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RETurn to work After stroKE (RETAKE)

Early vocational rehabilitation compared with usual care for participants: an individually randomised controlled multi-centre pragmatic trial with embedded economic and process evaluations

Final Version 7.0 6th August 2020

Short title:	**RETurn to work After stroKE**
Acronym:	**RETAKE**
ISRCTN:	12464275
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Sponsor reference:	17104
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The RETAKE study will at all times comply with current government and HRA advice regarding COVID-19 for the nation in which the study takes place. The Sponsor will ensure study activities will be amended as required in accordance with the latest guidance. Alternative methods to processes have been suggested throughout respecting COVID-19.

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2. Synopsis

Title	RETurn to work After stroKE: Early vocational rehabilitation compared with usual care for participants: an individually randomised controlled multi-centre pragmatic trial with embedded economic and process evaluations
Short title	RETAKE (RETurn to work After stroKE)
Chief Investigator	Dr Kathryn Radford, Associate Professor in Rehabilitation Research, University of Nottingham
Trial design	Individually randomised controlled multi-centre pragmatic trial with embedded economic and process evaluations.
Setting	Stroke Units and accompanying stroke rehabilitation services
Sample size estimate	760 (420 Early Stroke Specific Vocational Rehabilitation (ESSVR); 340 usual care) gives 90% power (5% alpha) to detect 13% difference in job retention at 12m; assuming 26% control rate , 20% loss to follow-up, clustering in intervention only (2 RETAKE OTs (clusters) per site), cluster size=11 , ICC=0.03, inflation factor=1.23)
Number of participants	760 participants (and their carers (if applicable)) will be recruited from approximately 20 NHS stroke units with accompanying stroke rehabilitation services.
Eligibility criteria	**Stroke Survivors** **Inclusion criteria:** • Age ≥18 years. • Admitted to hospital with new stroke (all severities). • In work at stroke onset (including self-employed, paid or unpaid). • Willing and have capacity to provide informed consent to participate in the study. • Have sufficient proficiency in English to contribute to the data collection required for research. **Exclusion criteria** • Not intending to work. **Carers** **Inclusion criteria:** • Nominated carer of consenting participant. • Willing and have capacity to provide informed consent to participate in the study. • Have sufficient proficiency in English to contribute to the data collection required for research. **Exclusion criteria:** • None

Description of interventions	The Early Stroke Specialist Vocational Rehabilitation (ESSVR) model (intervention) will be compared to a usual care (control) group. **Intervention group:** ESSVR will be delivered by a stroke specialist occupational therapist (OT) who is trained to assess the impact of the stroke on the participant and their job; coordinate appropriate support from NHS, employer and other stakeholders; negotiate workplace adjustments, monitor return to work and explore alternatives where current work is not feasible or cannot be sustained. It will be tailored to individual needs. **Usual care (UC) group:** Usual NHS rehabilitation provided by usual care team. This may involve outpatient/community physio-, speech- or occupational- therapy, psychology, medical follow-up.	
Duration of study	53 months: 9 months set-up; 26 months recruitment (including 6 month internal pilot); 12 months follow-up; 6 months analysis.	
Randomisation and blinding	Participants will be individually randomised in a 5:4 allocation ratio (ESSVR:UC) to ensure the study is powered for the primary objective while accounting for the partially nested design of the study. Randomisation will be performed using the CTRU automated randomisation service. Allocation will use a computer-generated minimisation program incorporating a random element, stratified by site; participant age and stroke severity. Participants and personnel delivering the ESSVR intervention will not be blind to allocation group. Processes will be put in place to minimise the risk of contamination between OTs. Outcome assessment will be performed blind to allocation, where possible.	
	Objectives	**Outcome Measures**
Primary	To establish whether Early Stroke Specialist Vocational Rehabilitation (ESSVR) plus usual care is more effective than usual care alone at improving participants self-reported work outcomes 12 months after randomisation.	Self-reported return to work of at least 2 hours per week at 12 months post randomisation.
Secondary All secondary outcomes are measured at 3, 6 and 12 months.	To establish whether work related outcomes are improved by the intervention.	Return to work with same employer, number of hours worked, number of days in work.
	To establish whether the intervention improves mood.	The Hospital Anxiety & Depression Scale (HADS)

		anxiety and depression scores.
	To establish whether the intervention improves physical function.	The Nottingham Extended Activities of Daily Living scale (NEADL) summary score.
	To establish whether the intervention improves social participation.	The Community Integration Questionnaire (CIQ) social and productivity scores.
	To assess work self-efficacy	Measured using a single question from the work ability index.
	To establish whether the intervention is cost effective and improves health-related quality of life.	Measured using the EuroQoL 5 dimension health questionnaire, 5 level (EQ-5D-5L).
	To establish if the intervention changes health and social care resource use, or has an impact on wider resource use (e.g. productivity, personal or carer costs).	Self-reported A&E attendances, hospital admission/readmission, number of work accidents, overall health and social care resource use, measured using a bespoke patient completed resource use questionnaire.
	To establish whether the intervention improves post-stroke confidence.	The Confidence after Stroke Measure (CaSM) summary score.
	To establish whether the intervention reduces carer burden.	The Modified Caregiver Strain Index (mCSI)
	To assess the impact of COVID-19 on trial participants.	Work status (including changes to this), current situation, financial difficulties, benefits applied for/obtained as a result of COVID-19.
Process Evaluation	To measure intervention compliance and understand how the intervention is experienced and understood by providers and recipients, and explore the organisational implications of embedding and sustaining the intervention in preparation for wider NHS roll-out.	Measured using an embedded mixed-methods process evaluation using a range of methods including observations, qualitative interviews with participants, carers, service providers, employers and mentors, non-participant observation in sites, document analysis (case records and intervention proformas) and care mapping in a random sample of cases (up to 5% of

		participants in both ESSVR and UC).
Internal Pilot (8 Sites)	To assess whether study recruitment and six-month follow-up rates meet the predefined progression criteria thresholds.	Recruitment rates at 4 – 6 months post randomisation; and follow-up rates after 12 months post-randomisation.
Statistical methods	A detailed statistical analysis plan will be drafted and will be finalised and agreed by the appropriate members of the research team before any analyses are undertaken. The primary analysis will compare the proportions of participants in work at 12 months post randomisation between arms using a mixed effects logistic regression model allowing for clustering of outcomes in the intervention arm. See section 17 for further details.	

3. Abbreviations

AE	Adverse Event
CaSM	Confidence after Stroke Measure
CEAC	Cost-effectiveness Acceptability Curve
CI	Chief Investigator
CIQ	Community Integration Questionnaire
CLAHRC	Collaborations for Leadership in Applied Health Research and Care
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
CRN	Clinical Research Network
CTRU	Clinical Trials Research Unit
DMEC	Data Monitoring & Ethics Committee
DWP	Department for Work and Pensions
EQ-5D-5L	EuroQoL 5 dimension health questionnaire, 5 level
ESSVR	Early Stroke Specialist Vocational Rehabilitation
GCP	Good Clinical Practice
GP	General Practitioner
HADS	The Hospital Anxiety & Depression Scale
HCP	Healthcare Professional
HRA	Health Research Authority
HTA	Health Technology Assessment
ICF	Informed Consent Form
ICF	International Classification of Function
ICMJE	International Committee of Medical Journal Editors
ISF	Investigator Site File
ISRCTN	International Standard Randomised Controlled Trial Number
LICTR	Leeds Institute of Clinical Trials Research
MRC	Medical Research Council
NEADL	The Nottingham Extended Activities of Daily Living scale
NHS	National Health Service
NIHR	National Institute for Health Research
NPT	Normalization Process Theory
NRES	National Research Ethics Service
OT	Occupational Therapist
PE	Process Evaluation
PI	Principal Investigator
PIS	Participant Information Sheet
PSS	Personal Social Services
QALY	Quality-adjusted Life Year
RA	Research Assistant
RCT	Randomised controlled trial
REC	Research Ethics Committee
RGF	Research Governance Framework
RTW	Return to Work
RUSAE	Related, Unexpected Serious Adverse Event
R&D	Research and Development department
SAE	Serious Adverse Event
SAS	statistical analysis software

SFQ	Feasibility Questionnaire
SOP	Standard Operating Procedure
SPSS	Statistical Package for the Social Sciences (SPSS)
SSNAP	Sentinel Stroke National Audit Programme
TIDieR	Template for Intervention Description and Replication
TSC	Trial Steering Committee
UC	Usual Care
UoN	University of Nottingham
VR	Vocational Rehabilitation

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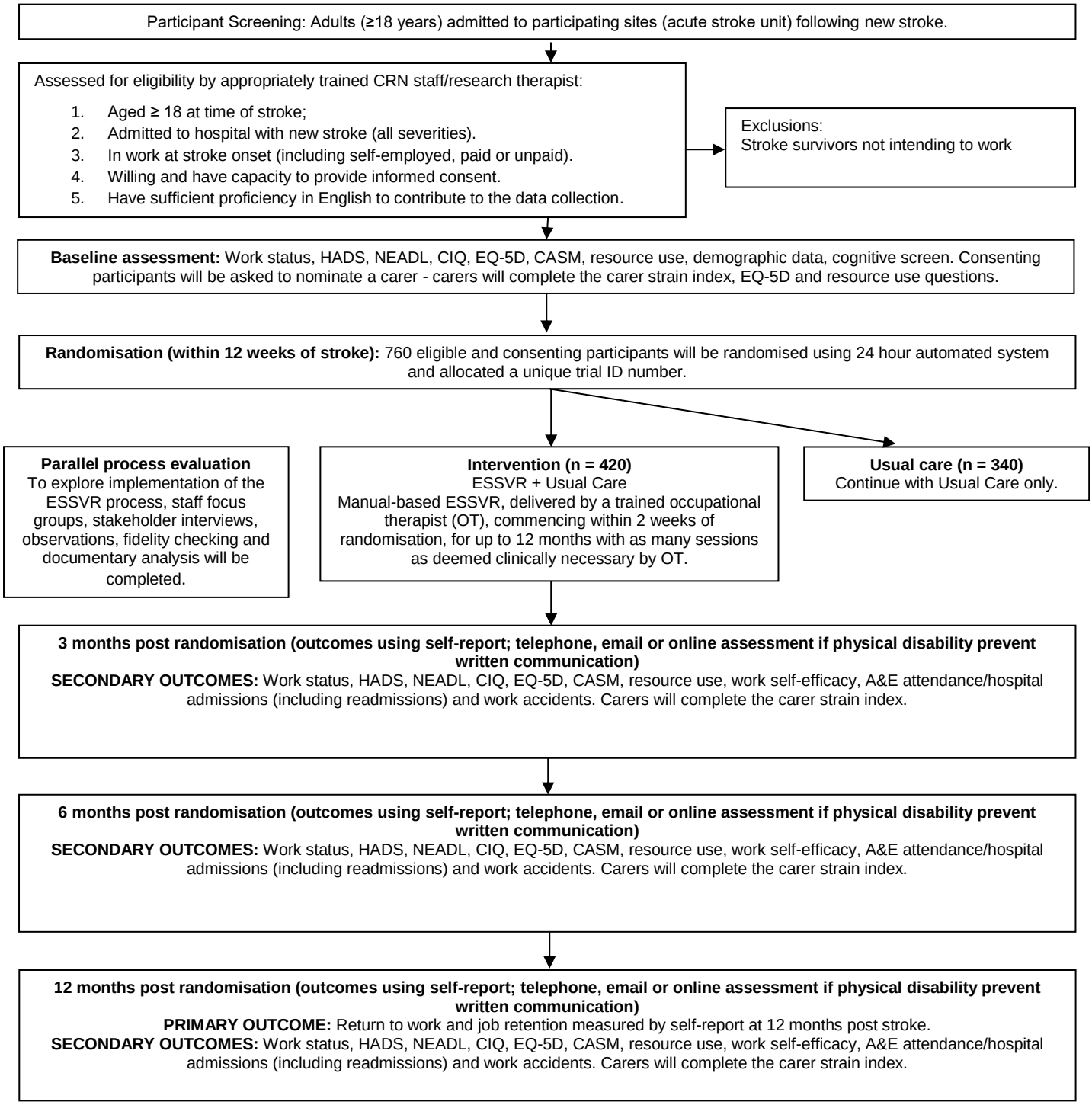
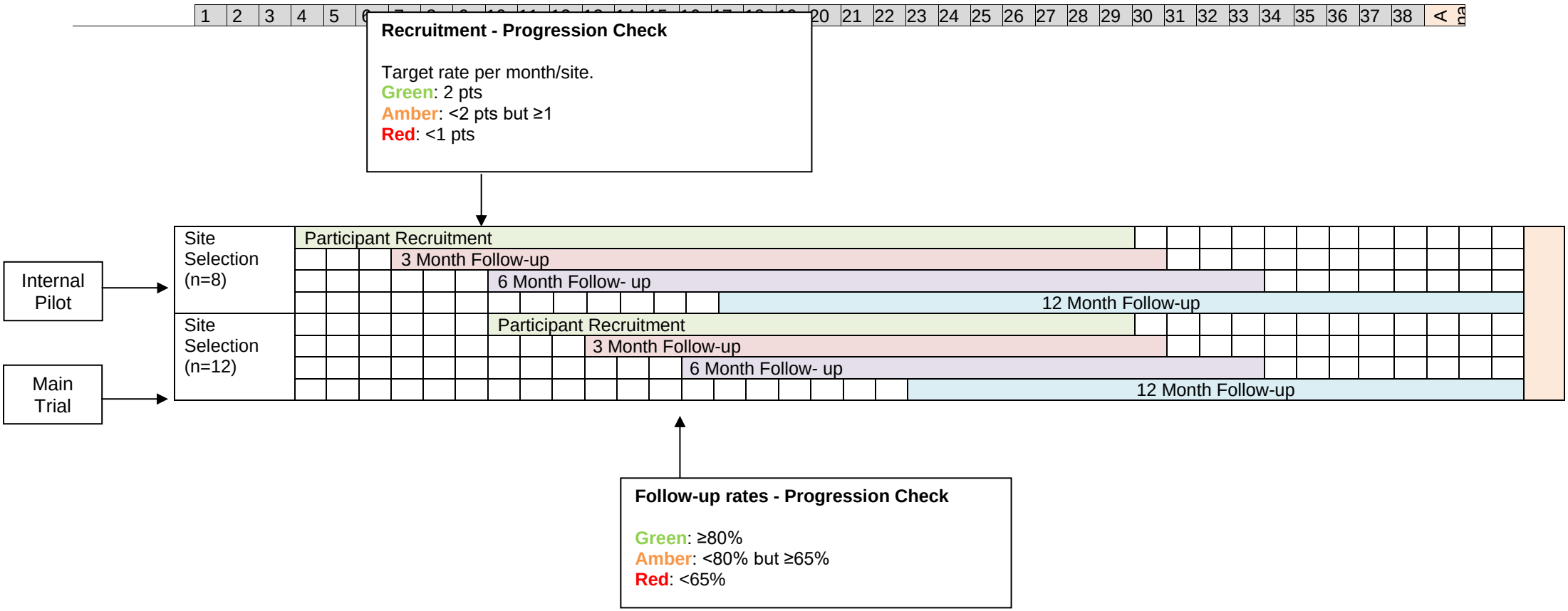
4. Flow Diagrams

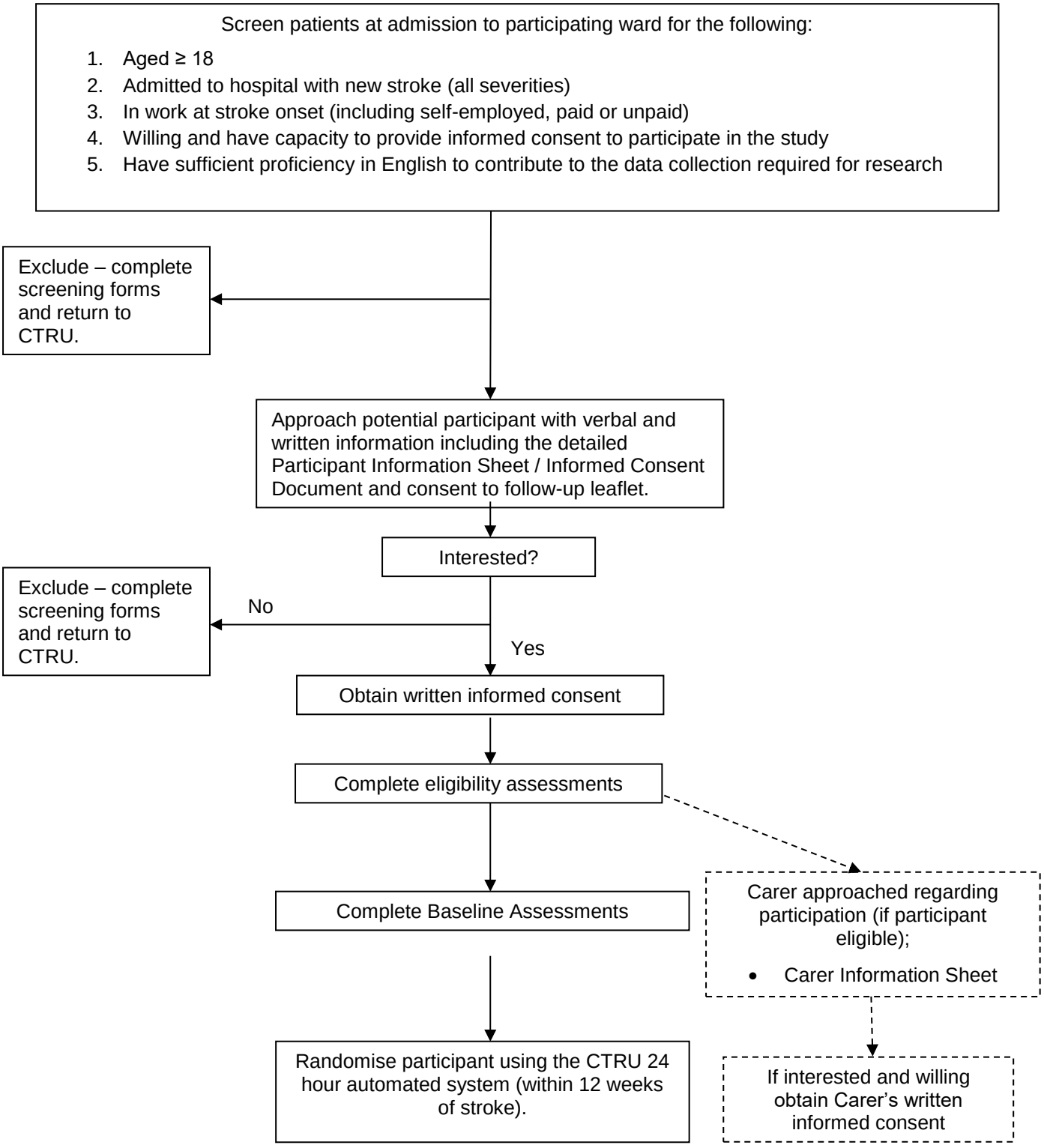
4.1 Flow Diagram 1 – Patient Pathway



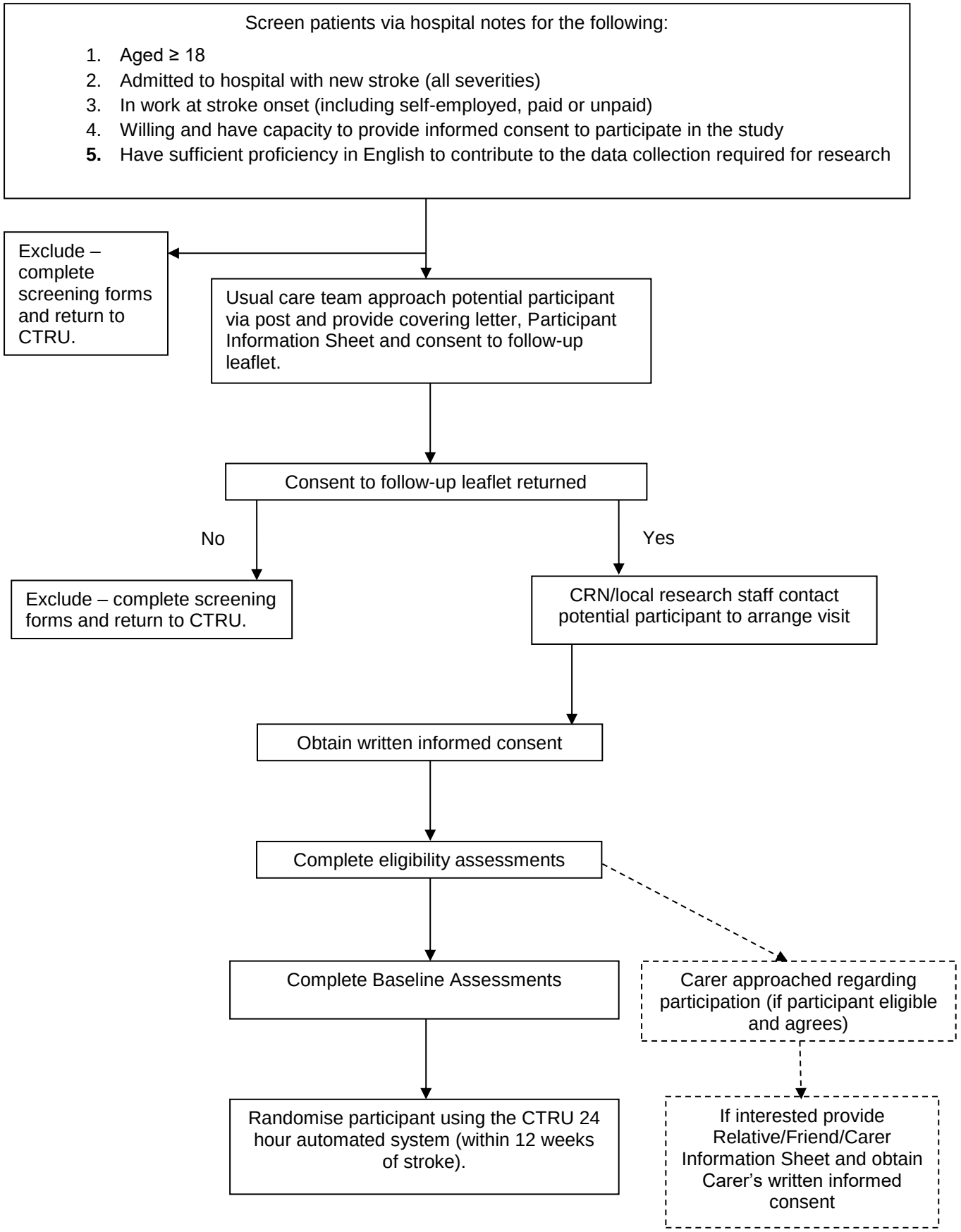
4.2 Flow Diagram 2 – Study Progression



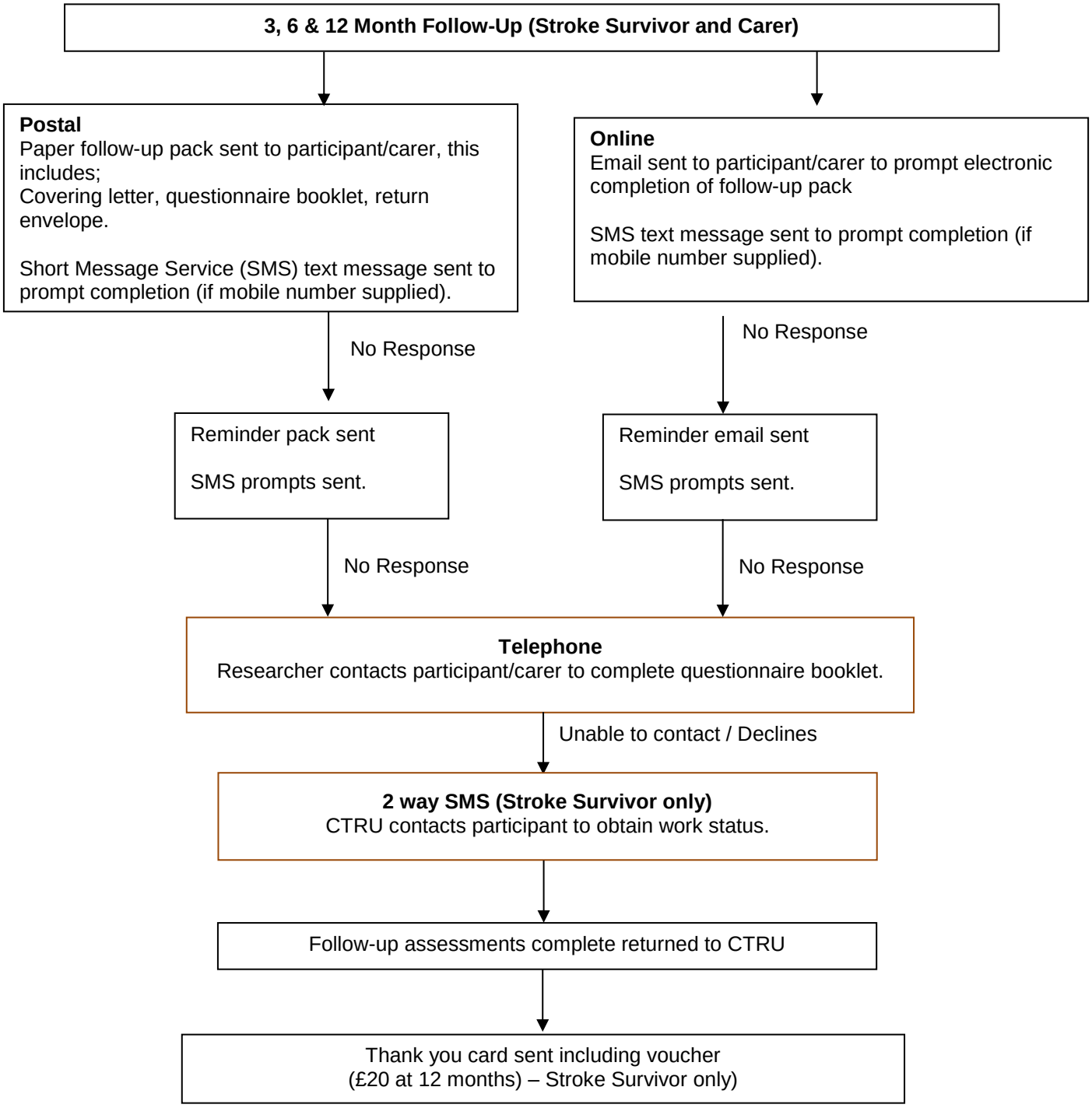
4.3 Flow Diagram 3 – Participant Recruitment in Hospital



4.4 Flow Diagram 4 – Participant Recruitment post-hospital discharge

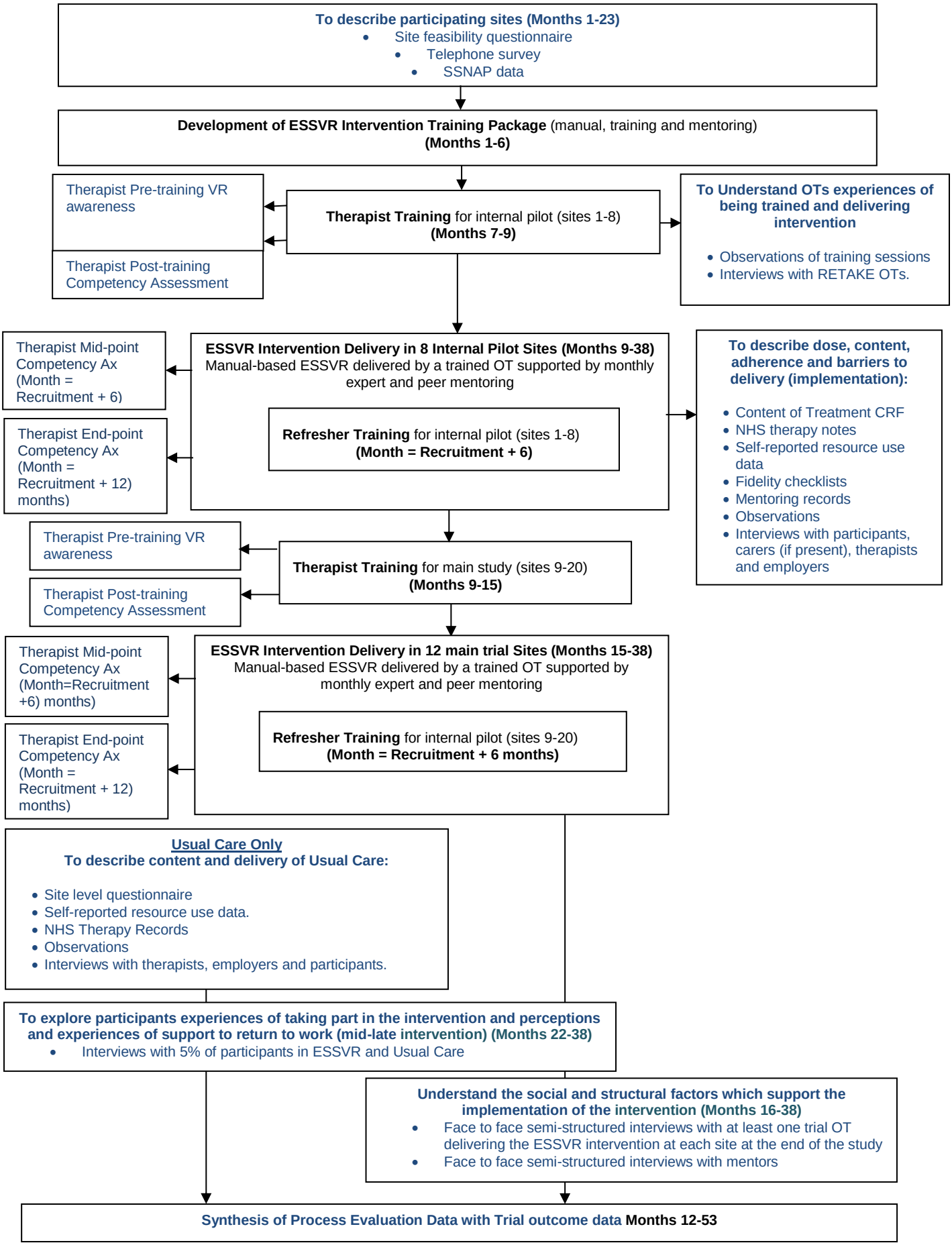


4.5 Flow Diagram 5 – Follow-up



We will seek consent from Stroke Survivors to share their details with the Department for Work and Pensions (DWP) to obtain information on their work status.

4.6 Flow diagram 6 – Process evaluation



5. Background and Rationale

Return to work after stroke (RETAKE) is a multicentre prospective individually randomised controlled trial (RCT) to test the effectiveness and cost-effectiveness of an Early Stroke Specific Vocational Rehabilitation (ESSVR) intervention on participants' 12 month work outcomes, with internal pilot and embedded process evaluation.

5.1 Background

Returning to work is a major goal for many participants but less than 50% of those working at stroke onset return (1). Residual physical, cognitive and language impairments limit the ability to return to a previous job or find new work (3,43). However, participant's beliefs (5), employer attitudes (6) and access to timely rehabilitation to support a return to an existing employer (7) may be more important determinants of success.

Vocational Rehabilitation (VR) involves helping people find work, prevent job loss and support career progression despite disability. The need for VR is recognised in Policy and Clinical Guidelines (8-15) yet it is not always seen as the job of health services (16) or routinely provided (16,17) by them. Only 37% of primary care trusts offer VR in stroke rehabilitation (16). Without a health based intervention, there is no obvious route to VR for participants (17).

Affording those who can work the opportunity, is a UK Government priority (11, 14), a recognised role for healthcare professionals (HCPs) (12, 14, 15) and an NHS outcome (26). Unfortunately NHS HCPs lack confidence to engage with employers, so despite clinical guidelines recommending partnership working between NHS and employment services, this doesn't routinely happen (27). However, participants and employers want to be supported by stroke specialists and employers welcome communication from NHS therapists (6,18).

5.2 Evidence explaining why this research is needed now

Every year 110,000 people in England have a stroke (11); 25% are working age (1). For many, a primary goal is to return to work (RTW) yet fewer than 50% of those working at onset do (1). This has huge economic impact. The societal cost of stroke, including health, social care, caregiving and lost productivity was estimated at £9 billion p.a. (£UK 2003) (18). This includes £4 billion direct treatment costs (5% of UK NHS costs), productivity losses of £1.5 billion and £841 million benefit payments. These costs will increase with increased incidence of stroke in younger people (20) improved survival, the ageing population and changes in retirement age provisions (21) resulting in increased strokes in employed people. Long term worklessness is associated with increased risk of depression, suicide and reduced quality of life (22).

People who can't RTW face a lifetime of state dependence. A survey of 2200 UK participants found 69% of 25-59 year olds were unable to RTW (23). McKevitt et al (24) surveyed 1251 UK participants, 1-5 years post-stroke, and identified unmet work needs in 52% and loss of income in 18%. A systematic review (2011) of VR post-stroke (29) identified only one US RCT (n=22, 7 people with stroke) of a case-coordination approach which led to 64% employment compared to 36% in UC at 6 months (30). There has subsequently been a South African RCT involving 94 participants in a 6-week workplace intervention, delivered by OT and physiotherapist alongside hospital rehabilitation (31); 60% of the intervention group RTW at 6 months compared with 20% in UC. But this was a small study in a non-UK setting, so needs replication in an adequately powered UK trial in the NHS.

Early Stroke Specific Vocational Rehabilitation (ESSVR) was developed combining best practice recommendations for VR in acquired brain injury (9) with expert consensus of stroke

specialists, VR experts and participants. The intervention, combining conventional OT with case coordination (32), is intended for delivery in the community as often as required, depending on individual needs determined by an OT with stroke expertise plus additional VR training. ESSVR includes (a) Assessing the impact of stroke on the patient and their job; (b) Educating patients, employers and families about stroke impact on work. Finding strategies to lessen impact e.g. memory aids, pacing to manage fatigue; (c) Work preparation: establishing routines with gradually increasing activity; opportunity to practice work skills e.g. computers to increase concentration, walking to increase stamina; (d) Liaison with employers & employment advisors to plan and monitor a phased RTW.

In the NIHR CLAHRC funded single centre randomised controlled feasibility trial of the ESSVR, the intervention was compared to usual NHS rehabilitation (usual care (UC)) in previously employed participants. 124 potential participants were screened; 92 (74%) were identified as eligible, 46 (36 men, mean 56 years (SD 12.7, range 18-78 years)) agreed to participate (50% of those eligible). Thirty four out of 46 (74%) participants had mild-moderate strokes, 30 (65%) were in professional roles, 10 (22%) self-employed at stroke onset. Thirty two (70%) were followed up at 12-months follow-up. Feasibility was demonstrated; it is possible to recruit from an acute stroke unit; randomise to the trial; deliver ESSVR and measure its effects and costs at 3, 6 and 12 months post stroke in people with mild-moderate stroke. With ESSVR, twice as many people were in work at 12 months post-stroke than with UC and those in work were less depressed (suggesting potential health benefits) (2).. However, as this was a small single-centre feasibility RCT we do not know if observed differences were related to the intervention or due to chance. An adequately powered multi-centre study is needed.

ESSVR may be more effective than usual NHS rehabilitation at helping participants return to or retain work. The study will generate new evidence to inform the clinical and cost effectiveness of supporting RTW in participants whilst highlighting contextual factors that limit clinical implementation and RTW outcome success. Without clinical and economic evaluation evidence, VR is unlikely to be implemented by the NHS (28) because it requires a co-ordinated approach and may be perceived as a non-NHS issue since the benefits are seen to fall outside the NHS (despite Government priorities for getting people into work). The study is likely also to generate lessons about partnership working with employment services for job retention in other populations.

6. Aims and Objectives

6.1 Aims

The aim is to determine whether ESSVR plus usual care is a clinically and cost effective therapy to help people return to work after stroke, when compared with usual care alone.

6.2 Primary Objective

To establish whether ESSVR plus usual NHS rehabilitation delivered by an occupational therapist is more effective than usual NHS rehabilitation alone at improving participants self-reported work outcomes 12 months after randomisation.

6.3 Secondary Objectives

1. To establish whether self-reported work related outcomes are improved by the intervention.
    a. Return to work with the same employer
    b. Number of hours worked per week
    c. Number of days worked
2. To establish whether the intervention improves mood.
3. To establish whether the intervention improves physical function.
4. To establish whether the intervention improves participation.
5. To establish whether the intervention improves health-related quality of life.
6. To assess work self-efficacy.
7. To establish whether the intervention improves post-stroke confidence.
8. To establish if the intervention changes overall health (including A&E visits, inpatient admissions, outpatient visits and primary care use including medications) and social care resource use.
9. To establish whether the intervention is cost-effective compared to usual care alone from an NHS and PSS perspective, in the base case, over the timeframe of the trial.
10. To establish whether the intervention reduces carer burden.
11. To assess the impact of COVID-19 on trial participants.

Secondary objectives will be measured at three, six and 12 months post randomisation, see section 12.1 for full table of assessments.

6.4 Internal Pilot Objectives

1. To assess whether study recruitment and follow-up rates meet the pre-defined progression criteria thresholds after 6 months of recruitment.

    Refer to section 14.3 for further details.

6.5 Process Evaluation Objectives

1. To measure fidelity to the intervention
    a. To ascertain intervention dose by calculating the number and length of intervention sessions delivered.
    b. To describe level of fidelity to the ESSVR intervention by coding content of CRFs completed by RETAKE OTs.
    c. To describe content and dose of usual care and ESSVR by coding content of treatment records completed by RETAKE OTs.
    d. To observe fidelity in practice.

2. To understand the social and structural context in which the intervention is delivered and to identify factors which may influence the quality of implementation.
    a. To describe participating centres in terms of number and grade of qualified staff, number of support staff and caseload.
    b. To understand professionals' experiences of being trained to deliver the intervention.
    c. To understand professionals' experiences of delivering the intervention.
    d. To understand the social and structural factors which support the implementation of the intervention.
    e. To understand participants' experience of being supported to return to work after stroke.

7. Study Design

RETAKE is a pragmatic, multi-centre individually randomised controlled trial (RCT) partially nested study design, including internal pilot with clear progression criteria and an embedded process evaluation.

The study aims to recruit 760 participants (420 ESSVR and 340 usual care) from 20 UK hospitals and linked early supported discharge/community services. An eight site internal pilot will assess recruitment after 6 months, when rates are stabilised, and follow-up after a further six months. The community-based case management intervention will be delivered by trained occupational therapists, and will consist of ESSVR in addition to usual care. Participants in the usual care arm are to receive unrestricted usual care provided by primary care, secondary care, community and social services. This approach has been taken to demonstrate it is feasible to provide our intervention (ESSVR) as part of routine care across the wider NHS, if benefit is demonstrated.

The primary outcome for the study is the proportion of participants in work (paid or unpaid) for at least 2 hours per week 12 months after randomisation. This outcome will be measured as a response to the question: 'Are you currently in work (paid or unpaid) for at least 2 hours per week?'. Data for this outcome will be collected using self-report (postal or online) questionnaires. To maximise data capture of the primary outcome telephone contact or SMS text messages will be used. We will also explore whether data on work status can be obtained from the Department for Work and Pensions (DWP). Data will also be collected at the Occupational Therapist (OT) level to assess adherence to / compliance with the intervention. Health and social care resource use will be collected by participant self-report questionnaires and therapy records in the intervention arm and used to define usual care.

As part of the process evaluation data will be obtained on intervention dose, duration, content and quality of intervention.

For a randomly selected 5% of participants in ESSVR and UC a case study design will be used to explore the content of care, therapist delivery and participant responsiveness to the intervention delivered/received in both arms of the trial. The case study will involve interviews with stroke survivors, their carers (if applicable), RETAKE OTs, other NHS staff and employers to explore their experiences of VR.

In addition, site level data will be gathered to assess staffing levels, current stroke pathways and services and proposed future service developments that may affect the intervention delivery.

7.1 Primary outcome

Self-reported return to work of at least 2 hours per week at 12 months post randomisation. This may be a return to a pre- stroke job or a new job. This will be recorded as a positive

response to the question: ‘Are you currently in work (paid or unpaid) for at least 2 hours per week?’

7.2 Secondary outcomes

Return to work with the same employer, including return to self-employed work.

Number of hours worked: As there is no consensus in the literature about what constitutes a successful work outcome (in terms of the number of hours worked per week or the duration of employment), we will record the mean self-reported hours worked per week at 3, 6 and 12 months as a proportion of the pre-stroke working hours

The number of days in work during the 12-month follow-up period, beginning from the date of randomisation.

Mood, using the Hospital Anxiety and Depression Scale (37). The questionnaire consists of 14 items, 7 measuring anxiety and 7 measuring depression. Participants rate distress experienced in the previous week on a four point scale where 0= no distress and 3 = much distress. Two scores are obtained, one by adding all the anxiety items and the other by adding the depression items. A cut off of 8 is used for both depression and anxiety to indicate caseness (40)

Functional ability measured using the Nottingham Extended Activities of Daily Living index (38), a measure of help needed with instrumental activities of daily living, including walking around outside; doing the housework; using the telephone. Scores are from 0 to 66, with higher values indicating greater independence.

Social participation measured using the Community Integration Questionnaire (39).The CIQ consists of 15 items relevant to home integration (H), social integration (S), and productive activities (P). It is scored on frequency of performing activities or roles, with secondary weight given to whether or not activities are done jointly with others. The social integration and productive activities subscales will be outcomes, ranging from 0 to 12 and 0 to 7 respectively, where a high score indicates good integration.

Health-related quality of life measured using the EuroQol EQ-5D- 5L (40, 41). The EQ-5D-5L is a measure of health utility (quality of life) comprising 5 dimensions: mobility; self-care; usual activities; pain/discomfort; and anxiety/depression. Each dimension has five levels: no problems; slight problems; moderate problems; severe problems; unable/extreme. The EQ-5D-5L can be valued in a number of ways. NICE (2017) (87) currently recommend using the mapping function developed by Van Hout (2012) (88) in the base or reference case analysis. We will value the EQ-5D-5L using the method preferred by NICE as the reference case at the time of analysis but may, if appropriate, value the EQ-5D-5L in more than one way in order to explore the impact the different approaches available.

Health and Social Care resource use will be elicited using a bespoke resource use questionnaire. In the base case, data will be collected relating to the use of health and personal social services (PSS) as recommended by NICE (2013) (58). This will include primary care, secondary care, emergency care, medication use and social services.

Work Self-efficacy measured using a single question from the work ability index 'Assume that your work ability at its best has a value of 10 points. How many points would you give your current work ability?’ which has been shown to be good predictor of retirement due to work disability and mortality in people with acquired brain injury including stroke (59). The lowest score is zero (0).

Confidence measured using the Confidence after Stroke Measure (CaSM) (42), which measures self-confidence, positive attitudes and social confidence after stroke, with

established validity (85) on a scale from 0-81, where high scores reflects the highest level of confidence.

7.3 Duration of the Study

The funded project is 53 months duration from 1st July 2017 to 30th November 2021. Nine months is for set-up period, 26 months recruitment (including 6 months internal pilot), 12 months follow-up and 6 months for analysis and write up.

Progression criteria have been incorporated to determine progression to the main trial at 6 months after the start of internal pilot (for recruitment) and 12 months after the start of internal pilot recruitment (for follow-up).

8. Randomisation and Blinding

8.1 Randomisation

Participants will be individually randomised within 12 weeks of stroke, after confirmation of eligibility, informed consent and collection of baseline data is complete. Informed written consent for entry into the study **must** be obtained prior to randomisation.

Randomisation will be performed using the CTRU automated 24-hour randomisation service, which will provide each participant with a unique Study ID. Usernames/authorisation codes and PINs, provided by the CTRU when all site specific approvals are in place, and used by authorised CRN/local research staff, will be required to access the randomisation service.

Participants will be individually randomised in a 5:4 allocation ratio (ESSVR + usual care: usual care) to ensure the study is powered for the primary objective while accounting for the partially nested design of the study. The increased proportion of participants allocated to the intervention arm accounts for a greater level of correlation anticipated in the outcomes for those receiving ESSVR, as a result of participants being treated by the same occupational therapy staff.

Allocation will use a computer-generated minimisation programme incorporating a random element, stratified by: site, participant age (<55, ≥55) and stroke severity.

The following details will be required at randomisation:

- Participant identifiers: initials, date of birth, NHS number;
- Recruiting site (site code);
- Confirmation of eligibility;
- Confirmation of informed consent;
- Confirmation of completion of baseline assessments;
- Stratification factors (site; age (i.e. date of birth derived as <55 years or ≥55 years); stroke severity)

Web address for 24-hour randomisation service:
https://lictr.leeds.ac.uk/webrand/
Telephone line for 24-hour randomisation service: 0113 343 2290

Following successful randomisation the CRN/local research staff completing the randomisation process will receive an automated email confirming randomisation, randomisation allocation and subsequent actions required.

The RETAKE OTs (or nominated delegate) will receive an automated email, detailing the participant identifiers, randomisation allocation and highlighting subsequent actions required e.g. arranging the first intervention visit with the participant (if allocated to intervention arm). RETAKE OTs will attempt to contact any participants allocated to ESSVR as soon as they are able, to inform them of their allocation.

RETAKE OTs (or nominated delegate) will keep a record of all recruited participants (both ESSVR and UC) to ensure RETAKE OTs do not treat UC participants.

All participants will be notified by CTRU of their allocation via letter, with details of subsequent actions (i.e. contact from RETAKE OTs / follow-up assessments).
CTRU will also inform the participant's GP of study participation, omitting allocation, via letter.

8.2 Blinding

Participants and personnel delivering the intervention will not be blind to allocation group. We have considered how knowledge of allocation status could influence participant and clinician behaviour change in relation to usual care, and have incorporated measures to limit these possibilities.

To minimise the risk of detection bias, baseline data will be collected prior to participant randomisation. CRN/local research staff who are blind to the allocation group will attempt to contact participants who do not return their postal/online follow-up questionnaires following the reminder letter/email.

Although GPs will be informed about trial participation, they will not be informed about allocation status following randomisation, reducing the risk of inducing GP behaviour change based on this knowledge. However, the ESSVR directed liaison with the GP is permitted as part of the intervention.

The wider health and social care team will not be informed about trial participation or allocation status. However, the ESSVR directed contact with the wider health and social care team is permitted as part of the intervention.

The Trial Management Group (TMG) and Trial Steering Committee (TSC) will be blind to the allocation and all reports reviewed by these groups will be presented in a blinded format. If requested by either committee (e.g. due to safety concerns), CTRU will break the blind by providing the relevant allocation status.

8.3 Unblinding

Every effort will be made in order to maintain the blinding for the trial. Where incidents of unblinding do occur, site staff will be asked to inform the CTRU as soon as possible providing detailed information on the circumstances surrounding the incident.

9.0 Trial/Study Management

9.1 Responsibilities

Detailed responsibilities are outlined in relevant Organisational sub-contracts, below provides a summary of general responsibilities.

9.1.1 Sponsor
The Sponsor is responsible for study initiation management and financing of the study as defined by Directive 2001/20/EC. The sponsor delegates some of these responsibilities to CTRU as detailed in the trial contract

9.1.2 Chief Investigator:
The Chief Investigator (CI): As defined by the NHS Research Governance Framework, the CI is responsible for the design, conduct, co-ordination and management of the trial.

9.1.3 Clinical Trials Research Unit (CTRU)

The CTRU will provide set-up, implementation and monitoring of study conduct to CTRU SOPs and MRC GCP standards including study design, protocol development, randomisation design and implementation, database development and provision, CRF design, monitoring schedule and statistical analysis and reporting. In addition, the CTRU will support main REC and Research and Development (R&D) submissions, and site set-up and on-going management including non-clinical training, monitoring reports and promotion of the study. The CTRU will be responsible for the database administrative functions, data management including postal follow-up and telephone reminders, safety reporting, and all statistical analyses.

9.1.4 University of East Anglia (UEA)

UEA will have overall responsibility for the design, analysis and writing up of the health economics component of RETAKE, but will draw upon the expertise of the wider research team to ensure, for example, the dataset is fit for purpose and that the health economic design and analysis is well-informed and appropriate. The health economists working on RETAKE are affiliated to Norwich Clinical Trials Unit (NTCU). A Health Economics Analysis Plan will be drafted in line with NTCU guidance and will draw upon the Statistical Analysis Plan to ensure consistency were appropriate. The HEAP will be reviewed by someone independent of the trial and finalised before trial database lock.

9.1.5 Kings College London

KCL will have overall responsibility for the process evaluation of RETAKE, drawing on the expertise of the wider research team, particularly in relation to evaluation of therapist training, and quantitative data collection.

9.1.6 Principal Investigator

Overall responsibly for conduct of the study at the participating site, including (but not limited to) assessment of eligibility, informed consent and patient safety.

9.1.7 Site Staff

Site research staff are responsible for the conduct of the study in accordance with the study protocol and terms of the statement of activities for the study. RETAKE OTs at site are responsible for delivering the intervention in accordance with the study protocol, the intervention manuals and terms of the statement of activities for the study.

9.2 Oversight / Trial Monitoring Groups

9.2.1 Trial Management Group (TMG): the TMG, comprising the CI, CTRU team, other key external members of staff involved in the trial, and a patient representative will be assigned responsibility for the clinical set-up, on-going management, promotion of the trial, and for the interpretation of results. Specifically the TMG will be responsible for:

- Input into and comment on the protocol, patient information and case report forms (CRFs) at the start of the trial and where amendments are required during the lifetime of the trial.
- Input into the development of the statistical and health economics analysis plan.
- Involvement in the day to day running of the trial, including supporting the Chief Investigator and Clinical Trials Research Unit (CTRU) by providing clinical or other expert guidance to the CTRU and participating sites on trial based matters such as eligibility or treatment queries and interpretation of information recorded on CRFs.
- Attend TMG meetings and provide availability for future TMG meetings.
- Respond to trial correspondence and any questions in a timely fashion.

- Input into the monitoring and classification of serious adverse events (SAEs) where required, including reviewing causality and expectedness (CLINICALLY QUALIFIED MEMBERS ONLY).
- Maintain awareness of accumulating external evidence and assess its impact and relevance.
- Input into the meetings of the Trial Steering Committee (TSC), where invited to do so.
- Provide responses to any issues or concerns raised by the TSC
- Consider the implications of any recommendations made by the TSC
- Promotion of the trial.
- Monitoring and encouraging recruitment.
- Input and advice on the trial monitoring plan.
- Input into the interpretation and writing up of the trial results.
- Allow contact details to be included in the protocol.

The TMG team will meet quarterly as a minimum, dependent upon the phase of the study and the input required as determined by the team.

9.2.2 Trial Steering Committee (TSC)

The TSC, with an independent Chair, will provide overall supervision of the study, in particular monitor study progress, and provide public, clinical, and professional advice, with pre-agreed terms of reference including completion of the pilot study according to pre-defined success criteria. It will include an Independent Chair, not less than two other independent members and a consumer representative. The CI and other members of the TMG may attend the TSC meetings and present and report progress. The Committee will meet annually as a minimum.

For a study of this nature, a separate Data Monitoring and Ethics Committee is not required. Rather, the TSC will adopt a safety function, with the constitution of a sub-committee of independent members to review safety issues, where this becomes necessary.

10. Selection and Withdrawal of participants

10.1 Participant Eligibility

The target population for this study is adults aged 18 years or over, admitted to hospital following a new stroke who are in paid or unpaid work prior to stroke onset. Eligibility waivers to inclusion / exclusion are not permitted.

10.1.1 Inclusion criteria

Patients meeting **all** of the following criteria **will be** considered eligible to take part in the study;

- Age ≥18 years at time of stroke.
- Admitted to hospital with new stroke (all severities).
- In work at stroke onset (including self-employed, paid or unpaid).
- Willing and have capacity to provide informed consent to participate in the study.
- Have sufficient proficiency in English to contribute to the data collection required for research.

Participants with a language barrier resulting from stroke (e.g. aphasia) will still be considered eligible providing capacity to consent can be established. Local sites will seek help from family members or suitably trained independent clinical professionals to include people who satisfy the eligibility criteria wherever possible.

10.1.2 Exclusion criteria

Patients meeting **any** of the following criteria **will not** be eligible to take part in the study;

- Not intending to work.

10.1.3 Expected duration of participation

Participants will be included in the study for up to 12 months from time of randomisation (or withdrawal of consent or death, if sooner). Participants randomised to the intervention will receive individually tailored ESSVR meaning that the number of sessions and time period will not be specified. However, the intervention will not continue beyond the 12 month point.

All participants will be followed up at 3, 6 and 12 months post-randomisation.

10.2 Carer Eligibility

In this study, a carer is defined as follows:

> *A main informal caregiver who provides the participant with support a minimum of once per week.*

10.2.1 Inclusion criteria:

- Nominated carer of consenting participant.
- Willing and have capacity to provide informed consent to participate in the study.
- Have sufficient proficiency in English to contribute to the data collection required for research.

10.2.2 Exclusion criteria:

- None

10.2.3 Expected duration of carer participation

Carers will be included in the trial for up to 12 months post randomisation (or withdrawal of carer or participant consent, or death of the carer or participant, if sooner).

All carers will be followed up at 3, 6 and 12 months post-randomisation.

10.3. Recruitment

10.3.1 Recruitment setting

Recruitment will be from approximately 20 stroke services from across the UK, the sites will have hospital registers of participants to facilitate early identification of participants. The ESSVR will be delivered in participants' homes, local community or in the workplace by trial trained occupational therapists.

Participant recruitment will vary by site dependent upon service infrastructure and patient pathways. These will be established during site set-up and strategies will be put in place to maximise identification and recruitment of potential patients. We plan to recruit adults who have suffered a stroke and their carers (if applicable) from:

- Hyper Acute Stroke Units
- Acute Stroke Units
- Stroke Rehabilitation Units
- Linked early supportive discharge and community rehabilitation services.

Participating sites will be required to have obtained local, ethical and management approvals and to have undertaken appropriate training prior to the start of screening and recruitment into the study. The recruitment target is 760 participants over a 26 month period.

10.3.2 Recruitment process

If required and only where face-to-face recruitment is not possible, recruitment may take place remotely – In these instances study information will be provided in person or via post/email, verbal consent to participate will be sought in the first instance and the baseline assessment administered via telephone / video / online technology with written consent returned via post/email following recruitment. If written consent cannot be obtained, verbal consent will be accepted (all efforts to obtain written evidence of consent must be made. Efforts may include an email from the stroke survivor confirming consent or acknowledging receipt of a copy of the verbal consent form sent via encrypted email or postal return of a signed copy of the original consent form. Printed copies of emails will be attached to the verbal consent form.

Following admission to the recruiting unit / service, the patient's usual care team will work closely with experienced and appropriately trained Clinical Research Network (CRN) / local research staff to screen out clearly ineligible patients and record reasons for ineligibility (e.g. age <18; not in paid or unpaid work at stroke onset). Only the patient's usual care team will have access to patient records prior to consent. The patient's usual care team will also provide detailed information about the eligibility criteria for participation in the trial, and will generate a list of potentially eligible participants to track throughout admission and up to 12 weeks post stroke.

10.3.3 Recruitment in hospital

Recruitment posters will be displayed at each site and will detail the relevant study contact (CRN/local research staff) to allow ward staff/relatives/friends to suggest potentially eligible participants.

Following verbal consent to be approached by a researcher (obtained by the patient's usual care team) the CRN/local Research staff will approach potentially eligible participants (and their carers if appropriate) and raise the possibility of study participation verbally. Potential participants who express an interest will be given verbal and written information and will be provided with an opportunity to have family members or a carer present for further discussion (if wished). During the initial approach the researcher will determine if the potential participant has a carer they wish to nominate, and will provide additional information regarding carer involvement if appropriate.

Potential participants will have a period of time to decide whether they wish to take part in the study. This time period will depend on the length of hospital stay with consideration of time required to support study procedures (i.e. participant recruitment / data collection). CRN/local research staff will confirm eligibility and obtain written informed consent and perform the baseline assessment.

10.3.4 Recruitment post hospital discharge

Potential participants who express an interest in the study during the initial approach in hospital and complete a consent to follow-up leaflet, but are discharged before consent/baseline data collection is obtained, will be contacted by the CRN/local researcher to arrange a visit either at the patient's home or at the hospital, answer any questions and, if applicable, confirm eligibility and obtain written informed consent and perform the baseline assessment.

For potential participants who are not approached during their hospital stay, the patient's usual care team, in liaison with CRN/local research staff, will review hospital notes for eligible patients. Only the patient's usual care team will have access to patient records prior to consent. Patients meeting the eligibility criteria will be sent a consent to follow-up leaflet and a participant information sheet with covering letter from their usual care team informing them about the project. The patient will be asked to return the completed consent to follow-up leaflet within 2 weeks if they are interested in study participation. If the potential participant expresses interest then the CRN/local research staff member will make contact to arrange a visit either at the patient's home or at the hospital, answer any questions and, if applicable, confirm eligibility and obtain written informed consent and perform the baseline assessment.

10.3.5 Carer Recruitment

Carers will only be recruited with consent from the participant i.e. they will not be approached until and unless the participant has identified this person and gives verbal consent for this approach to be made.

Consenting participants will be asked if they wish to nominate a carer during the recruitment process or at the baseline assessment visit.

Carers will be provided with a Relative/Friend/Carer Information Sheet (with covering letter and consent to follow-up leaflet if sent to their home address) informing them about the study.

If carers are interested in participating, CRN/local research staff will discuss what involvement may entail, answer any questions and obtain written/verbal informed consent and perform the baseline assessment.

In a random sample of 5% of participants, carers will be invited to take part in qualitative interviews to explore their experiences of vocational rehabilitation (VR).

10.4 Screening

Each recruiting site will be required to complete anonymised screening forms to monitor and identify potential participants against the eligibility criteria and demonstrate that those recruited are representative of the group as a whole, and record the proportion of refusals and reasons for refusal (where given). A screening form will be completed for all patients identified as potentially eligible (for both in hospital and post-hospital discharge recruitment).

Minimum data recorded will be: age (in years); gender; ethnicity; whether or not the eligibility criteria are satisfied; whether or not written informed consent was obtained (including reason(s) for non-consent if applicable) and; whether or not the patient was randomised.

Screened patients who are not randomised because they are ineligible or because they decline participation will also have the following information recorded: the reason not eligible for study participation OR the reason eligible but declined.

The anonymised screening forms will be returned to the CTRU on a monthly basis to allow timely identification of any issues in the identification or recruitment of participants.

Documented reasons for ineligibility or declining participation will be closely monitored by the central research team as part of a regular review of recruitment progress. This information will also allow for generalisation of study results in accordance with CONSORT reporting guidelines. This information will also be used to highlight any issues in the identification or recruitment of participants during the internal pilot.

CRN/local Research staff will monitor potential participants throughout their hospital stay and seek informed consent to ensure randomisation is within 12 weeks post stroke.

10.5 Informed consent

The Principal Investigator (PI) retains overall responsibility for the informed consent of participants at their site and must ensure that any person delegated responsibility to participate in the informed consent process is duly authorised, trained and competent to participate according to the ethically approved protocol, principles of Good Clinical Practice (GCP) and Declaration of Helsinki 1996 and any other regulatory requirements that might be introduced. Those delegated responsibility will be documented on the Authorised Personnel Log.

The PI or their nominee (CRN/local research staff) will explain the details of the study and provide the relevant information sheet either in person or via post/email, ensuring that the participant has sufficient time to consider their participation. The PI or their nominee will answer any questions that any potential participant has concerning study participation either in person or via telephone.

All participants will provide written informed consent. The Informed Consent Form will be signed and dated by the participant and the PI (or their nominee) prior to the participant undergoing procedures that are specifically for the purposes of the study and are out-with standard routine care at the participating site (including history taking and the collection of identifiable participant data). Where a participant is unable to sign his/her name, s/he will be asked to make a mark on a consent form. Where a participant is unable to sign or make a mark on the consent form verbal consent will be sought that will be witnessed by an independent observer (staff member, relative or friend). The Informed Consent Form will also be signed and date by the witness.

If recruitment is conducted remotely participants will provide verbal consent in the first instance, followed by return of written informed consent by post or email. The name of the participant and the date verbal consent was provided will be recorded on the verbal consent form and signed and dated by the PI or nominee prior to undertaking any study procedures. Following recruitment to the study the Informed Consent Form will be signed and dated by the PI (or their nominee) and sent to the participant by post or email – The participant will be asked to either sign and date the Informed Consent Form and return using the pre-paid envelope provided or reply to the email address provided to confirm agreement to participate.

On receipt of written informed consent the PI (or their nominee) will update the verbal consent form the reflect the method of written consent (post or email).

The right of a patient to refuse participation without giving reasons must be respected. Following informed consent, the participant must remain free to withdraw from the study at any time without giving reasons and without prejudicing his/her further treatment and will be provided with a contact point where he/she may obtain further information about the trial.

Should there be any subsequent amendment to the final protocol, which might affect a participant's participation in the study, continuing consent will be obtained using an amended Informed Consent Form which will be signed by the participant. It will be the responsibility of the PI to ensure this is done in a timely manner and according to any timelines requested by the Clinical Trials Research Unit (CTRU) at the University of Leeds. A record of the consent process, including the date of consent and all those involved, and confirmation that the participant meets all of the eligibility criteria will be kept in the participant's notes. The original consent form will be filed in the Investigator Site File, one copy will be kept by the participant, one retained in the patient's hospital records and one will be returned to the Clinical Trials Research Unit (CTRU) at the University of Leeds.

10.6 Site Identification and Eligibility

Clinical / rehabilitation leads for Stroke Services at NHS Acute Trust / rehabilitation sites will be approached to determine if they wish to take part in the study. Sites expressing an interest in the study will be invited to complete a Site Feasibility Questionnaire (SFQ) to determine that appropriate services are available to support recruitment and delivery of the intervention. The feasibility questionnaire will include details to support site set-up (e.g. current services, patient pathways and commissioning), data collection, and a review of current services. A summary of participating sites, including screening, and reasons for non-selection, will be maintained by the CTRU.

Potential sites will be screened to confirm eligibility based on the following:

10.6.1 Inclusion criteria

- Stroke service able to deliver ESSVR (this may include a hyper-acute stroke unit, acute stroke unit, stroke rehabilitation unit and linked early supported discharge and community rehabilitation services).
- Agreement by therapy service managers that a site recruitment target of 2 per month is feasible and acceptable for the service to support intervention delivery.
- Agreement by therapy service managers that ESSVR trained therapists will not treat Usual Care participants.

10.6.2 Exclusion criteria

- Routinely provide well defined and active VR for participants within 12 weeks of stroke.

Participating sites will be required to have obtained local management approvals and undertake appropriate training in the intervention and study procedures prior to the start of screening and recruitment into the study.

10.7 Withdrawal

Participants may be withdrawn from the trial either at their own request or at the discretion of the PI. The participants will be made aware that this will not affect their future care.

Participants will be made aware (via the Participant Information Sheet and Informed Consent Form) that should they withdraw, the data collected up to the date of withdrawal cannot be erased and will still be used in the final analysis. If a participant withdraws consent to participate, clarification will be sought on whether withdrawal is from, for example, participation in the intervention, questionnaire completion, receipt of text message. .

Individual assessments will not be carried out where the participant appears reluctant to participate (i.e. no response to postal/online questionnaires, telephone contacts), even if they have consented. However, outcome data that does not involve participant contact (e.g. from medical or healthcare records) will continue to be collected in these cases.

11. Treatment details

11.1 Usual Care

Usual care is defined as ‘The wide range of care provided in a community whether it is adequate or not, without a normative judgment’ (51)

To increase external validity and relevance of trial findings to clinical practice, we plan to use an unrestricted usual care approach. Whereby the trial protocol does not restrict access to usual care, in line with our pragmatic trial design (52) and the possibility for heterogeneity of usual care treatments for people with stroke.

Usual care will be provided by primary care, secondary care, community and social services and determined by local policies and practices. Usual care will be available to both intervention and usual care participants. For example, usual care will depend on participants' level of independence and social predicaments but is likely to include GP appointments for medical problems; rehabilitation packages such as early supported discharge offering rehabilitation for activities of daily living including, personal e.g. washing, dressing, toileting, domestic e.g. cooking and indoor and outdoor mobility including driving and transport use; the use of voluntary sector services e.g. Headway, and stroke support clubs.

11.2 ESSVR (plus Usual Care)

Patients randomised to the ESSVR intervention (plus Usual Care) will receive ESSVR delivered by an Occupational Therapist (OT) experienced in stroke rehabilitation who has undergone specific training, provided by the trial, in manualised ESSVR. On receiving communication that a participant has been randomised to ESSVR, the trial OT will attempt to make contact with the participant by telephone or letter. Thereafter, the trial OT and participant will agree to meet in the most appropriate setting. If a face-to-face meeting is not possible, then the trial OT will arrange a meeting to be conducted remotely, for example, telephone, video conferencing.

ESSVR is an early, individually tailored intervention that seeks to lessen the impact of stroke by assessing the patient's role as a worker and finding acceptable strategies to overcome problems e.g. assessing and addressing new disabilities which might have a direct impact on work activities in relation to work demands – these may be physical, cognitive, psychological or task/environment-based interventions.

The intervention will commence within 2 weeks of randomisation and last for as long as is needed up to 12 months post-randomisation. The intervention will predominantly be delivered face-to-face on a one-to-one basis in the community, in the participant's home or workplace but may also take place in an outpatient therapy setting or in hospital when the participant is hospitalised for a long time, or over the telephone, videoconferencing, email or text. The number of intervention sessions will be determined by participant need. Liaison with or about the participant may also take place by email, letter, videoconferencing, or over the telephone with calls or texts and may involve face-to-face or virtual meetings with others such as workplace representatives and other health or social care professionals. If a site is no longer able to provide a trial OT to deliver the intervention, for example if trained OTs are redeployed elsewhere and cannot be replaced, then the central team that includes expert OTs will seek to provide remote delivery of the intervention wherever feasible.

ESSVR is individually tailored in content, dose, intensity and duration according to:

- participants' needs;
- preferences e.g. whether the participant consents to employer liaison and workplace visits or whether the participant accepts advice only about employer liaison and;
- employment context e.g. where there is no employer to liaise with or, participants return to work early and are unable to meet the therapist in person at the intended frequency, resulting in online or telephone intervention.

Remote delivery of the intervention (and data collected as part of the remote assessments) should comply with trust policies and procedures at all times. Where necessary sites will be

asked to alert participants to the risks associated with the storage and transfer of electronic data (e.g. screenshots, photographs etc.)

11.2.1 Therapist Identification

OTs who are familiar with delivering community rehabilitation programmes to participants will be identified by the site to deliver the intervention. Identification of therapists to deliver ESSVR will vary by site dependent upon the size of the rehabilitation service and therapist capacity. Details on the therapist experience, ability and clinical role will be documented for accurate reporting as per the TIDieR checklist [22].

11.2.2 RETAKE OT Training Package

To minimise inter-therapist variation and enhance fidelity, RETAKE OTs will receive a training package, led by members of the RETAKE training team. Training will comprise:

- a manual detailing ESSVR;
- 2-days of intervention training delivered face-to-face or remotely during interactive workshops followed by refresher days after recruitment commences and;
- mentoring for the duration of the trial.

The training package will support RETAKE OTs to become knowledgeable, competent and confident to deliver ESSVR and support to overcome local barriers that may be faced during its delivery alongside existing NHS stroke rehabilitation service delivery. To account for staff turnover further site-level training will be available as and when required.

The training package will include role play, clinical scenarios and case studies in order to highlight learning about strategies for delivering ESSVR. ESSVR trained OTs will also be briefed on the RETAKE trial design, CRFs required to be completed by RETAKE OTs and issues pertaining to the delivery of the intervention in the context of a trial, including maintaining protocol timings to start intervention, duration of the intervention and contamination using group discussion and case studies. The two day workshop will run during the site set-up period, after which the trained RETAKE OTs will be encouraged to put this new learning into practice prior to commencing recruitment. This extended learning period will be supported by an appointed mentor who will monitor progress, skills and competency before intervention delivery to trial participants commences. Refresher training and online forums will be used to discuss cases.

Trained OTs will receive mentoring (approximately once a month) by the RETAKE training team. This will be either individual or at a group-level for up to an hour and will involve a semi-structured telephone discussion to monitor progress, skills and quality of intervention delivery for the duration of the study. Quality monitoring will assess adherence to the intervention (to ensure adherence to the ESSVR process as outlined in the intervention manual) during the trial (See Process Evaluation section).

Ad hoc support by email, video-conference and telephone will be provided to discuss cases by a member of the RETAKE training team.

RETAKE OT competency to deliver ESSVR will be assessed via the use of case vignettes in and post training, at 6 and 12 months into the intervention period. Competency will be scored by the RETAKE training team and will identify if RETAKE OTs demonstrate satisfactory levels of competence or require additional support. If additional support is required then additional mentoring will be provided and further training may be provided to ensure that fidelity to the intervention is achieved.

In addition, the RETAKE therapists will also be asked to complete measures to assess attitudes to evidence-based practice and confidence to implement evidence-based practice to determine whether these factors affect implementation fidelity. These measures will be administered prior to training using the Evidence Based Practice Attitudes and Beliefs Scale (EBPAS-36) (89). The EBPAS-36 measures 12 domains of EPB including: 1. intuitive appeal of EBP, 2. the likelihood of adopting EBP given requirements to do so, 3. openness to new practices, 4. the perceived divergence of one's usual practice with research-based/academically developed interventions, 5. the limitations of EBPs, 6. the EPB's fit within the values and needs of client and clinician, 7. negative perceptions of monitoring, 8. the balance between perceptions of clinical skills and science as important in service provision, 9. the time and administrative burden with learning EBPs, 10. job security related to expertise in EBP, 11. perceived organisational support and 12. positive perceptions of receiving feedback (89, 90, 91).

Confidence to implement evidence-based practice, or the RETAKE therapists' self-efficacy, will be measured using the Evidence-Based Practice Confidence Scale (EPIC) (92). An 11-item, self-reported measure which asks the user to rate their confidence in their ability to perform tasks relating to EBP ranging from 0% (not at all confident) to 100% (completely confident).

Details of training provision and mentoring, including content, attendance, duration, and training providers will be documented.

11.2.3 Delivery of the intervention

Following randomisation, the RETAKE OTs at the site will be notified of the participant treatment allocation via email. The trial OT will make arrangements to contact intervention participants to schedule the first contact (within 48 hours ideally). Participants should commence treatment within 2 weeks of randomisation. Delivery timelines will be reiterated in treatment allocation notifications to the RETAKE OTs and PI.

RETAKE OTs will follow the ESSVR manual that includes the core components of ESSVR and recommended guidelines for VR following stroke (21,22). The assessment and intervention aspects of ESSVR will be tailored to each participant based on their needs and involves;

- Assessing the impact of stroke on the patient and their job
- Educating patients, employers and families about stroke impact on work.
- Finding strategies to lessen impact e.g. memory aids, pacing to manage fatigue
- Work preparation: establishing routines with gradually increasing activity; opportunity to practice work skills e.g. computers to increase concentration, walking to increase stamina
- Liaison with employers & employment advisors to plan and monitor a phased RTW.

Management of RETAKE OTs will be by usual line management.

Data will be captured on, for example, the number of contacts and sessions, date and duration of sessions, mode of delivery, location and intervention components.

11.2.4 Contamination

The ESSVR intervention is a bespoke, manualised, early vocational rehabilitation intervention for participants that is unlikely to be replicated by existing community therapy

services. Where existing services offer rehabilitation to address work needs, it is often late after stroke to a minority of patients presenting with other primary problems.

To minimise the risk of contamination, RETAKE OTs should not treat usual care participants that may be referred to their service during the study period. RETAKE OTs will be notified of all participants recruited during randomisation and a list of all recruited participants will be maintained in order to avoid the Trial OT seeing usual care participants. Maintaining a record of usual care participants that are seen by the same community rehabilitation team, in which the trial OT normally works, will help to monitor provision of usual care.

It is possible that behaviour change in usual care participants, their carers and health and social care practitioners may be induced by study information, including knowledge of allocation status. All participants will be provided with general study information and informed about allocation. Usual care participants will not be provided with detailed information about the intervention.

Sources of contamination will be explored further during the pilot study and, if identified, appropriate strategies will be rolled out to minimise contamination.

We will collect data on usual care participants who are treated by a trial OT and this will be monitored.

11.2.5 Intervention adherence

Intervention compliance will be assessed as described below.

11.2.5.1 RETAKE OT Adherence

Adherence to the ESSVR manual will be monitored in two ways:

- RETAKE OTs will be provided with expert mentoring to deliver ESSVR during the entire trial intervention period. A mentoring record CRF will used to record mentoring received and deviations from the ESSVR process recorded and coded.
- Intervention delivery and adherence to the ESSVR core components will be monitored using a fidelity checklist completed during observations in a random selection of 5% of cases.

RETAKE OTs will record intervention delivery (content, duration and dose) via a content CRF and routine treatment records. Adherence will be monitored by coding of the therapists treatment records and content CRFs.

Reasons for non-adherence will also be documented (where possible) and further explored in interviews with RETAKE OTs as part of the process evaluation.

11.2.5.2 Participant Adherence

Participant adherence/responsiveness to the ESSVR intervention, will be assessed by attendance at first intervention session, number of sessions offered and attended and drop-out from / agreed ending of intervention. This will be collected via a content CRF completed by the trial OT at each intervention session.

Non-compliance will be determined by:

- No attendance from the first intervention session i.e. intervention did not commence.

Poor compliance will be defined as:

- Attendance at less than 30% of the offered intervention sessions.

OR

- Drop out from / agreed ending of intervention

Interviews with 5% of ESSVR participants will be used to describe factors affecting adherence/ participant responsiveness to the intervention.

In the usual care group we will attempt to record all relevant treatments received using the site level questionnaire, and self-reported resource use questions at 3, 6 and 12 months post-randomisation, however, the pragmatic nature of the trial means we will not be prescriptive about usual care. In a sub sample of 5% of participants randomly selected as case studies in the process evaluation routine NHS therapy records will be used to illustrate the usual care received, interviews and observations of usual care participants and therapists will describe the nature, content and delivery of care and offer a perspective on participant responsiveness.

12. Data Collection

Required data, assessment tools, collection time points and processes are described in detail in sections below and summarised in Table 1.

Informed consent must be obtained prior to the participant undergoing procedures that are specifically for the purposes of the study and are out-with standard routine care at the participating site.

Assessments will either be administered by CRN/local Research staff, or self-completed (online or paper). Proxy completion of self-completed data is not permitted, however, the level of support required to complete the questionnaires (if any) will be documented.

As part of study initiation, CRN/local Research staff will receive training on the completion of all study specific assessments to ensure standardised completion.

Participating sites will be expected to maintain a file of essential study documentation (Investigator Site File), which will be provided by CTRU, and to retain copies of all completed Case Report forms (CRFs) and questionnaires for the study as appropriate.

12.1 Table 1 – Summary of Assessments

Assessment	Type	Method of Completion	Timeline				
			Screening	Baseline	3 Months	6 Months	12 Months
PARTICIPANT DATA							
Screening (Demographics / assessment of eligibility)	CRF	Researcher	X				
Consent	Consent Form	Self-completion	X				
Eligibility / location of baseline assessment	CRF	Researcher		X			
Demographics (Age / Gender / Ethnicity / Relationship status/ Home circumstances / Employment details / Educational level/ / Driving status)	CRF	Researcher		X			

Oxford Cognitive Screen (OCS)	CRF	Researcher		X			
Details of stroke	CRF	Researcher		X			
Relevant co-morbidities / medical issues	Questionnaire Booklet	Researcher / Self-completion		X	X	X	X
Contact Details (E.g. Address / telephone numbers / preferred method of contact / GP details / employer details)	CRF	Researcher		X			
Change of contact details	CRF	Researcher / OT / CTRU		UNSCHEDULED (AS MADE AWARE)			
Impact of COVID-19	CRF	Researcher			X	X	X
Work status	Questionnaire Booklet	Researcher / Self-completion		X	X	X	X
Hospital Anxiety and Depression Scale (HADS)	Questionnaire Booklet	Researcher / Self-completion		X	X	X	X
Nottingham Extended Activities of Daily Living (NEADL)	Questionnaire Booklet	Researcher / Self-completion		X		X	X
Community Integration Questionnaire (CIQ)	Questionnaire Booklet	Researcher / Self-completion		X			X
Health Related Quality of Life (EuroQol EQ-5D-5L)	Questionnaire Booklet	Researcher / Self-completion		X	X	X	X
Resource Use (Primary care / Secondary care / Emergency care / Medications/ Social services / Wider societal costs (e.g. productivity costs, out of pocket costs))	Questionnaire Booklet	Researcher / Self-completion		X	X	X	X
Work Self-efficacy (single question from the work ability index)	Questionnaire Booklet	Researcher / Self-completion		X	X	X	X
Confidence after Stroke Measure (CASM)	Questionnaire Booklet	Researcher / Self-completion		X			X
Safety Reporting	Questionnaire Booklet / CRF	Researcher / Self-completion			X	X	X
Work status (DWP)	Routine data	Data transfer DWP > CTRU		DOWNLOADS TO BE AGREED WITH DWP TO ALLOW 12 MONTH DATA COLLECTION			
Usual Care Data	CRF	Researcher / Self-completion		X	X	X	X
CARER DATA							
Consent	Consent Form	Self-completion	X				
Eligibility	CRF	Researcher		X			
Contact Details (Address / telephone numbers / preferred method of contact / GP details)	CRF	Researcher		X			
Carer Demographics (Age / Gender / Ethnicity / Relationship to participant / Employment details)	Questionnaire Booklet	Researcher / Self-completion		X	X	X	X
Modified Caregiver Strain Index (MCSI)	Questionnaire Booklet	Researcher / Self-completion		X	X	X	X
Health Related Quality of Life (EuroQol EQ-5D-5L)	Questionnaire Booklet	Researcher / Self-completion		X	X	X	X

Resource Use (Health, social care and personal costs)	Questionnaire Booklet	Researcher / Self-completion		X	X	X	X
Questions relating to impact on carer's work	Questionnaire Booklet	Researcher / Self-completion		X	X	X	X
SITE DATA							
Site questionnaire (Site demographics, staffing levels, Existing stroke care pathways)	Questionnaire Booklet	Researcher		X		X	X
INTERVENTION DATA							
Assessment	**Type**	**Method of Completion**	**Timeline**				
			Training	**Refresher training**	**Intervention Period (Week 1 – 52)**		
Therapist details (e.g. Demographics, qualifications, country of OT training, length of experience in stroke rehab, length of experience in VR, grade, usual team, WTE hours worked)	CRF	Self-completion	X				
VR learning needs analysis	Vignette	Self-completion	PRE-TRAINING				
ESSVR 2-day training attendance	CRF	Trainer / RETAKE OT	X				
Therapist attitude and confidence (Evidence-Based Practice Attitude Scale (EBPAS-36; Evidence-based practice confidence scale (EPIC scale)	Questionnaire	Self-completion	PRE-TRAINING				
Refresher training attendance	CRF	Trainer / RETAKE OT		X			
ESSVR competency assessment	Examined vignettes	Trainer / Mentor	DURING TRAINING, POST-TRAINING	X			
Mentoring attendance and summary of session	CRF	Mentor			X		
ESSVR Intervention Data Collection	CRF	RETAKE OT			X		
PROCESS EVALUATION DATA							
Fidelity checklist	CRF	Researcher			X		
Interviews	Interview	Researcher			X		
Observations	Observations	Researcher			X		

12.2 RETAKE OT data – Pre, during and post training

For OTs who are identified as RETAKE OTs and attend the ESSVR training the following information will be completed;

- Therapist details

- Learning needs analysis
- Evidence-based practice confidence scale (EPIC scale)
- Evidence-based Practice Attitude Scale (EBPAS-36)
- ESSVR competency assessment

12.3 Participant Data –Baseline assessment

For participants that provide informed consent and are confirmed to meet the eligibility criteria the following information will be completed;

- Location of assessment
- Demographic data
- Cognitive screen
- Contact details
- Work status
- Hospital Anxiety and Depression Scale (HADS)
- Nottingham Extended Activities of Daily Living (NEADL)
- Community Integration Questionnaire (CIQ)
- Health Related Quality of Life (EuroQol 5-Dimension health questionnaire 5 level (EQ-5D-5L))
- Confidence after Stroke Measure (CASM)
- Work self-efficacy
- Resource Use

Baseline assessments will be collected face to face in hospital or at the participant's home following discharge. If required baseline assessments may be administered remotely via telephone / video / online technology Assessments should be completed as close as possible to, but prior to, randomisation (and within 12 weeks of stroke).

12.4 Carer Data –Baseline assessment

For carers nominated by the participant that provide informed consent and are confirmed to meet the eligibility criteria the following information will be completed;

- Location of assessment
- Demographic data
- Contact details
- Modified Caregiver Strain Index (MCSI)
- Health Related Quality of Life (EuroQol 5-Dimension health questionnaire 5 level EQ-5D-5L))
- Resource Use
- Questions relating to impact on carer's work

Baseline assessments will be collected face to face in hospital or at the carer's home. If required baseline assessments may be administered remotely via telephone / video / online technology. Assessments should be completed as close as possible to, but prior to, participant randomisation (and within 12 weeks of their stroke).

12.5 Collection and Use of Identifiable Information

In order to facilitate the follow-up and data collection of participants/carers, their full name, address and/or e-mail address, telephone numbers, NHS number, date of birth, national insurance number (not applicable for carers), and General Practitioner (GP) details will be collected and returned to the CTRU. This information will be used to verify the survival status (and current address prior to the mail out of follow-up questionnaires, if opted for paper completion) of participants/carers prior to the 12 month follow-up (where possible). It will also be used to obtain data from the DWP (e.g. the provider of employment status).

12.6 3, 6 and 12 month Follow-up Assessments

Self-reported follow-up questionnaires will be completed at three, six and twelve months post randomisation. At study enrolment, participants and their carers (if applicable) will be asked whether they are able and willing to complete the follow-up questionnaires online using QTool. Participants/carers who are unable or unwilling to use QTool will be able to complete paper questionnaires during follow-up. Priming calls, Initial and reminder letters/e-mails, and SMS prompts, will be used to maximise data return. A 2-way SMS text message will also be sent (if mobile number provided) to confirm work status only of stroke survivors.

In the event of no response, CTRU will highlight participant(s)/carer(s) requiring contact to local/central research staff to request a blinded staff member performs the follow-up assessments. Contact will be initiated with an attempt to complete the questionnaires over the telephone or via a face to face visit.

12.6.1 QTool

QTool is an internet based questionnaire software that allows participants to complete their questionnaires online. Participants/carers who choose to use QTool will require access to a computer (including mobile device/tablet) and the internet and will be required to provide their email address to CTRU. Participants will be provided with a username and a password in order to log in to the QTool system online. Participants/carers will also be given a user guide which will describe the process for logging in to QTool, provide answers to some common questions and details of who to contact if more help is needed. CTRU will send an email to participants/carers when a questionnaire is due to be completed. A thank you message will be displayed upon successful completion and submission of the questionnaire. Should a questionnaire not be completed on QTool by the required time point, CTRU will send a reminder email to the participant/carer. Should the QTool system be unavailable participants will be asked to complete their questionnaire by post.

12.6.2 Paper questionnaires

Participants/carers will receive follow-up questionnaires by post from the CTRU. Participants/carers will complete the questionnaires at home and return them to the CTRU using a pre-paid envelope. Should a completed questionnaire not be received at CTRU by the required time point, CTRU will send a reminder letter to the participant/carer.

12.6.3 Gift vouchers

Along with a thank you note, participants (stroke survivors only) will receive a £20 gift voucher upon receipt of their completed 12 month follow-up data.

12.6.4 Participant Data – 3, 6 and 12 month Follow-up Assessments

The following data will be collected from participants:

at 3, 6 and 12 months:

- Impact of COVID-19
- Work status
- HADS
- EQ-5D-5L
- Work self-efficacy

Resource UseAt 6 and 12 months only:

- NEADL

At 12 months only:

- CIQ
- CASM

12.6.5 Carer Data – 3, 6 and 12 month Follow-up Assessments

The following data will be collected from carers at 3, 6 and 12 months:

- MCSI
- EQ-5D-5L
- Resource Use
- Questions relating to impact on carer's work

12.6.6 Usual Care Data

We will attempt to measure and describe the current focus of usual care in several ways including participant self-report at 3, 6 and 12 months post-randomisation and a site level questionnaire to obtain information on current services. In a sample of usual care participants routine NHS therapy records will be reviewed and, observations and interviews will be completed to describe the care received and explore experiences of care received.

The follow-up questionnaire booklet includes questions intended to capture the nature of any relevant intervention received by the usual care group. This will be costed and described retrospectively.

Continued use of NHS / Supported Stroke Discharge / 3rd sector services is also anticipated alongside ESSVR intervention. We will attempt to capture and describe this as part of this study via participant self-report.

12.6.7 Intervention Data

Intervention data will be recorded by RETAKE OTs and will include details of each session (including date, duration of sessions, mode of delivery, what was delivered). Additional data to inform intervention fidelity will be collected as part of the process evaluation. Specific data will be collected to indicate any impact from COVID-19 on intervention delivery.

12.6.8 Site Data

The following data will be collected from each participating site prior to recruitment, approximately halfway through recruitment and at the end of the intervention period:

- Site demographics
- Staffing levels (e.g. number and grade of qualified staff, number of support staff and caseload)
- Existing stroke care pathways (including existing VR pathways, proposed VR service developments and/or changes in practice)

12.6.9 The Modified Caregiver Strain Index (MCSI)

A 13-item screening tool with good internal reliability (α =.86, [60]) that measures subjective and objective elements of caregiver strain in 3 dimensions, 'perception of caregiving', 'care-recipient characteristics', and 'emotional status' and resource use pertaining to the impact of the participants stroke on the carer's work ability and finances. Positive responses to seven or more items on the index indicate a greater level of strain.

12.6.10 Oxford Cognitive Screen (Baseline only)

A cognitive screen which assesses the major cognitive domains of memory, language, number, praxis, executive functions and attention. Designed to provide a rapid assessment of a patient's cognitive function (approximately 15minutes). Test items are presented both visually and verbally, with the possibility of selecting a correct answer from a multiple choice array. Sites routinely using this screen will not be asked to repeat this measure for study purposes if administered within the previous 2 weeks. If face-to-face administration is not possible, advice from the test developer will be followed to administer the screen remotely.

Remote delivery of the OCS (and data collected as part of the remote assessment) should comply with trust policies and procedures at all times. Where necessary sites will be asked to alert participants to the risks associated with the storage and transfer of electronic data (e.g. screenshots, photographs etc.)

12.6.11 Intervention Content

Developed by Phillips (2010) (33) and modified for use in stroke (2) measures components of the ESSVR intervention in 1-minute units.

12.7 Descriptive variables

Work status will be recorded using the International Classification of Function (ICF, 2010) definitions, and categorised as the proportion people in any of the following:

a) Returned to work in the same role with an existing employer
b) Returned to a different role with an existing employer
c) Returned to work with a different employer i.e. new work in the same or a different role.
d) Returned to self-employed work

Where work is defined as competitive employment (full or part time paid work in an ordinary work setting, paid at the market rate (57)).
Secondary return to work success will be all the above but where patients can also be in a graded return to work programme or vocational training.

Further work status will be categorised: 'Supported work', defined as employment in an 'open work' setting but with ongoing support e.g. Government funded Work Programme, 'Vocational training or Apprenticeships', 'Non-paid (voluntary) work', 'Student' in full time education defined as an average of 12 hours per week; Home maker; Retired; Unemployed (for health reasons); Unemployed (other reason).

Wider resource use will also be captured to reflect that vocational rehabilitation is designed to have an impact on productivity costs (including presenteeism), out of pocket expenses incurred by the participants, employers' costs, and wider public sector costs (for instance DWP contacts).

We will also record mortality and self-reported A&E attendance / hospital admission and work accidents; hospital readmission.

13. Definition of a protocol deviation

A protocol deviation is an unanticipated or unintentional divergence or departure from the expected conduct of a study inconsistent with the protocol, consent document or other study procedures.

Violations of eligibility criteria and other deviations from protocol will be assessed by TMG and discussed with the TSC during study evaluation before data lock. The process for this will be outlined in the Trial Monitoring Plan.

14. Statistics

14.1 General considerations

A detailed statistical analysis plan (SAP) will be drafted in accordance with current CTRU standard operating procedures and will be finalised and agreed by the appropriate members of the research team before any analyses are undertaken. Following analysis of the progression criteria from the internal pilot, no formal interim analyses are planned. A single final analysis is planned after the trial is closed to recruitment and follow-up and when the full database has been cleaned and locked.

All analyses will be conducted at the 5% significance level and reported according to CONSORT guidance. Data will be analysed using SAS software by the trial statistician, with oversight from the supervising statistician. Carer data will be analysed by descriptive statistics only.

Additionally, COVID-19 period will be taken into consideration in summaries and analyses to assess the level of COVID-19 impact on the trial robustness.

14.2 Screening

Numbers of approached and screened patients, and numbers of patients eligible for trial entry, consented and participating, with the reasons for non-entry, will be summarised.

14.3 Internal pilot

Data from the 8 sites participating in the internal pilot will be analysed initially using descriptive statistics to evaluate the progression criteria. Progression criteria will be assessed based on recruitment and follow-up rates after 6 months of recruitment based on a traffic light system of green (go), amber (review) and red (stop). Start of recruitment is defined as the first participant recruited into the trial.

Recruitment criteria will be assessed over months 4-6 to allow rates to stabilise; follow-up criteria will be assessed after a further six months (i.e. 12 months after the start of recruitment) based on the following:

- The recruitment criterion is a recruitment rate of at least 2 patients per site per month (green), at least one but less than two (amber), or less than one (red).
- The follow-up rate criterion is a follow-up rate of at least 80% (green), at least 65% but less than 80% (amber) or less than 65% (red).

The TSC will be provided with data on the above at approximately 6 and 12 months after the start of the recruitment. The TSC will also be provided with data on the number of sites and adherence to the intervention to inform a decision on continuation of the trial.

If any criteria are graded as amber or another issue is identified which could impact on the successful completion of the trial, a rescue plan will be developed outlining steps to be taken to improve recruitment, and/or follow-up (as appropriate), and will be approved by the TSC before submission to the HTA. If we fail to achieve the progression criteria (red), we will look to stop the trial.

Outcome data from participants in the internal pilot will be included in the main trial analysis.

14.4 Descriptive statistics

Baseline characteristics of participants will be summarised by the study arms and characteristics of those lost to follow-up will be compared with those not lost to follow-up to assess for bias. The number of participants providing outcome data at each visit will be summarised, as will numbers and reasons for withdrawal.

Receipt of the various components of the intervention will be recorded for each patient in the intervention group.

14.5 Sample size and justification

760 participants (420 ESSVR; 340 usual care) will be randomised to receive either ESSVR and usual care or usual care alone. This provides 90% power at the 5% significance level, to detect a 13% absolute difference in the proportion of people in work at 12 months (assuming 26% in control as per the feasibility study (2). It accounts for 20% loss to follow-up and clustering in the intervention arm (11 recruited per RETAKE OT, 2 RETAKE OTs per site, 20 sites, intra-cluster correlation coefficient (ICC) 0.03, inflation factor 1.234). Clustering will only exist in the intervention arm to account for between-therapist effects. An ICC of 0.03 has been assumed, given that standardised training and manuals for delivering the intervention will minimise the ICC. A review of similar trials supports an assumption of an ICC no greater than 0.03 (61, 62). NQuery v3.0 software was used in the calculation of the sample size.

14.6 Primary analysis

The primary analysis will compare the proportions of participants in work at 12 months post randomisation between arms, using a mixed effects logistic regression model allowing for clustering of outcomes in the intervention arm due to the effect of the therapists. The model will be adjusted for the stratified design factors of age, stroke severity and site.

Corresponding 95% confidence interval and p-values will be reported as well as the ICC for the intervention arm.

If a participant is unable to report their working status, e.g. if they are dead, this will be taken as a negative response to the question. Other missing data will be assumed missing at random for the primary analysis; multiple imputation for handling such missing data will be explored as a sensitivity analysis.

14.7 Secondary analyses

Secondary outcomes (return to work with the same employer, number of hours worked per week, number of days in work, mood, physical function, community participation, work self-efficacy, post-stroke confidence) at three, six and twelve months will be analysed using a similar modelling strategy as described for the primary analysis. Where outcomes are continuous, linear models will be fitted; where binary, logistic models will be fitted. Details of models to fit will be given in the Statistical Analysis Plan.

14.8 Assessment of safety

Secondary objectives related to safety (A&E attendances, hospital admission/readmission, work accidents and mortality) will be summarised.

14.9 Procedures for missing, unused and spurious data

Missing data is expected at the item, scale and timepoint levels. Where scales have published scoring protocols, detailing the handling of missing item data, these will be followed. If not, items will be prorated where 75% or more items for a scale are available. Mechanisms for missing data on variables/ key scales will be explored and a multiple

imputation model built covering the primary analysis. Sensitivity analysis will explore the impact of employing different missing data handling strategies.

Thorough assessment on the extent of missing data due to COVID-19 will be carried out. If data are missing due to COVID-19, the reason will be recorded and referenced COVID-19.

14.10 Definition of populations analysed

Analyses will be on the intention to treat population, which will include all randomised participants, regardless of non-adherence with the intervention, analysed in the study arm to which they were randomised. Sensitivity CACE analyses may be carried out, taking into account compliance with the intervention in the intervention arm. Compliance will be defined in terms of the individual components of the intervention (see section 14.2.5), with full details given in the SAP.

15. Health economic analysis

A within-trial economic evaluation (a cost utility analysis) will be conducted comparing the costs and QALYs in the ESSVR plus usual care group and usual care group alone in participants of working age from the perspective of the UK National Health Service (NHS) and Personal Social Services (PSS) in the base case as recommended (58) and from a wider perspective in secondary analysis to reflect the expected wider costs and benefits of the VR intervention.

The Intervention resource use (comprising training, mentoring and delivery) will be captured and recorded by the intervention OTs. This will be used to estimate a cost of the training and mentoring components to be used in the main economic evaluation. However, although delivery costs will be estimated using this data this won't be included in the economic evaluation as it was felt by the research team, which includes PPI members, that participants would not be able to distinguish between intervention OT visits and non-intervention OT visits such that participants are going to be asked explicitly to include all visits in their responses to the resource use questions. To avoid the potential for double counting we will therefore base resource use and costs on patient reported data and only use OT recorded delivery data to enable us to estimate a cost for the service. It should be noted that patient reports may deviate from the OT records. Levels of wider health, PSS and societal resource use at baseline, 3, 6, and 12 months will be captured using a bespoke resource use questionnaire designed for self-completion. We will attach published unit costs for a common recent price year (63, 64,65) to individual level quantities of resource use and estimate the mean cost per participant incorporating the cost of the intervention and wider healthcare and PSS resource use (primary care, secondary care, emergency care, medications, and social services). Secondary analysis will take a wider cost perspective including participants, carers, employers and wider public sector services perspective.

Health-related quality of life will be measured using the EQ-5D-5L (66) at baseline, 3, 6, and 12 months, and valued in line with guidance at the time of analysis (NICE, 2017). QALYs will be estimated for the trial period using linear interpolation and area under the curve analysis, adjusting for baseline values (67).

A regression-based approach (seemingly unrelated regression equations) (68) will be used for the statistical analysis if the necessary assumptions hold. The level of uncertainty associated with the decision over which option is most cost-effective will be explored using non-parametric bootstrapping (69) to construct the cost-effectiveness acceptability curve (CEAC) (70). Neither costs nor QALYs will be discounted reflecting the time frame of the trial. The planned analysis is subject to change to ensure it stays in line with any changes to accepted methodology during

the course of the study. However, a detailed Health Economics Analysis Plan will be finalised and reviewed by an independent health economist prior to the trial database being locked.

The importance and feasibility of extending the time horizon of the economic analysis will be considered as appropriate.

16. Safety reporting procedures

16.1 General Definitions

An adverse event (AE) is:

- any unintentional, unfavourable clinical sign or symptom
- any new illness or disease or the deterioration of existing disease or illness

A serious adverse event (SAE) is defined in general as an untoward event which:

- results in death
- is life threatening
- requires or prolongs existing hospitalisation
- is significantly or permanently disabling or incapacitating
- constitutes a congenital anomaly or a birth defect or
- is otherwise considered an important medical event by the clinician.

Judgement should be exercised in deciding if an AE should be classified as serious in other circumstances. This should include other AEs that are not immediately life-threatening or do not result in death or hospitalisation, but may jeopardise the participant and may require intervention to prevent one or more of the outcomes listed under SAEs above.

An SAE occurring to a participating participant which, in the opinion of the Chief Investigator, is related to the research and is unexpected will be reported to the Research Ethics Committee (REC).

The Health Research Authority (HRA) defines **related and unexpected SAEs (RUSAEs)** as follows:

- 'Related' – that is, it resulted from administration of any research procedures; and
- 'Unexpected' – that is, the type of event is not listed in the protocol as an expected occurrence.

16.2 Expected Adverse Events / Serious Adverse Events (non-reportable)

In this patient population, acute illness resulting in hospitalisation, new medical problems and deterioration of existing medical problems are expected. In recognition of this, events fulfilling the definition of an AE or SAE will not be reportable in this study unless they are specified in the section below or fulfil the definition of a Related and Unexpected Serious Adverse Event (RUSAE).

16.3 Related and Unexpected SAEs (RUSAEs)

A serious adverse event that is unexpected in its severity and seriousness and deemed directly related to or suspected to be related to the trial intervention shall be reported to the ethics committee that gave a favourable opinion as stated below.

This may include:

- Accidental injury resulting from working with equipment or work place adaptations recommended by the RETAKE OT;

- Work accidents resulting in injury requiring hospital treatment.

The above events will be collected by self-report (via the patient reported questionnaires at 3, 6, and 12 months or via a site notifying the CTRU or member of the research team. The event shall be reported immediately of knowledge of its occurrence to the Chief Investigator.

The Chief Investigator will:

- Assess the event for seriousness, expectedness and relatedness to the trial treatment or intervention.
- Take appropriate medical action, which may include halting the trial and informing the REC and Sponsor of such action.
- If the event is deemed related to the trial treatment or intervention the CTRU, on behalf of the Chief Investigator, shall inform the REC using the reporting form found on the HRA web page within 15 days of knowledge of the event.
- Shall send any follow-up information and reports to the REC.
- Make any amendments as required to the study protocol and inform the REC as required

16.4 Participant removal from the study due to adverse events

Any participant who experiences an adverse event may be withdrawn from the study at the discretion of the Investigator. This will be reported to the CTRU and reviewed by the Chief Investigator.

16.5 Deaths

Deaths should be notified to CTRU within 7 days of becoming aware. It is anticipated that deaths will be identified by local CRN/research staff, RETAKE OTs, CTRU via ongoing checks of survival status (prior to requesting completion of 12 month questionnaire data) and at the end of the study.

16.6 Reporting to External Bodies

Summaries of reportable SAEs / RUSAEs, deaths and withdrawals will be reported to the TSC and will also be reported annually to the main Research Ethics Committee (REC) in routine annual progress reports.

Reporting of RUSAEs to the REC and the Sponsor will be subject to current HRA guidance, CTRU SOPs and Sponsor requirements.

17. Process Evaluation

17.1 Aims and design

We will conduct a parallel process evaluation, nested within the trial to 1) measure fidelity to the intervention and 2) understand the social and structural context in which the intervention is delivered and to identify factors which may influence the quality of implementation. This includes identifying enablers and barriers to the deployment of the intervention, contextual factors that may be associated with variations in outcome across the intervention groups, and factors that would support the implementation of the intervention into routine practice. The process evaluation will use quantitative process indicator data being collected as part of the trial, and qualitative data collection methods.

17.2 Fidelity measurement

17.2.1 Objectives

1. To ascertain intervention dose
2. To describe content of usual care and ESSVR
3. To describe levels of adherence to the ESSVR intervention
4. To conduct observations of the delivery of UC and ESSVR.

17.2.2 Methods

To meet Objectives 1 and 2, we will use a combination of data collection methods including CRFs completed by the RETAKE OTs designed to collect the number, frequency, length and content of each ESSVR intervention session.

Content of ESSVR will also be described via routinely collected data (NHS therapy notes) and self-reported resource use data from CRFs collected at follow up.

In Usual Care content will be ascertained from the site questionnaire (administered prior to recruitment, halfway through and at the end of the intervention period), and participant self-reported resource use data at 3, 6 and 12 month follow-up.

In addition, we will measure therapist attributes including years post qualification, stroke rehabilitation experience, formal training in VR, age, and competency post training. The RETAKE therapists will be asked to complete measures to assess attitudes to evidence-based practice (using the Evidence Based Practice Attitudes and Beliefs Scale (EBPAS-36) (89) and confidence to implement evidence-based practice using the Evidence-Based Practice Confidence Scale (EPIC) (92) prior to the training to determine whether these factors affect implementation fidelity.

Data from the questionnaires will be measured against therapist adherence to the core (non-modifiable) components of the ESSVR logic model to determine the relationship between therapist attributes and implementation fidelity.

Participant adherence and engagement in the therapeutic vocational rehabilitation process will be measured in observations taking place in a random selection of 5% of case studies in both arms indicated in 17.4.4 (objective 4) using the working alliance inventory observer form (93)

In a sample of usual care participants usual care content will be ascertained from routine NHS therapy records. These participants will also be invited to take part in interviews to explore the extent to which support, similar to ESSVR, is delivered in usual care.

To meet Objective 3; The content of the intervention recorded by RETAKE OTs (CRFs and therapy records), RAs (fidelity checklists) and ESSVR mentors (mentoring records) will be coded and compared to an ESSVR logic model (based on the feasibility trial and ratified by the research management group together with the stakeholder and expert advisory group).

To meet Objective 2 and 4, we will observe 5% of participants recruited to the trial (both ESSVR and UC), using a fidelity checklist to record practices (for ESSVR participants).

17.3 Analysis of quantitative data from the process evaluation

The dose, duration and frequency of the ESSVR intervention will be calculated using data from completed CRFs in combination with NHS therapy records. The total time spent delivering the ESSVR intervention (face to face and non-face to face contact (liaison with the patient, employer and other stakeholders by letter/phone etc.), administration and travel) will be identified. Details relating to the content of intervention sessions will be extracted to identify whether core components of ESSVR were delivered as intended (i.e. as specified in the intervention manual and logic model)). Associations between therapist attributes, contextual factors and intervention fidelity (measured by deviations from the RETAKE core process) will be explored using regression models. Analysis will be conducted using Statistical Package for the Social Sciences (SPSS) (version 21.0 for Windows). In addition, a fidelity monitoring CRF will be used to check whether the ESSVR process is followed.

17.4 Social and structural context

27.4.1 Objectives

1. To describe participating sites.
2. To understand professionals' experiences of being trained to deliver the intervention.
3. To understand professionals' experiences of delivering the intervention.
4. To understand the social and structural factors which support the implementation of the intervention.
5. To understand participants' experience of being supported to return to work after stroke.

17.4.2 Theoretical framework

The qualitative study will draw on normalization process theory (NPT) (72) developed to understand the introduction of complex interventions into healthcare settings as representing a programme change with implications for organizations, staff, and service users. NPT draws attention to two separate categories that warrant consideration, the process itself and the organisational and structural setting in which new interventions are to be implemented. In this context, NPT proposes that four generative mechanisms can help explain how new interventions are embedded and 'normalized' within standard service models. These are: coherence (how the work that defines and organizes a practice/intervention is understood, made meaningful and invested in at individual and collective levels); cognitive participation (commitment to and engagement of participants with the intervention; collective action (the work needed to implement the intervention, and anticipated pay-off (or cost) this work may bring); and reflexive monitoring (participants' individual and collective on-going formal and informal appraisal of the intervention) (73). Equally, NPT has been applied to qualitative investigation and analysis of patient experience of and engagement in care, drawing attention to the implementation of tasks that treatments require, embedding and integrating these in daily life. NPT therefore proposes that the same generative mechanisms can help to understand how patients engage with a specific intervention. (74). NPT will be used to help design data collection tools (interview topic guides) and to guide qualitative data analysis and interpretation.

17.4.3 Data collection methods

1. To meet Objective 1 we will use routinely collected data from all sites and SSNAP data where relevant. This will be combined with data collected from the site questionnaire prior to recruitment, halfway through and at the end of the intervention period to provide a description of existing stroke care pathways, services for supporting participants in return to work and to record current stroke pathway, staffing information (i.e. number and grade of qualified staff, number of support staff and caseload), proposed VR service developments and /or changes in practice that are not evidence based.

To meet Objective 2 the RA will;

1) Observe up to four training sessions delivered by the training team

2) Conduct semi-structured interviews with up to 20 participating RETAKE OTs purposively selected according to geographical location, urban vs rural and size.

To meet Objectives 3 – 5 the RA will:

3) Conduct face to face semi-structured interviews with at least one trial OT delivering the ESSVR intervention at each site at the end of the study, to explore views of the intervention and organisational, social and other factors contributing to the delivery of the intervention.

4) Use a longitudinal case study design to map the care received for a random sample of up to 5% of participants in both ESSVR and UC. This will entail non-participant observations of face to face intervention delivery and employer interactions in each site. Interviews will be conducted at up to three time points with participants, carers (if present), therapists (to discuss the rehabilitation process and identify obstacles to delivery) and employers.

5) An additional 5% sample of participants recruited to the study will be invited to take part in face to face semi-structured interviews at the end of the study to explore experiences of taking part in the intervention, perceptions and experiences of support to return to work.

6) Conduct face-to-face semi-structured interviews with the mentors to explore their perspective of supporting RETAKE OTs to deliver the intervention and to explore views of organisational, social and other factors contributing to the delivery of the intervention.

Interviews will be conducted using a topic guide developed with reference to the theoretical framework and examples previously used in similar studies.

Non-participant observation will be conducted using a prompt for structured observation and unstructured fieldnotes and the Working Alliance Inventory – Observer Form (93). Consent will be sought from all parties (participant, therapists, employers) prior to observations.

17.5 Trial OT Recruitment

OTs trained to deliver the ESSVR intervention will be recruited to participate in interviews as part of the process evaluation.

Up to 20 RETAKE OTs, will be invited to participate in interviews. They will be contacted by telephone by a member of the research team and sent a copy of an information sheet and consent form. Informed consent will be obtained prior to interview. These interviews will be conducted by telephone or in person by a RA.

17.5.1 Inclusion criteria

- OTs who received training to deliver the ESSVR intervention in each of the participating trial sites.

17.5.2 Exclusion criteria

- None

17.5.3 Expected duration of staff participation

OTs trained to deliver the ESSVR intervention will be involved in the study for up to 30 months (Training period, Recruitment (26 months + 12 months follow-up), post-trial interviews.

17.6 NHS Staff Recruitment

NHS staff involved in the management, commissioning or delivery of stroke rehabilitation will be recruited to participate in interviews as part of the process evaluation.

Up to 45 NHS staff will be invited to participate in interviews. They will be contacted by telephone by a member of the research team and sent a copy of an information sheet and consent form. Informed consent will be obtained prior to interview. These interviews will be conducted by telephone or in person by a RA.

17.6.1 Inclusion criteria

- NHS staff involved in the management, commissioning or delivery of stroke rehabilitation in each of the participating trial sites.

17.6.2 Exclusion criteria

- None

17.6.3 Expected duration of staff participation

- One off interview lasting up to 45 minutes.

17.7 Employer Recruitment

Employers of ESSVR participants (who consent to their employer being contacted) randomly selected as case studies in the process evaluation, will be contacted by telephone by a member of the research team and sent a copy of an information sheet and consent form. Informed consent will be obtained prior to interview. The interview will be conducted by telephone / video-conferencing or in person by a RA. at a mutually agreed time to explore their views of the ESSVR intervention.

17.7.1 Inclusion criteria

- Employers of stroke participants in ESSVR intervention and usual care who consent to their employer being approached by the study team.

17.7.2 Exclusion criteria

- None

17.7.3 Expected duration of Employer participation

In the ESSVR intervention (where participants consent for their employer to be contacted) employers are routinely involved in the process of supporting an employee in a return to work. This may last for up to 12 months from the point of randomisation. Consenting employers who have engaged with the RETAKE OTs as part of the intervention will be interviewed, once the participant has given consent for this to occur. This will take place only once and interviews are likely to last for up to 45 minutes.

Employers identified by participants in Usual Care who are selected to take part in the longitudinal case studies for the process evaluation will be invited to participate in a one off interview lasting up to 45 minutes.

17.8 Mentor Recruitment

Mentors who support RETAKE OTs to deliver the intervention will be recruited to participate in interviews as part of the process evaluation.

RETAKE Mentors will be invited to participate in interviews. They will be contacted by telephone by a member of the research team and sent a copy of an information sheet and consent form. Informed consent will be obtained prior to interview. These interviews will be conducted by telephone or in person by a RA.

17.8.1 Inclusion Criteria

- Mentors who deliver mentoring to the RETAKE OTs.

17.8.2 Exclusion Criteria

- None

17.8.3 Expected duration of mentor participation
Mentors will be involved in the study for up to 30 months (Training period, Recruitment (26 months + 12 months follow up), and will be asked to participate in interviews.

17.9 Sampling strategy

For professional and patient interviews, we will use a purposive sampling strategy to ensure diversity in terms:

- geographical location (e.g. urban vs rural centres)
- level of staff seniority
- participant sociodemographic variables (including gender and socio-economic status)

17.10 Data analysis

Data will be uploaded to QSR NVivo software for management. Analysis will combine both inductive (new insights emerging from the data) and deductive (informed by NPT) approaches. It will proceed iteratively with data collection to identify whether data saturation has been achieved. It will be conducted by at least two members of the research team and follow a standard approach of data familiarisation, line by line coding, development and refinement of broader conceptual explanatory categories, and iterative testing of interpretation through feedback with study participants and research team discussions (75).

17.11 Data collection and storage

All interviews will be audio recorded, following agreement from the interviewee and will be professionally transcribed. Only the research team and the transcriber will listen to the interview audio files. Process evaluation participants and sites will not be identified by personal details or name but will be given a randomly generated number by the lead researcher. This number will only be known to the lead researcher and stored as an encrypted digital file within password protected folders and storage media. Audio recordings will be destroyed at the end of the study.

All written notes (e.g. observation forms, interview notes) will only have the participants' randomly generated number on the sheet as a form of identification. Paper notes will be stored in a lockable filing cabinet in the PE researcher's university office.

18. Records

18.1 Case Report Forms

Each participant will be assigned a trial identity code number (participant ID; made up of their recruitment site code and a unique sequential trial number), allocated at randomisation, for use on CRFs, other trial documents and the electronic database. The documents and database will also use their initials and date of birth (dd/mm/yy).

CRFs will be treated as confidential documents and held securely in accordance with relevant regulations. The Principal Investigator will hold a confidential record of the participant's name, date of birth, local hospital number or NHS number, and Participant Trial Number (the Trial Recruitment Log), to permit identification of all participants enrolled in the trial, in accordance with regulatory requirements and for follow-up as required.

CRFs shall be restricted to those personnel approved by the local Principal Investigator and recorded on the 'Authorised Personnel Log.'

18.2 Source documents

Source documents shall be filed at the PI site and may include but are not limited to, consent forms, current medical records, laboratory results and records. A CRF may also completely serve as its own source data. Only trial staff as listed on the Authorised Personnel Log shall have access to trial documentation other than the regulatory requirements listed below.

18.3 Direct access to source data / documents

The CRFs and all source documents, including progress notes and medical/psychological and other agencies test results shall made be available at all times for review by the Chief Investigator, the CTRU, Sponsor's designee and inspection by relevant regulatory authorities.

19. Quality Assurance and Ethical Considerations

19.1 Insurance and Indemnity

Insurance and indemnity for trial participants and trial staff is covered within the NHS Indemnity Arrangements for clinical negligence claims in the NHS, issued under cover of HSG48. There are no special compensation arrangements, but trial participants may have recourse through the NHS complaints procedures.

The University of Nottingham as research Sponsor indemnifies its staff, research participants and research protocols with both public liability insurance and clinical trials insurance. These policies include provision for indemnity in the event of a successful litigious claim for proven non-negligent harm.

19.2 Record Retention and Archiving

19.2.1 End of study

The end of the study is defined as the date of the last participant's last data item (i.e. the date of the 12 month follow-up of the last participant randomised).

19.2.2 Archiving

In compliance with the ICH/GCP guidelines, regulations and in accordance with the University of Nottingham Research Code of Conduct and Research Ethics, the Chief or local Principal Investigator will maintain all records and documents regarding the conduct of the study. These

will be retained for at least 7 years or for longer if required. If the responsible investigator is no longer able to maintain the study records, a second person will be nominated to take over this responsibility.

The Trial Master File and trial documents held by the CTRU on behalf of the Sponsor shall be finally archived at secure archive facilities at the University of Nottingham. This archive shall include all trial databases and meta-data. Where data has been encrypted, decryption keys will be provided.

19.2.2.3 Trial data and documents held by research sites

Research sites are responsible for archiving all trial data and documents (ISF and all essential documents therein, including CRFs) at the participating research site until authorisation is issued from the Sponsor for confidential destruction. The research site will be responsible for providing a key contact who will take responsibility for archiving.

19.2.2.4 Participant medical records held by research sites

Research sites are responsible for archiving trial participant medical records in accordance with the site's policy and procedures for archiving medical records of patients who have participated in a clinical trial.

20. Discontinuation of the Trial by the Sponsor

The Sponsor reserves the right to discontinue this trial at any time for failure to meet expected enrolment goals, for safety or any other administrative reasons. The Sponsor shall take advice from the Trial Steering Committee as appropriate in making this decision.

21. Data Protection and Confidentiality

All trial staff and investigators will endeavour to protect the rights of the trial's participants to privacy and informed consent, and will adhere to the Data Protection Act, 1998 (and future updates). The CRF will only collect the minimum required information for the purposes of the trial. All information, including personal information (name, address, telephone number, date of birth) collected during the course of the study will be kept strictly confidential.

Information from the main study will be held securely on paper and electronically at CTRU, University of Leeds. Access to the information will be limited to the trial staff and investigators and relevant regulatory authorities.

Trial data, including the database, will be stored on CTRU owned and managed servers. The underlying storage is encrypted to AES 128 or higher and is kept in locked racks within University of Leeds data centres. Access to servers is restricted by use of firewalls and only permits the minimum level of access required to allow CTRU owned and managed devices to connect to services. Access to file storage areas, databases and services is further controlled by the use of usernames, passwords and roles to restrict access to just the individuals authorised to access it.

Information about the trial in the participant's medical records / hospital notes will be treated confidentially in the same way as all other confidential medical information.

Data collection forms that are transferred to or from the CTRU will be coded with a study number and will include two identifiers, usually their initials and date of birth. Appropriate storage, restricted access and disposal arrangements personal and clinical details will be put in place.

The CTRU will comply with all aspects of the 1998 Data Protection Act (and future update) and operationally this will include:

- Consent from participants to record personal details including name, date of birth, address and telephone number, National Insurance number, NHS number, hospital number, GP name and address.
- Appropriate transfer, electronic and physical storage, restricted access and disposal arrangements for personal and clinical details of participants.
- Consent from participants for access to their medical records by responsible individuals from the research staff or from regulatory authorities, where it is relevant to study participation.
- Consent from participants for the data collected for the study to be used to evaluate safety and develop new research.
- Where anonymisation of documentation is required, sites are responsible for ensuring only the instructed identifiers are present before sending to CTRU.

All data collected as part of the Process Evaluation will be transferred and stored securely at the University of Nottingham in accordance with the Data Protection Act 1998 (and future updates). Recordings of semi-structured interviews will be transcribed verbatim. This may be conducted by a UK-based third party with an appropriate confidentiality and data security agreement.

Medical information may be given to the participant's medical team and all appropriate medical personnel responsible for the participant's welfare.

If information is disclosed during the study that could pose a risk of harm to the participant or others, the researcher will discuss this with the CI and where appropriate report accordingly.

Data generated as a result of this trial will be available for inspection on request by the participating physicians, the University of Nottingham representatives, the REC, local R&D Departments and the regulatory authorities.

22. Quality Assurance

The study will be conducted in accordance with the principles of Good Clinical Practice (GCP) in clinical studies, as applicable under UK regulations, the NHS Research Governance Framework (RGF), and through adherence to CTRU and Sponsor SOPs as applicable and study specific guidance implemented to ensure delivery of the study in accordance with this protocol.

22.1 Serious Breaches

Investigators are required to promptly notify the CTRU if a serious breach occurs (as defined in the latest version of the HRA SOP). This is defined as a breach of the protocol or of the conditions or principles of GCP which is likely to affect to a significant degree the safety or physical or mental integrity of the study subjects, or the scientific value of the research.

In the event of doubt or for further information, the Investigator should contact the Chief Investigator.

22.2 Criteria for terminating trial

The trial may be stopped at the end of the internal pilot if the progression criteria are not met (see section 17.2). Other reasons to stop the trial might include a change of opinion of the REC or overwhelming evidence of major safety concerns or issues with the study conduct (e.g. poor

recruitment, loss of resources). Adverse events will be recorded throughout the trial following GCP principles and local governance procedures as described below.
Should concern warranting discontinuation of the trial arise, the decision to terminate will be reached by the Trail Steering Committee and the Trial Sponsor. If evidence is limited to one centre a decision to stop in only one centre may be made.
Should a decision to terminate the study as a whole or in a single centre be made, research data will not be destroyed and will be archived according to the archiving section.

22.3 Ethics committee and regulatory approvals

Recruitment will not commence until the protocol, informed consent forms and participant information sheets have received approval / favourable opinion from the Research Ethics Committee (REC), the respective National Health Service (NHS) or other healthcare provider's Research & Development (R&D) department, and the Health Research Authority (HRA). The trial will be registered on the ISRCTN registry. Should a protocol amendment be made that requires REC approval, the changes in the protocol will not be implemented until the amendment and revised informed consent forms and participant information sheets have been reviewed and received approval / favourable opinion from the REC and R&D departments in accordance with most recent HRA guidance at time of amendment. A protocol amendment intended to eliminate an apparent immediate hazard to participants may be implemented immediately providing that the REC are notified as soon as possible and an approval is requested. Minor protocol amendments only for logistical or administrative changes may be implemented in accordance with the most recent HRA guidance at time of change.

The CTRU and / or CI will provide the main REC with a copy of the final protocol, information sheets, consent forms and all other relevant study documentation.

The trial will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, 1996; the principles of Good Clinical Practice, and the Department of Health Research Governance Framework for Health and Social care, 2005.

22.4 Informed consent and participant information

The process for obtaining participant informed consent will be in accordance with the REC guidance, and Good Clinical Practice (GCP) and any other regulatory requirements that might be introduced. The investigator or their nominee and the participant (and their witness, if required) shall both sign and date the Informed Consent Form before the person can participate in the study.

The participant will receive a copy of the signed and dated forms and the original will be retained in the Investigator Site File. A second copy will be filed in the participant's medical notes and a signed and dated note made in the notes to confirm that the patient met the eligibility criteria and that informed consent was obtained for the trial. A third copy will be sent to the CTRU at the University of Leeds.

The decision regarding participation in the study is entirely voluntary. The investigator or their nominee shall emphasise to them that consent regarding study participation may be withdrawn at any time without penalty or affecting the quality or quantity of their future medical care, or loss of benefits to which the participant is otherwise entitled. If participants of the proposed study withdraw consent form further participation their data will be included in the final study analysis unless they specifically withdraw consent for their data to be used. No trial-specific interventions will be done before informed consent has been obtained.

The investigator will inform the participant of any relevant information that becomes available during the course of the study, and will discuss with them, whether they wish to continue with the study. If applicable they will be asked to sign revised consent forms.

If the Informed Consent Form is amended during the study, the investigator shall follow all applicable regulatory requirements pertaining to approval of the amended Informed Consent Form by the REC and use of the amended form (including for ongoing participants).

22.5 Safeguarding of adults

It is possible that, during discussions, participants may disclose information to the research team (CRN / local Researcher), or they may have concerns that the individual may be experiencing abuse, or is at risk of abuse. In such circumstances the researcher will follow their NHS Trusts' Safeguarding Adults policy (or equivalent document).

22.6 Trial Monitoring

A Trial Monitoring plan will be developed and agreed by the Trial Management Group (TMG) and Trial Steering Committee (TSC). This will be informed by a Trial Risk Assessment which will consider the safety or physical or mental integrity of the study participants and the scientific value of the research (including the potential risk associated with the implementation of the intervention and recruitment which can, if not monitored and mitigated, affect the integrity and smooth running of this study). This monitoring plan will detail the timing and content of reports to monitor study conduct and implementation and adherence with the Consolidated Standards of Reporting Trials (CONSORT).

For a study of this nature, a separate Data Monitoring and Ethics Committee is not required. Rather, the TSC will adopt a safety monitoring role, with the constitution of a sub-committee to review safety issues where this becomes necessary.

22.7 Data Monitoring

Data will be monitored for quality and completeness by the CTRU in accordance with SOPs and guidelines, using established verification, validation and checking processes. Missing data, except individual data items collected via the participant reported questionnaires, will be chased until they are received, confirmed as not available, or when the study is at analysis. Reminders will be sent to participants if postal/online questionnaires are not returned on time, supported by text, email and telephone reminders, where appropriate.

22.8 Clinical Governance Issues

The Sponsor for the study is University of Nottingham. The Sponsor will ensure responsibility and accountability for study conduct and procedures associated with the protocol.

To ensure responsibility and accountability for the overall quality of care received by participants during the study period, clinical governance issues pertaining to all aspects of routine management will be brought to the attention of the TSC and where applicable to individual NHS Trusts.

23. Publication and Dissemination Policy

The study will be registered with an authorised registry, according to the International Committee of Medical Journal Editors (ICMJE) Guidelines, prior the start of recruitment.

The success of the study depends upon the collaboration of all participants. For this reason, credit will be given to those who have collaborated through authorship and contributorship. Uniform requirements for authorship for manuscripts submitted to medical journals will guide authorship decisions. These state that authorship credit should be based only on substantial contribution to:

- Conception and design, or acquisition of data, or analysis and interpretation of data;
- drafting the article or revising it critically for important intellectual content;
- and final approval of the version to be published;
- and that all these conditions must be met (www.icmje.org).

In light of this, the Chief Investigator, Co-Applicants, UoN staff, and relevant senior CTRU staff and those involved in the economic evaluation and process evaluation will be named as authors in any publication, subject to journal authorship restrictions. In addition, all collaborators will be listed as contributors for the main study publication, giving details of roles in planning, conducting and reporting the study.

The TMG / TSC will agree a publication plan and must be consulted prior to release or publication of any study data.

Individual collaborators must not publish data concerning their participants which is directly relevant to the questions posed in the study until the main results of the study have been published. Local collaborators may not have access to study data until after publication of the main study results.

NIHR Heath Technology Assessment

The NIHR must be notified of all outputs (i.e. publications). A copy of any outputs and any information pertaining to it must be sent to NIHR at the same time as submission or at least 28 days before the date intended for publication, or it being placed in the public domain, whichever is earlier.

All publications must acknowledge NIHR HTA as the study's funding source and include an appropriate disclaimer regarding expressed views and opinions (example text is provided on the HTA website).

On completion of the research study a draft final report will be submitted to the HTA programme (trial funder) by the CTRU, within 14 days. This will be peer reviewed and then published on the NIHR HTA website. The Trial team is obliged to provide HTA with advanced notice of any publication relating to the trial. Copies of any materials intended for publication

will be provided to NIHR HTA at least 28 days prior to submission for publication, and this will be co-ordinated by the CTRU

23.1 Authorship Guidelines

The agreed first author of abstracts is responsible for circulating these to the other members of the TMG for review at least 15 days prior to the deadline for submission.

The agreed first author of manuscripts is responsible for ensuring:

- timely circulation of all drafts to all co-authors during manuscript development and prior to submission
- timely (and appropriate) circulation of reviewers' comments to all co-authors

- incorporation of comments into subsequent drafts
- communication with the TSC (i.e. ensuring submission is in line with TSC publication plan, and ensuring TSC receive the final draft prior to submission)

The first author is responsible for submission of the publication and must keep the TMG and all authors informed of the abstract's or manuscript's status. The TSC will be kept informed of rejections and publications as these occur. On publication, the first author should send copies of the abstract or manuscript to the TSC, the TMG, the Sponsor and to all co-authors, and ensure communication with the NIHR.

23.2 Access to the final study dataset

To maintain the scientific integrity of the study, data will not be released prior to the end of the study, either for study publication or oral presentation purposes, without the permission of the Trial Steering Committee or the Chief Investigator or CTRU. In addition, individual collaborators must not publish data concerning their patients which is directly relevant to the questions posed in the study until the main results of the study have been published.

The Chief Investigator is the data custodian of the Data. Leeds shall collect and hold the Data during the course of the Project in accordance with the Protocol. On completion of the Project, the Data shall be transferred to Nottingham in encrypted format, along with any information needed to de-encrypt the Data, for final archiving. Following completion of the Project, any Party may apply to Nottingham for access to the Data for the purposes of further academic research in the public interest. The University of Nottingham and the University of Leeds shall establish an information governance committee to govern access to the Data following completion of the project.

23.2.1 Data source

Data from the CTRU main study database in Leeds must be used for data analyses (main trial, health economics and process evaluation) for all abstracts and publications relating to the questions posed within the study protocol, with the exception of additional Process Evaluation data. Furthermore, the statistical team at the CTRU shall perform all such analyses, with the exception of: the health economics analysis which will be undertaken within the Health Economics Group at the University of East Anglia using data pre-identified in the Health Economic Analysis Plan as necessary for the health economic analysis; the independent statistician review and the sponsor as required.

23.2.2 Data release

To maintain the scientific integrity of the study, data will not be released prior to the first publication of the results of the study, either for study publication or oral presentation purposes, without the permission of the TSC.

24. User and Public Involvement

The trial team have established a PPI stroke research partnership group at the University of Nottingham and we have identified and invited one participant and a physician with an acquired brain injury to join our Trial Management Group. Their involvement will ensure that the protocol, information sheets recruitment materials, the planned management and dissemination is informed by personal insight and experiences. We will also draw on a wider network of participant's through their existing roles in Different Strokes and Headway. Reimbursement is in accordance with INVOLVE guidance,

25. Funding

25.1 Funding source

This study is funded by the National Institute for Health Research Health Technology Assessment (NIHR HTA) Programme (Grant reference 15/130/11).

25.2 Participant payments

Participants will be provided with a maximum of £20 voucher for return of questionnaires.

26. Signature Pages

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

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

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

For and on behalf of the Study Sponsor:	
Signature:	Date: ...../...../.....
Name (please print):	
Position:	

Chief Investigator:	
Signature:	Date: ...../...../.....
Name: (please print):	

Statistician:	
Signature:	Date: ...../...../.....
Name: (please print):	
Position:	

27. References

1. DANIEL, K. WOLFE, C. BUSCH, M. MCKEVITT, C. (2009) What Are the Social Consequences of Stroke for
Working-Aged Adults? A Systematic Review. Stroke. 40. p.431-40.
2. Grant M (2015) Developing, delivering and evaluating stroke specific vocational rehabilitation: a feasibility randomised controlled trial, University of Nottingham
3. CORR, S. WILMER, S. (2003) Returning to work after a stroke: An important but neglected area. British Journal of Occupational Therapy. 66(5). p.186-92.
4. VESTLING, M. TULVESSON, B. IWARSSON, S. (2003) Indicators for return to work after stroke and the importance of work for subjective well -being and life satisfaction. Journal of Rehabilitation Medicine.
35. p.127-4.
5. LINDSTRÖM, B. RÖDING, J. SUNDELIN, G. (2009) Positive attitudes and preserved high level of motor performance are important factors for return to work in younger persons after stroke: A national survey, Journal of Rehabilitation Medicine, Vol 41, (9), pp. 714-718(5)
6. RADFORD, KA. WALKER, M. (2008) Impact of stroke on return to work. Brain Impairment. 9 (2). p.161
7. COOLE, C. RADFORD. K. GRANT, M. TERRY, J. (2013) Returning to Work After Stroke: Perspectives of Employer Stakeholders, a Qualitative Study. Journal of Occupational Rehabilitation. 23(3). p.406 -18.
8. BLACK, C. (2008) Working for a healthier tomorrow: Dame Carol Black's Review of the health of
Britain's working age population. London: The Stationery office.
9. TYERMAN, A. MEEHAN, MJ. (2004) Vocational assessment and rehabilitation after acquired brain injury: Inter-agency guidelines. London: British Society of Rehabilitation Medicine/Royal College of Physicians.
10. DEPARTMENT OF HEALTH. (2007) National Stroke Strategy.
11. NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE (2013) Stroke rehabilitation: long-term rehabilitation after stroke (clinical guideline CG162).
12. NHS ENGLAND (2014) Five Year Forward View. Available at: http://www.england.nhs.uk/wpcontent/uploads/2014/10/5yfv-web.pdf Accessed 11.6.15
13. ISWP (2012) National Clinical Guideline for Stroke. 4th ed. London: Royal College of Physicians.
14. DEPARTMENT FOR WORK AND PENSIONS (2004) Building Capacity for Work. A UK Framework for Vocational Rehabilitation. London: DWP.
15. BLACK, C. FROST, D. (2011) Health at work – an independent review of sickness absence.
16. RADFORD, K. CROMPTON, A. STAINER, K. (2013) Commissioning vocati onal rehabilitation after stroke:Can the Cinderella services get to the ball? A qualitative study. Journal of Health Services Research & Policy. 18(1 suppl). p. 30-8.
17. CARE QUALITY COMMISSION. (2011) Supporting Life After Stroke: A Review of Services for People who have had a Stroke and their Carers.
18. SINCLAIR, E. RADFORD, K. GRANT, M. TERRY, J. (2013) Developing stroke-specific vocational rehabilitation: a soft systems analysis of current service provision. Disability and Rehabilitation. 36 (5).
p.409-17.
19. SAKA, RO. MCGUIRE, A. WOLFE, CDA. (2005) Economic burden of stroke in England. London: National
Audit Office.
20. TOWNSEND, N. WICKRAMASINGHE, K. BHATNAGAR, P, ET AL. (2012) Increased incidence stroke in younger people. Coronary heart disease statistics 2012 edition. British Heart Foundation: London.
21. Repeal of Retirement Age Provisions Regulations (legislation.gov.uk, 2011)
22. ARAUZ, A. (2013) Return to work after stroke: the role of cognitive deficits. Journal of Neurology, Neurosurgery and Psychiatry. 84(3). p.240.

23. WADDELL,G, AYLWARD M (2010) Models of sickness and disability: applied to common health problems, Royal Society of Medicine Press Ltd, London
24. STROKE ASSOCIATION (2015) State of the Nation: Stroke Statistics January 2015. Available from https://www.stroke.org.uk/sites/default/files/stroke_statistics_2015.pdf Accessed 31.7.15
25. MCKEVITT, C. FUDGE, N. REDFERN, J. ET AL. (2011) Self-reported long-term needs after stroke. Stroke. 42(5). p.1398-403.
26. The NHS Outcomes Framework 2014/15. (2013) www.gov.uk/dh accessed 21.9.16
27. PLAYFORD, ED. RADFORD, K. BURTON, ET AL. (2011) Mapping Vocational Rehabilitation Services for people with Long term neurological conditions: Summary report . Department of Health.
28. BRITISH SOCIETY OF REHABILITATION MEDICINE (2003) Vocational rehabilitation - the way forward (2nd Edition): report of a working party (Chair: Frank AO). London, British Society of Rehabilitation Medicine.
29. BALDWIN, C. BRUSCO, NK. (2011) The effect of vocational rehabilitation on return to work rates post stroke: a systematic review. Topics in Stroke Rehabilitation. 18(5). p.562-72.
30. TREXLER, LE. TREXLER, LC. MALEC, JF. ET AL. (2010) Prospective randomised controlled trial of resource facilitation on community participation and vocational outcome following brain injury. Journal of Head Trauma Rehabilitation. 25(6). p.440-446.
31. NTSIEA, MV. VAN ASWEGEN, H. LORD, S. OLORUNJU, S. (2014) The effect of workplace intervention programme on return to work after stroke: A randomised controlled trial. Clinical Rehabilitation. doi:10.1177/0269215514554241
32. FADYL, J. MCPHERSON, K. (2009) Approaches to vocational rehabilitation after traumatic brain injury: a review of the evidence. Journal of Head Trauma Rehabilitation. 24. p. 195-212.
33. RADFORD, KA. PHILLIPS, J. DRUMMOND, A. ET AL. (2013) Return to work after Traumatic Brain Injury:Cohort Comparison and Economic Evaluation, Brain Injury. 27(5). p. 507–520.
34. SAMPSON C, EDWARDS C, RADFORD KA, Return to work after stroke: feasibility economic analysis, in preparation
35. RADFORD, KA. GRANT, MI. SINCLAIR, EJ. ET AL. (2013) Stroke Specific Vocational Rehabilitation (SSVR): A Feasibility Trial. International Journal of Stroke. Vol 8 (Suppl 3). p. 1-75.
36. BOND, GR. DRAKE, RE. BECKER, DR. (2012) Generalizability of the Individual Placement and Support (IPS) model of supported employment outside the US. World Psychiatry. 11(1). p. 32 -39.
37. ZIGMOND, AS. SNAITH, RP. (1983). The hospital anxiety and depression scale. Acta psychiatrica Scandinavica. 67(6). p.361-70. Epub 1983/06/01.
38. NOURI, F. LINCOLN, N. (1987) An extended activities of daily living scale for stroke patients. Clinical Rehabilitation.1(4). p.301-5.
39. WILLER B (1994) THE COMMUNITY INTEGRATION QUESTIONNAIRE: A Comparative Examination. American Journal of Physical Medicine & Rehabilitation, - Volume 73 - Issue 2, 75-
40. HERDMAN M, GUDEX C, LLOYD A, JANSSEN M, KIND P, PARKIN D, BONSEL G, BADIA X (2011) Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual Life Res;20(10):1727-36. doi: 10.1007/s11136-011-9903-x.
41. OPPE, M, DEVLIN, N., VAN HOUT, B, KRABBE, P AND DE CHARRO, F (2014) A Program of Methodological Research to Arrive at the New International EQ-5D-5L Valuation Protocol. Value in Health, 17(4), 445 – 453.
42. HORNE, J (2016) Measuring confidence after stroke. University of Nottingham.
43. FRANK AO, THURGOOD J (2006) Vocational rehabilitation in the UK: opportunities for the health care professions. International Journal of Therapy and Rehabilitation;13(3):126-34
44. LOISEL P,DURAN MJ, BERTHELETTE D, VÉZINA N, BARIL R,GAGNON D, LARIVIÈRE C, TREMBLAY C (2001)
New Paradigm for the Management of Occupational Back Pain, Disease Management and Health Outcomes 9(7):351-360 DOI: 10.2165/00115677-200109070-00001

45. GRANT M, RADFORD K, SINCLAIR E, WALKER M (2014) Return to work after stroke: recording, measuring and describing occupational therapy intervention, British Journal of Occupational Therapy, 77(9) 457-465
46. Equality Act 2010, http://www.legislation.gov.uk/ukpga/2010/15/pdfs/ukpga_20100015_en.pdf, accessed 21.9.16
47. BRITISH SOCIETY OF REHABILITATION MEDICINE (2010) Vocational Assessment and Rehabilitation for People with Long-Term Neurological Conditions: Recommendations for Best Practice. British Society of Rehabilitation Medicine, London.
48. VRA, 2007 Vocational Rehabilitation Association (VRA) UK Standards of Practice, VRA, 2007
49. RADFORD KA, PHILLIPS P, JONES T, GIBSON A, SUTTON C, WATKINS C, SACH T, DULEY L, WALKER M, DRUMMOND A, HOFFMAN K, O'CONNOR R, FORSHAW D, SHAKESPEARE D (2015) Facilitating return to work through early specialist health-based interventions (FRESH): protocol for a feasibility randomised controlled trial, Pilot and Feasibility Studies, 2015, 1:24 (17 June 2015) doi:10.1186/s40814-015-0017-z
50. World Health Organisation (WHO) (2001) International Classification of Functioning Disability and Health (ICF). Geneva: WHO.
51. SMELT AF, VAN DER WEELE GM, BLOM JW, GUSSEKLOO J, ASSENDELFT WJ (2010) How usual is usual care in pragmatic intervention studies in primary care? An overview of recent trials. British Journal of General Practice. 60(576):e305-18.
52. DAWSON L, ZARIN DA, EMANUEL EJ, FRIEDMAN LM, CHAUDHARI B, GOODMAN SN (2009) Considering usual medical care in clinical trial design. PLoS Med. 6(9):e1000111.
53. Sentinel Stroke National Audit Programme Clinical Audit April—June 2015 public report, National results, September, 2015, https://www.strokeaudit.org/ accessed 21.9.16
54. DESHPANDE P AND TURNER-STOKES L (2004) Survey of vocational rehabilitation services available to people with acquired brain injury in the UK. In Tyerman A and Meehan MJ eds. Vocational assessment and rehabilitation after acquired brain injury: Inter-agency guideline, BSRM.
55. DEPARTMENT OF HEALTH (2001) ICH-GCP, Research Governance Framework for Health and Social Care.
56. GRANGER C (1998) The emerging science of functional assessment: our tool for outcomes analysis. Archives of Physical Medical Rehabilitation Mar;79(3):235-40
57. CROWTHER R, MARSHALL M, BOND G, HUXLEY P (2004)Vocational rehabilitation for people with severe mental illness. CochraneDatabase of Systematic Reviews 2004, Issue 2. [DOI:10.1002/14651858.CD003080]
58. NICE. Guide to the methods of technology appraisal 2013. Assessed on line on 18th August at: https://www.nice.org.uk/process/pmg9/chapter/1-foreword
59. ILMARINEN J, TUOMI K (1993) Work Ability Index for aging workers, in Ilmarinen J Ed, Ageing and Work, Helsinki Finnish Institute of Occupational Health, 142-151.
60. ROBINSON, B (1983). Validation of a Caregiver Strain Index. Journal of Gerontology. 38:344 -348.
61. HANKEY, GRAEME J (xxxx) Training caregivers of disabled patients after stroke, The Lancet , Volume 382 , Issue 9910 , 2043 - 2044
62. FORSTER A, MELLISH K, FARRIN A, BHAKTA B, HOUSE A, HEWISON J, et al. (2014) Development and evaluation of tools and an intervention to improve patient- and carer-centred outcomes in Longer-Term Stroke care and exploration of adjustment post stroke: the LoTS care research programme. Programme Grants Appl Res;2(6)
63. CURTIS L (2015) Unit Costs of Health and Social Care. PSSRU. http://www.pssru.ac.uk/projectpages/ unit-costs/2015/ (accessed 22nd April 2016.
64. DEPARTMENT OF HEALTH. NHS reference costs 2014/15. https://www.gov.uk/government/publications/nhs -reference-costs-2014-to-2015 (accessed 22nd April 2016.
65. HSCIC. Prescription Cost Analysis, England - 2015. http://www.hscic.gov.uk/article/2021/Website-Search?productid=20437&q=prescription+cost+analysis&sort=Relevance&size=10&page=1&area=both

#top (accessed 8th April 2016.
66. CHEN P, LIN KC, LIING RJ, WU CY, CHEN CL, CHANG KC (2016) Validity, responsiveness, and minimal clinically important difference of EQ-5D-5L in stroke patients undergoing rehabilitation. Qual Life Res. 25(6):1585-96. doi: 10.1007/s11136-015-1196-z.
67. MANCA, A., N. HAWKINS, AND M.J. SCULPHER (2005) Estimating mean QALYs in trial -based costeffectiveness analysis: the importance of controlling for baseline utility. Health Econ,. 14(5): p. 487-96.
68. WILLAN AR, BRIGGS AH, HOCH JS. (2004) Regression methods for covariate adjustment and subgroup analysis for non-censored cost-effectiveness data. Health economics 13(5): 461 -75
69. BRIGGS AH, WONDERLING DE, MOONEY CZ (1997) Pulling cost-effectiveness analysis up by its bootstraps: A non-parametric approach to confidence interval estimation. Health economics; 6(4):327-40.
70. FENWICK E, CLAXTON K, SCULPHER M (2001) Representing uncertainty: the role of cost-effectiveness acceptability curves. Health economics; 10(8): 779-87.
71. MOORE, GF. AUDREY, S. BARKER, M. ET AL. (2015) Process evaluation of complex interventions:Medical Research Council guidance. British Medical Journal.350. h1258
72. MAY, C. MURRAY, E. FINCH. T. ET AL. (2010) Normalization Process Theory On-line Users' Manual and Toolkit. Available from: http://www.normalizationprocess.org [Accessed 9th August 2011]
73. http://www.normalizationprocess.org/accessed 20.9.16
74. GALLACHER K, MAY, CR, MONTORI, VM, & MAIR, FS (2011) Understanding Patients' Experiences of Treatment Burden in Chronic Heart Failure Using Normalization Process Theory. Annals of Family Medicine, 9(3), 235–243.
75. RITCHIE J, LEWIS J. Qualitative Research Practice (2003) A Guide for Social Science Students and Researchers. London, England: Sage Publications.
76. BORELLI, B. (2011) The Assessment, Monitoring, and Enhancement of Treatment Fidelity In Public Health Clinical Trials, Journal of Public Health Dentistry 71 (Suppl 1):S52-63. DOI: 10.1111/j.1752-7325.2011.00233.x
77. HAWE, P. SHEIL, A. RILEY, T. (2004) Complex interventions: how "out of control" can a randomised controlled trial be? British Medical Journal. 328., p.1561 - 1563.
78. NICE (2016) Stroke in Adults QS2 ISBN: 978-1-4731-1806-5, https://www.nice.org.uk/guidance/qs2, accessed 21.9.16
79. ALASZEWSKI A, ALASZEWSKI H, POTTER J, PENHALE B (2007) Working after stroke: survivors' experiences and perceptions of barriers to and facilitators of the return to paid employment. Disability and Rehabilitation, 29(24): 1858-1869.
80. MEDICAL RESEARCH COUNCIL (2008) Developing and evaluating complex interventions: new guidance, London: Medical Research Council.
81. CORRIGAN JD, HARRISON-FELIX C, BOGNER J, DIJKERS M, TERRILL MS, WHITENECK G (2003) Systematic bias in traumatic brain injury outcome studies because of loss to follow-up. Archives of Physical Medicine and Rehabilitation; 84:153–160.
82. PARKER C, DEWEY M (2000) Assessing research outcomes by postal questionnaire with telephone follow-up. Int. J. Epidemiol. (2000) 29 (6): 1065-1069. doi: 10.1093/ije/29.6.1065
83. MURRAY J, FORSTER A, YOUNG J (2013) Response and completion rates for postal outcomes booklets in stroke rehabilitation International Journal of Therapy and Rehabilitation. http://dx.doi.org/10.12968/ijtr.2007.14.10.27395
84. FORSTER A, MELLISH K, FARRIN A, BHAKTA B, HOUSE A, HEWISON J et al. (2014) Development and evaluation of tools and an intervention to improve patient- and carer-centred outcomes in Longer-Term Stroke care and exploration of adjustment post stroke: the LoTS care research programme.Programme Grants Appl Res 2014;2(6)
85. HORNE, J C, LINCOLN, NB, LOGAN, PA (2015) Developing a new, patient reported Confidence after Stroke Measure (CaSM). International Journal of Stroke, 10 (Suppl. 5), 5-76.

86. HOFFMANN TC, GLASZIOU PP, BOUTRON I, MILNE R, PERERA R, MOHER D et al. (2014) Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. BMJ. 2014;348:g1687
87. NICE. NICE's position statement on EQ-5D-5L. August 2017.
88. Van Hout B, Janssen M, Feng Y et al. (2012) Interim scoring for the EQ-5D-5L: Mapping the EQ-5D-5L to EQ-5D-3L value sets. Value in Health, 15: 708-15.
89. RYE, M, TORRES, EM, FRIBORG, O, SKRE, I, AARONS, GA. (2017) The Evidence-Based Practice Attitude Scale-36 (EBPAS-36): A brief and pragmatic measure of attitudes to evidence-based practice validated in US and Norwegian samples. Implementation Science, 12:44, DOI 10.1186/s13012-017-0573-0
90. AARONS GA. (2004) Mental health provider attitudes toward adoption of evidence-based practice: the Evidence-Based Practice Attitude Scale (EBPAS). Ment Health Serv Res., 6(2):61–74.
91. AARONS GA ET AL (2012) Expanding the domains of attitudes towards evidence-based practice: the evidence based practice attitude scale-50. Adm Policy Ment Health, 12;39(5):331–40.92. SALBACH NM JAGLAL SB (2011) Creation and validation of the evidence-based practice confidence scale for health care professionals. Journals of Evaluation in Clinical Practice, 17, 794-800.
93. HORVATH, A. O. & GREENBERG, L. S. (1986). The development of the Working Alliance Inventory. Inh. S. Greenberg and W. M. Pinsof (Eds.), The Psychotherapeutic Process: A Research Handbook (pp. 529-556). New York: Guilford.

28. Appendices

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