Assessing psychological support for people with emotional distress and difficulties in relationships: The SPS study.

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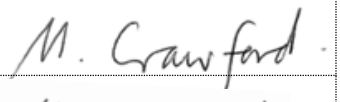
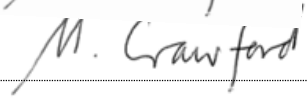
Summary of protocol changes

Version	Date	Summary of changes made
2.0	22 Dec 2022	Prior to the start of recruitment, a change to the platform on which study data is captured. Addition of a section defining expected SAEs. Addition of further details on study procedures and making clearer the description of the sample size calculation and planned analyses
3.0	21 Mar 2023	Updated eligibility criterion so that people on a waiting list for a psychological treatment for personality disorder are only excluded if the waiting list is less than one year. Added a separate 12 month visit to collect details of any psychological treatment received during participation.
4.0	18 July 2023	Increased number of months for participant recruitment and total study period. Amended recruitment rate.
5.0	07 Dec 2023	Removal of the Patient Satisfaction Questionnaire at 6-month follow-up. Addition of option for posting the self-completion follow-up surveys.

Protocol authorised by

Name & Role	Date	Signature
Professor Mike Crawford	22 Dec 2022	
Professor Mike Crawford	21 Mar 2023	
Professor Mike Crawford	18 July 2023	
Professor Mike Crawford	21 Dec 2023	

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Sponsor

Imperial College London/ is the main research Sponsor for this study. For further information regarding the sponsorship conditions, please contact the Head of Regulatory Compliance at:

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Funder

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This protocol describes the SPS study and provides information about procedures for entering participants. Every care was taken in its drafting, but corrections or amendments may be necessary. These will be circulated to investigators in the study. Problems relating to this study should be referred, in the first instance, to the Chief Investigator.

This study will adhere to the principles outlined in the UK Policy Frame Work for Health and Social Care Research. It will be conducted in compliance with the protocol, the Data Protection Act and other regulatory requirements as appropriate.

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GLOSSARY OF ABBREVIATIONS

AD-SUS	Adult Service Use Schedule
AE	Adverse Event
AR	Adverse Reaction
CI	Chief Investigator
CRF	Case Report Form
DERS	Difficulties in Emotional Regulation Scale
DSM	Diagnostic and Statistical Manual
DSUR	Development Safety Update Report
EQ-5D-5L	EuroQual 5 Dimensions 5 Levels
GAD	Generalised Anxiety Disorder
GCP	Good Clinical Practice
GP	General Practitioner
HRA	Health Research Agency
IDMEC	Independent Data Monitoring and Ethics Committee
ISRCTN	International Standard Randomised Controlled Trial Number
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NIHR	National Institute for Health Research
PHQ	Patient Health Questionnaire
PI	Principal Investigator
PIS	Participant Information Sheet
PSS	Personal Social Services
QUALY	Quality of life - Adjusted years
R&D	Research and Development
RCT	Randomised Control Trial
REC	Research Ethics Committee
SAP	Statistical Analysis Plan
SAR	Serious Adverse Reaction
SAE	Serious Adverse Event
SCID	Structured Clinical Interview for DSM
SOP	Standard Operating Procedure
SPS	Structured Psychological Support
TAU	Treatment as Usual
TSC	Trial Steering Committee
UAR	Unexpected Adverse Reaction
WSAS	Work and Social Adjustment Scale

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KEYWORDS

Economic evaluation; Mental health; Personality Disorder; Process evaluation; Psychological treatment; Randomised Controlled Trial

STUDY SUMMARY

TITLE	**Assessing psychological support for people with emotional distress and difficulties in relationships: The SPS study.**
DESIGN	Multi-centre, individually randomised, parallel group, researcher-blinded, controlled trial.
AIMS	1) To conduct a trial to test whether, for people with probable personality disorder, Structured Psychological Support is a clinically effective and cost-effective intervention for improving mental health and social functioning. 2) To conduct a parallel process evaluation to generate a contextualised analysis of the delivery of the intervention and outcome generation.
OUTCOME MEASURES	Social functioning (primary outcome), mental health, suicidal behaviour, health-related quality of life, patient-rated experience, service utilisation and costs, in the 12 months after randomisation.
POPULATION	People aged 18 and over who have probable personality disorder and are being treated by mental health staff working in primary or secondary care settings.
ELIGIBILITY	A score of four or more on the Standardised Assessment of Personality – Abbreviated Scale, willing and able to provide written informed consent. We will exclude people who have a co-existing organic or psychotic mental disorder, and those who are currently receiving psychological treatment for personality disorder or are on a waiting list of less than one year for such treatment.
DURATION	36 months

1. INTRODUCTION

1.1. BACKGROUND

The one-in-twenty people in Britain who meet diagnostic criteria for personality disorder have impaired social functioning, high levels of emotional distress, and greatly reduced quality of life. [1-3] It is estimated that the annual cost of providing NHS care for people with personality disorder will be over £1 billion per year by the middle of this decade. [4] Psychological interventions can help people diagnosed with personality disorder, but existing treatments are usually highly intensive and require people to attend group sessions over many months or years.
Most people diagnosed with personality disorder do not have access to these intensive interventions. Even when they do, as many as half do not engage with them. [5] As a result, very few people with personality disorder receive any evidence-based treatment. [6]

The most prevalent type of personality disorder in mental health settings is borderline personality disorder. Current NICE guidelines for borderline personality disorder explicitly state that short-term interventions should not be used. [7] However, this recommendation is based on expert opinion in the absence of evidence from high quality research.

Concerns have repeatedly been expressed about the poor quality of health care that people with personality disorder receive. [8-10] There are no licensed pharmacological treatments. [11] Current evidence-based psychological interventions are highly intensive, [7] and considered unsuitable for many patients including those with the most severe problems. [5,12] Improving services for people with personality disorder is a national service priority. NICE have called for all people with borderline personality disorder to be offered choice in the duration and intensity of therapy they are offered. [13] But options for patients are currently limited by the lack of evidence-based low intensity interventions. The NHS in England are currently funding the expansion of services for people with personality disorder. [14,15] But there is uncertainty about how these resources can be most effectively used.

1.2. RATIONALE FOR CURRENT STUDY

A recent Cochrane review found that, for people with borderline personality disorder, psychological interventions are more effective than usual treatment at reducing symptom severity and improving social functioning. [16] Most trials were of high-intensity interventions. A more recent systematic review that focussed on low-intensity interventions, reported that most were group-based and did not follow participants up after treatment had ended. The authors concluded that it was unclear if initial benefits seen during therapy are sustained, or if low-intensity interventions provide a cost-effective use of resources.

In 2016, the NIHR Research for Patient Benefit programme funded a study to develop a low intensity intervention for people with a diagnosis of personality disorder. [17] Qualitative data from people with a diagnosis of personality disorder indicated a strong preference for individual sessions, as most patients reported not being able to get personalised support within a short-term group setting. [17] This led us to develop ‘Structured Psychological Support’ (SPS), which we subsequently examined in a feasibility trial. [18] Data from the trial revealed clinically and statistically

significant differences at six months favouring SPS for both social functioning and patient satisfaction with care. [18]

This trial will provide a fully powered evaluation of this promising intervention. We will test whether SPS is a clinically effective and cost-effectiveness intervention for people with personality disorder.

2. STUDY OBJECTIVES

2.1. PRIMARY OBJECTIVE

To test whether people with probable personality disorder who are offered Structured Psychological Support have improved social functioning over a one-year period compared to those offered enhanced treatment as usual.

2.2. SECONDARY OBJECTIVES

To investigate the effectiveness of SPS compared to enhanced treatment as usual across six and 12 months, on social functioning, mental health, suicidal behaviour, patient-rated experience of care and on the incidence of adverse events.

2.3. HEALTH ECONOMIC OBJECTIVES

To examine the cost-effectiveness of SPS compared to enhanced treatment as usual for people with probable personality disorder. To do this we will examine the effects of SPS on health-related quality of life using the EQ-5D-5L over 12 months. We will compare use of health and social care services as well non-NHS costs such as accommodation and voluntary sector costs, between those in the active and control arm of the trial, and examine the within trial cost-effectiveness of SPS, compared to enhanced treatment as usual over 12 months using QALYs based on EQ-5D-5L and costs.

2.4. PARALLEL PROCESS EVALUATION

The process evaluation will provide a contextualised analysis of intervention delivery and outcome generation. Informed by a logic model, we will characterise the treatments to which trial participants are exposed. We will also examine the organisational and professional context within which SPS is delivered. Should the trial generate evidence of patient benefit, we will use the results of the process evaluation to support the wider delivery of this low intensity intervention throughout the NHS.

3. STUDY DESIGN

Multicentre, individually randomised, parallel group, researcher-blinded, randomised controlled trial, of Structured Psychological Support plus treatment as usual versus enhanced Treatment as Usual, including a parallel process evaluation and an integrated economic evaluation. Details of study interventions can be found in section 3.4 to 3.6 below).

The trial will involve two linked phases:
Phase 1 – A four-month internal recruitment pilot study. The planned recruitment rate in month one is 24, and in month two onwards is 32 per month. Data from the internal pilot will be presented to the Trial Steering Committee indexed against a priori stop/go criteria, which are detailed below. The TSC will then advise the funder and the sponsor on whether the study should progress to phase 2.

Phase 2 - Full trial over a further eight-month recruitment period, with a rate of recruitment of 30-35 per month. All participants will be followed-up for 12 months

Progression criteria	Red (%)	Amber (%)	Green (%)
Number of centres open to recruitment	3 or fewer (<60)	4 (80)	5 (100)
Total number recruited	Fewer than 60 (< 50%)	61 to 139 (50 to 99%)	140 (100%)
Uptake of the intervention in active arm of the trial (attends one or more session)	Less than 65%	65-99%	100%

All trial participants will receive enhanced treatment as usual from mental health services, ensuring that all have a jointly developed crisis plan. In addition, participants will be randomised to either no additional treatment or Structured Psychological Support.

3.1. STUDY SAMPLE

We will recruit 308 study participants (see section 7.1 for sample size calculation). For the parallel process evaluation, we will interview 40 trial participants, 10 non-participants and 45 clinicians and managers.

3.2. RANDOMISATION

Randomisation will be via a secure fully automated service operated by the North Wales Organisation for Randomised Controlled Trials in Healthcare (NWORTH), Bangor University. We will use a sequentially randomised dynamic adaptive algorithm stratified by gender (male/female/non-binary or other)and study centre with a 1:1.15 TAU:SPS ratio. [19] Within the Structured Psychological Support for people with personality disorder randomisation algorithm, the likelihood of the participant being allocated to each treatment group is recalculated based on the participants already recruited and allocated. This recalculation is done at the overall allocation level and within stratification (gender and study centre). By undertaking this re-calculation, the algorithm ensures that balance is maintained within acceptable limits of the assigned allocation ratio while maintaining unpredictability.
After a participant has consented, the site researcher will provide the trial coordinator at Imperial College with the participant's contact details. The trial coordinator will use the automated service to allocate the participant to a treatment group and then inform the participant and the participant's key worker of their allocation. For those in the active arm of the trial, the trial coordinator will also liaise with the local SPS supervisor, including providing the contact details of the participant, so that the participant can be allocated to a local therapist.

3.2.1. Blinding of study personnel

The research staff at sites, and the senior statistician will remain blinded throughout the trial. Staff in the trial coordinating team, individuals delivering and supervising the intervention, and the trial statistician will be unblinded.

3.3. STUDY OUTCOME MEASURES

3.3.1. Descriptive measures

We will collect basic demographic and clinical data on age, gender, ethnicity, disability, relationship status, employment status, and duration of contact with mental health services. We will assess the range of personality-related difficulties that participants have using the Personality Assessment Questionnaire for ICD-11 personality trait domains (PAQ-11) [20] and use items from the Structured Clinical Interview for Axis II Personality Disorders (SCID-II) [21] to determine whether they meet diagnostic criteria for borderline personality disorder. The SCID-II provides a reliable assessment of borderline personality disorder.[22] This will enable us to establish what proportion of participants meet the most prevalent form of the condition, with associated NICE guidelines.[7,13] We will also assess whether potential participants meet criteria for Post-Traumatic Stress Disorder, using the International Trauma Questionnaire.[23]

3.3.2. Primary outcome measures

Social functioning measured at baseline, six and 12 months after randomisation using the total score on the Work and Social Adjustment Scale (WSAS). [24] Social dysfunction is important to people with personality disorder because of the impact it has on quality of life and other long-term outcomes. [25,26] The WSAS is a widely used measure for assessing social dysfunction among people with mental health conditions, and rated more highly than other measures of social dysfunction by patients. [27] It is short, reliable, and sensitive to change. [28]

3.3.3. Secondary outcomes measures

All secondary outcome measures will be collected at baseline, six and 12 months after randomisation.

i. We will assess mental health using the 16-item Difficulties in Emotion Regulation Scale, [29] the nine-item Patient Health Questionnaire (PHQ-9) [30,31] and the seven-item Generalised Anxiety Disorder (GAD-7). [32,33]
ii. Suicidal thoughts and behaviour using items from the National Household Survey of Psychiatric Morbidity.[34]
iii. Health-related quality of life will be assessed using the EQ-5D-5L. [35] The EQ-5D-5L provides a brief and reliable measure of health-rated quality of life, which is responsive to change in people with personality disorder. [36]
iv. Patient experience, measured using the patient-rated global improvement [37]
v. Patient satisfaction with care (12 months only). [38]
vi. Standardised Assessment of Personality – Abbreviated Scale (12 months only)

3.3.4. Resource use and costs

We will collect data on use of resources using the Adult Service Use Schedule (AD-SUS) adapted for use in this trial based on previous research involving people with personality disorders. [39,40]This questionnaire collects detailed data on use of all hospital and community health and social care services. At baseline we will use the AD-SUS to record service use over the previous six months, at trial follow-ups we will use the AD-SUS to record service use since the previous assessment. In order to ensure that the key cost drivers are measured as accurately as possible, we will

also collect data on inpatient mental health admissions via computer records from the host NHS Trusts.

3.3.5. Qualitative data for the process evaluation

Semi-structured interview schedules have been designed in consultation with the Lived Experience Advisory Panel and other members of the project team. The interview schedules should be applied flexibly and may be modified after initial interviews have been conducted to take account of emergent themes. We estimate that it will take 5 to 10 minutes to complete interviews with people who declined to take part, 30 to 60 minutes to complete interviews with those who complete the six-month follow-up visit, 20 to 30 minutes to complete interviews with allied health professionals and 30 to 45 minutes to complete interviews with therapists.

3.4. STUDY INTERVENTIONS

SPS is an individual intervention delivered in six to ten, sessions over a period of three to six months. These sessions may be delivered face-to-face or online via a web-based conference platform such as MS Teams. It is a person-centred approach, which allows therapists to determine the exact number, frequency, and duration of sessions based on clinical judgement and patient preference. SPS draws on the longer-term evidence-based treatments for people with personality disorder including Dialectical Behaviour Therapy [41] and Mentalization Based Treatment [42] and has five key components:

1. Information about personality and mental health and the role of health services;
2. Validation and radical acceptance aimed at reducing self-blame and motivating self-efficacy;
3. Support to help the participant develop psychological skill(s) for managing their main difficulties;
4. Discussion of the role of relationships and structured activities in achieving better mental health, and
5. Use of a ‘mentalizing stance’ to highlight the importance of mental states.

During the first two sessions, therapists assess the patient’s presenting complaints, understanding of their problems, and their coping strategies. They then use this to provide tailored advice and validation and to formulate a treatment plan, including a crisis plan. The patient and the therapist agree a focus for the remaining sessions and the therapist summarises the plan in a letter, which is given to the patient and, if consent is given, shared with their General Practitioner. After the regular sessions have been completed, patients are offered a follow-up review session within a one-month period. This provides an opportunity for the patient to talk about their experience of using the skills they have learned and for the therapist to provide additional advice and support. In most instances, patients are then discharged to their GP, but patients can be referred back to general or specialist mental health services if this is clinically indicated.

For each participant in the SPS arm, the number, length and modality (in-person versus online) of SPS sessions will be recorded,

3.5. TRAINING AND SUPERVISION FOR STAFF DELIVERING SPS

Each member of staff who delivers SPS will be given a copy of the treatment manual and will have completed 12 hours of training (three four-hour sessions), before they

treat their first study participant. In addition to this, they will attend fortnightly one-hour supervision sessions throughout the period when they are delivering the intervention. Supervision will be delivered by a local clinician who has completed training in high intensity evidence-based treatments for people with personality disorder and has attended three four-hour sessions on supervising colleagues who deliver SPS. Each of these supervisors will be asked to attend a monthly one-hour supervision session for supervisors via videoconference.

3.5.1. Treatment fidelity

Treatment fidelity will be maintained by regular clinical supervision and assessed by an independent clinical expert using audio recordings obtained from a random sample of clinical sessions. Using a fidelity measure developed during the feasibility study,[18] they will rate the extent to which they judge that therapists have delivered the five key components of SPS on a 10-point Likert scale (where zero is not delivered, five is delivered and 10 is delivered in full). We will select a stratified random sample of two sessions per therapist during the pilot phase of the trial (total = 60) and one session per therapist during the remainder of the study (total = 30). In all cases, we will also ask staff delivering SPS to self-complete a proforma for every participant, which records the number and length of face-to-face, telephone and email/text contacts they had with patients. This will provide a measure of adherence to the study protocol in terms of the number and length of sessions and total treatment duration. We will also ask therapists to self-rate treatment fidelity using the same assessment tool as the independent clinical expert as part of the proforma recording information about the session content. This will enable us to assess the validity of self-assessment while also providing data that links with the process evaluation (See section 7.2.2) and enables the characterisation of the content of sessions at patient and aggregate level.

3.6. ENHANCED TREATMENT AS USUAL

Enhanced treatment as usual will be delivered by staff working in mental health teams. It will comprise assessment, care planning, and review. Even though there are no licensed medications for the treatment of personality disorder, patients are regularly prescribed psychotropic drugs. As part of enhanced treatment as usual, some patients may be referred to specialist community services at times of crisis, and arrangements may be made for inpatient treatment if it is not possible to safely manage patients in the community during these crises. Staff delivering enhanced treatment as usual will also be able to refer participants to psychological treatment where these are not for personality disorder. During participation, study participants may also be added to the waiting list for both low intensity and long-term high intensity psychological treatment programmes for personality disorder, with a view to initiating the therapy after completion of the 12-month follow-up phase of the study. According to current NICE guidelines, all people with personality disorder should be offered a care plan and crisis plan, but evidence suggests that almost half do not receive this.[44] To try to ensure adherence to NICE-recommended care, we will assess whether all participants in the trial have a crisis plan during their baseline assessment. At each study site, a clinician will develop a person-centred crisis plan with any patient in the control arm who does not currently have one.

4. PARTICIPANT ENTRY

4.1. PRE-REGISTRATION EVALUATIONS

Pre-registration evaluations will determine whether potential participants are aged 18 years or over, have probable personality disorder, do not have a co-existing organic or psychotic mental disorder, and are not currently receiving psychological treatment for personality disorder or are on a waiting list of less than one year for such treatment.

The primary focus for recruitment will be Community Mental Health teams (which are increasingly referred to as Mental Health Hubs). In some areas, 'Primary Care Liaison Mental Health Teams' operate separately from Mental Health Hubs and provide short term support to patients who are mainly managed in primary care. Primary Care Liaison Mental Health Teams will also be an important source of potential recruits. Any patient that is identified as potentially eligible by a member of their clinical team will be invited to speak to a researcher, who will meet them to explain the rationale for the study and give them a copy of the Patient Information Leaflet. Assessment of eligibility will be completed if the patient gives written informed consent to take part.

4.2. INCLUSION CRITERIA

To be eligible for the trial, an individual must be age 18 or over, and being treated by mental health staff working in primary or secondary care NHS settings.

4.3. EXCLUSION CRITERIA

People will be excluded if they do not meet criteria for probable personality disorder on the Standardised Assessment of Personality Abbreviated Scale, if they are unable or unwilling to provide written informed consent, if they have a co-existing organic or psychotic mental disorder, and if they are already receiving psychological treatment for personality disorder or are on a waiting list of less than one year for such treatment. Anyone currently a participant in a clinical trial or other interventional research will not be eligible to take part until their participation is complete.

4.4. WITHDRAWAL CRITERIA

In accordance with the current revision of the Declaration of Helsinki (amended October 2000, with additional footnotes added 2002 and 2004), a participant will have the right to withdraw from the trial at any time and for any reason, without prejudice to his or her future medical care by the physician or at the institution, and is not obliged to give his or her reasons for doing so.

4.5. ENTRY CRITERIA FOR STAFF IN THE PROCESS EVALUATION

To take part in the process evaluation, staff will need to provide written informed consent. In the pilot phase of the trial, we will interview up to 10 clinicians who are delivering active and control treatments. Staff will be selected purposively, to ensure a mix of demographic characteristics and a range of study sites.
In the main phase of the trial, we will interview a team manager, a clinical lead and one of the therapy supervisors at five of the study sites. We will also interview 10 members of staff delivering the active intervention and 10 members of staff delivering the control intervention. The qualitative researcher based at Middlesex

University will work with the researchers at study sites to identify participants and staff that were involved in the study. Staff participants will be contacted by email or telephone by the researcher leading the process evaluation and asked to confirm their willingness to take part in an interview. Arrangements will then be made to find a mutually convenient time to meet. Consent and interviews may be completed in person, by telephone or online according to participant preference.

5. ADVERSE EVENTS

5.1. DEFINITIONS

Adverse Event (AE): any untoward medical occurrence in a patient or clinical study subject.

Serious Adverse Event (SAE): any untoward medical occurrence or effect that:

- **Results in death**
- **Is life-threatening** – *refers to an event in which the subject 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.*
- **Requires hospitalisation, or prolongation of existing inpatients' hospitalisation**
- **Results in persistent or significant disability or incapacity**
- **Is a congenital anomaly or birth defect**

Medical judgement will be exercised in deciding whether an AE is serious in other situations.
Important AEs that are not immediately life-threatening or do not result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, will also be considered serious.

5.2. REPORTING PROCEDURES

Depending on the nature of the event the reporting procedures below should be followed. Any questions concerning adverse event reporting should be directed to the Chief Investigator in the first instance

5.2.1. Non serious AEs

Non-serious adverse events will be operationally defined as treatment on an urgent or emergency basis, defined as attendance at an Emergency Department, referral to a Home Treatment Team or First Responders Team, as these events are expected to occur in the study population. Researchers will collect this information during follow-up interviews every three months. At six and 12 months the information will be collected as part of questions on service use (part of the ADSUS). At three and nine months researchers will collect this information as part of their check-in (during which we will also thank people for taking part in the study, confirm that contact details are correct and check arrangements for completing formal follow-up interviews).
Non-serious adverse events meeting this definition will be recorded on an adverse event log at the site.

5.2.2. Serious AEs

A non-CTIMP SAE form will be completed and emailed to the Chief Investigator within 24 hours. However, hospitalisations for elective treatment of a pre-existing condition will not be reported as SAEs.

All SAEs will be reported to the London-Bromley Research Ethics Committee where in the opinion of the Chief Investigator, the event was:

- 'related', i.e., resulted from the administration of any of the research procedures; and
- 'unexpected', i.e., an event that is not listed in the protocol as an expected occurrence (see section 5.3 below for the definition of expected SAEs in this study)

Reports of related and unexpected SAEs will be submitted within 15 days of the Chief Investigator becoming aware of the event, using the NRES SAE form for non-CTIMP studies. The Chief Investigator will also notify the Sponsor of all related and unexpected SAEs.

Local investigators will report any SAEs as required by their Local Research Ethics Committee, Sponsor and/or Research & Development Office.

Contact details for reporting SAEs
RGIT@imperial.ac.uk
CI email: m.crawford@imperial.ac.uk
Please send SAE forms to: psych_trials@imperial.ac.uk
Tel: 020 7594 3253 (Mon to Fri 09.00 – 17.00, leave voicemail if no answer)

5.3. EXPECTED SERIOUS ADVERSE EVENTS

A serious adverse event that results in hospitalisation, prolongation of existing hospitalisation, or is life threatening will be considered expected if it follows a pre-existing pattern that is a known symptom of the participant's existing mental health diagnosis. For example, where a participant has a history of self-harm that results in the need for in-patient treatment and an event occurs that is similar in nature and severity, and there is not an evident change in the frequency of such events.

6. ASSESSMENT AND FOLLOW-UP

We will follow up all study participants six and 12 months after randomisation, using all items listed in table 3 below.

Table 3: Study Assessment Schedule.

Assessments	Screening	Baseline	6-month follow-up	12- month follow-up	Unblinded 12-month follow-up
Structured Assessment of Personality – Abbreviated Scale	X [1]	-	-	X [4] *	-
Personality Assessment Questionnaire for ICD-11 Personality Trait Domains (PAQ-11)	X [2]	-	-	X [5] *	-
Structured Clinical Interview for Axis II Borderline Personality Disorders (SCID-II)	X [3]	-	-	-	-
International Trauma Questionnaire (PTSD items)	X [4]	-	-	X [12] *	-
Work and Social Adjustment Scale (WSAS)	-	X [1]	X [1] *	X [1] *	-
Difficulties in Emotion Regulation Scale (DERS)	-	X [2]	X [2] *	X [2] *	-
Patient Health Questionnaire (PHQ-9)	-	X [3]	X [3] *	X [3] *	-
Generalised Anxiety Disorder (GAD-7)	-	X [4]	X [4] *	X [6] *	-
Suicidal Thoughts and Behaviour from the National Household Survey of Psychiatric Morbidity	-	X [5]	X [5] *	X [7] *	-
Patient-rated Global Improvement	-	X [6]	X [6] *	X [8] *	-
Patient Satisfaction with Care*	-	X [7]	-	X [9] *	-
Adult Service Use Schedule (ADSUS)	-	X [8]	X [7] *	X [10] *	-
EuroQoL EQ-5D-5L level	-	X [9]	X [8] *	X [11] *	-
Trial Arm allocation guess	-	-	-	X [12]	-
Medical Records check of concomitant psychological treatment	-	-	-	-	X [1]

[*Number***]** refers to the order in which the scales appear.
* Measure can be self-completed or completed at interview with researcher.

Follow-up assessments will be carried out by researchers who are blinded to the participant's allocation status, through either in-person meetings or remotely via telephone or using a secure videoconferencing service. Participants and members of their clinical team will be aware which arm of the trial they have been allocated to. To help maintain blinding, researchers will work separately from unblinded clinicians and trial coordinator. Prior to follow-up interviews, participants will be asked not to reveal their treatment group. If any researcher becomes inadvertently unblinded, we will arrange for another (blinded) researcher to collect all further data. We will also ask the researcher that conducts the follow-up interviews to guess the participant's trial arm allocation at 12 months for sensitivity analysis. A final check of the participant's medical record will be made at 12 months to determine whether they received a psychological intervention for personality disorder during the previous 12 months (other than SPS in the context of the trial). This may unblind the researcher if the participant's medical record details their study treatment. For this reason the check will always be done after 12 month follow-up with the participant is completed.

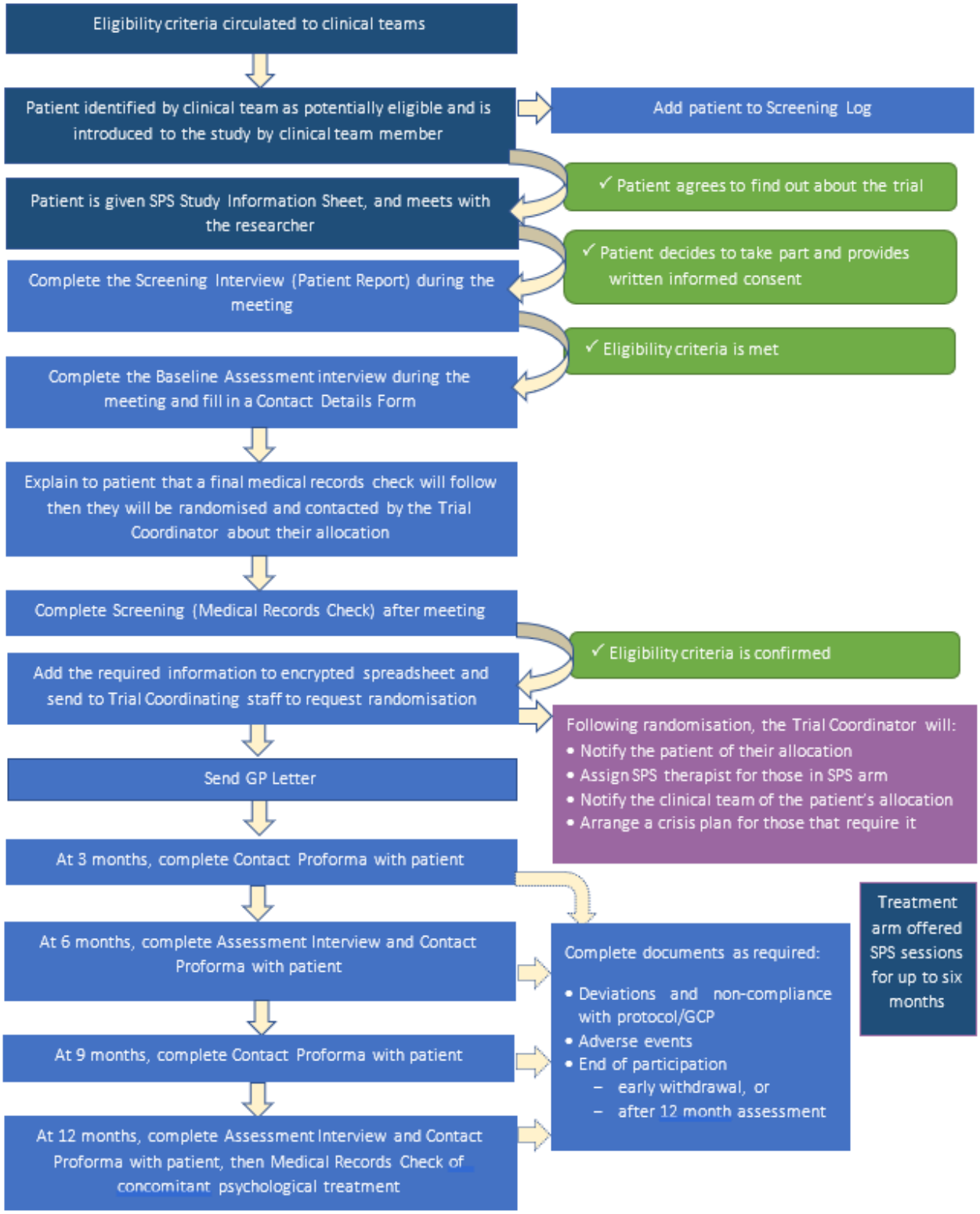
Study participants will be contacted at three and nine months to thank them for their participation in the study, enquire about adverse events, remind them of their forthcoming follow-up interviews and confirm their contact details. In order to maximise the rate of follow-up we will ask participants for consent to use medical records to check their current contact details. We will also ask them what their preferred method of contact is (telephone, text, email etc).

Information collected as study data will not usually be reported to the participant's clinical team. In the event that a participant tells us something which involves a risk to their safety or the safety of someone else, we would encourage them to share this information with others involved in their treatment e.g., the crisis team. The PI (or CI where the PI is not available) would be involved in the plan for obtaining urgent clinical support and, if it is judged that there is a major risk to safety this information may be shared with appropriate agencies (a mental health crisis team, Emergency Department or ambulance service), without their agreement. Under these circumstances we would let the person know of our intention to pass on the information and why we were doing so.

All study participants will be asked if they would like to be sent a summary of the study findings once these are available. This summary will be prepared by the Trial Management Group in collaboration with members of the Lived Experience Advisory Panel.

The process for an individual taking part in the SPS study is shown in Figure 1.

Figure 1: Procedure flowchart for the SPS study



6.1. DEFINITION OF END OF TRIAL

The end of trial is defined as the last 12-month follow-up assessment of last participant.

7. STATISTICS AND DATA ANALYSIS

7.1. SAMPLE SIZE

The sample size calculation is based on the primary hypothesis that people with personality disorder who are offered Structured Psychological Support will have improved social functioning over a one-year period, compared to those offered enhanced treatment as usual. We have powered the study to detect a minimum clinically significant difference of 3.8 points on the on the Work and Social Adjustment Scale, which, with a 9.5 standard deviation, equates to an effect size of 0.4. This compares with an effect size of 0.63 found in our feasibility trial,[18] and 0.42 reported in a recent systematic review of small-scale trials of individual low-intensity interventions for people with personality disorder.[43]

A four-point difference in total score on the WSAS equates to a major reduction in disability associated with one of the five items on the scale, for instance slightly impaired ability to work rather than severe impairment. It also equates to a small difference (e.g. from very severe impairment to severe impairment), in four out of the five items on the scale.

We conducted the sample size calculation using the ANCOVA method and PASS 16 software (NCSS, LLC. Kaysville, Utah, USA). This calculation shows that we will need to analyse data from 200 participants. With a 0.5 correlation between baseline and follow-up scores, this would give 90% power to detect a 0.4 Cohens D effect size (MD 3.8, SD 9.5) on the WSAS scale with a 5% significance level. We used a Variance Inflation Factor of 1.15 to account for clustering in the intervention arm of the trial assuming an average cluster size of 4 completers and an ICC of 0.05. Each therapist will need to treat 4 completers in the study, including 30% attrition this would be 5.69 participants. Therefore, each therapist will need to treat approximately 5-6 patients and approximately 29 therapists are required, 5-6 per site. Applying the VIF to the intervention group this means that we will need to analyse data from 215 participants (approximately 115 receiving SPS and 100 receiving TAU). To take account of 30% loss to follow-up we will aim to recruit 308 participants (approx. 165 receiving SPS and 143 receiving TAU).

7.2. DATA MANAGEMENT

7.2.1. Quantitative data from the trial

Consent Forms and Contact Details Forms recording identifiable data will be paper based only and stored in the Investigator Site File at the research site when completed. Quantitative screening, baseline, and follow-up data from patient interviews will be recorded on paper CRFs and then transcribed onto a web-based electronic database in MACRO. This database will be stored on a dedicated web server on a network drive at Bangor University, which is backed-up daily.

For the six- and 12-month follow-up assessments, there will be the option for participants to be sent a link to complete the data themselves without a researcher present. A web-based survey of the assessments from the paper CRF will be created in Qualtrics, a secure online survey tool. Qualtrics has ISO 27001

certification, meaning that it meets the international standard for managing confidential and sensitive data. Data is entered onto this web-based platform over encrypted SSL connections. All data transfers to Imperial College London use TLS encryption. Imperial College will be the data controller and there is a service-level agreement in place between Imperial College and Qualtrics. Only where a participant refuses to complete the assessment during an interview with a researcher, a unique link to the survey will be provided to the participant with a request for them to complete the questions independently.

Participants will be identified by their study ID number only in the MACRO database and Qualtrics. Access to the data held on both systems will be limited to individuals delegated the role, with these users allocated an identifier and password for login. Where web-based survey completion is not possible, the participant may be posted a paper copy of the questions along with a return envelope. A study specific data management plan will define in detail the procedures for data collection, entry, validation, verification, processing, transfer and archiving. It will also describe systems validation processes and list the data management personnel.

7.2.2. Qualitative data for the process evaluation

Qualitative data from interviews with study participants, researchers and staff will be audio recorded during in-person interviews on handheld digital recorders with encryption. Where in-person interviews are not possible, interviews may be conducted using a web-based conference platform (e.g., MS Teams), the interview recorded, and the audio data encrypted and saved. For participants that wish to take part in the interview but do not want to be audio-recorded, we will make contemporaneous notes, and then dictate as soon as possible after the interview has been completed.

These encrypted audio files will be stored on computers at Middlesex University and also transferred to a transcription service for professional transcribing prior to data analysis. This will use end to end encrypted transfer and encrypted storage. The audio files are immediately deleted from the transcription service's system on confirmation of receipt of the transcripts.

7.2.3. Audio recordings for assessing treatment fidelity

Therapy sessions may be audio-recorded by the therapist and then stored on an NHS computer. These may also be emailed to an independent clinician for the purpose of assessing treatment fidelity.

Audio-recordings of therapy sessions will be made on encrypted devices including mobile phones and laptops where this is necessitated by the location of the therapy (i.e. no desktop computer is in the room). These will be transferred to an NHS desktop computer for storage and the file immediately deleted from the original device if this was a portable device. For the purpose of supervision these recordings will be played during supervisory sessions from the NHS computer. Where the audio-recording needs to be sent to an independent clinician for evaluation of treatment fidelity, it will be emailed in an encrypted format and remain encrypted whilst stored. Once the recording is evaluated it will be immediately deleted from the email and computer of the clinician concerned.

7.3. DATA ANALYSIS

A fully documented Statistical Analysis Plan (SAP) will be written and agreed by the co-applicants and the independent committees before data collection has been completed.

The primary endpoint is 12 months. Our primary outcome is social functioning measured over 12 months using the total score on the Work and Social Adjustment Scale. The primary analysis will fit a Linear-mixed model to compare WSAS scores across the 12-month period (allowing for change across the three time points – baseline, 6 month and 12 month) adjusting for allocation group and study centre. There will also be consideration of accounting for clustering in the intervention group in the analysis model. Any additional covariates or factors to be included in the model will be assessed for their appropriateness and defined a priori in the SAP. Data will be analysed on an intention to treat (ITT) basis. Analysis of secondary outcomes will follow the same analysis model as the primary analysis where possible. Patterns of missing data will be assessed and predictors of missingness will be investigated and considered for inclusion in the models. Multiple imputation will be employed to address missing outcomes where appropriate. Test modelling and missing data assumptions via sensitivity analyses will be undertaken. All treatment effect estimates will be presented with 95% confidence intervals. Sensitivity analysis will also be undertaken for pre-planned variables: (i) whether participants meet diagnostic criteria for borderline personality disorder from the SCID II, (ii) whether participants meet diagnostic criteria for complex Post-Traumatic Stress Disorder from the ITQ and (iii) differences in the modality and components of the intervention that participants receive. Participants will have variables indicating which elements of the intervention they received. These variables will be added into the models as factors to assess if there is a potential impact on the results.

In a planned secondary analysis, we will compare the primary outcome among those participants who were randomised to and received SPS and no other psychological treatment for personality disorder with those who received no psychological treatment for personality disorder during the 12-month follow-up period.

7.3.1. Analysis of economic data

Prior to the completion of data collection, a fully documented Health Economics Analysis Plan will be written and agreed by the co-applicants and approved by DMEC. The economic evaluation will take an NHS/PSS perspective, and relevant non-NHS/PSS costs such as accommodation and use of voluntary sector services which are relevant in this patient group.

The economic evaluation will take a broad approach encompassing NHS, PSS and relevant non NHS/PSS costs such as accommodation and use of voluntary sector services which are relevant in this patient group.[45] Data on the use of health and social services will be collected using a modified version of the Adult Service Use Schedule. During the set-up phase of the trial, the questionnaire will be modified based on a literature review and input from other members of the research team. For each service use item, a relevant and suitable unit cost will be identified. Differences in service use over follow-up will be explored descriptively. While statistical differences in total costs by randomised group will be calculated using standard t-tests,[46] the focus of the analysis will be on the impact of costs and outcomes together. The primary cost-effectiveness analysis will consider costs alongside QALYs and will thus report on the incremental cost per QALY, in keeping with the

requirements of analyses for use in NICE guidance.[45] A secondary cost-effectiveness analysis will report the incremental cost per unit improvement in social functioning measured using the Work and Social Adjustment Scale. We will use data on number of hours worked per week and on out-of-pocket costs to study participants to widen the perspective to include non-health and social care costs as part of a secondary cost-effectiveness analysis. Statistical uncertainty around the estimates of cost-effectiveness will be explored using net benefit calculations and through the construction of cost-effectiveness acceptability curves.[47] Sensitivity analyses will be completed to test the assumptions used in the economic evaluation.

7.3.2. Analysis of qualitative data from the process evaluation

Interviews will be transcribed verbatim and uploaded to the NVivo computer package (Scolari/Sage) to manage data and support analysis. After familiarisation with the data (reading transcripts) an initial coding frame will be developed built upon both a priori research questions (notably relating to the anticipated relationship between resources, actions, outputs and outcomes described in the logic model) and themes developed in the data. This coding frame will be developed and refined as data collection and analysis progress. The framework will be applied to the data (indexing) with the aim of allocating all data to a theme (either already defined or emergent at this point). Whilst full copies of transcripts are retained to ensure context is maintained, NVivo supports the allocation to themes of disaggregated data. At the analytical stage constant comparison is used to discern patterns and divergences in the data and to support the identification of concepts and categories that enable a comprehensive and detailed response to the research questions.

Data and all appropriate documentation will be stored for a minimum of 10 years after the completion of the study, including the follow-up period.

8. REGULATORY ISSUES

8.1. ETHICS APPROVAL

This research has obtained approval from the London-Bromley Research Ethics Committee (REC) and Health Research Authority (HRA), and confirmation of capacity and capability from each participating NHS Trust before accepting participants into the study or any research activity is carried out. The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964, and later revisions.

8.2. CONSENT

Consent to enter the study must be sought from each participant only after a full explanation has been given, an information leaflet provided, and time allowed for consideration. Written consent will be obtained from all participants and the right of the participant to refuse to participate without giving reasons will be respected. After the participant has entered the study, the clinical team remains free to give alternative treatment to that specified in the protocol at any stage, other than a psychological treatment for personality disorder. Participants may be placed on a waiting list for such treatments during the follow up period. In cases where participants inadvertently receive a low intensity psychological treatment for personality disorder during the 12-month follow-up period, they will remain in the

trial. We will keep a record of all psychological treatments that study participants receive during the 12-month follow-up period and conduct a secondary 'per protocol analysis' of the cohort according to the psychological treatments that participants receive. All participants are free to withdraw at any time from the protocol treatment without giving reasons and without prejudicing further treatment.

8.3. CONFIDENTIALITY

The Chief Investigator will preserve the confidentiality of participants taking part in the study and is registered under the Data Protection Act.
CRF data entered onto the web-based online survey tool or collected during the process evaluation will be pseudonymised.
These data will be transferred to North Wales Clinical Trials Unit, Bangor University.

8.4. INDEMNITY

Imperial College London holds negligent harm and non-negligent harm insurance policies which apply to this study.

8.5. SPONSOR

Imperial College London will act as the main Sponsor for this study. Delegated responsibilities will be assigned to the NHS trusts taking part in this study.

8.6. FUNDING

The study has been funded by the National Institute for Health research Health Technology Assessment Programme. Reference NIHR133027.

All participants will be given a £10 honorarium following completion of the baseline interview, a £20 honorarium for completing the 6-month follow-up interview and a further £20 honorarium for completing the 12-month follow-up interview.

8.7. AUDITS

The study may be subject to audit by Imperial College London under their remit as sponsor and other regulatory bodies to ensure adherence to GCP and the UK Policy Frame Work for Health and Social Care Research.

9. STUDY MANAGEMENT

The day-to-day management of the study will be co-ordinated by the Trial Coordinating Office, Division of Psychiatry, Imperial College London 2nd Floor, Commonwealth Building, Du Cane Road, London, W12 0NN
Email: psych_trials@imperial.ac.uk
Bangor University will create and manage the trial database, clean and analyse the data collected in the database.
Middlesex University are responsible for all aspects of the process evaluation including data collection, analysis and reporting.

9.1. TRIAL OVERSIGHT COMMITTEES

A Trial Steering Committee and an Independent Data Monitoring and Ethics Committee will be in place prior to the start of the study. Each group will have an independent Chair and a majority of other independent members.

These committees will provide overall supervision of the trial and ensure that it is conducted in accordance with the study protocol and current legislation. It will also review trial data in order to identify patterns in the data that may suggest the need to halt the trial. The IDMEC will also monitor (1) recruitment of study participants, (2) ethical issues of consent, (3) quality of data (including missing data), (4) the incidence of adverse events, and (5) any other factors that might compromise the progress and satisfactory completion of the trial.

A Trial Management Group will also be set-up prior to the start of the study and will include those individuals responsible for the day-to-day management of the trial, such as the Chief Investigator, Principal Investigators and trial management staff. In addition, a research assistant and Expert by Experience, who is able to contribute a patient and wider public perspective will be included in the group. The role of the group will be to monitor all aspects of the conduct and progress of the trial, ensure that the protocol is adhered to and take appropriate action to safeguard participants and the quality of the trial itself. The group will consider and act on the recommendations of the TSC, IDMEC, and REC. The terms of reference for these committees are provided in a study SOP on trial oversight committees.

10. PUBLICATION POLICY

We will use a broad range of methods to communicate the results of this research to all stakeholders including both those who provide and use mental health services for people with personality disorder. This will include written reports, presentations at conferences, social media, service user groups and professional bodies. We will publish our findings on the website of the National Institute for Health Research and in widely read high-quality peer-reviewed open access journals. We will present the results of the study at the leading conferences for mental health and personality disorder including the Annual Conference of the British and Irish Group for the Study of Personality Disorder and the Annual Congress of the Royal College of Psychiatrists.

11. DISCLAIMER

This study is funded by the NIHR Health Technology Assessment Programme name of NIHR programme (Reference NIHR133027). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

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