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FReSH START Feasibility Study

A feasibility study of an intervention to improve quality of life and other outcomes in people who repeatedly self-harm

Study Title:	Function REplacement in repeated Self-Harm: Standardising Therapeutic Assessment and the Related Therapy (WP3 – Feasibility)
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The FReSH START study will at all times comply with current government and HRA advice regarding COVID-19. The Sponsor will ensure study activities will be amended as required in accordance with the latest guidance.

UNIVERSITY OF LEEDS

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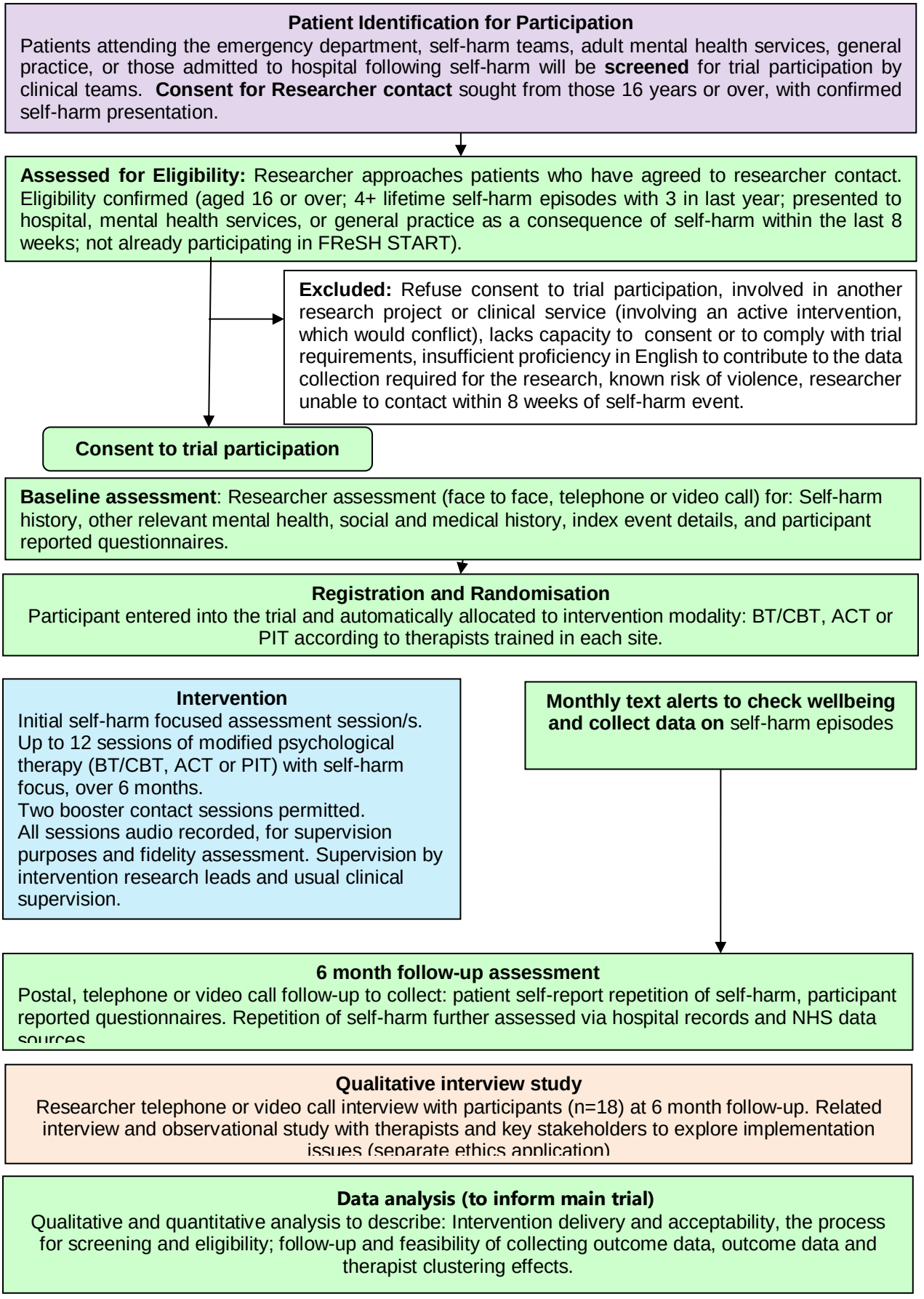
3. TRIAL FLOW CHART



4. GLOSSARY OF TERMS

AE	Adverse Event
ACT	Acceptance and Commitment Therapy
BHS	Beck Hopelessness Scale
BT/CBT	Behaviour Therapy/ Cognitive Behaviour Therapy
CLRN	Comprehensive Local Research Network
CORE-OM	Clinical Outcomes in Routine Evaluation – Outcome Measure
CRF	Case Report Form
CTRU	Clinical Trials Research Unit
CTS	Cognitive Therapy Scale
DBT	Dialectical Behaviour Therapy
ED	Emergency Department
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation
GP	General Practitioner
ITT	Intention-to-Treat
LIHS	Leeds Institute of Health Sciences
LTHT	Leeds Teaching Hospitals Trust
LYPFT	Leeds and York Partnership NHS Foundation Trust
REC	Research Ethics Committee
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NIHR	National Institute for Health Research
NRES	National Research Ethics Service
PIT	Psychodynamic Interpersonal Therapy
PHQ9	Patient Health Questionnaire 9
PMG	Programme Management Group
PSC	Programme Steering Committee
REC	Research Ethics Committee
RCSI	Reliable and Clinically Significant Improvement
RCT	Randomised Controlled Trial
R&D	Research and Development
RUSAE	Related, Unexpected Serious Adverse Event
SAE	Serious Adverse Event
SH	Self Harm
SMS	Short Message Service
SOP	Standard Operating Procedure
SSA	Site Specific Assessment
TMG	Trial Management Group
UC	Usual Care

5. BACKGROUND

5.1. Nature of the problem

Self-harm is a major public health challenge with estimated lifetime prevalence of 5-6% (1) and some 220,000 hospital attendances annually in England and Wales (2). Repetition of self-harm is common with 70% of hospital attenders reporting previous episodes of self-harm (3). Up to 20% of those who present to hospital give a history of over five acts (3) and about 25% attend hospital for a subsequent act during 18 month follow-up (3). For those seen in hospital after an episode which represents at least their third attendance, more than 50% will go on to a further repeat attendance (4). We know most about hospital attendance because of ease of data collection, but it is apparent that many additional episodes do not lead to hospital attendance (5, 6). A reasonable assumption is therefore that some 40-50,000 hospital attendances a year are accounted for by those who repeatedly self-harm, with as many episodes again not leading to hospital attendance (7).

Repeated self-harm especially is associated with other problems such as depression and misuse of alcohol, with poor quality of life and with problems with interpersonal and social function (8): the risk of suicide is higher in the presence of a history of repeated episodes (9). Multiple repetition bears a significant cost both to the individual and the healthcare system; total healthcare costs rise significantly in the six month period following hospital attendance if the episode is number five or greater compared to a first episode (10).

An intervention that improves the quality of life of people who repeatedly self-harm and that could be delivered without the need for expensive specialist services would be of potential benefit to tens of thousands of those who attend hospital each year. In addition to the personal and social benefits, a reduction in hospital attendance would be of benefit to the health service (local estimates are that each ED attendance and assessment costs £12-1400) and a reduction in primary care attendance would reduce burden on GPs who have little specific to offer.

5.2. Existing evidence

There is a useful distinction between acts of self-harm that are a response to recent stressors that are associated with acute distress and often not repeated once the stress is resolved, and multiple (repeated) acts associated with longer-term social and psychological problems (11). A recent Cochrane review showed little evidence for the benefit of existing therapies for the problem of multiply-repeated self-harm (12). Therapies that have been studied are intensive, of long duration (6-12 months), in specialist services, and require specialist therapists; there is no published evidence of cost-effectiveness. The latest Cochrane review, NICE guidelines in the longer-term management of self-harm in adults (13) (CG133) and expert commentaries (14) all point to the need for new research to test the effectiveness of interventions in this population.

5.3. Rationale for the present approach

Despite the importance of reducing repetition, we know from working with people who have experience of self-harm that a therapeutic approach that works with service users to identify valued (positive) goals is a more acceptable approach than therapies focused on reduction of the act itself.

Our approach involves modifying three existing therapies, behavioural/cognitive behavioural therapy (BT/CBT), acceptance and commitment therapy (ACT), and psychodynamic interpersonal therapy (PIT), specifically for use with people who multiply self-harm. We have selected therapies that can be easily adapted to deliver a new therapeutic approach for self-harm, have an evidence-base, and are accessible to the large numbers of people who repeatedly self-harm and are seen in mainstream NHS practice. Where the therapy is not already available in certain centres, each can easily be taught and learned by mental health professionals who work with people who repeatedly self-harm.

The three approaches overlap in several ways, particularly in the consideration of positive functions or values for the individual as a central tenet. Treatment goals are formulated as responses to these over-arching values, so that the individual is enabled to develop a broader values-concordant repertoire of activities. The therapies differ in other specific ingredients, which are particular therapeutic actions e.g., thinking about and responding to the world in a less maladaptive way in Behavioural Therapy/Cognitive Behaviour Therapy (BT/CBT), improving interpersonal relationships in psychodynamic interpersonal therapy (PIT), being more accepting of one's self in acceptance and commitment therapy (ACT).

Although the therapies will retain their own essential ingredients, all three will incorporate the same specific self-harm adaptation in order to provide a new approach to self-harm, differing from previous interventions which emphasise negative drivers such as affect dysregulation or hopelessness. It is important to emphasise that the new strategies are not to be presented as straight substitutes of a behavioural sort, but are likely to involve changes in social and interpersonal activities.

A key modification, common to the three therapies, will involve adaptation of the initial assessment which will focus upon elements of practice that people who self-harm find particularly helpful, in particular, recognising the positive benefits that they experience from self-harm (e.g. relief of tension) and the important role it plays in their lives. The assessment will include a focus on exploring the core values of the client, their problems and difficulties and potential risk issues. Prominence will be given to formulation and understanding of the potential positive or protective benefits that self-harm plays, by undertaking a functional analysis of self-harm behaviour. The assessment will also address the expectations of the client regarding treatment and work collaboratively to develop a positive rationale for psychological treatment, which directly addresses the expectations of the client and includes potential goal setting.

The work to modify the therapies is currently on-going and involves a systematic review of the relevant qualitative literature in this field, a thorough search of relevant grey literature and a Q-sort study to understand the attitudes and values held by people who self-harm. We are working with PPI to help us refine our research methods and synthesise data.

6. SUMMARY OF NIHR PROGRAMME GRANT FOR APPLIED RESEARCH (PGFAR)

This feasibility study forms part of a National Institute for Health Research (NIHR) funded research programme, which seeks to develop and evaluate an intervention to improve outcomes in people who repeatedly self-harm. The intervention will modify three existing psychological therapies (behavioural activation, acceptance and commitment therapy, psychodynamic interpersonal therapy) to target factors leading to repeated self-harm and associated psychological problems, aiming to improve quality of life and minimise self-damaging behaviour.

6.1. Programme Aims

To develop and evaluate the clinical and cost-effectiveness of a modified approach to psychological therapy for people who repeatedly self-harm and who are being treated in mainstream NHS practice.

6.2. Programme Objectives

1. Develop a clinical assessment that identifies both positive and negative functions of self-harm from the individual's perspective, that is acceptable to patients and that can be used by therapists trained in therapeutic approaches that are currently available in the NHS.
2. Produce therapeutic materials based upon this work and develop therapy-specific training programmes and intervention manuals to allow this new clinical assessment and self-harm-specific approach to be used as part of existing therapies.
3. Identify and train therapists experienced in relevant therapies or self-harm treatment, who are willing to undertake training and deliver the intervention in a research setting.
4. Evaluate the feasibility and acceptability (to patients and therapists) of the intervention
5. Evaluate the effectiveness and cost-effectiveness of the intervention in a Phase 3 RCT with an internal pilot and process evaluation.
6. Investigate the processes of delivery, including mechanisms of change, for the intervention.

This protocol is for objective 4, to evaluate the feasibility and acceptability of the intervention.

7. FEASIBILITY STUDY AIMS AND OBJECTIVES

7.1. Aims

The aim of this feasibility study is to 1) assess intervention delivery and acceptability 2) assess the feasibility of conducting, and 3) inform the design of the subsequent definitive randomised controlled trial of the Intervention versus Usual Care (UC) for adults.

7.2. Objectives

Objectives of the feasibility study are to:

Intervention delivery and acceptability

- Measure intervention delivery (number of sessions delivered / attended; key components)
- Measure researcher and therapist rated therapist fidelity to the intervention for both the:
    - self-harm focus common across the modified therapies, in the initial assessment and subsequent sessions
    - individual psychological therapeutic approach
- Finalise therapist rated fidelity checklists for use in future RCT (Work Stream 4)
- Measure acceptability of therapy to patients
- Measure acceptability of therapy to therapists
- Produce an updated version of the intervention and its delivery for use in future RCT (Work Stream 4)
- Undertake qualitative study of experience of, and acceptability of interventions

Recruitment methods, uptake and follow-up

- Measure rates of identification, eligibility and consent, recruitment
- Measure participant follow up rates.

Follow-up data collection

- Assess the feasibility of obtaining the full trial's primary outcome measure 'Quality of life using Clinical Outcomes in Routine Evaluation - Outcome Measure (CORE-OM)' and secondary outcome data (hopelessness; depression; social connectedness; Quality-adjusted life years and healthcare resource use) via postal or online administration (or telephone or face to face interviews if appropriate) at 6 months.
- Assess the acceptability and feasibility of obtaining the full trial's secondary outcome 'repetition of self-harm' via monthly text message data collection,
- Measure self-harm follow-up rates for text, postal/online (or face to face interviews if appropriate) administration and telephone interviews at 6 months, and through hospital records via researcher data collection.
- Assess through qualitative interviews the experience of, acceptability of, and the burden of, collecting participant reported outcomes.

Statistical outcomes

- Summarise outcome data and assess variability of outcomes
- Refine the sample size calculation for the main trial, including an estimate of clustering due to therapist effects

Progression Criteria

Review feasibility study results against pre-defined progression criteria for continuation to the definitive randomised controlled trial for: intervention delivery and acceptability, recruitment, and follow-up, (section 15.1).

8. DESIGN

The FReSH START feasibility study is a single arm trial, taking place across four sites, aiming to recruit 30 participants aged 16 years or older and reporting a self-harm episode in the preceding three months that is at least their 3rd episode in the preceding 12 months and their lifetime 4th.

To ensure that our intervention is compatible with NHS practice we will recruit through mechanisms which mirror NHS pathways. Thus we will recruit participants who present to health services – most commonly hospital Emergency Departments (ED), but also adult mental health teams and primary care.

Eligible, consenting participants will be registered and allocated to receive the trial intervention, comprising one of the three psychological therapies modified specifically for use with people who multiply self-harm: Behavioural Therapy/Cognitive Behaviour Therapy (BT/CBT), Psychodynamic Interpersonal Therapy (PIT), and Acceptance and Commitment Therapy (ACT). Delivery of the intervention will be by a therapist recruited and trained in one of the modified psychological therapies for the feasibility trial; therapy (BT/CBT, PIT or ACT), and therapist will be randomly allocated to participants.

Participants will be followed-up for 6 months from registration. Patient reported outcome data will be collected at 6 months post registration via postal or online administration (or telephone if appropriate) and via monthly text alerts for self-reported self-harm episodes. Repetition of self-harm will also be collected directly from hospital electronic records by the researcher during the follow up phase. Details on participant intervention provision and adherence will be recorded. Therapist level data will be collected, including demographics, experience and competencies, training, and ongoing supervision attendance. Fidelity to each of the intervention will be measured, including fidelity to the self-harm adapted approach, and to each of the three psychological therapies (BT/CBT, IPT and ACT). Inclusion of the key ingredients of the self-harm adaptation will be further recorded for the first assessment session of each therapy.

A parallel study will approach a sample of therapists and participants to take part in an interview study to refine the intervention and logic model ahead of the definitive multicentre RCT.

Along with screening and eligibility rates, this data, detail regarding appropriate data collection methods, and therapeutic delivery will be used to inform the design of the confirmatory, multi-centre RCT.

9. ELIGIBILITY

Inclusion criteria will be assessed by the clinical team in the emergency department (ED) or by the self-harm team during the patients' psychosocial assessment. Initial assessment will focus on potential participants' number of previous SH episodes.

Exclusion criteria will be assessed later by the study Researcher when following up patients who have consented to Researcher contact.

9.1. Inclusion criteria:

- Aged 16 years or over
- Presenting at ED, adult mental health services or general practice as a consequence of self-harm within the last 8 weeks, defined as: intentional acts that directly harm a person's own body. This includes methods like cutting, burning, scratching, banging or hitting parts of the body, or interfering with wound healing and it also includes self-poisoning, such as taking overdoses of drugs.
- Self-harm episode in the preceding three months that is at least their 3rd episode in the preceding 12 months and their lifetime 4th or more episodes.
- Has mental capacity to provide fully informed written consent

9.2. Exclusion criteria

- Receiving a specific psychological intervention that is similar to the trial intervention, or where a specific intervention is indicated for a related condition (e.g. anorexia nervosa or drug addiction) and would conflict with trial participation.
- Lacks capacity to comply with study requirements
- Insufficient proficiency in English to contribute to the data collection
- Known risk of violence (for example reported by ED or liaison psychiatry staff)
- 16 or 17 years of age and attending school and/or not eligible for treatment by local adult mental health services
- Researcher unable to contact participant within eight weeks following self-harm event

Participants may not be registered more than once. However, they can be screened on more than one occasion if not registered following first screening, as both eligibility and willingness to participate may change. Prospective waivers to eligibility criteria are not permitted.

10. RECRUITMENT PROCESS

10.1. Recruitment Setting

A total of 30 participants will be recruited following attendance at hospital ED, to self-harm teams, adult mental health services or general practice. Allocated therapy will be delivered by study-trained therapists located within the catchment area of the recruiting site.

10.2. Eligibility Screening During ED Attendance

Clinicians in the referring services will be provided with information about the study and a simple summary card (study card) for potential participants. Patients attending hospital following self-harm will initially receive an ED consultation and receive any required treatment. Patients who potentially

meet the eligibility criteria will be verbally informed of the study (by either the involved clinician or a clinical studies officer) and given the FReSH START study card, which briefly describes the study and will be asked for their permission for Researcher contact. If they agree to this contact, they will be asked to provide their contact details on the study card which will be sent directly to the Researcher. They will not be asked to consent to any study procedures or study involvement at this stage.

10.3. Researcher Contact

A study researcher will work with staff from participating sites to follow up those consenting to researcher contact. The Researcher will contact the patient to explain the study in more detail and, if the patient is still interested, establish full eligibility over the phone.

Where patients are not interested or not eligible, details will be recorded on the appropriate CRF and returned to CTRU. Referring clinical staff will discuss further care with ineligible patients. Self-referrals will be advised by the research team about seeking help in the NHS.

Where patients are eligible and remain willing to consider participation, the Researcher will arrange the baseline visit to obtain consent and undertake the baseline assessment. This can be a face to face meeting (in an appropriate and safe location, and with appropriate personal protective equipment PPE as per current NHS guidance). Alternatively the baseline visit may be performed by telephone or video calling*. In the meantime the patient will be sent the Participant Information Sheet to read prior to the Researcher visit. This will include information about the rationale, design and personal implications of the trial. Patients will be given at least 24 hours to read and digest the information provided, and will have the opportunity to discuss this with their family and other healthcare professionals if they so wish before being asked whether they would be willing to take part in the trial. There will also be the opportunity to ask the Researcher questions (either via the phone or video call, or at the arranged visit).
*Only video calling software which has been approved by the relevant NHS Trust and by the University of Leeds will be used.

10.4. Informed Consent

At the baseline visit the Researcher will invite patients to provide informed, written consent. The right of the patient to refuse consent without giving reasons will be respected. Further, the patient will remain free to withdraw from the study at any time without giving reasons and without prejudicing any further treatment.
If the visit is performed via telephone or video call the researcher will use a telephone consent script which covers all clauses of the consent form. Each clause will be initialed by the researcher following the participant's response. The researcher will sign the consent form and send a copy to the participant.

The original consent form will be sent to CTRU by the Researcher. A copy will be given to the participant. A further copy will be sent to the treating clinician for inclusion in the hospital notes (as appropriate).

10.5. Registration

Following confirmation of written informed consent and eligibility, and subsequent to the baseline assessment being performed, participants will be registered and allocated to a treating therapist by the study Researcher via the CTRU's automated 24-hour registration system. Authorisation and PIN codes, provided by the CTRU, will be required to access the registration system. These will be released when all relevant study approvals are in place for the participating site.

The following information will be required at registration:

- Name of researcher (who obtained informed consent and is undertaking registration)
- Researcher authorisation code and PIN
- Participant details: initials, gender, date of birth
- Name of trial research site and site code
- Confirmation of eligibility
- Confirmation of written informed consent and date
- Consent to researcher contact for process evaluation interviews obtained Y/N

On registration participants will be allocated a study number, and randomly allocated to receive one of the three possible psychological therapies available for delivery within the research site:

- Behavioural Therapy/Cognitive Behaviour Therapy (BT/CBT),
- Psychodynamic Interpersonal Therapy (PIT),
- Acceptance and Commitment Therapy (ACT).

Within each research site at least two of the three therapies should be available for delivery, and it is anticipated that at least two therapists per therapy will be trained and recruited to the feasibility study.

Participants will be randomised to therapy on an equal basis (1:1 where two therapies are available, or 1:1:1 basis, where all three therapies are available) within each research site using stratified permuted block randomisation, stratified by site. Participants will be further allocated to a trained therapist within the research site to deliver the intervention using stratified permuted block randomisation, stratified by allocated therapy and site, with an allocation ratio proportional to therapist availability., however where only one therapist exists for a particular therapy, the therapist will automatically be selected for the registered participant.

If necessary, for instance where only one therapy were to be available at a site or where randomisation to therapy causes logistical issues, we will use a simplified randomisation process by allocating participants to a trained therapist directly (similarly using stratified permuted block randomisation, stratified by site, with an allocation ratio proportional to therapist availability). This will maintain the credibility of the randomisation process and retain approximate balance in the number of participants across the different therapies.

Direct line for 24-hour registration +44 (0)113 343 2290

Web address for 24-hour registration: https://lictr.leeds.ac.uk/webrand/

Following registration, the Researcher will contact the participant to inform him/her of the therapy allocation and will liaise with the allocated therapist to initiate the intervention.

11. INTERVENTION DETAILS

11.1. Intervention Delivery

Recruited participants will receive up to 12 sessions of the intervention over a maximum of 6 months; with an additional option of 1-2 booster sessions (typically by telephone) within 3 months of completion of therapy. Sessions will commence as soon as possible following entry in to the trial. The intervention will be delivered in accordance with guidance notes developed for each of the modified therapies, and will be undertaken at appropriate Trust premises.

Sessions may be delivered face to face, via telephone or video call, will last for 45 to 50 minutes in duration and will occur where possible on a weekly basis. Mode of delivery will be determined by current Trust practice, therapist preference and participant preference. All sessions will be audio-recorded for use in supervision and independent fidelity assessment. Where sessions are delivered via video calling only audio will be recorded.

Rules for non-attendance are in line with practice from similar RCT for this patient group (for example DBT trials). Participants will be allowed a maximum of four appointments for which they fail to attend or cancel at the last minute.

11.2. Intervention therapies and self-harm

The intervention consists of one of three modified psychological therapies, Behavioural Therapy/CBT, Acceptance and Commitment Therapy, and Psychodynamic Interpersonal Therapy, each adapted to comprise core intervention aspects relevant to self-harm.

All three therapies will be adapted in a similar fashion to focus on self-harm and will incorporate a self-harm assessment package, which will comprise the first session of therapy.

The therapeutic assessment will focus upon elements of practice that people who self-harm find particularly helpful, in particular, recognising the positive benefits that they experience from self-harm (e.g. relief of tension, sense of control, opportunities for self-care) and the important role it plays in their lives. The session will include a focus on exploring the core values of the client, their problems and difficulties and potential risk issues. Prominence will be given to formulation and understanding

of the potential positive or protective benefits that self-harm plays, by undertaking a functional analysis of self-harm behaviour. The session will also address the expectations of the client regarding treatment and work collaboratively to develop a positive rationale for psychological treatment, which directly addresses the expectations of the client and includes potential goal setting.

Subsequent sessions will have a more specific focus on: helping participants notice patterns of thoughts, feelings, relationships and situations that are associated with self-harm; making choices that make life better for the participant, which may involve finding different ways to engage with strong or unpleasant feelings and impulses that quickly lead to self-harm; considering ways to improve well-being outside of self-harm, via discussion of overarching values and goals.

11.2.1 Behavioural Therapy/ Cognitive Behaviour Therapy (BT/CBT)

BT/CBT draws on cognitive and behavioural approaches to understanding emotional distress. Cognitive approaches see the way we think about events as influencing our emotional reaction to them. Fundamental beliefs (a schema) once activated gives rise to negative thoughts which maintain emotional difficulties through a series of feedback loops, including behaviours. Behavioural approaches involve trying to understand the pattern of relationships between behaviours and emotional responses in terms of the function of the behaviour and then seeking to introduce new patterns of behavior. The two theoretical approaches inform CBT treatment techniques, though different types of CBT may place more or less emphasis on one theoretical approach.

11.2.2 Acceptance and Commitment Therapy (ACT)

ACT is a newer form of cognitive behaviour therapy that aims to engender a quality called 'psychological flexibility', which can be defined as: '…the capacity to persist or to change behaviour in a way that includes conscious and open contact with thoughts and feelings (openness), appreciates what the situation affords (awareness), and serves one's goals and values (engagement). Consequently, in ACT, a clinician will use a range of therapy methods and techniques to enhance psychological flexibility: conversation, mindfulness, values-elicitation, self-compassion and perspective-taking exercises etc. For example, a clinician might help a person connect with their own over-arching goals and values by asking questions about what or whom is important in their life, then helping them to consider ways to match their behaviours with their values.

11.2.3 Psychodynamic Interpersonal Therapy (PIT):

This is a psychodynamic form of therapy which aims to manage feelings in the context of interpersonal relationships. It focuses upon interpersonal problems or ways of relating which may underpin symptomatic or problem scenarios. There is a strong focus on developing a strong therapeutic alliance from which interpersonal problems can be identified and solved. The different components of the model are as follows: 1) focus on feelings 2) encourage the client to stay with feelings 3) explore what associated thoughts, images, memories come to mind 4) explore links or patterns in interpersonal relating that are problematic 5) acknowledge these problematic patterns 6) test out new ways of behaving both in the session with the client and in personal relationships outside. A goodbye letter is given to the client at the end of the therapy to summarise the work.

11.3. Therapist identification

The intervention will be delivered by health professionals (mental health nurses, psychologists, OTs or psychiatrists, counsellors) who have either prior experience of work with people who self-harm and managing risk, or who are trained in one of the three therapies. Some prior experience of delivering any form of recognised therapy is desirable but not essential. Good interpersonal skills are essential as judged by being able to form strong working alliances with clients/users.

Potential therapists will be identified at each site following discussion with the relevant service managers. All therapists will have a recognised mental health professional background (eg. Nursing, occupational therapy, clinical psychology, psychiatry, CBT therapist, counsellor). We aim to recruit two therapists for each type of therapy at each site, with at least two of the three therapies made available at each site.

11.4. Therapist training

All therapists will undergo a therapy specific training according to the type of therapy they will deliver in the study. Training will be delivered by the co-investigator therapy leads and will consist of a 3 day workshop, with additional online materials provided as necessary. The workshop shall be delivered in virtual format when required. Therapists will be expected to demonstrate an acceptable standard of adherence and competence to their specific training, as judged by expert supervision, before participating as a study therapist. Following training the first two participants seen by each therapist (and recruited to the feasibility trial) will act as training cases, with their 12 session therapy closely supervised by the co-investigator therapy leads.

11.5. Supervision and risk management

11.5.1 Therapy-specific research supervision

All therapists will receive therapy-specific group supervision (maximum 3-4 people per group) lasting 90 minutes every 2 weeks. This will be face-to-face, phone, or via video if appropriate confidentiality safeguards can be agreed. Details of supervision sessions, including number of sessions, format, attendance and issues identified will be documented to monitor adherence to the supervision process. Supervision will be provided by the co-investigator therapy leads (co-ordinated by LIHS). Encrypted audio-recordings of therapy sessions may be used in supervision.

11.5.2 Clinical supervision

All sites will have a designated clinician who will be available for consultation regarding any risk issues or other questions related to wider clinical management. Therapists will manage and escalate risk as per routine clinical practice and through discussion with their psychotherapy supervisor and designated site clinician.

11.5.3 Risk Escalation Protocol

Should a participant become upset/distressed during or immediately after data collection, or phone the research number and indicate they are in distress:

1. (If during data collection), the researcher will ask them if they would like to stop. Some participants may feel upset but wish to continue with the activity. The researcher will remind them that that they do not have to continue. Participants can take a break during the activity if they need to or completely stop.
2. For participants who call the research number, or if participants remain distressed once they have stopped the activity, the researcher will acknowledge their distress and provide information about resources they can access (e.g. Samaritans, GP, support worker, crisis team).
3. If participants are still distressed, (they ask for more help and/or indicate that they are worried about how they are feeling, ask if they would like the researcher to support them in accessing the help outlined in step 2), the researcher should discuss the actions with a senior clinician on the research team.
4. If the researcher has serious concerns about a participant's immediate safety, the researcher will inform the participant that they need to speak to someone about the participant's concerns as they are worried about their immediate welfare. The researcher will immediately contact a senior clinician on the research team who will discuss options for accessing support for the participant.

11.6. Monitoring participant and therapist adherence (fidelity)

Adherence of participants to the intervention will be recorded by the number of sessions offered and attended, and reasons for ending therapy,

Fidelity assessments will be made via therapist reported fidelity using an adherence checklist for all sessions and through researcher rated assessment of audio recordings. Fidelity will assess the following components of the intervention:

- adaptations for working with people who self-harm in the initial assessment and subsequent sessions, common across the modified therapies
- individual psychological therapeutic approach

All initial sessions, and 1-2 additional sessions of each participants subsequent sessions, will be rated for fidelity, adherence and competence.

Assessment of the individual psychological therapeutic approach will be made using items from therapy-specific scales: the Sheffield Psychotherapy Rating Scale for PIT; the Cognitive Therapy Scale Revised for BT/CBT, and the ACT Fidelity measure for ACT. Assessment will be performed by the relevant co-investigator therapy lead or delegate.

11.7. Withdrawal of Treatment

In line with usual clinical care, cessation or alteration of regimens at any time will be at the discretion of the clinicians or the participants themselves.

Withdrawal from, or non-attendance for, treatment and non-compliance with follow-up questionnaires are NOT classed as withdrawal from the trial, and follow-up will continue as planned, unless a participant specifically expresses a wish to withdraw from trial processes.

11.8. Withdrawal of consent

The right of a participant to refuse participation without giving reasons will be accepted. The participant will remain free to withdraw at any time from the study without giving reasons and without prejudicing his/her further treatment. If participants of the proposed study withdraw consent from further participation their data collected up to that point will be included in the final study analysis. This will be made clear to the participants at the time of consent and when they withdraw from the study.

12. ASSESSMENTS/DATA COLLECTION

Participating site teams will be expected to maintain a file of essential trial documentation (Investigator Site File) which will be provided by CTRU, and to keep copies of all completed case report forms (CRFs) for the trial, except questionnaires which will be sent to CTRU and stored centrally.

Participant assessments will take place at:

- Baseline (prior to registration) for complete measures
- Monthly post-registration up to 6-months for self-reported self-harm episodes via text message follow-up
- 6-months post-registration for complete measures via postal/questionnaire, supplemented by a maximum of two reminders and phone, video call or face-to-face interviews to maximise follow-up rates. Follow-up at 6 months will therefore correspond with the expected completion of the participant's therapy sessions, including any booster sessions.

Required data, assessment tools, collection time points and processes are described in detail in sections 12.1 to 12.5. This is summarized in table 1 below. A window of up to two weeks prior to registration will be recommended for baseline data (ideally baseline and registration will occur on the same day) and plus or minus two weeks from the target of 6 months post- registration for outcome data. The feasibility of these windows will be recorded.

Table 1: Summary of Assessments

Assessment (including who is involved)	**Timeline (months post-randomisation)**

	Baseline	monthly	6 months
Eligibility and consent			
- Eligibility assessment (inclusion criteria assessed by clinician, exclusion criteria assessed by Researcher)	X		
- Consent (R)	X		
Background and Demographics (P and R)			
- NHS number	X		
- GP details	X		
- Participant's contact details	X		
- Education and employment	X		
- Date of index event	X		
- Details of 'index' event	X		
- Date of hospital attendance / contact with services	X		
- Self-harm history	X		
- Current co-morbid physical / mental health	X		
- Social and medical history	X		
- Current psychotropic medications	X		
- Source of referral	X		
Follow-up data (P, R and T)			
- Therapy details including method of delivery	X		
- Therapist details including gender, age, qualifications and experience	X		
- Therapist training details including competency assessment	X		
- Therapist supervision details (supervisor)			X
- Referrals to and attendance at other services			X
- Medication details			X
- Admissions to / attendance at hospital relating to self-harm			X
- Admissions to / attendance at hospital for other reasons			X
- Repeat of self-harm (T)	Ongoing collection at therapy sessions and monthly text messages		
- Serious adverse event reporting	Ongoing collection		
- Details of further self-harm episodes since consent (collected via 2-way SMS from Participant)		X	X
Questionnaires (Researcher admin at baseline, CTRU postal admin at 6 months)			
- Clinical Outcomes in Routine Evaluation - Outcome Measure (CORE-OM)	X		X
- Hopelessness - Beck Hopelessness Scale	X		X
- Depression PHQ 9	X		X
- Social connectedness – The Social Connectedness Scale - Revised	X		X

Self-reported episodes of self-harm			X
- Self-reported resource use	X		X
Qualitative Interview Study (R & P interview at 6 months – n=18))			
- Acceptability and perceived burden of questionnaire completion			X
- Details of treatment received and views on this			X

P = Participant, R = Researcher, T = Therapist

12.1. Screening Data

Clinicians in ED / appropriate hospital departments will provide data on the screening logs. This will include age, gender, reason not approached or not-eligible, where possible. In addition, routinely collected anonymous summary audit data on ED attendance and liaison psychiatry referrals will be used where available.

12.2. Registration and Baseline Data

Patients who satisfy the eligibility criteria and provide written or telephone informed consent at the Researcher visit will enter the trial.

The Researcher will provide data at registration / baseline, to include the following:

- NHS number
- GP address
- Participant's contact details, as appropriate: address, telephone number, mobile number, email address, and (optional) contact details for an individual nominated by the participant (who can be contacted if contact with participant is lost)
- Education and employment
- Date of index* event
- Details of index event (including categorisation of methods used (self-injury, self-poisoning, combined))
- Date of hospital attendance / contact with services
- Self-harm history (including number of self-harm events in the last 12 months and lifetime)
- Current co-morbid physical / mental health, (including COVID19 related data if appropriate)
- Social and medical history (current living accommodation, education, employment, co-morbidities, alcohol use, substance use)
- Current psychotropic medications
- Source of referral

**The 'index event' is defined as the most recent event that led to contact with services, prior to the baseline assessment*

The following questionnaires will be completed at baseline, prior to registration, via face-to-face, telephone or video call Researcher administration:

- Clinical Outcomes in Routine Evaluation - Outcome Measure (CORE-OM)
- Hopelessness - Beck Hopelessness Scale
- Depression - PHQ-9

- Social connectedness -The Social Connectedness Scale-Revised
- Self-reported resource use – primary and community care and medications and private financial burden due to self-harm (trial-specific).

Researchers who have a face to face meeting with a participant on NHS Trust property will adhere to the current government, NHS and Trust guidance on Personal Protective Equipment (PPE).

Researchers who visit participants in their home will follow the University of Leeds policy for working alone.* The researcher will take a mobile phone on all visits. S/he will have a study contact and will inform the study contact of when s/he is conducting an interview, will arrange an agreed contact time, and will provide the study contact with the anonymous participant ID. The researcher will telephone the study contact when the interview has been completed.
*Home visits will only take place if and when such contact can be fully compliant with government guidelines on social distancing.

12.3. Follow-Up Data

Participant-completed data
Questionnaires will be completed at 6 months post-registration via postal follow-up. Participants will be alerted to questionnaires being posted via text, and a maximum of two reminders will be sent to the participant. The Researcher may also telephone or video call the participant in an attempt to obtain the data if necessary. If the Researcher speaks to the participant and they do not wish to provide this, then this data will not be chased further.

The following data will be collected at 6 months:
- Clinical Outcomes in Routine Evaluation - Outcome Measure (CORE-OM)
- Hopelessness - Beck Hopelessness Scale
- Depression - PHQ-9
- Social connectedness -The Social Connectedness Scale-Revised
- Self-reported episodes of self-harm
- Self-reported resource use – primary and community care and medications and private financial burden due to self-harm (trial-specific).

Text messages
Text messages will be sent to the participant monthly to record occurrence of self-harm. The responses will not be routinely fed back to therapists, as they will be seeing clients weekly, and will be discussing self-harm issues on a regular basis with their clients. Separate consent will be sought for the texts and there will be an option for the participants to stop the messages by texting STOP. No free text responses will be possible. A contact telephone number and email address will be provided to allow respondents to raise questions with the research team if they wish.

Clinical data:
Data will be recorded on hospital attendances (including number and details of attendance / admission).

Therapy details will be collected from the therapist, and will include: therapy details (type, session offered and attended, dates, contact between sessions, method of delivery); therapy supervision details; referrals / attendance at other services; therapy content; repeat of self-harm, and medication details.

Therapist data:
Details on each therapist will be recorded and will include gender, age, qualifications and experience. Training data will also be recorded for each therapist, and will include the date and competency assessment. Supervision data will be recorded, and will include dates and details of each session.

12.4. Maximising Follow-Up

All participants who enter the study will be considered part of the intention to treat population and efforts will be made to follow up whenever appropriate.

12.5. Patient reported Assessment Instruments

The assessment instruments will be incorporated into visit-specific participant assessment packs for ease of completion. Details on scoring methods will be included in the Statistical Analysis Plan, together with interpretation of scores.

Clinical Outcomes in Routine Evaluation - Outcome Measure (CORE-OM)(15, 16)
The Clinical Outcomes in Routine Evaluation - Outcome Measure (CORE-OM) is a 34 item measure, used to assess levels of psychological global distress across four dimensions of well-being, symptoms (depression, anxiety, physical and trauma), functioning and risk. Quality-adjusted life years (QALYs) can be generated via the preference-based measure the CORE-6D(17) based on six questions from the CORE-OM34.

The CORE-OM is acceptable to patients to complete and is widely used in primary and secondary care services in the NHS. It is our proposed primary outcome measure for the follow-on definitive trial, to measure QoL. Quality of Life (QoL) is the most important patient-centred outcome as it can capture positive life changes (15, 18) - although reduction in the episodes of self-harm would be expected, the one does not necessarily mediate the other. We have chosen the CORE-OM as our main outcome measure, instead of the EQ-5D-5L (or other generic QoL measure), as its item content and domains better capture problems experienced by people who repeatedly self-harm

Beck Hopelessness Scale
The Beck Hopelessness Scale (BHS) is a 20-item self-report inventory and is used to measure feelings about the future, loss of motivation, and expectations.

PHQ-9(19, 20)
The Patient Health Questionnaire- 9 (PHQ-9) is the depression module of the larger Patient Health Questionnaire(21) and is used to assess mental and emotional conditions, providing a reliable and valid measure of depression severity.

The Social Connectedness Scale-Revised
The Social Connectedness Scale – revised (SCS-R) is a 20 item scale used to measure social connectedness as a sense of belonging.

Self-reported resource use
Within the Health Economics questionnaire designed for use in this study, information will be collected on primary, secondary and community care utilisation, medications and private financial burden due to self-harm.

12.6. Fidelity assessment instruments

Fidelity assessment of assessment and therapy sessions in the intervention arm will be made using a selection of items from the therapy-specific scales described below for fidelity to the individual psychological therapeutic approach, supplemented with additional items to assesses adaptations for self-harm.

For comparability across therapies, a single fidelity measure that captures common features across therapies will be scored, based upon responses in each of these therapy-specific measures.

BT/CBT: The Cognitive Therapy Scale (Revised) (CTS-R).
The Cognitive Therapy Scale (Revised) (CTS-R) is a widely used measure of competence for Cognitive Behavioural Therapies (22). It assesses the competence with which specific behavioural and cognitive techniques are used in therapy along with an assessment of more general therapeutic skills (e.g., interpersonal effectiveness, collaboration, pacing).

PIT: The Sheffield Psychotherapy Rating Scale
The Sheffield Psychotherapy Rating Scale is a 59 item scale using 7-point rating scales. It assesses the therapist's adherence to manuals for cognitive and interpersonal therapy. Trained raters rating the extent to which the therapist engages in each of the required behaviours (Shapiro, D and Startup, M., (2010) *Measuring Therapist Adherence in Exploratory Psychotherapy,* Psychotherapy Research, 2:3, 193-203). This measure has been validated for people with depression.

ACT: ACT Fidelity measure (ACT-FM)
The ACT Fidelity Measure (ACT-FM) records the fidelity of therapist behaviours the ACT treatment model. It includes 25 items, grouped into sub-domains recording pre-scribed and pro-scribed therapist behaviours in relation to ACT. It was developed recently via an expert Delphi study and field test with practicing clinicians. The measure shows acceptable inter-rater reliability and is rated as practicable by raters.

Therapist completed adherence checklist
An adherence checklist will be designed for use in the study, to be completed by the treating therapist following each intervention session.

12.7. Definition of End of Trial

The end of the trial is defined as the date of last participant 6 month follow-up.

13. PARTICIPANT SAFETY

13.1. Definitions

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

13.2. Expected Adverse Events/ Serious Adverse Events (non-reportable)

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).

13.3. Expected serious adverse events – standard reporting

The following events are expected within the study population and will be collected from date of consent until six months post-registration:

- Hospital admissions and re-admissions
- Life-threatening repeated self-harm not leading to hospital admission
- Death (including Suicide)

Deaths

With a sample this small we would not *expect* any deaths; however the expected rate of deaths for those who self-harm is approximately 60-100 times that of the population as a whole, thus it is possible that some people may die as a consequence of self-harm during the course of the study. Additionally there may be deaths due to other causes within the study population.

All deaths occurring from the date of consent up to six months post-registration must be recorded on the Death Form and faxed to the CTRU **within 24 hours** of staff or researchers becoming aware of the event. The original form should also be posted to the CTRU in real time and a copy retained at site.

Reports will be reviewed by the Chief Investigator within one working day of receipt by CTRU. The Programme Steering Committee (PSC), Funder and Sponsor will be informed of the death within one month of reporting by site.

It is possible that families and / or coroners may wish to speak to someone representing the trial about trial participant deaths, as well as to local Mental Health Service staff who have provided treatment. The Chief Investigator would be available for such meetings if required.

As deaths are more likely within this population they will not be subject to expedited reporting to the main REC, unless the PSC advises that the frequency of self-harm related and / or all deaths observed within the trial population is significantly higher than that expected in the general self-harm population.

Hospital admissions and re-admissions

Hospital attendance details will be obtained by researcher review of local hospital records and participant self-report, and monitored on a regular basis by the PMG and PSC. Any safety concerns identified by the PSC must be reported to Main REC and the Sponsor by CTRU within 15 days of identification, and appropriate action taken.

13.4. Related and Unexpected SAEs – expedited reporting

All Related/Unexpected SAEs occurring from the date of consent up to six months post registration must be recorded on the Related/Unexpected Serious Adverse Event (RUSAE) Form and faxed to the CI within 24 hours of the clinical research staff becoming aware of the event.
For each Related/Unexpected SAE the following information will be collected:

- date of SAE
- full details in medical terms with a diagnosis, if possible
- its duration (start and end dates; times, if applicable)
- action taken
- outcome

Any follow-up information should be communicated with the CI as soon as it is available. Events will be followed up until the event has resolved or a final outcome has been reached. The original RUSAE Form(s) should be retained by site until the event has reached a final outcome and all queries have been resolved.

All Related / Unexpected SAEs will be reviewed by the Chief Investigator, notified to the sponsor within one working day, and are subject to expedited reporting to the main REC by the CTRU on behalf of the Chief Investigator within 15 days.

Responsibilities of the Chief Investigator, CTRU, PSC and Sponsor will be detailed in a study specific guidance document

14. HEALTH ECONOMICS

14.1. Overall objectives for HE in the feasibility study

Although the standard economic evaluation framework has been developed in such a manner that it can be used to assess any use of scare resources to achieve improved health related quality of life improvements, interventions in mental health have specific idiosyncrasies which require additional attention. Whilst the evaluation of the full programme will meet NICE reference case standards and meet the CHEERS guidance in reporting outcomes, the feasibility study analysis will be limited to considering those elements which are considered most uncertain in the economic evaluation of mental health interventions. For example, we will not be considering the collection of secondary care costs in the feasibility study as we know complete records can be collected via Hospital Episode Statistics (HES). A consequence of this is that it is not really possible to draw conclusions about the overall economic argument from the feasibility trial, though we note this is not the underlying purpose of the feasibility study. In addition we will not use the feasibility study to determine the overall framework of analysis which will compare incremental Quality-Adjusted Life Years (QALYs) against incremental costs from both an NHS perspective but also from a wider societal perspective.

The feasibility study will assess the instruments we intend using for a) the measurements of Health Related Quality of Life (HRQoL) and therefore construction of QALYs and b) the measurements of resource use which are not captured by routine databases such as HES.

14.2. Feasibility of HRQoL Instrument

Whilst there is usually a preference for a completely generic measure of HRQoL such as the EQ-5D as suggested by NICE, there is sufficient evidence to suggest that the instrument is not particularly sensitive for use in all MH assessments. For this reason the CORE-6D instrument (derived from the CORE-OM) will be used. We will use the feasibility study to assess the completeness of response and the variation in self-reported HRQoL across patients and over time.

14.3. Feasibility of Resource Use Instruments

The feasibility study will also be used to assess the instruments used to capture self-reported resource use. From a medication/treatment perspective we will ask respondents to self-report use over the previous 3 months on the basis of providing a sufficient period of time in which to extrapolate over longer periods without incurring too much of a risk of recollection bias. The standard form is to identify the unit of resource use (medication, GP visit, residential rehabilitation centre stay) and quantify the number of units used. Much of this is standard in the economic evaluation of any technology. An important distinction from the cost-perspective is whether we can determine which are personal costs and which are costs to the NHS.

A key element in the assessment of the costs of MH interventions is the impact on the ability to work. There are no standardized or validated instruments for use in all economic evaluations in mental healthcare settings (23). In addition to the lack of standardized measure for use in MH, we also wish to explore the possibilities of distinguishing between costs due to unemployment, absenteeism and presenteeism. Ultimately they may have different costs associated with them but we also wish to explore the possibility of using these measures in the larger trial to understand transitions across these dimensions and we use the feasibility study to trial questions which have been drawn from a number of sources. In the event that these data are not well completed we will revert to a simpler set of workforce participation questions.

14.4. Modelling and Analysis perspective

Finally we will use the feasibility study to gain greater understanding of the mechanisms of the intervention and the population of patients. This is to better understand what the economic analysis of the full trial may look like and to pick up on any important drivers of costs or HRQoL which are not apparent from the wider literature. Any unanticipated outcomes from the study need to be assessed in terms of the likely impact on the economic evaluation.

15. OUTCOMES

The outcomes relate to intervention delivery, acceptability and feasibility of recruitment, follow-up and outcome data collection, as follows :

Intervention delivery and acceptability

- Number and proportion of therapists undergoing training and deemed competent.
- Therapy delivery by randomly allocated therapist, cross over of patients to therapists.
- Proportion of participants attending therapy, completing the required number of therapy sessions, number of early drop-outs from treatment, reasons for early drop outs, overall and by therapy type (BT, ACT, PIT).
- Availability and uptake of other treatments and services accessed by participants
- Proportion of participants taking up telephone "top up" contact at end of therapy.
- Proportion of participants and therapists delivering key intervention components, overall and by therapy type (BT, ACT, PIT) as recorded by the therapist
- Proportion of treatment sessions by method of delivery
- Participant and therapist fidelity to the intervention including fidelity to the self-harm modifications and to the individual psychological therapeutic approach overall and by therapy type (BT, ACT, PIT) as recorded by the researcher rated audio-recordings.
- Number and attendance of therapy specific supervision sessions.

Recruitment methods, uptake and follow-up

- Number of patients screened for eligibility, overall and by site
- Number of study cards given out and proportion completed, overall and by site
- Method of referral e.g. Emergency Department, self-harm team, clinical staff, general practice.
- Proportion of patients who complete the study card, who could be followed-up by the Researcher to assess eligibility and proportion of those found eligible for the study, overall and by site
- Proportion of patients that consent and are registered to the study out of those found eligible
- Reasons for non-participation, overall and by site
- Proportion of patients completing the study out of those registered, number of withdrawals from follow-up data collection, reasons for withdrawal, overall and by site
- Number of losses to follow-up and characteristics of participants lost to follow-up

Follow-up data collection

- Proportion of participants with available monthly self-reported repetition of self-harm data
- Proportion of participants with 6 month self-reported outcome data, proportion obtained through postal, online, telephone or face to face administration
- Proportion of participants with self-harm follow-up obtained through hospital records, text, and 6 month self-report
- Overall and item completion rates, and time spent on self-reported questionnaires.
- Proportion of participants reporting questionnaires as acceptable

Statistical outcomes

- Estimates and variability of self-reported outcomes at baseline and 6 months post-randomisation with 95% Confidence Intervals
    - Psychological global distress as measured by the CORE-OM.
    - Hopelessness as measured by the Beck Hopelessness Scale (BHS)
    - Depression as measured by the Patient Health Questionnaire- 9 (PHQ-9)

    - Social connectedness as measured by the Social Connectedness Scale – revised (SCS-R)
- Proportion of participants with reliable and clinically significant improvement (RCSI) defined as defined on the CORE-OM (16, 24, 25) as: change in CORE-OM of 5 or more points (reliable) and movement from the clinical range (≥10/40) to the non-clinical range (<10/40) (clinically significant).
- Clustering effect (ICC) of the CORE-OM by therapist and by therapy modality

16. QUALITATIVE INTERVIEW STUDY

The feasibility will include an embedded qualitative interview study to explore the acceptability of the approach from a service user perspective and to gain insights into how service users feel the therapy may work in practice This qualitative study will complement a related interview and observational study with the therapists and other key stakeholders to explore key implementation issues from a service perspective (approved by the University of Leeds School of Medicine Ethics Committee). Findings from both these studies will be used to refine the therapist training and finalise recruitment and follow-up procedures for the definitive trial. The findings will also be used to finalise a logic model that can guide the process evaluation of the definitive trial.

16.1. Sample identification:

Participants will be asked at time of enrolment to the feasibility study if they are willing to be approached to take part in this qualitative study. A sample of participants who consent (n=18) will then be approached by a study researcher to take part in this study.

16.2. Procedure:

Participants
Consenting participants will be interviewed at the end of therapy to explore their experiences of the therapy and the perceived impact on their social and psychological well-being. Participants will be asked about the appropriateness and acceptability of the measures and procedures for recruitment and follow-up. In addition, the effects of the COVID19 pandemic and the lockdown will be explored. A topic guide will be used to guide the interview. Interviews can be held via telephone or video call.

16.3. Data collection and storage:

Interviews will be audio recorded*, following agreement from the interviewee, using a digital audio recording device and will be professionally transcribed by University of Leeds approved GDPR compliant transcribers. During transcription, any potentially identifying information that may be contained in the interview discussions will be anonymised or removed. Only the research team and the transcriber will listen to the interview audio files. Audio files will be securely transferred in encrypted format, and securely stored at LIHS, accessible to only those members of the study team requiring such access. Field notes from observations and interviews will also be stored at LIHS. Where interviews are held via video calling only audio will be recorded.

16.4. Analysis:

Data from the interviews will be analysed for content thematically using a framework approach. The framework will be developed from the intervention development work in earlier stages of the programme of work. Intervention development also involves interviewing therapists involved in the feasibility study; this element of the project is dealt with in a separate protocol. The output from this analysis will be the refined training materials and finalised procedures for the definitive trial.

A second, theory driven analysis will explore participants' responses to identify how their experiences resonate with, and help to refine, our initial theories as to how this intervention might work to enact change. For example, a programme theory from our initial logic model is "identifying an individual's values through understanding the function of self-harm for them will facilitate engagement with therapy as clients feel respected". Analysis will explore where participant experience confirms or refutes initial theories and identify potential adjustments to, or caveats on, programme theories. The output from this analysis will be a logic model that can be used to guide the process analysis of the definitive trial.

17. STATISTICAL CONSIDERATIONS

17.1. Sample size:

We plan to recruit 30 participants to provide sufficient data to assess progression criteria to inform the decision to move to a definitive randomised Phase III evaluation (WP4). As this study is designed to determine the feasibility of a confirmatory trial and not to assess proof of concept or evaluate effectiveness, formal power calculations are not appropriate

Progression criteria will assess recruitment, follow-up, delivery and acceptability of the intervention using a traffic light system (Table 2). With 30 participants, the 95% CI around our green (go) criteria will exclude values in the red zone, relating to our stopping criteria. Therefore, with 30 patients, should we meet the go criteria we can be sufficiently confident that follow-up, delivery and acceptability will not fall to unacceptable levels as defined by the red (stop) criteria.

Recruitment of 30 participants will take place over four months in four centres, with approximately two to three participants recruited per month per center. With at least two therapists per center, this corresponds to one to two new participants a month per therapist, in line with recruitment and capacity requirements for the planned definitive trial (WP4).

Table 2 Feasibility study progression criteria

	Red	Amber	Green (95% CI)
Recruitment : Average no. patients recruited / month	<4	4-7	>7

Follow-up : % patients completing 6m primary outcome	<60%	60-75%	>75% (95% CI: 59.5%, 90.5%)
Delivery: % therapist delivering key intervention components (overall and by each therapy)	<60%	60-80%	>80% (95% CI: 65.7%, 94.3%)
Acceptability: % participants attending 1st session	<50%	50-70%	>70% (95% CI: 53.6%, 86.4%)

17.2. General Considerations

Statistical analysis is the responsibility of the CTRU Trial Statistician under the supervision of the Supervising Statistician. The analysis plan outlined in this section will be reviewed and a detailed, final statistical analysis plan will be written before any analysis is undertaken. The analysis plan will be written in accordance with current CTRU standard operating procedures (SOPs) and guidelines and will be finalised and agreed by the following people: the Trial Statistician, the Supervising Statistician, the Chief Investigator, the CTRU Principal Investigator and the Senior Trial Manager. Any changes to the finalised analysis plan and reasons for change will be documented.

17.3. Analysis Populations

All analyses and data summaries will be conducted on the intention-to-treat (ITT) population which is defined as all participants registered regardless of non-compliance with the protocol or withdrawal from the study.

17.3.1 Frequency of Analyses

No formal analyses are planned until after the trial is closed to recruitment and the required number of patients have been registered. Final analysis of the feasibility study will be carried out when all available outcome data has been received, no earlier than 6 months after the close of recruitment.

17.3.2 Outcome Analysis

Analysis will report descriptive statistics and confidence interval (CI) estimates rather than hypothesis testing. Estimates will be obtained for data relating to outcomes (section 13) and progression criteria (Section 15.1).

Recruitment methods, uptake and follow-up

The feasibility and success of the recruitment strategy will be evaluated by summarising the screening, eligibility, consent and registration processes, including numbers of participants involved during each stage. Reasons for non-participation in the study will be summarised. Participant retention during follow-up, including number of participants completing/withdrawing from the study and reasons for withdrawal will be presented by therapeutic modality. Characteristics of participants lost to follow-up will be compared to those completing the study.

Intervention delivery and acceptability

Delivery of intervention by allocated therapist will be summarised as will cross over of therapist. Retention rate in the intervention will be evaluated by summarising the proportion of patients successfully completing the required amount of therapy, the number of early dropouts and reasons for drop-out, overall and by therapeutic modality. The methods for measuring adherence and fidelity to the intervention will be agreed and summarised including the number of therapy sessions attended/missed, evidence of delivery of key intervention components, supervision, and fidelity to self-harm approach and individual psychological therapy, by both the participant and therapist. The range of treatment-as-usual available and taken up by participants in addition to the trial intervention will be summarised.

Follow-up data collection

The feasibility and success of obtaining the self-reported self-harm data monthly via text message will be assessed by summarising the proportion of participants with available repetition of self-harm data monthly up to 6 months post-randomisation, and compared to self-harm data obtained through hospital records and self-report at 6 month follow-up. The feasibility and best method of obtaining self-reported six month outcome data will be assessed by summarising the proportion of participant's with available data by method of obtainment. Acceptability of questionnaires will be assessed by summarising overall and item level completion rates, time spent on questionnaires, and participants reported acceptability.

Statistical outcomes

To check our assumptions for the sample size for the definitive trial, we will assess the variability (standard deviation) of the self-reported outcomes at baseline and 6 months post-randomisation, and report summary statistics and 95% confidence intervals. For the primary outcome of the full trial, the CORE-OM, we will report change from baseline (with 95% confidence intervals), and the proportion of participants with reliable and clinically significant improvement (RCSI). An investigation of the clustering effect (ICC) relating to the therapists will be carried out and reported for the CORE-OM at 6 months with 95% confidence interval. Descriptive summaries will be used to explore self-reported outcomes at 6 months post-randomisation by method of intervention delivery (face-to-face, telephone or video call).

18. TRIAL MONITORING

A Monitoring Plan will be developed and agreed by the Trial Management Group (TMG) and PSC based on the trial risk assessment; this may include on site monitoring.

18.1. Programme Steering Committee (PSC)

The PSC will provide overall supervision of the study - in particular, study progress, adherence to protocol, participant safety, and consideration of new information. The committee will meet once during the set-up period and at least annually thereafter for the duration of the study. A subcommittee of the PSC will be convened where necessary to monitor safety data.

18.2. Data Monitoring

Data will be monitored for quality and completeness by the CTRU. Missing data will be chased until it is received, confirmed as not available or the study is at analysis. However missing data items will not be chased from participants (although missing questionnaires will be where appropriate). The CTRU/Sponsor will reserve the right to intermittently conduct source data verification exercises on a sample of participants, which will be carried out by staff from the CTRU/Sponsor. Source data verification will involve direct access to patient notes at the participating hospital sites and the ongoing central collection of copies of consent forms and other relevant investigation reports.

18.3. Clinical Governance Issues

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 PSC and, where applicable, to individual NHS Trusts.

19. QUALITY ASSURANCE AND ETHICAL CONSIDERATIONS

19.1. Quality assurance

The study will be conducted in accordance with current MRC Good Clinical Practice (GCP) guidelines, UK Policy Framework for Health and Social Care Research 2017 and complies with the Mental Capacity Act (2005), through adherence to CTRU standard operating procedures (SOPs) and relevant study-specific SOPs.

19.2. Serious Breaches

Investigators are required to promptly notify the CTRU of a serious breach (as defined in the latest version of the National Research Ethics Service (NRES) SOP). A 'serious breach' is defined as a breach of the protocol or of the conditions or principles of GCP (or equivalent standards for conduct of non-CTIMPs) which is likely to affect to a significant degree the safety or physical or mental integrity of the trial subjects, or the scientific value of the research.

In the event of doubt or for further information, the Investigator should contact the Trial Manager at the CTRU.

19.3. Ethical considerations

The trial will be performed in accordance with the recommendations guiding physicians in biomedical research involving human subjects adopted by the 18th World Medical Assembly, Helsinki, Finland, 1964, amended at the 52nd World Medical Association General Assembly, Edinburgh, Scotland, and October 2000. The right of the patient to refuse participation without giving reasons must be respected. The patient must remain free to withdraw from the trial at any time without giving reasons and without prejudicing their care or treatment. The trial documentation will be submitted by CTRU to the identified Research Ethics Committee (REC). The trial must be approved by that REC and receive Management approval from each participating site prior to any participants entering the trial.

19.4. Submission of Study Data

Case Report Forms
Data will be recorded by researchers / site staff on trial-specific paper CRFs and submitted by post to the CTRU at the University of Leeds. Only the participant's trial number plus date of birth and initials will be added to CRFs in order to identify the participant. The site / researcher is responsible for obliterating all other personal identifiable data prior to sending CRFs and any other reports to the CTRU (with the exception of the patient consent form which will include the patient's name and signature). Following receipt, the CTRU will contact the trial site to resolve any missing or discrepant data queries.

The CTRU will seek to adopt all reasonable measures to record data in accordance with the protocol. Under practical working conditions some minor variations may occur due to circumstances beyond the control the CTRU. All such deviations will be documented on the study records, together with the reason for their occurrence; where appropriate, deviations will be detailed in the published report.

Interview data
Data collected through observations (field notes and observational records, audio and/or video recorded interviews, summaries of documentary analysis), and reflective reports will be anonymised and stored at LIHS.

20. CONFIDENTIALITY

All information collected during the course of the study will be kept strictly confidential. Information will be held securely on paper and electronically at the Clinical Trials Research Unit (CTRU). The CTRU and LIHS will comply with all aspects of the 2018 Data Protection Act and operationally this will include

- consent from participants to record personal details including name, date of birth, address and telephone number, email address, NHS number, GP name and address
- appropriate storage, restricted access and disposal arrangements for participant personal and clinical details
- 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 trial participation.
- consent from participants for the data collected for the trial to be used to evaluate safety and develop new research.
- participant name, address and telephone number will be collected when a participant is registered into the trial but all other data collection forms that are transferred will be coded with a trial number and will include two participant identifiers, usually the participant's initials and date of birth.
- where central monitoring of source documents by CTRU / LIHS (or copies of source documents) is required, the participant's name must be obliterated before sending.

- where anonymisation of documentation is required, sites are responsible for ensuring only the instructed identifiers are present before sending to CTRU/LIHS.

To ensure confidentiality of the data collected when published, fictitious site names and pseudonyms or study numbers not linked to sites or persons will be used. All identifiable data such as research site names, address, date of birth and participants' names will be removed.

Consent will be obtained from participants for the data collected to be used to develop new research. We will consider co-enrolment in other studies on a case by case basis.

If a participant withdraws consent from further collection of data, their data will remain on file and will be included in the final study analysis.

21. ARCHIVING

At the end of the study, data will be securely archived at the CTRU/LIHS for a minimum of 5 years. Data held by the CTRU / LIHS will be archived in the Leeds Sponsor archive facility and site data and documents will be archived at site. Following authorisation from the Sponsor, arrangements for confidential destruction will then be made.

22. STATEMENT OF INDEMNITY

The proposed study is sponsored by the University of Leeds. The NHS has a duty of care to patients treated, whether or not the patient is taking part in a research study, and the NHS remains liable for clinical negligence and other negligent harm to patients under this duty of care. The University of Leeds, as the employer of the Chief Investigator will be liable for negligent harm caused by the design of the study.

23. STUDY ORGANISATIONAL STRUCTURE

23.1. Responsibilities

23.1.1 Chief Investigator

As defined by the UK Policy Framework for Health and Social Care Research 2017, the Chief Investigator is responsible for the design, management and reporting of the study.

23.1.2 Operational structure

The **Programme Steering Committee (PSC)** – The PSC, with an independent Chair, will provide overall supervision of the programme, in particular progress, adherence to protocols, safety and

consideration of new information. It will include an Independent Chair, no fewer than two other independent members and a patient representative. The CI and other members of the PMG may attend the PSC meetings and present and report progress. The Committee will meet annually as a minimum.

The **Programme Management Group** (PMG), which oversees the FReSH START Programme Grant, comprises of the Chief Investigator, Programme Manager, Co-Applicants, Co-Investigators, and NHS host. The PMG will oversee the whole programme of studies**.**

The **Study Management Group** (SMG) is located within the Institutes of Health Sciences and Clinical Trials Research Unit at the University of Leeds. The SMG comprises of the Chief Investigator, the Programme Manager, key Co-Applicants, research fellows and CTRU staff. The SMG will meet at key points during the study to oversee the study including the set-up, on-going management, promotion of the study and the results.

It is anticipated that the Chief Investigator, the research fellows and CTRU staff will regularly meet to discuss the study. They will be responsible for the set-up of the study, including gaining ethical and R&D approval, appointment of additional researchers if required, management and overall supervision of the study team, collection and analysis of data, and drafting/finalizing publications. The Chief Investigator will be responsible for the day-to-day running of study.

The CTRU will be responsible for: registration, database development and provision, CRF design, data management and quantitative analysis.

24. PUBLICATION POLICY

The study will be registered with an authorised registry, according to the International Committee of Medical Journal Editors (ICMJE) Guidelines. The success of the study depends upon the collaboration of all participants. For this reason, credit for the main results will be given to all 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 and relevant members of the PMG staff will be named as authors in any publication.

The timing of any publication from the programme and this study will ensure scientific integrity is maintained. Individual collaborators must not publish data concerning their participants which is directly relevant to the questions posed in the study until the first publication of the analysis is

reported. The publication policy for this study will follow the publication policy agreed by the Programme Management Group.

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