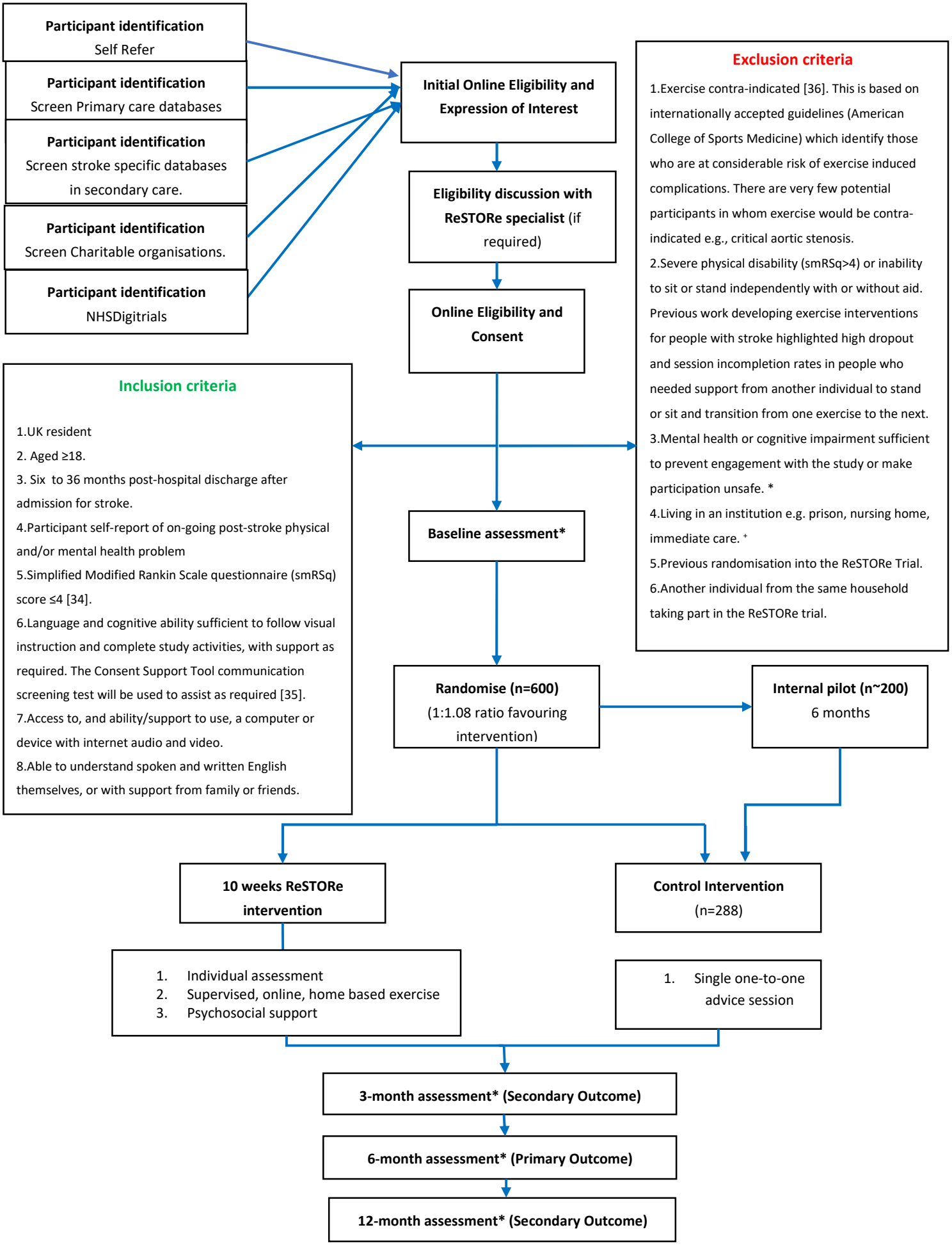
Internal pilot

During months one to three (from first randomisation), we will enrol ~64 participants (~three intervention groups) [6]. In months four to six, we aim to recruit ~45 participants/month (~two intervention groups) before progressing seamlessly to the main trial (total n=109). If achieving less than 50% of our targets, we will consider recruitment unlikely to be feasible; if 50% to 99%, the TMG will review recruitment strategies, report to TSC/DMC/HTA, and continue with modified protocol and close monitoring

Table 1: Pilot trial success criteria for recruitment

Target	Red	Amber	Green
Trial recruitment	<50%	50-99%	≥100%
Recruitment rate (participants per month)	<17	17 - 33	≥33
Number of PIC sites open	<1	1-2	≥2
Indicative number of participants recruited overall	<100	100 - 199	≥200
Decision	Decision to progress will be made by the TSC in association with the funder.	Progress to main trial with additional PIC sites being recruited.	Progress to main trial following a review. Any barriers to recruitment will be addressed.

Figure 1 Study flow diagram


Participant identification
Self Refer
Participant identification
Screen Primary care databases
Participant identification
Screen stroke specific databases in secondary care.
Participant identification
Screen Charitable organisations.
Participant identification
NHSDigitrials
Initial Online Eligibility and Expression of Interest
Eligibility discussion with ReSTORe specialist (if required)
Online Eligibility and Consent
Exclusion criteria
1.Exercise contra-indicated [36]. This is based on internationally accepted guidelines (American College of Sports Medicine) which identify those who are at considerable risk of exercise induced complications. There are very few potential participants in whom exercise would be contra-indicated e.g., critical aortic stenosis.
2.Severe physical disability (smRSq>4) or inability to sit or stand independently with or without aid. Previous work developing exercise interventions for people with stroke highlighted high dropout and session incompletion rates in people who needed support from another individual to stand or sit and transition from one exercise to the next.
3.Mental health or cognitive impairment sufficient to prevent engagement with the study or make participation unsafe. *
4.Living in an institution e.g. prison, nursing home, immediate care. +
5.Previous randomisation into the ReSTORe Trial.
6.Another individual from the same household taking part in the ReSTORe trial.
Inclusion criteria
1.UK resident
2. Aged ≥18.
3. Six to 36 months post-hospital discharge after admission for stroke.
4.Participant self-report of on-going post-stroke physical and/or mental health problem
5.Simplified Modified Rankin Scale questionnaire (smRSq) score ≤4 [34].
6.Language and cognitive ability sufficient to follow visual instruction and complete study activities, with support as required. The Consent Support Tool communication screening test will be used to assist as required [35].
7.Access to, and ability/support to use, a computer or device with internet audio and video.
8.Able to understand spoken and written English themselves, or with support from family or friends.
Baseline assessment*
Randomise (n=600)
(1:1.08 ratio favouring intervention)
Internal pilot (n~200)
6 months
10 weeks ReSTORe intervention
1. Individual assessment
2. Supervised, online, home based exercise
3. Psychosocial support
Control Intervention
(n=288)
1. Single one-to-one advice session
3-month assessment* (Secondary Outcome)
6-month assessment* (Primary Outcome)
12-month assessment* (Secondary Outcome)

2.2 Aims and objectives

To assess the clinical and cost-effectiveness of a supervised, live online, home-based, group rehabilitation programme to support long-term physical and mental health recovery (ReSTORe) versus best-practice usual care, for people with mild to moderate disability, 6–36 months post-hospital discharge after stroke.

2.2.1 Primary objective

To determine if the ReSTORe rehabilitation intervention improves HRQoL at six months post-randomisation compared to best-practice usual care in people with long-term (≥6 months) mild to moderate physical and/or mental health disability after stroke.

2.2.2 Secondary objective

To determine if the ReSTORe rehabilitation intervention improves clinical and patient reported outcomes at three, six- and 12-months post-randomisation compared to best-practice usual care in people with long-term (≥6 months) mild to moderate physical and/or mental health disability after stroke.

2.2.3 Process Evaluation objective

1. To explore the experiences of participants in the intervention and control groups, including enablers of, and barriers to, lifestyle change amongst participants.
2. To highlight any contextual issues that may affect the outcome or delivery of the study and/or intervention.

2.3 Outcome measures

2.3.1 Efficacy

Primary Outcome

Health-related quality of life (HRQoL) at six months post-randomisation using the PROMIS-Preference Score (PROPr). The PROPr score is generated from seven sub-scores: depression, fatigue, sleep disturbance, pain interference, physical function, social roles/activities and cognitive function [1, 2], all of which are important areas identified by long-term stroke survivors. The score ranges from -0.022 to 1.0 where 0 indicates a health state equivalent to death and 1.0 indicates perfect health [33]. The measure was sensitive to change in HRQoL and fatigue in our recent REGAIN trial[11].

Secondary Outcomes

The following outcomes will be measured at baseline, three, six- and 12-months post-randomisation.

1. PROMIS 29+2 Profile
    - PROPr score (three and 12 months).
    - Sub-scores: depression, fatigue, sleep disturbance, pain interference, physical function, social roles/activities and cognitive function [1, 2].
    - Sub-scales: anxiety and pain intensity.
2. PROMIS Neuro-QoL short-form v2.0 - Cognitive Function. An 8-item neurological condition specific assessment of cognitive function [3].
3. Health utility: EQ-5D-5L, a validated, generic HRQoL measure consisting of 5 dimensions, each with 5 levels of response. Each combination of answers can be converted into a health utility score. It has good test-retest reliability, is simple to use, and gives a single preference-based index value of health status for cost-effectiveness analysis [4].
4. Physical Activity: International Physical Activity Questionnaire Short-Form (IPAQ-SF) which provides a measurement of both volume and intensity of physical activity participation [5].
5. General health: self-report of current overall health compared to baseline.
6. Health and social care resource use: participant self-report.
7. Recurrent stroke.
8. All-cause/cardiovascular mortality.
9. Adverse events attributable to the trial.
10. Serious adverse events.
11. Simplified Modified Rankin Scale questionnaire (smRSq) score ≤4 [34]

Follow-up

Patient reported outcomes will be collected online at baseline pre-randomisation, and at three, six- and 12-months post-randomisation. Participants will receive an email notification and/or text message to ask them to complete the online questionnaires at each follow-up time point. In the case of non-response, reminder messages and calls will be utilised and if required, a data collection call will be made with priority on collecting the two key outcomes, the PROPr (primary outcome) and EQ-5D-5L. Contact can be via any of the approved methods. If a participant fails to complete a follow-up questionnaire, they will be followed-up at the next timepoint and data collected until the end of the trial unless they have explicitly withdrawn consent for the trial.

2.4 Participant identification and enrolment

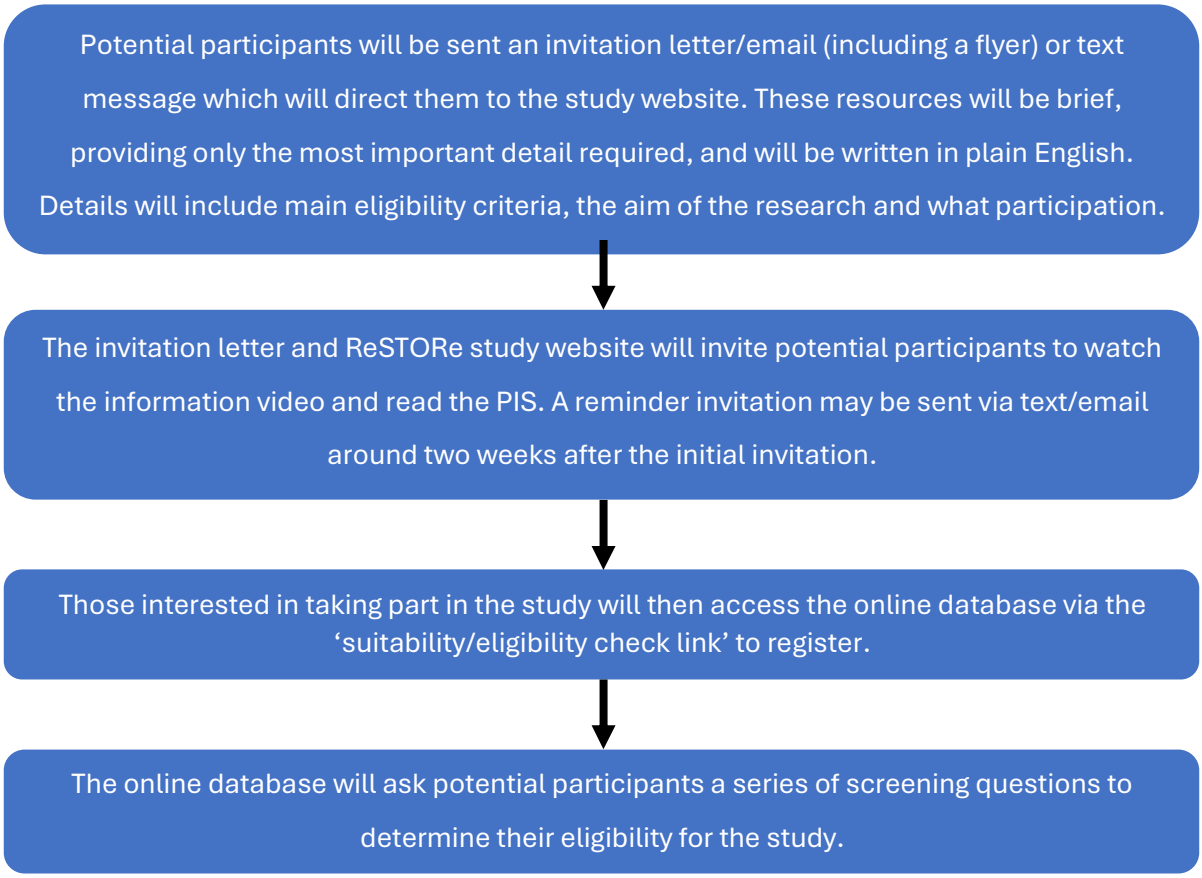
Participants will be identified via a variety of recruitment routes. These include:

1. **Primary Care -** The Regional Research Delivery Network (RRDN England), Scotland NHS Research Scotland Primary Care Network, and Health and Care Research Wales can screen local primary care databases to identify stroke patients. These searches can be conducted at scale, involving GP hubs to identify potential participants to invite to the study. A member of the GP practice with support of a Research Facilitator will run a search on the practice database. It is advised that practices undertake screening of the patient list to ensure that no individual is contacted in error. The Research Facilitators will have an NHS-to-NHS Letter of Access. Invitation letters and flyers will then be sent via an external service provider (Docmail).
2. **Secondary Care and Community Health Sites -** NHS hospitals in England and Wales that currently upload stroke patient data to the Sentinel Stroke National Audit Programme (SSNAP), or to other local databases that hold stroke patient data, will be invited to act as Participant Identification Centres (PICs). These sites will screen their databases to identify potential participants for contact by post/email/text message.
3. **Self-Referral -** Potential participants may self-refer through study advertisements and promotional materials (e.g. posters, the ReSTORe website, and social media platforms) which will provide information on how to contact the study team directly.
4. **Public health/research databases and charities –** e.g. Be Part of Research, SHARE Scotland, the Stroke Association and Different Strokes among other national databases/charities. The ReSTORe study will be listed on the relevant registry/charity websites, enabling potential participants to view study information and eligibility criteria. An email/letter/text template prepared by WCTU will be used for contacting potential participants and will be issued by the nominated person on behalf of the study team.
5. **NHS Digitrials –** NHS Digitrials will identify potential participants who meet the study's eligibility criteria by securely accessing NHS secondary care discharge data further in accordance with CAG approval (Confidentiality Advisory Group). The service will manage the initial approach to participants via letters. The recruitment model enables targeted mailouts to specific geographical areas to support the recruitment of a representative sample.

With all screening methods via the recruitment methods above, lists will be filtered to exclude those who have 'opted out' of being contacted about research.

Individuals expressing interest through the methods described above will undergo an initial screening process prior to completing the eligibility forms.

Participant Invitation and Registration Process



2.5 Eligibility criteria

Individuals are eligible to be included in the study if they meet the following criteria:

2.5.1 Inclusion criteria

1. UK resident
2. Aged ≥18.
3. 6 to 36 months post-hospital discharge after admission for stroke.
4. Participant self-report of on-going post-stroke physical and/or mental health problem
5. Simplified Modified Rankin Scale questionnaire (smRSq) score ≤4 [34].
6. Language and cognitive ability sufficient to follow visual instruction and complete study activities, with support as required. The Consent Support Tool communication screening test will be used to assist as required [35]. *
7. Access to, and ability/support to use, a computer or device with internet audio and video.

8. Able to understand spoken and written English themselves, or with support from family or friends.

2.5.2 Exclusion criteria

1. Exercise contra-indicated [36]. This is based on internationally accepted guidelines (American College of Sports Medicine) which identify those who are at considerable risk of exercise induced complications. There are very few potential participants in whom exercise would be contra-indicated e.g., critical aortic stenosis. *
2. Severe physical disability (smRSq>4) or inability to sit or stand independently with or without aid. Previous work developing exercise interventions for people with stroke highlighted high dropout and session incompletion rates in people who needed support from another individual to stand or sit and transition from one exercise to the next.
3. Mental health or cognitive impairment sufficient to prevent engagement with the study or make participation unsafe. *
4. Living in an institution e.g. prison, nursing home, immediate care. [+]
5. Previous randomisation into the ReSTORe Trial.
6. Another individual from the same household taking part in the ReSTORe trial.

*** As advised by a ReSTORe specialist.**

[+] This exclusion criterion is in place to minimise the risk of cross-contamination between trial arms. If two members of the same household were to be randomised, one allocated to the control group and the other to the ReSTORe intervention, there is a potential risk that the control participant could be inadvertently exposed to elements of the ReSTORe intervention. This could compromise the integrity of the control arm and affect the reliability and validity of the trial outcomes. To prevent this, the WCTU CDMS system will not permit a second individual from the same household to be randomised, and such cases will be excluded.

2.6 Eligibility check and informed consent

Potential participants will be invited to register for the trial by completing a brief initial screening form online and if suitable continue to the full online eligibility check. The initial screening form will also have the option for participants to indicate if they have any difficulties with communication. Participants that indicate they may have difficulties with communication will be contacted directly by one of the ReSTORe specialists to complete a further check using

elements of the Consent Support Tool communication screening test as required [35] to ensure that the study is suitable for them.

If the potential participant passes the screening form, they will be asked to enter their contact details including GP details. GP details must be provided in order for the potential participant to register interest into the study. This is required so that the participant's GP can be contacted if any medical concerns are raised during the study. If a potential participant does not pass the screening form, a message will appear on screen to inform them that the ReSTORe study is not suitable for them.

If the potential participant passes the screening form, they will automatically receive a link to the main eligibility form (unless they require a further check with a ReSTORe specialist). Upon completion of the main eligibility form, if the participant is eligible, they will automatically receive a link to the online consent form. If they are not eligible for the trial, a message will appear on screen to inform them that the ReSTORe study is not suitable for them.

If the individual indicates that they may have difficulties with communication, the additional check must be completed after screening and prior to consent. After the additional check, the participant will be informed of whether the study is suitable for them or not by the ReSTORe specialist conducting the check. If the study is suitable for them, the participant will receive a link to the main eligibility form and if required, a ReSTORe specialist may assist them with completing this and if applicable the consent form via phone/videoconference.

Individuals will be able to complete the consent form in their own time. Potential participants will be provided with contact details for the WCTU ReSTORe team should they have any questions or wish to discuss the study further. Participants will need to confirm they have read each of the consent items before agreeing to take part in the study. A copy of the completed consent form will then be sent to them by email upon completion. Once the consent form has been completed and submitted, the participant will be sent another link to access the baseline questionnaire. Participants will receive reminders via text/email and phone call to complete any outstanding forms throughout the process (additional screening, eligibility, consent and baseline).

Once both the consent form and baseline questionnaires have been completed, the participant will be automatically randomised into the study by the UoW online system (CDMS). The participant will receive a notification confirming that they have been successfully randomised and will be informed that a ReSTORe specialist will be in touch shortly to let them know their allocation and to arrange their first appointment.

In our REGAIN trial[11] (n=585), despite extensive, costly translation work into the five most spoken non-English languages (Bengali, Gujarati, Urdu, Punjabi, Mandarin), we did not recruit any non-English speakers. For ReSTORe, participants must be able to understand basic spoken and written English themselves, or with support from family or friends. If the ReSTORe intervention is effective in English speakers, further research will look at transferability for non-English speakers outside this trial, including translating materials and delivering the intervention in selected languages. Future research can evaluate delivery in these groups and develop an implementation plan for non-English speakers. Our online approach will facilitate delivery in language and culturally specific groups.

A third of stroke survivors have aphasia, resulting in difficulties understanding written and spoken language, and in speaking and writing. Additional support to facilitate access to interventions is important for this group. We have detailed how participants with communication impairments will be supported to understand trial information and how the intervention delivery and workbooks will be adapted. The Consent Support Tool communication screening test [35]developed by our team, will be used online as required during the initial eligibility and consent process to form an individualised prescription of the communication strategies that will aid participant understanding. This will ensure information and support is tailored to the individual throughout trial procedures, the intervention, and outcomes assessments.

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

New information: Any new information that arises during the study will be reviewed by the TSC. If this new information may affect participants' willingness to take part in the study, it will be communicated to all participants. Participants will be contacted by a member of the WCTU ReSTORe team and asked whether they still wish to continue participating in the study. Participants will be provided with an updated PIS and asked to complete a revised consent form as necessary.

Incidental findings: Incidental findings relating to participants' medical conditions or general health, will be discussed with the participant's GP and communicated to the participant as required. The participant will be advised to make an appointment with their GP to discuss the findings and will be informed that a letter will also be sent to their GP if required.

2.6.1 Consent for qualitative interviews

At the point of consent for the main study, participants will be asked for their consent to be contacted at a later stage about an interview with a qualitative researcher. Although consent will be recorded for everyone on entry to the ReSTORe study, only some participants will be contacted for interview. If they are selected for interview, participants will receive an email inviting them to consider the interview study and be directed to the study website where they can read the interview PIS. For information on participant selection, please refer to section 3.2.

If they do not respond to the invite, a qualitative research fellow from the WCTU ReSTORe team will make contact to answer any questions they may have and provide support with following links and with online forms where required. If the participant declines the interview and provides a reason, this will be documented electronically. If they choose to participate, they can complete an online interview consent form linked to the study database. Following receipt of the consent form, a qualitative researcher from the ReSTORe team will contact the participant to discuss the interview study, answer any questions they may have, and if they remain happy to proceed, arrange a date for the interview to take place. The interviewer will confirm the consent form has been completed before the interview is conducted by telephone or video call.

2.6.2 Consent for photographs and video clips

At the point of consent to the main study, participants will be asked if they consent to have photographs or short video clips taken during the live exercise sessions and support sessions for use at presentations or for study publicity. Declining consent for this will not impact on their eligibility for the trial.

2.6.3 Consent for qualitative practitioner interviews

The ReSTORe intervention will be delivered online from a single trial hub – UHCW. There will be between five and 10 specialists involved in delivery of the study (control and intervention). At the end of their time on the study, and with their consent, we will interview a sample of specialists involved in the study. Interviews will be conducted by a qualitative researcher from the ReSTORe team. For more information on specialist selection, please see section 3.2.

2.7 Site Staff Training

Staff training will be documented on training logs held at WCTU. Study responsibilities will be documented on delegation logs to be held at WCTU (electronic). The CI will retain overall responsibility for conduct of the study.

ReSTORe Specialist: Specialists delivering the ReSTORe intervention will be Clinical Exercise Physiologists or Physiotherapists with appropriate professional registration, relevant continued professional development (CPD), and good clinical practice (GCP) training. All specialists will be based at UHCW, and an exercise lead will be responsible for ensuring study procedures are followed and standardised for intervention delivery.

Training: ReSTORe specialists will be experienced and trained in stroke communication (by a specialist stroke speech & language therapist) and psychosocial, motivational, and behavioural support (health psychology). Specialists have completed a single day of ReSTORe training to ensure an appropriate level of clinical knowledge and skills for exercise rehabilitation in long-term stroke survivors. This training will be supported by a detailed practitioner manual.

Specialist Manual*:* A detailed manual will guide specialists through each component of the intervention, graphically and with written instruction. It will also include general information about the trial, key components of GCP, and contact details of the study team. The content will reflect information delivered during the ReSTORe specialist training. Trial manuals will be made available in public repositories on publication of main trial findings.

Exercise intervention: To enhance specialist' knowledge of exercise assessment and prescription in long-term stroke survivors, ensuring intervention efficacy and safety, the manual will provide an overview of key evidence and exercise guidance. To provide an appropriate level of standardisation, parameters within which the exercise intervention should be delivered will be detailed. *Psychosocial and motivational intervention:* The manual will give a detailed description of each psychosocial topic, with hints and tips of questions to ask, and session aims. The content will map onto the intervention participant manual, allowing the practitioner to tailor the discussion.

Participant workbook: A comprehensive resource detailing, in a patient-friendly fashion, relevant trial information. It will be adapted from existing materials and refined and finalised with our patient partners. In the form of a workbook, this resource will be introduced to the participant at the 1:1 assessment and will include: 1) general trial information; 2) information about living with stroke; 3) schedule for the participant's exercise programme and psychosocial and motivational support sessions; 4) general advice on safe and effective lifestyle physical activity.

2.8 Randomisation

2.8.1 Randomisation

Pre-randomisation eligibility checks will be carried out by the WCTU ReSTORe team/ReSTORe specialists to ensure that potential participants meet the eligibility criteria and are not randomised in error. Consent for entry into the study must have been completed prior to baseline assessment. Participants will be randomised once they have been registered as eligible for randomisation on the web-based system and completed the required baseline questionnaires.

Randomisation will be undertaken automatically by the UoW CDMS following completion of the baseline questionnaire using a computer-generated randomisation sequence, performed by minimisation, and stratified by:

1. age (<65 or ≥65 years),
2. sex (male or female)
3. simplified modified Rankin Scale (≤2 or 3-4)

GP notification: After randomisation, the participant's GPs will be informed by letter that they are taking part in the study. This will be sent by the WCTU ReSTORe team.

2.8.2 Post-randomisation withdrawals and exclusions

Participants may decline to continue involvement in the study at any time, without prejudice. Participants can discontinue from the trial intervention (treatment discontinuation), and they can also choose to withdraw from the trial completely. This will not affect the standard of care they receive. For participants withdrawing from the study altogether, data obtained prior to the point of withdrawal, will be retained for the final analysis unless explicitly withdrawn at the participant's request. For participants who withdraw, a withdrawal CRF will be completed including reason for withdrawal if provided. Willingness to continue in the study will also be monitored and recorded throughout the intervention period by ReSTORe specialists conducting the interventions. Participants may be withdrawn from the study or trial intervention, at any time, at the discretion of the chief investigator and specialist.

2.9 Study interventions

2.9.1 Study treatment(s) / intervention(s)

The ReSTORe intervention will be delivered online from a single trial hub – UHCW. There will be approximately five to 10 ReSTORe specialists (Clinical Exercise Physiologist/Physiotherapists)

based at UHCW who will deliver the study interventions as described below. Additional ReSTORe specialists may be identified as needed.

2.9.2 Best practice usual care (Control) intervention

We recognise the challenges of recruiting people to studies where the usual care arm receives no additional treatment or care; our patient partners consistently raise this as an issue of concern and inequity. Therefore, for our control arm, we will deliver a *'best-practice usual care'* intervention. This will comprise of an individual ReSTORe specialist appointment, with general advice on safe physical activity and living with stroke, supplemented with freely available Stroke Association leaflets, including aphasia-friendly and translated versions.

A 30-minute 1:1 online appointment will allow the practitioner to discuss individualised ways in which the participant can independently engage in self-directed physical activity. Participants will not be provided with a structured exercise plan, rather comprehensive information detailing ways in which physical activity can be incorporated into their everyday lives. No specific psychological techniques will be used when providing this information. This allows us to offer the control group best-practice usual care, whilst retaining the aim of the study comparing a group who receive a supervised online rehabilitation programme with a group who do not.

2.9.3 ReSTORe Rehabilitation Intervention

The ReSTORe intervention has three components:

1. **Individual assessment:** One-hour, online, 1:1 assessment with a ReSTORe specialist (Clinical Exercise Physiologist or Physiotherapist), trained and supported by a Health Psychologist and stroke communication specialist (Speech & Language Therapist), to screen, assess and risk stratify, and provide personalised rehabilitation advice.

2. **Exercise:** Up to 45 minutes, 2-3 times/week for 10-weeks consisting of individualised, multi-modality, equipment-free (or minimal equipment) aerobic and resistance exercise at a manageable intensity. In line with patient partner preferences, the ReSTORe exercise intervention includes:
   a. Live (end-to-end encrypted, password protected) online group sessions led by ReSTORe specialists to allow group exercise with real time instruction and feedback. Groups will have approximately eight participants and will be age, ability, culturally, and communication impairment specific (smaller discrete groups) as required.

b. Signposting to pre-recorded on-demand sessions, adapted for those with additional communication needs, and graded by ability, including a range of modalities from breathing exercises and Pilates to chair-based and standing moderate intensity functional exercise.

c. Participant workbook with instructions on safe and effective exercise.

3. **Psychosocial and motivational support:** Participants will attend six online 45-60-minute group support sessions facilitated by a ReSTORe specialist, with training and support from a health psychologist and stroke communication specialist. Sessions will cover the cognitive and emotional impact of living with stroke, and support engagement with the exercise components of the intervention by addressing potential barriers such as fear avoidance of activity. The Intervention is underpinned by behaviour change theory and designed in accordance with complex intervention (MRC/NIHR) frameworks. We also draw on guidance for designing behaviour change interventions based on the target population, target behaviours, hypothesised mechanism of change, and behaviour change technique [39].

Stroke survivors have complex reasons for sedentary behaviour including fatigue, disability, emotional and motivational factors, and environmental barriers [26]. Stroke impacts on cognitive, psychological and social determinants of behaviour, thus ReSTORe is underpinned by social cognitive theory [41] and the bio-psychosocial model [42]. Cognitive problems, memory, concentration, attention, and executive functioning will be addressed with a range of educational and interactive materials, handouts, workbooks, short videos and opportunity to pace the sessions. Social factors including feelings of isolation, relationships with family, friends, carers and healthcare professionals, and psychological factors related to grief and loss to self, emotional impact, mood, anxiety, and stress will be covered during the support sessions as outlined below.

The content and structure of the sessions are informed by the COM-B framework (capability, opportunity, motivation). Specifically, capability - knowledge about stroke and rehabilitation, and psychological skills training; opportunity - including social and peer support, environmental adaptations, and use of tools to engage in the intervention; and motivation - mapped onto goal setting and planning, feedback and monitoring, and shared experiences.

Group-based learning [43] is also important, including group formation and cohesion which can promote engagement with the intervention and behaviour change. Each session will include specific behaviour change techniques [44] including instruction, knowledge, goal

setting, problem solving, action planning, self-monitoring of behaviour and reflection, information about social, environmental and health consequences, social support, and framing and reframing. The sessions will be delivered using a CBT approach [45, 46].

The six sessions, as suggested to be important by our patient partners, will be:

Session 1: Introduction, exercise after stroke, goal setting
Session 2: Fear avoidance of activity
Session 3: Managing Post-Stroke Fatigue
Session 4: Mood and emotions
Session 5: Stress and anxiety management
Session 6: Reflection and long-term change

4. **Delivery:** The intervention will be delivered UK-wide from UHCW by ReSTORe specialists. This delivery model is directly transferrable, with minimal adaptation, from our recent trials [37, 47, 48] for which we implemented fully functional online trial and intervention delivery platforms. The model allows concentration of professional expertise and experience, standardised delivery, and time and resource-efficient trial and intervention procedures.

   For participants, decentralised online delivery supports accessibility for those who would otherwise not be able to take part in centre-based rehabilitation programmes due to poor heath, cost, transport, and time pressures. People with communication impairments may be accommodated in smaller discrete groups, ReSTORe specialists will be trained by stroke communication specialists, and a 'co-pilot' (additional practitioner) will provide technical assistance.

5. **Safety:** The ReSTORe specialists are experienced in remote online assessment, prescription, and delivery of physical activity for multi-morbid clinical populations. Troubleshooting and screening before and during live exercise and support sessions will assess safety, progress, health, and any adverse effects. Participants will be advised to initially have another person nearby whilst exercising. A comprehensive emergency procedure has been developed and implemented in existing trials, ensuring, in the unlikely event of someone becoming unwell during live sessions, protocols are in place to efficiently manage the situation.

Emergency procedure: In advance of each session, the ReSTORe specialist will have access to contact details for each participant. During the sessions, the ReSTORe specialist will be able to see each participant individually on a large screen. In the event of an emergency, the ReSTORe specialist will alert the designated 'co-pilot' for the session who will be able to communicate directly with the participant in question (via the live call or telephone) outside of the group and alert the emergency services if required.

6. **Intervention/control delivery:** Specialists trained in the ReSTORe intervention will be able to deliver the programme to groups of participants anywhere in the country using pre-recorded and live exercise and psychological support sessions.

2.9.4 Compliance

Compliance with ReSTORe intervention: Attendance at live online exercise sessions and the psychological support sessions will be logged by the ReSTORe specialist for each participant every week. Participants will be identified using their email address. The completion of intervention (individual assessment, online live exercise sessions, and psychological support sessions) and control sessions will be recorded as one measure of compliance.

Definition of compliance with intervention: The impact of compliance on outcomes will be assessed using a compliers average causal effect (CACE) analysis. A detailed statistical analysis plan will be written and approved by the Data Monitoring Committee (DMC) including definitions of full and partial compliance for the intervention group.

Fidelity: Most live exercise sessions and psychological support sessions will be recorded to reduce the risk of those delivering the intervention behaving differently when being recorded. The psychological support sessions will be recorded and scored against criteria. From these sessions, a purposively selected subset (~10%) of recordings will be analysed across relevant intervention sessions by the qualitative researcher.). This will enable assessment of fidelity, and an understanding of areas and issues that generated discussion.

The control group and intervention group individual practitioner appointments will also be recorded and scored against criteria.

2.10 Concomitant illness and medication

2.10.1 Concomitant illness

At the start of the study, potential participants will be screened during their eligibility assessment for any concomitant illnesses other than stroke. If the illness influences the potential participant's eligibility to continue in the study (e.g. serious mental health problems that exclude participation in a group intervention) the individual will be informed, and they will not be eligible to participate.

2.10.2 Concomitant medication

Participants will be asked to record all medications they are taking at each follow-up time point.

2.11 Co-enrolment into other trials

Co-enrolment of ReSTORe participants onto other interventional studies will be considered as required where there is no conflict with the ReSTORe study objectives and the participant is willing to do so. The CI will review the protocols for other studies and will consider co-enrolment in conjunction with the Trial Management Group where appropriate. Based on this, a list of appropriate and agreed studies will be produced and updated throughout the trial. Co-enrolment is not an agreement for data sharing, rather an agreement for participants to be approached about participating in more than one research study.

2.12 End of study

The study will end when all participants have completed their 12-month follow-up. For the process evaluation, up to n=25 participants in the control arm and n=25 from the intervention arm will be interviewed **after** their three-month follow-up.

The study will be stopped prematurely if:

- Mandated by the Ethics Committee
- Following recommendations from the Data Monitoring Committee (DMC)
- Funding for the study ceases

The Research Ethics Committee (REC) will be notified in writing within 90 days when the study has been concluded or within 15 days if terminated early.

3. METHODS AND ASSESSMENTS

3.1 Schedule of delivery of intervention and data collection

Table 2. Study assessments

	Pre-randomisation		Post-randomisation			
Online assessment	**1**	**2**	**3**	**4**	**5**	**6**
Assessment time point	**Screening**	**Enrolment/ randomise (Baseline)**	**Intervention Delivery** 10 weeks	**3m (± 2w)**	**6 m (± 1 m)**	**12 m (± 1 m)**
Invitation	✓					
Initial Screening Check	✓					
Eligibility Assessed	✓					
Concomitant Illnesses		✓				
Additional screening check* (telephone if required)		✓				
Informed consent		✓				
Patient Demographics		✓				
Intervention delivery			✓			
Health and medication use		✓		✓	✓	✓
Simplified Modified Rankin Scale		✓		✓	✓	✓
PROMIS-PROPr		✓		✓	✓	✓
PROMIS® 29+2 Profile v2.1 (PROPr)		✓		✓	✓	✓
PROMIS Neuro-QoL		✓		✓	✓	✓
EQ-5D-5L		✓		✓	✓	✓
IPAQ-SF		✓		✓	✓	✓
General health (self-report)		✓		✓	✓	✓
Recurrent stroke		✓		✓	✓	✓
Adverse events			✓	✓	✓	✓
Death			✓	✓	✓	✓
Health and Social Care resource use				✓	✓	✓
Semi-structured interviews (Process evaluation)				✓		

*** Additional screening check based on the Consent Support Tool will be performed as required for some participants over the telephone by a trained member of the WCTU ReSTORe team.**

3.2 Embedded process evaluation

Semi-structured interviews with participants*:* Information about interviews will be provided to all participants during study recruitment. Participants will be asked to consent (or not) to being contacted around three months after they have entered the study to share their views and experiences of the intervention or control. Participant interviews will be completed by phone or video call by a qualitative researcher from the WCTU ReSTORe team. Online consent will be taken prior to the interview taking place.

Pilot study interviews

Interviews with up to five people in each arm recruited to the internal pilot to check intervention acceptability, and identify obstacles or facilitators to participation, uptake, and completion. We will use this internal pilot to optimise recruitment and retention by identifying challenges, and solutions which will be discussed with our patient partners. The model used for interviews in the pilot study will differ from the main study in that participants will be interviewed within three months of randomisation rather than after three months.

Main Study interviews

Intervention and control participants will be interviewed to investigate their experiences, contextualise quantitative findings, and explore factors that helped or hindered participation, thus informing interpretation and wider implementation. Interviews will take place after the three-month follow-up outcome data collection, so that the interview itself does not introduce bias to the analysis. A purposive sample of up to n=25 intervention and n=25 control participants will be interviewed at three months post randomisation to ensure a diverse range of perspectives are included. Our sample size of up to 25 per group follows guidance [49] indicating that while code saturation ('when researchers have *heard it all*') was reached at nine interviews, 16 to 24 interviews were needed to reach meaningful saturation ('*to understand it all*'). The interviews will use a topic guide that will include participant experiences of a stroke, and any obstacles or enablers to participation, adherence, and recovery. We will explore what components were used/dropped/never used. The interviews will last about one hour and be recorded.

4. ADVERSE EVENT MANAGEMENT

4.1 Definitions

4.1.1 Adverse Events (AE)

An Adverse Event (AE) is defined as any untoward medical occurrence involving a participant, which does not necessarily have a causal relationship with the intervention or study.

AEs exempt from formal recording

For the intervention group, common AEs listed in Table 3 that are identified during or after intervention sessions will be recorded on the intervention notes (not an AE form), for clinical purposes only.

Table 3. AEs exempt from formal recording

Events
Participants' normal post-stroke symptoms and sequelae e.g. fatigue, muscle ache, headache.
Normal post exercise symptoms e.g. moderate levels of shortness of breath, tiredness/fatigue, light headedness/dizziness, muscle and/or joint soreness/stiffness including delayed onset of muscle soreness (DOMS).
Exacerbation of pre-existing musculoskeletal conditions (e.g. osteoarthritis) as long as not more than 72hrs in duration.

Any AEs that are not listed above should be recorded using the AE form on the UoW CDMS. Forms should be completed by the intervention team or WCTU ReSTORe team as appropriate, as soon as possible after becoming aware of the AE. All AEs should be assessed within 24 hours of identification to check if they constitute a 'Serious Adverse Event' as per section 4.1.2 below. If assessed as a Serious Adverse Event, it should be reported within 24 hours, following the procedures outlined in section 4.2.3 and not recorded on the AE form.

4.1.2 Serious Adverse Events (SAEs)

An SAE is any untoward medical occurrence that fulfils one or more of the following criteria:

- Results in death
- Is immediately life-threatening
- Requires hospitalisation or prolongation of existing hospitalisation

- Results in persistent or significant disability or incapacity
- Is a congenital abnormality or birth defect
- Intervention is required to prevent one of the above or is an important medical condition

SAEs exempt from reporting

The following event in Table 4 that fulfils the criteria for 'serious' is common in the clinical population being studied and **does not** need to be reported to WCTU as an SAE for this trial. This will be recorded as part of follow-up data collection in the participant questionnaires or in the relevant section(s) of the CRF.

Table 4. SAEs exempt from reporting

Events
Treatment, which was elective or pre-planned, for a pre-existing condition.

4.2 Recording Adverse Events and Reporting Serious Adverse Events

4.2.1 Recording and reporting period

Intervention group: All AEs and SAEs (unless otherwise specified) occurring from the time of informed consent until the six month follow-up time-point must be recorded and reported as appropriate. Participants will be asked about anything that might constitute a SAE during their three and six-month follow-up questionnaire and will also be given the opportunity to identify any events at every live exercise and support session or by email during the intervention period.

Usual care group: The usual care group will be asked about anything that might constitute a SAE during their three and six-month follow-up questionnaire only. It will not be possible to collect a comparison dataset for the usual care group within this period without contaminating the control intervention. This is a pragmatic study, and the participants will not be contacted during the intervention period, unlike the intervention group. It is important not to contact the usual care group more than is necessary so as not to introduce bias. We anticipate a low risk of adverse events arising from best practice, usual care i.e. from a single session of advice.

4.2.2 Recording and assessing AEs/SAEs

Participants in the intervention group will have the opportunity to indicate whether they have experienced any AEs by completing pre- exercise session poll questions. Responses indicating the participant has potentially experienced an AE will be evaluated by the practitioner and the participant contacted to confirm the details. Specialists should also monitor any information volunteered by a participant at any time during a live exercise session and will ask if anyone has anything to report at the end of the session to remain online after the session or to call/email any concerns.

Participants in the intervention group will also have contact details (generic email address and phone number) for the study team and specialist. Whilst participants will not be actively encouraged to report AEs via this route, they may seek advice and help from the team which may result in AEs being disclosed/discussed. Any AEs except those listed in Table 3 will be recorded on the AE form on the ReSTORe database unless they fulfil the criteria for a 'Serious Adverse Event' in which case they will be reported to WCTU via the SAE form (see section 4.2.3 below).

All AEs should be assessed by a ReSTORe specialist/WCTU ReSTORe team within 24 hours of identification to determine if they meet the criteria to be reported as SAEs as defined in section 4.1.2. If any AEs meet these criteria, they must be reported to WCTU ReSTORe team by completing the SAE form on the ReSTORe database within 24 hours of becoming aware. The WCTU ReSTORe team will notify the WCTU Quality Assurance team of any reported SAEs. If the follow-up questionnaire received from a participant indicates events that may fulfil an SAE, then they should be contacted for further information and an SAE form completed if applicable.

All SAEs should be reported to WCTU ReSTORe team, irrespective of their relationship to the intervention unless they are exempt from reporting (see section 4. 1.2). Once received, the WCTU ReSTORe team will review the SAE and request further information if required from the intervention team, participant or participant's GP as appropriate.

For each **SAE** the following information will be collected:

- event type
- event start date/time and date research team were aware
- event details in medical terms and any relevant medical history
- causality
- outcome

The causality of SAEs (i.e. relationship to study intervention) will be assessed by the chief investigator and another appropriately delegated clinical trial team member using the classifications in Table 5 below.

Table 5. SAE Causal relationships

Relationship to study intervention	Description
Unrelated	There is no evidence of any causal relationship.
Unlikely to be related	There is little evidence to suggest there is a causal relationship (e.g. the event did not occur within a reasonable time after administration of the study intervention). There is another reasonable explanation for the event (e.g. the patient's clinical condition, other concomitant treatment).
Possible relationship	There is some evidence to suggest a causal relationship (e.g. because the event occurs within a reasonable time after administration of the study intervention). However, the influence of other factors may have contributed to the event (e.g. the patient's clinical condition, other concomitant treatments).
Probable relationship	There is evidence to suggest a causal relationship and the influence of other factors is unlikely.
Definitely related	There is clear evidence to suggest a causal relationship and other possible contributing factors can be ruled out.

4.2.3 Expected SAEs

There are no expected SAES previously documented for this intervention. Therefore, any that are assessed as having a causal relationship to the intervention will not undergo expectedness assessment and will be expedited to the REC as per section 4.2.4 below.

4.2.4 Reporting SAEs

The trial management team at WCTU will liaise with the intervention specialist/participant to compile all the necessary information. Once the SAE form has been completed, two independent causality assessments will take place as per section 4.2.2 above. SAEs that are deemed possibly, probably or definitely related to the trial intervention by either causality assessor will be notified to the REC and sponsor within 15 days.

4.2.5 Follow-up of reported SAEs

ReSTORe specialists or the WCTU ReSTORe team will monitor for changes to unresolved SAEs via intervention poll responses or through contact with the participant. If a ReSTORe specialist becomes aware of any change of condition or other follow-up information it should be reported to the WCTU ReSTORe team by completion of the SAE Follow-Up form as soon as it is available. Events will be followed up until the event has resolved or a final outcome has been reached where possible.

4.3 Responsibilities

ReSTORe Specialist	Checking for AEs when participants attend for exercise session or via pre -exercise poll responses: **1.** Ensuring that all SAEs are recorded and reported to WCTU ReSTORe team within 24 hours of becoming aware of the event and provide further follow-up information as soon as available. Ensuring that reported SAEs are chased with WCTU ReSTORe team if a record of receipt is not received within 2 working days of initial reporting
Chief Investigator/delegate OR Independent clinical reviewer	**1.** Clinical oversight of the safety of patients participating in the study, including an ongoing review of the risk / benefit **2.** Using clinical judgement in assessing causality **3.** Review of all related and unexpected SAEs

	4. Review of specific SAEs in accordance with the study risk assessment and protocol as detailed in the Trial Monitoring Plan
Trial team delegate (e.g. TM/TC/Statistician)	1. Central data collection and verification of SAEs, according to the study protocol 2. Expectedness assessment of related SAEs 3. Reporting safety information to the CI, delegate, or independent clinical reviewer for the ongoing assessment of the risk / benefit according to the Trial Monitoring Plan 4. Reporting safety information to the independent oversight committees identified for the study (Data Monitoring Committee (DMC) and / or Trial Steering Committee (TSC)) according to the Trial Monitoring Plan 5. Expedited reporting of related and unexpected SAEs to the REC within required timelines 6. Notifying Investigators of related and unexpected SAEs that occur within the study
Sponsor delegate	Review SAEs that are deemed possibly, probably or definitely related to the trial intervention.
Trial Steering Committee (TSC)	In accordance with the Trial Terms of Reference for the TSC, periodically reviewing safety data and liaising with the DMC regarding safety issues.
Data Monitoring Committee (DMC)	In accordance with the Trial Terms of Reference for the DMC, periodically reviewing unblinded overall safety data to determine patterns and trends of events, or to identify safety issues, which would not be apparent on an individual case basis.

4.4 Notification of deaths

All deaths, when they are identified (up to the 12-month follow-up time-point), will be reported to the sponsor by the WCTU ReSTORe team, overseen by the CI, irrespective of whether the death is stroke-related, intervention-related, or an unrelated event. Deaths identified between six and 12 post-randomisation will be recorded for outcomes purposes but will not be classed as an SAE.

4.5 Reporting urgent safety measures

If any urgent safety measures are taken the CI/Sponsor shall immediately and in any event no later than three days from the date the measures are taken, give written notice to the relevant REC of the measures taken and the circumstances giving rise to those measures.

5. DATA MANAGEMENT

Personal data collected during the study will be handled and stored in accordance with the UK General Data Protection Regulation (UK GDPR).

Personal identifiable information will be collected via the online database and stored electronically at WCTU. Participant details will be stored and accessed by staff at WCTU and UHCW via the UoW CDMS to confirm eligibility and consent; inform GP of trial participation; allow postage of participant workbooks; contact participants during the study; allow delivery of intervention and control procedure and contact for qualitative interviews. Handling of personal and confidential data will be clearly documented in the participant information sheet and consent obtained.

ReSTORe specialists at UHCW will also keep paper records of participant contact details and medical health information for those participants randomised to the ReSTORe intervention. This is required for study delivery to ensure participants are exercising at the appropriate level and to be used if a medical emergency occurs. These paper records will be stored securely in locked filing cabinets only accessible to study staff until three months post intervention. These records will not be passed onto WCTU.

Disclosure of confidential information will only be considered if there is an issue which may jeopardise the safety of the participant or another person, according to UoW SOPs (UoW SOP 15 part 1) and the UK regulatory framework.

For information on data storage and archiving timelines, please refer to section 5.8.

5.1 Data collection and management

The CRFs and questionnaires have been developed by the Trial Manager in consultation with the CI, Statistician, Health Economist, programming team and other relevant members of the study team to collect all required study data.

All data will be entered directly by participants, ReSTORe specialists or WCTU ReSTORe team members onto a secure online study database (UoW CDMS) hosted by WCTU as outlined in the data management plan and in accordance with UoW SOPs. Data entered onto the online study database and collected during the intervention- will be source data. These will be stored safely and securely. On all study-specific documents, other than the completed consent form, the participant will be referred to by the study participant number, not by name. During the intervention sessions the participant details including email and name (if entered by the participant) will be visible to specialists and other attendees.

Various methods will be used to chase missing data including phone, text and email via a third-party service (Twilio). Participants will receive a reminder to complete the online questionnaires at each study time point. If a participant has not completed a study questionnaire following the reminder, the WCTU ReSTORe team will contact the participant to encourage them to complete the questionnaire online, and to provide support where required. If data remains missing following this chase, the WCTU ReSTORe team will contact the participant to attempt to collect the outcome measurements with priority on the core measures (PROPr and EQ5DL). The procedures for managing this will be outlined in the data management plan and appropriate consent will be sought to contact participants.

Data will still be collected for participants who discontinue or deviate from the intervention protocol or miss a follow-up questionnaire unless they withdraw their consent (section 2.9).

5.2 Database

The database (UoW CDMS) is developed by the Programming Team at WCTU and all specifications (i.e. database variables, validation checks, screens) are agreed between the programmer and appropriate study staff.

5.3 Online video platform

Microsoft Teams will be used for the ReSTORe study interventions. This platform will enable live streaming of intervention sessions. The freely available prerecorded online videos produced by national stroke charities will be available in a link for the participant that will take them to YouTube.

5.4 One-to-one consultation platform

All one-to-one consultations between the ReSTORe specialists and a study participant will take place on an online video platform (Microsoft Teams). This will include the best practice usual care advice consultation in the control group and the individual assessment component of the ReSTORe intervention.

5.5 Data storage

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

5.6 Data access and quality assurance

Most data will be received directly from participants who will enter their data into the online study database. Following the completion of the initial screen form (which includes an initial eligibility check and provision of contact details) participants will be contacted using the contact details that they have provided to confirm eligibility. Participants will complete an online consent form. After the collection of the baseline demographic data for each participant and following randomisation, data where possible will be pseudonymised. Confidentiality will be strictly maintained and names, addresses or personal identifiable information will not be disclosed to anyone other than the staff involved in running the study. All electronic participant-identifiable information will be held on a secure, password-protected database accessible only to authorised personnel. Direct access to source data (online study database) will be available for study-related monitoring or audit by UHCW or WCTU for internal audit or regulatory authorities.

5.7 Data Shared with Third Parties

Requests for data sharing will be managed in accordance with UoW SOP 15 Part 3. The datasets generated during and/or analysed during the current study will be available upon request after publication of the main study results. The publication of a study protocol, study results and study data will comply with the NIHR standard terms and will follow Warwick SOP 22: Publication & Dissemination. Data will be shared with the following parties:

- Twilio
- APPEN (Transcription service)
- NHS Digitrials

5.8 Archiving

Study documentation and data will be archived for at least five years after completion of the study at the UoW WCTU. Study documentation and data at UHCW will be archived for 10 years after completion of the study. Study documentation and data held by NHS PIC sites will be stored in line with their local trust policy.

If the decision is made that records held by the sponsor/coordinating centre no longer need to be retained, the reasons for destruction of essential documents should be documented and signed by the Head or Deputy Head of Operations.

This record/certificate of destruction should be retained (by the WCTU QA team for WCTU managed studies) for a further five years from the date that the essential documents were destroyed. There is no need to destroy documents after the minimum archive period is reached as long as all commitments regarding personal data have been met and there is sufficient funding available.

Personal data will be securely removed after it has been used for stated purposes. The removal process will depend upon the software used to secure the data. Personal data associated with research participants should not be stored on the network drive without use of additional encryption, where possible it should be contained within the CDMS (ReSTORe Database).

6. STATISTICAL ANALYSIS

6.1 Power and sample size

Sample size: We will recruit 600 participants (control arm: 288; intervention arm: 312; allocation ratio 1:1.08) (51) with 5% significance level, 90% power, and 20% loss to follow-up to detect our target difference between trial arms. The following justifications have been used to choose the parameter values for the estimation of the sample size:

1. Effect size and standard deviation: We have used a target difference of 0.04 on the PROPr score based on data from the National Institute for Health (NIH) (52), and a standard deviation of 0.18 using data from our REGAIN trial [11].

2. Correlation: The required sample size will be lower if there is a correlation between the baseline and 6-month primary outcome timepoints (53). In our REGAIN trial, with the same primary outcome, we observed such a correlation. For ReSTORe we have used a correlation value of 0.7 (lower limit of 95% CI from REGAIN data) in the sample estimation.

3. Intra-class correlation coefficient (ICC): To account for the possible dependency between the primary outcome values in a cluster in the intervention arm, we used an ICC value 0.03 from the REGAIN trial [11].

4. Cluster size in the intervention arm: We have used a mean cluster size in the intervention arm of 8 (as per our REGAIN trial,[11]).

5. Loss to follow-up rate: We have assumed a 20% loss to follow-up (the REGAIN trial had approximately 17% loss of follow-up data on the primary outcome). To account for a higher than expected dropout rate the study will over recruit until sufficient participants meet the primary end point. Recruitment will be within approximately 10% of the original target and end of recruitment will be determined by the trial statistician in consultation with the trial management team/TMG as appropriate.

6.2 Statistical analysis of efficacy and harms

6.2.1 Statistics and data analysis

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

Data will be summarised and reported as per CONSORT, using intention-to-treat analyses.

For the primary outcome measures, treatment effects (with 95% Confidence Intervals) will be estimated using a partially nested heteroscedastic regression model, adjusted for clinically important variables. This is to accommodate for the clustering in the intervention group and the individual patient observation in the control arm. We will examine the clustering effect and, if this is significant, we will fit the above models with the clustering variable as a random effect; otherwise, it will be fitted as a fixed effect. We will use an Estimand Framework to assess intercurrent events (ICEs) and handle any missing data. Intercurrent events will include non-compliance (as defined by criteria agreed with the DMC and the trial management committee), assessed using CACE (Complier Average Causal Effect) analysis.

Other secondary outcomes which are continuous will be analysed in a similar way to the primary outcome. For categorical secondary outcomes, analogous models will be computed with summaries based on odds ratio and 95% confidence interval of odds ratios. Withdrawal and adverse event data will be compared between the arms using chi-squared test statistics. Graphical plots will be produced displaying the means and confidence intervals from baseline over the 3 follow-up periods. There are no formal interim analyses for this study.

6.2.2 Planned recruitment rate

A recruitment rate of ~50 participants per month will be required after the six-month internal pilot (n~200). Participants will be from primary and secondary care registers in addition to participants identified via public health/research registries. The target recruitment rate for the study has been discussed with and agreed by the Trial Management Group (TMG).

6.3 Subgroup analyses

Pre-specified, exploratory sub-group analysis will include age (<65 or ≥65), sex and simplified modified Rankin Scale (≤2 or 3-4). The sub-group effects will be assessed using regression modelling with the interaction term of sub-group and treatment. As the sub-groups are not powered, the results will be reported using 95% confidence intervals.

6.4 Health economic evaluation

A prospectively planned economic evaluation will be conducted from a NHS and personal social services perspective, according to the recommendations of the NICE reference case [50].

The costs associated with implementing the intervention and control will be captured by the trial team. Additionally, participants' health service contacts will be recorded at three, six and twelve months, this includes: healthcare, local authority-provided day care and NHS residential services. Time lost from work (paid/unpaid) and patient-borne health costs (e.g. wheelchair by type, home adaptations, feeding aids, walking aids, home-help, support from relatives) will also be recorded to examine a broader social perspective. Healthcare resource use will be costed using most recently available published national reference costs, reflated to a common year [51, 52].

Generic health-related quality-of-life will be assessed at baseline, three, six, and twelve months using the EQ-5D-5L questionnaire. EQ-5D-5L scores will be converted to health status scores using the UK value set recommended by NICE guidance at the time of analysis [53]. Using the trapezoidal rule, the area-under-the-curve of health status scores will be calculated, providing patient-level QALY estimates. Reflecting the one-year timeframe, costs and QALYs will be undiscounted.

Mechanisms of missingness of data will be explored and multiple imputation methods will be applied where appropriate to impute missing data. Imputation sets will be used in bivariate analysis of costs and QALYs, using the STATA MI framework. Within-study (12 month) incremental cost per QALY estimates and confidence intervals will be estimated [54-57]. Findings will be analysed and visualised in the cost-effectiveness plane, as cost-effectiveness acceptability curves, net monetary benefit and value of information analysis. At the time of writing no method is available to analyse one-arm clustering within a bivariate regression framework. Ignoring clustering may result in some over-precision of findings if the clustering effect is significant, although have limited scope to systematically bias findings. The importance of clustering will be explored within a hierarchical univariate sensitivity analysis of net monetary benefit (NMB) at varying thresholds of willingness to pay. If incremental costs and benefits are non-convergent within the study follow-up then extrapolated modelling will be considered.

6.5 Qualitative data analysis

The semi-structured interviews with ~n=25 intervention group, ~n=25 control and ~n=5 practitioner's will be recorded, subject to the permission of each participant/practitioner, pseudonymised, and transcribed verbatim. Framework analysis will be used to analyse the data [58].

This will involve:

- Data familiarisation: listening to digital recordings, reading transcripts, and re-reading field notes;
- Identifying a thematic framework: key issues and themes identified, and an index of codes is developed;
- Indexing: this index is applied to all data;
- Charting: a summary of each passage of text is transferred into a chart to allow more overall and abstract consideration of index codes across the data set and by each individual;
- Mapping and interpretation: understanding the meaning of key themes, dimensions and broad overall picture of the data and identifying and understanding the typical associations between themes and dimensions. We will remain vigilant for any new themes emerging from the data as we progress. The computer package NVivo 12 will be used to organise the data.

The charting process provides an opportunity to code data from numerous perspectives. The computer package NVivo 12 will be used to organise the analysis.

The findings of the qualitative work will be reported as a separate chapter in the final report but will also be incorporated in the discussion to bring together a synthesis of all the results, thus helping to explore and explain the overall 'value' of the interventions. Quantitative and qualitative data will be integrated using a mixed methods matrix' where quantitative responses can be compared to interview data and recorded on a matrix. This is particularly useful to reveal gaps between quantitative and qualitative insights.

From the intervention delivery recordings (initial practitioner assessment, the exercise familiarisation session and the psychological support sessions) and control (1:1 session) recordings, a purposively selected subset (10%) of recordings will be analysed, with a checklist to assess fidelity and using the qualitative approach detailed above to help understand which areas generated discussion and what issues were discussed. Intervention fidelity will be assessed using the tenets highlighted by Mars et al[59].

7. STUDY ORGANISATION AND OVERSIGHT

7.1 Sponsorship and governance arrangements

University Hospitals Coventry and Warwickshire NHS Trust will act as Sponsor for the study and undertake the responsibilities as defined by the UK Policy Framework for Health and Social Care

Research and Good Clinical Practice guidelines. An authorised representative of the Sponsor has approved the final version of this protocol with respect to the study design, conduct, data analysis and interpretation and plans for publication and dissemination of results.

Study management will be undertaken at Warwick Clinical Trials Unit, University of Warwick. A sub-contract agreement is in place between UHCW and WCTU who will provide full research management services. This will specify whose SOPs will be adhered to for each aspect of the study.

PIC agreements will also be in place between the Sponsor and each research site, with clear delegation of roles and responsibilities.

7.2 Ethical approval and consideration

All ethical approvals will be sought using the Integrated Research Application System. The study will be conducted in accordance with relevant regulations and guidelines. The REC and sponsor will be notified of the end of the study (whether the study ends at the planned time or prematurely). The CI will submit a final report to the required authorities with the results, including any publications, within one year of study end.

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

Substantial protocol amendments (e.g. changes to eligibility criteria) will be communicated by the study team to relevant parties i.e. investigators, participants, NHS Trusts and study registries once approved.

Relevant data, including identifiable data, will be entered directly by participants into a secure online database provided by WCTU (UoW CDMS), although in some instances, data may be entered into the database by ReSTORe specialists at UHCW or WCTU ReSTORe team during telephone calls with study participants. These data will be considered as source data for the study.

We will ensure that staff undertaking study recruitment are trained in GCP and consent procedures.

All study staff will ensure that participants' anonymity is maintained. Participant identifiable information collected for the study will be stored securely on the electronic database. All data will be stored securely and will only be accessed by study staff and authorised personnel.

ReSTORe will comply with relevant UK data protection legislation, which requires data to be pseudonymised as soon as it is practical to do so. Identifiable data will be deleted after the final results have been published.

7.3 Study Registration

The study will be registered on the International Standard Randomised Controlled Trial Number (ISRCTN) Register.

7.4 Notification of serious breaches to GCP and/or study protocol

Trial protocol deviation and violations

Deviation	Change or departure from the protocol, other key trial documents and/or GCP that does not result in harm to the participants or significantly affect the scientific value of the reported results of the study.
Violation	Failure to comply with or variance from GCP and/or the final approved protocol. This results from error, fraud or misconduct. These cases should be documented in the protocol deviation and violation section of the case report form for the trial and appropriate corrective and preventative actions taken. Deviations will be included and considered when the clinical trial report is produced, as they may have an impact on the analysis of the data.
Serious Breach	A Serious Breach which is likely to effect to a significant degree –

	(a) the safety or physical or mental integrity of the subjects of the study; or **(b)** the scientific value of the study The sponsor will be notified immediately of any case where the above definition applies during the study conduct phase and will notify the licensing authority in writing of any serious breach of **(a)** the conditions and principles of GCP in connection with that study; or **(b)** the protocol relating to that study, as amended from time to time, within seven days of becoming aware of that breach

The above should be aligned with the UoW SOP 31v5.0

7.5 Indemnity

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

7.6 Study timetable and milestones

Year	Apr-Jun 2024	July-Sep 2024	Oct-Dec 2024	Jan-March 2025	April-June 2025	July-Sep 2025	Oct-Dec 2025	Jan-March 2026	April-June 2026	July-Sep 2026	Oct-Dec 2026	Jan-March 2027
Month	-3 - 0	1 - 3	4 - 6	7 - 9	10-12	13-15	16-18	19-21	22-24	25-27	28-30	31-33
Approvals/set-up/pre-pilot												
Mailouts												
Internal pilot												
Recruitment												
Intervention												
3-month FU												
6-month FU												
12-month FU												
Analysis/reporting												
TSC/DMC												
Close-down												

Month 0 estimated to commence 01st July 2024.

7.7 Administration

The study coordination will be based at Warwick Clinical Trials Unit, University of Warwick.

7.8 Trial Management Group (TMG)

The Trial Management Group, consisting of the project staff and co-investigators involved in the day-to-day running of the study, will meet regularly throughout the project. Significant issues arising from management meetings will be referred to the Trial Steering Committee or Investigators, as appropriate.

The full remit and responsibilities of the TMG will be documented in the Charter which will be signed by all members.

7.9 Trial Steering Committee (TSC)

The study will be guided by a group of respected and experienced personnel and trial methodologists as well as at least one 'lay' representative. The TSC will have an independent chairperson. Meetings will be held at regular intervals determined by need but not less than once a year. Routine business is conducted by email, post or teleconferencing.

The Steering Committee, in the development of this protocol and throughout the study will take responsibility for:

- Major decisions such as a need to change the protocol for any reason
- Monitoring and supervising the progress of the study
- Reviewing relevant information from other sources
- Considering recommendations from the DMC
- Informing and advising on all aspects of the study

The membership of the TSC is shown on page 5.

The full remit and responsibilities of the TSC will be documented in the Committee Charter which will be signed by all members.

7.10 Data Monitoring Committee (DMC)

The DMC will consist of independent experts with relevant clinical research, and statistical experience. The DMC meeting frequency will be guided by the DMC chair but will be suggested to be three months into the recruitment phase and regularly thereafter, as directed by the DMC chair. Confidential reports containing recruitment, protocol compliance, safety data and interim assessments of outcomes will be reviewed by the DMC. The DMC will advise the TSC as to whether there is evidence or reason why the study should be amended or terminated. The membership of the DMC will be approved and appointed by the NIHR.

DMC meetings may also be attended by the CI and Trial Manager (for non-confidential parts of the meeting) and the trial statistician.

The full remit and responsibilities of the DMC will be documented in the Committee Charter which will be signed by all members.

7.11 Essential Documentation

A Trial Master File will be set up in accordance with UoW SOP 11 - Essential Documentation and held securely at WCTU. Investigator Site Files will be prepared electronically and the content for the investigator site files will be uploaded to the study website for sites to download. UHCW will hold and maintain a Sponsor oversight file.

7.12 Financial Support

This study has been funded by NIHR Health Technology Assessment (HTA) Programme - NIHR157510.

8. MONITORING, AUDIT AND INSPECTION

The study will be monitored by the Research and Development Department at UHCW as representatives of the lead Sponsor (the monitor will be appropriately trained in accordance with UHCW R&D SOP 18), and by the Quality Assurance team at WCTU as representatives of the study coordinating centre and academic lead, to ensure that the study is being conducted as per protocol, adhering to Research Governance and GCP. The approach to, and extent of, monitoring will be specified in a study monitoring plan determined by the risk assessment undertaken prior to the start of the study. A Trial Monitoring Plan will be developed and agreed by the TMG and TSC based on the study risk assessment, including on site monitoring if applicable. Processes to be considered in the monitoring plan will include participant enrolment, consent, eligibility, and allocation to study groups; adherence to study interventions and policies to protect participants, including reporting of harm and completeness, accuracy, and timeliness of data collection. The plan will be available from the study coordination centre and will also be lodged with the sponsor. Whilst the monitors work in the same institution as the study team (WCTU), they will act independently in this role.

If UHCW has evidence that the study protocol and procedures are not being adhered to, an on-site monitoring visit may be triggered.

9. PATIENT AND PUBLIC INVOLVEMENT (PPI)

We have set up a reference group of stroke survivors sourced from the University of Sheffield. The PPI group will advise on intervention content, study processes and outcomes. As part of setting up this group, we will identify two further Stroke survivors to join the Trial Management Group and Steering Committee.

Our lay co-applicants will sit on the trial management group (TMG), initially meeting monthly and subsequently quarterly, and will have a pivotal role in steering the conduct of the study. They will review the ethics application to ensure that study documentation e.g. participant information sheet, is user appropriate. They will be given the opportunity to engage in study publicity and the

dissemination of findings through appropriate channels i.e. social media, lay conferences, public engagement events, service provider events, newsletter articles. They will be viewed as members of the research team, with experience and skill that can contribute fully to the successful conduct of the study and will be asked to be involved in measuring and reporting research impact. A role description and terms of reference for lay co-applicants has been produced in collaboration with our lay partners. This will ensure that both parties understand the nature and extent of the collaboration, and their expectations of each other.

In addition to reviewing ethics documentation, we will ask our lay partners to work closely with the research team, acting as critical reviewers, in finalising the resources for ReSTORe - practitioner manual and the control group information. This is essential to ensure creation of feasible, acceptable and participant friendly resources. They will also help develop the interview topic guide and will contribute to the interpretation of qualitative data analysis.

Lay co-apps and partners will be supported by the Chief Investigator, study coordination team, and through the peer support of lay partners on existing clinical trials. All activity will be appropriately reimbursed at INVOLVE rates, for which there is adequate provision in the budget. Lay partners will also benefit from training and support from WCTU's existing one-day face-to-face training programme for patient and public partners which was developed in collaboration with a patient partner from another study who suggested the original need for, and content of, the course.

10. DISSEMINATION AND PUBLICATION

Full results of the study will be prepared by the research team and lay partners and submitted to funders as a final report. Findings will be submitted to peer-reviewed journals and disseminated to the medical and exercise rehabilitation communities. We will publish papers in open-access journals describing the development and refinement of the ReSTORe intervention, and the study protocol, as per recommended guidance for transparent reporting, the Consolidated Standards of Reporting Trials (CONSORT) guidelines (www.consort-statement.org), the NIHR standard terms, and UoW SOP 22: Publication & Dissemination. UHCW NHS Trust as Sponsor will review and approve all publications. We will submit abstracts to national and international conferences.

The ReSTORe intervention will be fully manualised and available for public access once the study has completed. If appropriate, we will develop a practitioner training programme to support the implementation of ReSTORe.

Our lay partners will help prepare the final report and assist with dissemination of study results. We will produce a lay summary for participants and the hospitals/centres involved. Results will be publicised via the study website. At the end of the study, we will host a joint investigator and participant event to promote key findings. The ReSTORe study will be relevant to the NHS thus outputs will follow the usual route into the NHS system and wider society.

HRA guidance on information for participants at the end of a study will be followed: *https://www.hra.nhs.uk/about-us/consultations/closed-consultations/guidance-participant-information-end-study-consultation/*

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12. APPENDICES

12.1 Appendix 1 - Logic model for the ReSTORe psychological intervention.