PROSPER

Pilot trial of an evidence-based low intensity psychosocial intervention delivered by lay therapists for asylum seekers and refugees (PROSPER)

PROSPER Protocol V5.0 Dated: 11/12/2019

Trial Sponsor:
University of Liverpool
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ISRCTN: 15214107

Research Ethics Ref: 19/NW/0345

Sponsor Ref: UoL001469

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UNIVERSITY OF LIVERPOOL

LIVERPOOL CLINICAL TRIALS CENTRE LCTC

NHS National Institute for Health Research

The PROSPER trial is funded by the NIHR Public Health Research Programme. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

PROTOCOL APPROVAL

I, the undersigned, hereby approve this clinical study protocol:

Authorised by Chief Investigator:

Signature: _____ **Date:** 11/12/19

Professor Christopher Dowrick
Professor of Primary Medical Care, Department of Health Services Research, University of Liverpool

Authorised on behalf of Sponsor:

Signature: _____ **Date:** _____

Mr Alex Astor
Head of Research Support, Research Support Office, University of Liverpool

Authorised on behalf of the Lead Statistician:

Signature: _____ **Date:** 18/12/19

Dr Girvan Burnside
Senior Lecturer in Biostatistics, Liverpool Clinical Trials Centre, University of Liverpool

PROTOCOL APPROVAL

I, the undersigned, hereby approve this clinical study protocol:

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Signature: _____ **Date:** _____

Professor Christopher Dowrick
Professor of Primary Medical Care, Department of Health Services Research, University of Liverpool

Authorised on behalf of Sponsor:

Signature: _____ **Date:** 16 Dec 19

Mr Alex Astor
Head of Research Support, Research Support Office, University of Liverpool

Authorised on behalf of the Lead Statistician:

Signature: _____ **Date:** _____

Dr Girvan Burnside
Senior Lecturer in Biostatistics, Liverpool Clinical Trials Centre, University of Liverpool

GENERAL INFORMATION

This document describes the PROSPER Pilot including detailed information about procedures and recruitment. The protocol will not be used as an aide-memoir or guide for the treatment of other participants; every care was taken in its drafting, but corrections or amendments may be necessary. These will be circulated to the registered investigators in the trial, but sites entering participants for the first time are advised to contact the coordinating centre (Liverpool Clinical Trials Centre (LCTC)) to confirm they have the most up to date version. Clinical problems relating to this trial will be referred to the relevant Chief Investigator, Professor Christopher Dowrick, via the LCTC.

This protocol defines the participant characteristics required for trial entry and the schedule of treatment and follow-up. Participant recruitment will be undertaken in compliance with this document and applicable regulatory and governance requirements and waivers to authorise non-compliance are not permitted.

Incidence of protocol non-compliance, whether reported prospectively (e.g. where an intervention treatment cannot be delivered on a scheduled date as a result of public holidays) or retrospectively noted (e.g. as a result of central monitoring) are recorded as protocol deviations, the incidence of which are monitored and reported to trial oversight committees.

The template content structure is consistent with the SPIRIT (Standard Protocol Item: Recommendations for Interventional Trials 2013) and has regard for the Health Research Authority guidance. Regulatory and ethical compliance information is located in section 8.

Relationship Statements

Roles and responsibilities are fully described on page 15.

The University of Liverpool is the sponsoring organisation and will formally delegate specific sponsoring roles to the Chief Investigator and LCTC, but remains legally responsible for the trial.

The LCTC at the University of Liverpool in collaboration with the Chief Investigator, Professor Christopher Dowrick, will have overall management responsibility and will be responsible for the co-ordination of sites.

The LCTC as part of the Liverpool Clinical Trials Collaborative has achieved full registration by the UK Clinical Research Collaboration (www.ukcrc.org) as their standards and systems were assessed by an international review panel as reaching the highest quality. The LCTC has a diverse trial portfolio underpinned by methodological rigour, a GCP compliant data management system, and core standard operating procedures.

CONTACT DETAILS

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Centre for Health Economics and Medicines Evaluation Bangor University Bangor Gwynedd LL57 2PZ Tel: +44 (0) 1248 383201 E-mail: e.winrow@bangor.ac.uk	Department of Health Services Research University of Liverpool 1st Floor Block B Waterhouse Building 1-5 Brownlow Street Liverpool L69 3GL Tel: +44 (0) 151 794 5599 Email: cfd@liverpool.ac.uk
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Individual Authorised to Sign the Protocol and Protocol Amendments on behalf of the Sponsor:	**Chief Investigator (CI):**
Mr Alex Astor Research Support Office University of Liverpool 2nd Floor Block D Waterhouse Building 3 Brownlow Street Liverpool L69 3GL Tel: +44 (0) 151 794 8739 Email: sponsor@liverpool.ac.uk	Professor Christopher Dowrick Professor of Primary Medical Care Department of Health Services Research University of Liverpool B121 Waterhouse Buildings 1-5 Brownlow Street Liverpool L69 3GL Tel: +44 (0) 151 794 5599 Email: cfd@liverpool.ac.uk
Clinical Expert who will advise on Protocol Related Clinical Queries and Evaluate SAE Reports (in case CI is unavailable):	**Back Up Clinical Expert who will advise on Protocol Related Clinical Queries and Evaluate SAE Reports:**
Dr Ross White Doctorate in Clinical Psychology Department of Psychological Sciences University of Liverpool G10 Whelan Building Quadrangle Brownlow Hill Liverpool L69 3GB Tel: +44 (0) 151 794 5532 Email: ross.white@liverpool.ac.uk	Professor Atif Rahman Professor of Child Psychiatry Department of Psychological Sciences University of Liverpool Block B Waterhouse Buildings 1-5 Brownlow Street Liverpool L69 3GL Tel: +44 (0) 151 794 6938 Email: atif.rahman@liverpool.ac.uk
Department of Health Services Research Expert to advise on non-clinical Protocol Related Queries:	**WHO PM+ certified Master Trainer to advise on intervention queries:**
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PSS Clinical Lead	**PSS Supervisor**
Lynn Learman Person Shaped Support (PSS) Eleanor Rathbone House Connect Business Village 24 Derby Road Liverpool L5 9PR Tel: +44 (0) 151 702 5555 E-mail: Lynn.Learman@pss.org.uk	Rachel McCluskey Person Shaped Support (PSS) Eleanor Rathbone House Connect Business Village 24 Derby Road Liverpool L5 9PR Tel: +44 (0) 151 702 5555 E-mail: Rachel.McCluskey@pss.org.uk

Additional Contacts:

The contact details of other individuals involved in the trial are detailed in documents supplementary to the protocol and stored in the Trial Master File.

TABLE OF CONTENTS

GLOSSARY

AE	Adverse Event
AS&R	Asylum Seeker and Refugee
CI	Chief Investigator
CRF	Case Report Form
CSRI	Client Service Receipt Inventory
DSM-5	Diagnostic and Statistical Manual of Mental Disorders (5th edition)
GP	General Practitioner
HADS	Hospital Anxiety and Depression Scale
HIC	High Income Countries
HRA	Health Research Authority
IAPT	Increasing Access to Psychological Therapies
IDSMC	Independent Data and Safety Monitoring Committee
LCTC	Liverpool Clinical Trials Centre
LMIC	Low and Middle Income Countries
NGO	Non-Governmental Organisation
NHS	National Health Service
NRES	National Research Ethics Service
NIHR CRN	National Institute for Health Research Clinical Research Network
PHQ-9	9-item Patient Health Questionnaire
PI	Principal Investigator
PIA	Participant Information Agency
PM+	Problem Management Plus
PMG	Project Management Group
PSS	Person Shaped Support
PSYCHLOPS	Psychological Profiles Instrument
PTSD	Post-Traumatic Stress Disorder
R&D	Research & Development
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
RSI	Reference Safety Information
RSO	Research Support Office
SAE	Serious Adverse Event
SDV	Source Data Verification
SOP	Standard Operating Procedure
TSC	Trial Steering Committee
WHO	World Health Organisation
WHO-5	World Health Organisation Five Wellbeing Index
WHODAS	World Health Organisation Disability Assessment Schedule

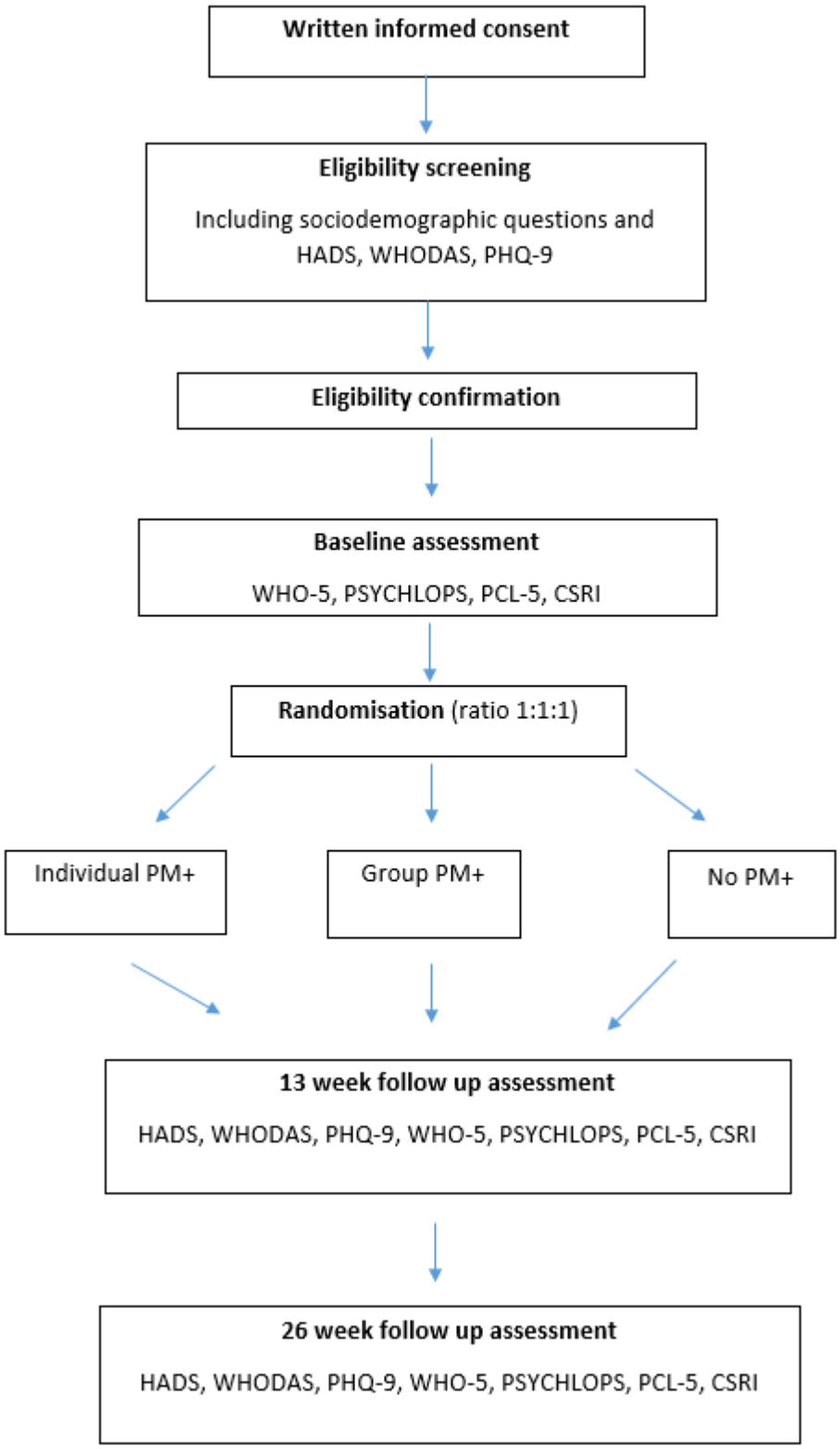
PROTOCOL SUMMARY

Full Title:	Pilot trial of an evidence-based low intensity psychosocial intervention delivered by lay therapists for asylum seekers and refugees
Acronym:	PROSPER
Phase:	Pilot randomised controlled trial
Target Condition:	Adult asylum seekers (including those refused leave to remain) and refugees who are in contact with participating NGOs, primary care teams including out of hours services, and other community-based welfare agencies.
Sample size:	105
Inclusion Criteria:	a. Asylum seekers and refugees b. Age ≥18 years (self-reported); c. Score of ≥8 on either the depression or anxiety subscale of HADS and score of ≥17 on WHODAS; d. Have conversational English; e. Registered with a GP in Liverpool City Region. f. Willing to provide relevant socioeconomic data (age, medical information etc.) g. Provided written informed consent
Exclusion Criteria:	a. New arrivals to the UK (<28 days) b. In Initial Accommodation and receiving Section 98 support for <28 days, due to high likelihood of dispersal outside the region c. Imminent risk of suicide; d. Complex mental disorder (bipolar disorder/manic depression, or schizophrenia); e. Cognitive impairment (moderate/severe intellectual disability, any dementia); f. Substance misuse; g. Currently receiving a formal psychological therapy.
Trial Centres and Distribution:	Liverpool City Region. Site: University of Liverpool research team (Department of Health Services Research) Site and Counselling NGO: PSS (Person Shaped Support) Participant Information Agencies will include NGOs whose primary function is to provide advice and support for asylum seekers and refugees. See Section 2.1 for more information
Participant Study Duration:	26 weeks per participant
Overall Trial Duration:	12 months (including 6 months recruitment)

Intervention:	**Intervention:** Problem Management Plus (PM+) **Control:** Usual care and peer support within each of the participating NGOs	
	Objectives	**Outcome Measures**
Primary	Assess severity of combined anxiety and depressive symptoms at 13 weeks post-baseline.	HADs
Secondary	1. Severity of combined anxiety and depressive symptoms at 26 weeks post-baseline 2. Subjective wellbeing 3. Functional impairment 4. Progress on problems for which participant has sought help. 5. Post-traumatic stress disorder 6. Depressive disorder 7. Service and support use	1. HADS 2. WHO-5 3. WHODAS 2.0 4. PSYCHLOPS 5. PCL-5 6. PHQ-9 7. CSRI

Protocol Summary - continued

Schematic of Study Design



ROLES AND RESPONSIBILITIES

Sponsor

The Sponsor is the University of Liverpool and is legally responsible for the trial. They will formally delegate specific roles to the Chief Investigator, Department of Health Services Research and Clinical Trials Unit.

Funder

The PROSPER feasibility study (hereinafter referred to as the 'Feasibility Study') incorporating the PROSPER pilot trial (hereinafter referred to as the 'PROSPER Pilot') is funded by the NIHR Public Health Research Programme. This funding source had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

Protocol Contributors

Individuals who contribute substantively to protocol development and drafting should have their contributions reported using the table below:

Name	Affiliations	Contribution to protocol
Christopher Dowrick	Department of Health Services Research, University of Liverpool	Protocol development, clinical and scientific arrangements, trial design and conduct
Carolyn Hopkins	LCTC, University of Liverpool	Protocol development, governance arrangements and trial conduct
Becky Rawlinson	LCTC, University of Liverpool	Protocol development, governance arrangements and trial conduct
Girvan Burnside	LCTC, University of Liverpool	Statistical arrangements, trial design and conduct
Clare Jackson	LCTC, University of Liverpool	Data management, trial design and conduct
Ross White	Department of Psychological Sciences University of Liverpool	Clinical and scientific arrangements, trial design and conduct
Anna Chiumento	Department of Psychological Sciences University of Liverpool	Intervention development, trial design and conduct
Katie Neville	LCTC, University of Liverpool	Quality Assurance review

Chief Investigator: Professor Christopher Dowrick is the Chief Investigator for the trial and is responsible for overall design and conduct of the trial in collaboration with other members of the study team.

Clinical Trials Unit: The LCTC at the University of Liverpool in collaboration with the Chief Investigator will have overall management responsibility and will be responsible for trial

management activities including (but not limited to) study planning, budget administration, Trial Master File management, safety reporting, data management, randomisation, statistical analysis and participating site coordination.

Department of Health Services Research: The Department of Health Services Research at the University of Liverpool is responsible for data collection and participant management.

Oversight Committees

PROSPER Pilot is subject to oversight from the following committees:

Project Management Group (PMG)
A Project Management Group (PMG) has been formed comprising the Chief Investigator, other lead investigators (clinical and non-clinical), staff from the LCTC and staff from the participating NGOs. The PMG is responsible for the day-to-day running and management of PROSPER Pilot and meets at least monthly.

Trial Steering Committee (TSC)
The Trial Steering Committee consists of an independent chairperson plus independent experts in the fields of refugee mental health, health economics and biostatistics.

The role of the TSC is to provide overall supervision for PROSPER Pilot and provide advice through its independent chairperson. The ultimate decision for the continuation of PROSPER Pilot lies with the TSC. The TSC first convened in February 2019 and will meet regularly during the trial (at least annually).

Independent Data and Safety Monitoring Committee (IDSMC)
The Independent Data and Safety Monitoring Committee consists of an independent chairperson and independent members who are experts in the fields of refugee mental health, participatory research and medical statistics.

The IDSMC will be responsible for reviewing and assessing recruitment, interim monitoring of safety and effectiveness, trial conduct and external data. The IDSMC first convened in February 2019 and will meet regularly during PROSPER Pilot (at least annually). No formal interim analysis is planned. The IDSMC will provide a recommendation to the TSC concerning the continuation of PROSPER Pilot.

Further information regarding conduct and membership of oversight committees is maintained in the Trial Master File in the following documents:

- Oversight Committee Membership Document
- Project Management Group Terms of Reference
- Trial Steering Committee Terms of Reference
- Independent Data and Safety Monitoring Committee Charter

1 INTRODUCTION

1.1 Background

PROSPER Pilot is being conducted as part of an overarching research project (the Feasibility Study) and is designed to assess the feasibility of an evidence-based low intensity psychosocial intervention (PM+) delivered by lay therapists for asylum seekers and refugees (AS&Rs). The Department of Health Services Research, based at the University of Liverpool, is carrying out the Feasibility Study under the supervision of Professor Christopher Dowrick (details of the Feasibility Study are described in a separate protocol: IRAS: 247920, REC: 18/NW/0441).

AS&Rs have higher prevalence of psychological morbidity, including depression, anxiety and post-traumatic stress disorder (PTSD), and functional impairment compared to other migrant groups and local majority populations (Lindert 2009, Close 2016, Priebe 2016). Mental health problems are particularly prevalent amongst war refugees (Bogic 2015), with rates of PTSD up to 10 times higher than in the general population (Fazal 2005, Slewa-Younan 2014). Persistence of mental health problems after resettlement is related to poor socio-economic conditions, acculturation-related stressors, economic uncertainty and ethnic discrimination (Priebe 2016, George 2015). As a result, AS&Rs encounter extensive barriers to accessing health care (Priebe 2016) and have substantial unmet mental health needs (Bradby 2015).

Making psychological therapies more accessible for AS&Rs is a national research priority (Samele et al 2007). Psychosocial interventions for AS&Rs resettled in high-income countries (HICs) may provide significant benefits, however there are few studies of good quality (Nosè 2017). Evidence for the applicability of psychological interventions by non-specialists in low and middle-income countries (LMICs) has increased significantly (Wiley-Exley 2007, Rahman 2008, Bolton 2014). Many countries, including the UK, are seeking to improve health care delivery by extending the roles of health professionals (Delamaire, 2015), increasing workforce capacity and enhancing quality of care (Sibbald, 2009, Kings Fund 2013). Innovations developed in low- and middle-income countries (LMICs), including task-sharing (Padmanathan 2013), have the potential to address current challenges for mental health care in high-income countries (HICs) (Sashidharan 2016).

Problem Management Plus (PM+) is a trans-diagnostic psychosocial intervention, designed to be delivered by lay therapists. Developed by World Health Organisation (WHO) as part of its Mental Health Gap Action Programme (mhGAP), using the GRADE[1] evidence-base (Dua, 2011), PM+ has shown significant benefit in trials in LMICs (Dawson 2015, Rahman 2016). However, to date there is no evidence of effectiveness or cost-effectiveness of interventions such as PM+ offered by lay therapists to AS&Rs in HICs.

PROSPER Pilot builds on the feasibility work and patient and public involvement (PPI) undertaken to date during the Feasibility Study which has consisted of the following activities:

Systematic review:
Barriers and facilitators to uptake of psychosocial interventions delivered by lay therapists to improve mental health and wellbeing of asylum seekers and migrants are being examined. An

[1] GRADE (Grading of Recommendations, Assessment, Development and Evaluations) is a transparent framework for developing and presenting summaries of evidence and provides a systematic approach for making clinical practice recommendations

initial bibliographic database search has yielded over 14,000 citations. Screening of titles and abstracts is currently in progress, and approximately 30 relevant papers are expected to be identified. Preliminary assessment of this literature suggests that barriers to uptake include: lack of understanding of UK health systems; lack of understanding of role of researcher and rules for research participation (including confidentiality); and differences in explanatory models for distress. Facilitators of uptake include: cultural adaptation of intervention, including strengths-based approaches; matching of therapist and participant characteristics, e.g. using 'peer-navigators; and access to safe spaces for therapy.

Focus groups:
Six focus groups with 24 participants have been conducted. Participants include asylum seekers and refugees, voluntary and community development workers, accommodation agents, GPs, community nurses, psychological therapists and health commissioners. Participants noted high levels of mental health problems, distress and trauma, often related to the asylum process. They reported barriers in accessing health care include limited provision, lack of trust in authorities, and problems with availability and utility of interpreters. They considered the psychoeducation of PM+ to be potentially helpful, in that managing problems assists in building mental strength and establishing realistic expectations. They noted the need to ensure that involvement with PM+ does not add to existing financial and practical difficulties, and for caution in providing support beyond the parameters of PM+.

PM+ training:
Two wellbeing mentors, employed by Person Shaped Support (PSS), were appointed in September 2018 as part of the Feasibility Study. The following month the wellbeing mentors and their supervisor received five days of intensive training, delivered by two PM+ Master Trainers (from Liverpool and Amsterdam). This focused on the delivery of the PM+ intervention strategies, and on training and supervision skills. Subsequently the wellbeing mentors have taken on practice cases to embed their skills, and receive regular monthly supervision which will continue throughout the Feasibility Study and PROSPER Pilot.

Lay therapists:
Fifteen lay therapists have been recruited via social media and two open meetings at PSS: nine are women and six are men; their languages include English (all), Arabic (3), Farsi (5), Urdu (4) and French (1). Training began in March 2019 and includes education in mental disorders, basic counselling skills, delivery of intervention strategies and self-care. Lay therapists will receive a total of eight days of training, and will be trained to deliver either individual or group PM+. This will be followed by training cases and a competency assessment which will be successfully completed prior to delivery of PM+ to participants in PROSPER Pilot.

PPI open meetings:
Meetings were held on 20 June 2018 and 20 February 2019, to describe and discuss progress with the Feasibility Study and PROSPER Pilot. More than 40 stakeholders participated, including from statutory and voluntary agencies, and people with experience of asylum seeking.

Contextual modifications:
Aspects of the delivery model have been considered to promote uptake and relevance of PROSPER Pilot. Modifications include:

- Focus on English, Arabic, Farsi and Urdu, identified as four most common languages currently spoken by AS&Rs in Liverpool City Region.
- Decision to exclude new arrivals and those in temporary accommodation: on grounds of a) high probability of dispersal and hence unavailability for intervention and/or follow-up; and b) low probability of being registered with a GP and hence unable to access trial safeguarding procedures.

- Alteration to text of PM+ manuals to reflect life in western urban settings, rather than south Asian rural settings: e.g. 'home' not 'hut', 'reading' not 'rearing poultry', 'visit job centre' not 'speak with village elder'.
- Lay therapists to be trained in either individual or group PM+.
- Matching therapists and participants on basis of gender and language, but not on basis of religion, politics or culture.
- Identification of 'safe spaces' for research interviews and delivery of PM+ sessions, including availability of child care.
- Reimbursement of travel expenses for lay therapists and participants.
- Supervision and support of lay therapists to include boundary issues between therapy and involvement in participants' lives.

1.2 Rationale

The Red Cross (2017) estimates that 65 million people throughout the world have been forced to flee their homes as the number of protracted conflicts has increased. This has created more than 22 million refugees worldwide, of whom an estimated 118,995 live in the UK (2017 figures). The UK received 38,500 asylum applications in 2016. Home Office (2018) figures show that, for 2014-2016, 35% of asylum applications were granted initially, rising to 52% after appeal. Many applications are initially refused because it is difficult to provide the evidence needed to meet the strict criteria of a refugee.

AS&Rs experience levels of emotional distress and functional impairment much higher than other migrant groups and local majority populations (Fazel 2005, Lindert 2009, Nose 2017). These are related to their reasons for leaving their country of origin, their experiences in transit and their receptions on arrival, including their experiences regarding asylum applications (Priebe 2016). There are particular reasons for concern over the mental health of asylum seekers without leave to remain, who are at risk of destitution since they are neither eligible for state benefits nor allowed to undertake paid employment. Despite this, AS&Rs commonly have inadequate access to mental health care appropriate to their needs (Priebe 2016). Their contact with statutory agencies is often crisis-driven and mediated through voluntary third sector organisations, whose staff can lack knowledge and skills in the management of psychosocial distress. The situation is especially problematic for asylum seekers without leave to remain who, from August 2017, are now required to pay for specialist health care (NRPF, 2017).

Although it is possible for some AS&Rs to access psychological therapies either through the NHS, in the form of Increasing Access to Psychological Therapies (IAPT) services, or through the voluntary sector, these are limited in scope and availability and in practice most AS&Rs do not access psychosocial interventions appropriate to their needs. There is therefore a need to offer and evaluate an accessible intervention (to which there are no direct comparators), designed to address the mental health and associated practical problems experienced by asylum seekers and refugees in the UK.

The rationale for undertaking a pilot trial of PM+ for AS&Rs, rather than proceeding to a full multi-centre trial, is that there are several areas of uncertainty regarding trial viability. These include the feasibility of recruiting and retaining AS&Rs as study participants, the fidelity of intervention delivery, and the acceptability and utility of proposed study measures. There may also be inequalities in mental health and wellbeing between AS&R groups, depending on their age, gender, nationality, education, occupational status, length of stay, access to resources and their current legal status in the UK which could inform the design of a full trial. As North West England has the largest number of asylum seekers in dispersal accommodation in England (9524 in first quarter of 2017) it is a suitable setting for the Feasibility Study.

1.3 Risk and Benefits

1.3.1 Asylum seekers and refugees

Risks:
For those PROSPER Pilot participants not granted leave to remain, participation in research may raise anxieties about public visibility and heightened risk of deportation. This risk can be mitigated by participants registering their contact details as their NGO or their primary care team. A potential risk for all participants is being offered support from a lay therapist who has a similar linguistic and cultural background but antithetical political or religious views; this will be mitigated by training on ethical practice by lay therapists. The risk of stigma associated with mental illness in some cultures is mitigated by the focus in PM+ on problems of living rather than on illness.

There is a risk to lay therapists of being overwhelmed by participants' distress; this will be mitigated by training and supervision, including focus on boundary issues of who they can and cannot feasibly support; the provision of ongoing support mechanisms; and signposting to appropriate care pathways for participants in need of additional care. Lay therapists' personal safety will be enabled by ensuring that PM+ sessions with participants are conducted on the premises of supervised voluntary or statutory organisations, not in participants' homes.

Benefits:
PROSPER Pilot offers support to distressed and functionally impaired AS&Rs, who may otherwise have no means of receiving evidence-based psychosocial support. If this study enables a full trial to be implemented, we anticipate benefits to PROSPER Pilot participants in terms of improving the mental health and functioning of AS&Rs, and in reducing inequalities in their mental health and wellbeing. If the effectiveness of PM+ in this population is demonstrated, AS&Rs can expect reduced symptoms of anxiety, depression and post-traumatic stress disorder, and improved functioning and subjective wellbeing. This in turn may enhance their equity of access to existing statutory health and social care services.

PROSPER Pilot will offer the lay therapists training and experience in a set of transferable skills.

1.3.2 Society and NHS

Risks: Given the current level of political controversy over the status of AS&Rs, there is a risk that this study may generate adverse publicity and lead to policy decisions designed to make life in the UK more difficult, especially for asylum seekers refused leave to remain. There is a risk that a psychosocial intervention designed to empower participants may encourage them to make greater use of health and social care services, generating extra demand on already hard-pressed services. However, this risk is likely to be mitigated by a reduction in use of unplanned and emergency care. The time-limited nature of the intervention will be carefully explained to minimise the risk of AS&Rs assuming continued access to the intervention beyond the scope of the trial.

Given that the participating NGOs are subject to the vagaries of external funding during a period of sustained austerity, and that one or more could reduce or cease their function during the lifetime of the study, there is a risk that their involvement in the management and delivery of PROSPER may compromise our ability to deliver on our objectives. This risk will be mitigated by paying careful attention to NGO funding sources and, if necessary, by advocacy to commissioners and funding agencies.

Benefits: The PROSPER study will generate new knowledge of benefit to the NHS and to society. PM+ is recommended by WHO as an intervention that can be delivered by lay therapists, and as an effective intervention for vulnerable populations living in conditions of adversity. It is innovative in that it takes task-sharing strategies that have been used in LMICs and applies them to a HIC, bringing global mental health to HIC (Sashidharan, 2016). This study will ascertain whether lay therapists in NGOs can be trained to deliver PM+ with demonstrable evidence of capacity. It will provide early indications whether PM+ can lead to evident improvements in mental health and function for distressed AS&Rs in current UK settings. It will take forward the Increasing Access to Psychological Therapies (IAPT) initiative, by identifying potential new pathways for access to care for these vulnerable groups.

There is currently a lack of evidence on feasibility of conducting research into psychosocial interventions in these circumstances, and this study will address this gap in the evidence-base. We anticipate that the study will provide clear evidence on the key parameters needed for a definitive randomised controlled trial in this field. Such a definitive trial has the potential to improve mental health, wellbeing and functional ability amongst AS&Rs, and to reduce health inequalities. This is likely to lead to more equitable and effective use of health care, with a shift from receiving emergency care to managed, proactive and preventive care.

From a societal perspective, cost effectiveness and cost-benefit analyses following the definitive trial will indicate the extent to which the intervention confers both direct and indirect benefits. PPI involvement will ensure that the project delivers high quality, original evidence that has the potential to have a significant impact on the design of the definitive intervention and, subsequently, on policy and practice.

1.4 Objectives

PROSPER Pilot is part of the Feasibility Study, the overall aim of which is to determine whether it is possible to conduct a randomised controlled trial in the UK of an evidence-based psychosocial intervention based on PM+, delivered by lay therapists for distressed and functionally impaired asylum seekers and refugees.

The objectives of the Feasibility Study are to:

1. adapt the form and content of PM+ to the needs of AS&Rs in the UK;
2. assess the feasibility of the proposed PM+ training procedures, including involvement of refugees as lay therapists;
3. assess the feasibility of the proposed procedures for recruiting distressed AS&Rs as study participants;
4. assess the feasibility of retaining both lay therapists and study participants through to trial completion;
5. assess the fidelity of delivery of the intervention;
6. assess the acceptability and utility of the proposed study measures, considering levels of literacy and any linguistic and cultural barriers.

Minor adaptations to the form and content of PM+ (objective 1) have been made prior to PROSPER Pilot and the adapted PM+ will be used as the intervention. Information and data generated during conduct of PROSPER Pilot will be used to address elements of the remaining objectives (2 – 6) as described in more detail below.

1.4.1 Primary Objective

The primary objective of PROSPER Pilot is to provide preliminary information on the potential effectiveness of group or individual PM+ versus standard care for AS&Rs, assessed using severity of combined anxiety and depressive symptoms at 13 weeks post-baseline measured using the Hospital Anxiety and Depression Scale (HADS).

1.4.2 Secondary Objectives

To provide preliminary information on the potential effectiveness and cost-effectiveness of group or individual PM+ versus standard care for AS&Rs with regards to:

- Severity of combined anxiety and depressive symptoms
- Subjective wellbeing
- Functional impairment
- Progress on problems for which an individual has sought help
- Post-traumatic stress disorder
- Depressive disorder
- Use of services and supports from NHS, social care and voluntary sectors

The following table details the proposed measures for quantifying the secondary objectives and will be assessed during a 26 week follow up period:

Item	**Proposed Measure for Assessment**
Severity of combined anxiety and depressive symptoms	Hospital Anxiety and Depression Scale (HADS)
Subjective wellbeing	WHO (Five) Well-being Index (WHO-5)
Functional impairment	WHO Disability Assessment Schedule 2.0 (WHODAS)
Progress on problems for which an individual has sought help	The Psychological Outcome Profiles instrument (PSYCHLOPS)
Post-traumatic stress disorder	Posttraumatic Stress Disorder Checklist for DSM-5 (PCL-5)
Depressive disorder	Patient Health Questionnaire (PHQ-9)
Use of services and supports	Adapted Client Service Receipt Inventory (CSRI)

2 TRIAL DESIGN

The PROSPER Pilot (forming part of the Feasibility Study) is designed as a three-arm pilot study of the design features of a proposed future definitive randomised controlled trial. Data generated as part of PROSPER Pilot will be used to inform decisions regarding design and conduct of a substantive multi-centre trial.

PROSPER Pilot aims to randomise 105 AS&Rs in a 1:1:1 ratio to individual PM+, group PM+ or usual care. Details of the intervention and usual care are provided in Section 4.

2.1 Trial Setting

PROSPER Pilot will be conducted in Liverpool City Region (Halton, Knowsley, Liverpool, St Helens, Sefton and Wirral). It will utilise collaborative working between the following organisations: University of Liverpool (Department of Health Services Research and LCTC), Liverpool John Moores University, Bangor University, PSS[2] (Person Shaped Support), Asylum Link[3], British Red Cross[4] and Refugee Women Connect[5].

Asylum Link, British Red Cross and Refugee Women Connect are local NGOs whose primary function is to provide advice and support for AS&Rs.

PSS will be responsible for delivering the intervention. It is a health and social care charity delivering a wide array of services to create homes, empower communities, promote wellbeing and strengthen families. PSS includes Spinning World, a specialist psychological therapies service for AS&Rs and others who have experienced human right abuses and traumatic events.

2.1.1 Selection of Participating Sites and Participant Information Agencies

For the purposes of PROSPER Pilot there will be two participating sites:

Department of Health Services Research (based at the University of Liverpool):
The research team based at the Department of Health Services Research will be responsible for Investigator Site File maintenance, participant recruitment, assessment and confirmation of eligibility, randomisation, data capture and participant follow up. Evidence of informed consent, participant screening and eligibility assessment and other relevant source documentation will be maintained securely. Site set up and training will be conducted as per usual LCTC processes.

PSS:
As PSS staff will be delivering the intervention and will have some responsibility for participant safety and data collection they will also be considered a site. Source data regarding intervention delivery will be maintained at site in a secure and confidential manner. Staff training will be managed as per local PSS processes. Trial-specific training will be conducted and will be evidenced in ISF.

[2] http://www.psspeople.com
[3] https://www.asylumlink.org.uk/
[4] https://www.redcross.org.uk/
[5] https://www.refugeewomenconnect.org.uk/

Due to the nature of PROSPER Pilot there are no specific geographical 'sites' at which the research is being conducted. Follow up appointments will be arranged at locations convenient to the participant and researcher, and the locations for intervention delivery will be determined opportunistically.

Local NGOs, primary care teams and other agencies who have contact with AS&Rs will be used as Participant Information Agencies (PIAs). They will identify potential participants opportunistically and refer them to the research team. The participant identification and referral process, including details of specific PIAs, is described in Section 5.1.

2.2 PROSPER Pilot Outcomes

There are specific outcome measures proposed for use in any full trial of this intervention which will be tested as part of PROSPER Pilot. These are detailed in the table below.

Objective	**Outcome Measures**	**Timepoint(s) of evaluation**
Efficacy:		
To provide preliminary information on the potential effectiveness of group or individual PM+ versus standard care with regards to:		
- **Severity of combined anxiety and depressive symptoms**	**Hospital Anxiety and Depression Scale (HADS)**	Baseline, **13 week*** and 26 week follow up assessments
- Subjective wellbeing	WHO-5 Wellbeing Index	
- Functional impairment	WHO Disability Assessment Schedule (WHODAS)	
- Progress with problems for which participant has sought help	Psychological Outcomes Profile (PSYCHLOPS)	
- Post-traumatic Stress Disorder (PTSD)	Post-traumatic Stress Disorder Checklist for DSM-5 (PCL-5)	
- Depressive Disorder	9-item Patient Health Questionnaire (PHQ-9)	
Health Economics:		
To provide preliminary information on the potential cost-effectiveness of group or individual PM+ versus standard care with regards to:		
- use of services and supports from NHS, social care and voluntary sectors	Adapted Client Service Receipt Inventory (CSRI)	Baseline, 13 week and 26 week follow up assessments

* HADS score at 13 weeks post-baseline is proposed as the potential primary outcome to be used in any future trial (see Section 2.3 and 7 for more detail of how this will be assessed).

2.3 Further Feasibility Outcomes

Other elements of PROSPER Pilot will be assessed and used to inform the feasibility of conducting a full trial:

Objective	Outcome Measure	Timepoint(s) of evaluation
To assess the feasibility of the proposed procedures for recruiting distressed AS&Rs as study participants	Number of AS&Rs recruited	Baseline
To assess feasibility of randomisation	Successful randomisation of participants	Baseline (randomisation)
To assess the feasibility of retaining study participants through to trial completion	Number of study participants in the trial (assessed in individual arms)	26 weeks
To assess the acceptability and utility of specified primary and secondary outcome measures	Completion of study measures and estimation of between group differences[a] Evaluation of outcomes[b]	Baseline, 13 weeks, 26 weeks

[a] Estimates of between group differences in outcomes measures will be used to assess if clinically important improvements of outcomes would be plausible in a full trial (see Section 7, Statistical Considerations, for more detail).

[b] The specified primary and secondary outcomes of PROSPER Pilot will be evaluated with regards to their potential acceptability and suitability for a subsequent definitive trial via qualitative process evaluation which will be carried out by the research team in Department of Health Services Research (see Section 5.5.4 for more information).

2.4 Feasibility Study Progression Criteria

The feasibility of progression to a definitive multi-centre randomised controlled trial will be informed by the extent to which the criteria below have been met using a go, amend, stop system:

Progression Criteria	Go	Amend	Stop
Recruitment of trial participants	≥70% of target	50-69% of target	<50% of target
Retention of trial participants	≥70% retained	50-69% retained	<50% retained
Protocol adherence	≥70% of intervention delivered per protocol	50-69% of intervention delivered per protocol	<50% of intervention delivered per protocol

Completion of outcome measures	≥70% of measures are complete	50-69% of measures are complete	<50% of outcome measures are complete

If criteria meet 'amend' targets, reasons for this will be investigated with an aim to identify aspects amenable to change.
If criteria meet 'stop' targets, reasons will be analysed and discussion within the PMG and independent oversight committees. If it is determined that these rates cannot be improved then a full trial would not be recommended.

Other progression criteria involving data from PROSPER Pilot that will be further assessed by the research team are:

- Recruitment of supervisors and lay therapists
- Retention of lay therapists
- Acceptability of outcome measures
- Whether clinically important improvement in outcomes are plausible.

3 ELIGIBILITY CRITERIA

3.1 Inclusion Criteria

a. Asylum seekers and refugees[6]
b. Aged ≥18 years (self-reported)
c. Score of ≥8 on either the depression or anxiety subscale of HADS and score of ≥17 on WHODAS
d. Have conversational[7] English
e. Registered with a GP in Liverpool City Region
f. Willing to provide relevant socioeconomic data (age, medical information etc.)
g. Provided written informed consent

3.2 Exclusion Criteria

a. New arrivals to the UK (<28 days)
b. In Initial Accommodation[8] and receiving Section 98 support[9] for <28 days, due to high likelihood of dispersal outside the region
c. Imminent risk of suicide
d. Complex mental disorder (bipolar disorder/manic depression, or schizophrenia)
e. Cognitive impairment (moderate/severe intellectual disability, any dementia)
f. Substance misuse
g. Currently receiving a formal psychological therapy

3.3 Notes Regarding Eligibility

If the researcher has any concerns or uncertainty about responses, eligibility must be discussed with the Chief Investigator (or nominated deputy).

Eligibility criteria are to be considered alongside the following notes;

Exclusion Criterion	Note
c. Imminent suicide risk	Assessed by researchers using formal protocols with supervision and arbitration from qualified healthcare professionals – see Safety Reporting section.
d. Complex mental disorder	Assessment by researcher will be on basis of: a) participant self-reporting a diagnosis and/or b) participant currently in receipt of antipsychotic medication, defined as medication listed in British

[6] Including all categories of asylum seekers (i.e. pre-asylum; leave to remain pending, refused, discretionary or indefinite; humanitarian protection; refugee status; stateless; vulnerable person resettlement programme)
[7] Ability to converse comfortably in said language, as self-assessed by potential participant
[8] Reception centres which are the usual first accommodation for asylum seekers. http://www.asylumineurope.org/reports/country/united-kingdom/reception-conditions/housing/types-accommodation
[9] http://www.legislation.gov.uk/ukpga/1999/33/section/98

	National Formulary Chapter 2 section 2.3 (bipolar disorder and mania) and section 2.6 (psychoses and schizophrenia) If required, further clinical assessment will occur using standard formal protocols.
f. Substance misuse	Assessment by researcher will be on basis of participant response to the question: 'are you currently having problems with alcohol, cocaine, marijuana or any other drugs?' If response is yes or equivocal, then participant will be excluded. If required, further clinical assessment will occur using standard formal protocols.

3.3.1 Co-enrolment Guidelines

To avoid potentially confounding issues, ideally participants will not be recruited into other trials during their participation in PROSPER.

Where a PROSPER participant is considering recruitment into another trial, this should be discussed with the Chief Investigator.

4 INTERVENTION

Participants will be randomised to receive individual PM+, group PM+ or the control (no PM+), in a ratio of 1:1:1.

4.1 Problem Management Plus (PM+)

Problem Management Plus (PM+), is a manualised brief multi-component intervention (Dawson, 2015), recommended by the World Health Organisation as part of its mhGAP guidelines (http://www.who.int/mental_health/mhgap/en/). It is specifically developed to be amenable to cultural and linguistic adaptation for the local context. Based on evidence-based problem solving and behavioural techniques, the intervention is trans-diagnostic by which we mean it applies the same intervention strategies across common mental health problems clients may be experiencing. Addressing multiple problems at one time through shared emotional mechanisms is efficient, reducing the practical challenge of making differential diagnoses and learning multiple treatment manuals for different mental health diagnoses (Wilamowska et al, 2010; Bullis et al, 2014)).

The PM+ intervention consists of five weekly face-to-face sessions, delivered either one-to-one or in groups. The first session opens with psychoeducation, including information on common reactions to adversity, the rationale for PM+, goal setting, and brief motivational interviewing. Sessions one to four each introduce an intervention strategy: (i) Managing Stress (slow breathing exercise); (ii) Managing Problems (using problem solving techniques); (iii) Get Going, Keep Doing (applying behavioural activation techniques); and (iv) Strengthening Social Support. These strategies are applied by participants during the intervention session to problems they are facing. Each strategy is reviewed in subsequent sessions, with application of strategies between sessions encouraged to enhance learning through repetition. The final session involves a revision of learning, education on preventing relapse, and ends with a culturally appropriate closing ceremony.

To enhance accessibility for groups the group PM+ intervention is structured around locally relevant and appropriate pictorial materials and adopts a narrative format to support engagement and individual disclosure of personal difficulties which can be more difficult in a group format. Specifically, a case example of a woman or a man (depending on the gender of group participants) experiencing common functioning and emotional problems is shared each week, with participants following their progress through PM+ Group.

4.2 Training and Supervision

Training in PM+ was delivered by 2 WHO-approved Master Trainers, who delivered a 5 day training course in October 2018 to two appointed Wellbeing Mentors. The Wellbeing Mentors have counselling qualifications and previous experience of delivering training programmes. The course included training in the PM+ intervention, how to train and supervise others, and monitoring the safety of intervention participants and self-care needs of lay therapists. Following completion of the training course, the Wellbeing Mentors gained experience of delivering the PM+ intervention in clinical practice.

The Wellbeing Mentors subsequently cascade training to the lay therapists. The individual and group PM+ intervention trainings is delivered over 8 days (1 day per week over 8 weeks) to groups of lay therapists. Each lay therapist will either be trained to deliver the individual PM+ intervention or the group PM+ intervention. This will be followed by training cases and a competency assessment which will be successfully completed prior to delivery of PM+ to participants in PROSPER Pilot. One of the Master Trainers will directly observe some of the lay therapist training sessions to ensure that they are being delivered accurately. She will provide fortnightly supervision to the Wellbeing Mentors throughout the period of lay therapist training and will keep a formal written record of all contact with the Wellbeing Mentors.

Consistent with an apprenticeship model (Murray et al, 2011), protocol adherence is ensured through regular (at least fortnightly) supervision of the lay therapists provided by two Wellbeing Mentors. Involving all individual or group lay therapists in a group, supervision will last up to three hours and will entail reviewing the progress of intervention delivery, including case-management of participants and additional refresher training on intervention components. The group PM+ lay therapists will receive the same as individual PM+ lay therapists, in addition to refresher training on group facilitation skills, through role-play.

The Wellbeing Mentors are in turn provided supervision by one of the Master Trainers, conducted at least monthly during the trial and lasting two hours. In addition, Wellbeing Mentors have the day-to-day support of their line manager at PSS who also participated in the 5-day PM+ training with Master Trainers, and who participates in the monthly supervision sessions with the Master Trainer to ensure supervision consistency.

Intervention fidelity will be monitored through independent observations of 15% of randomly selected sessions of each lay therapist against tailored checklists, conducted by the Wellbeing Mentors. Session logs (per participant) will be completed by lay therapists after each PM+ session and will capture information regarding timing, length and content of sessions. The logs will be passed to the Wellbeing Mentors at weekly supervision meetings. A small number of sessions may be audio- or video-recorded as an additional assessment of intervention fidelity.

Lay therapists will be employed on a voluntary basis by PSS and will be required to sign an agreement outlining what is expected of them in their role.

4.3 Adaptation of the PM+ intervention

Minor adaptations were made to the individual and group PM+ manuals to make them appropriate for delivery in the UK. Details of all adaptations are listed on the adaptation sheets within the TMF.

4.4 Venue for delivery of intervention

All PM+ sessions will take place at mutually convenient and safe locations, where support is available if required. Sessions will be delivered within organisations which have on-site staff with experience and training in managing emotional distress: PSS, Asylum Link, British Red Cross, Refugee Women Connect and similar organisations devoted to the care of asylum seekers and refugees.

No face-to-face sessions should take place in the home of either a participant or lay therapist.

4.5 Control (no PM+ intervention)

Participants randomised to the control arm will not be offered any PM+ but will be able to access all usual care and peer support offered by the participating NGOs. To control for time and attention, participants randomised to the control arm will be invited to attend a local AS&R NGO of their choice. They are put in contact with other AS&Rs from similar backgrounds and encouraged to meet together with these others on a weekly basis for five weeks.

4.6 Assessment of Compliance

Intervention compliance will be measured by assessing adherence to the PM+ protocol with regards to attendance at sessions.

4.7 Concomitant Medications/Treatments or Restrictions

If antipsychotic medication is recorded at the baseline review, the researcher will discuss clinical investigators who will make a decision regarding eligibility.

Participation in a formal psychological therapy would preclude participation.

Participating in PROSPER Pilot does not require any restrictions or lifestyle changes.

5 PARTICIPANT TIMELINE AND ASSESSMENTS

The participant pathway includes discrete activities that must be conducted in the correct order. Details are provided under the relevant headings below.

5.1 Participant Identification

Potential participants will be identified primarily through NGOs and their associated networks, and primary care teams, all designated as Participant Information Agencies (PIAs). Specific NGO PIAs include, but are not limited to, Asylum Link, British Red Cross and Refugee Women Connect (see section 2.1). Primary care participant identification will focus on working with GP practices who receive Local Enhanced Service payments. Other organisations acting as PIAs include, but are not limited to, Urgent Care 24[10], Mersey Care Social Inclusion Team[11], Liverpool Community Development Service[12] and Serco[13].

PIAs will be provided with a short summary of the study including the main inclusion and exclusion criteria. They will be asked to display posters and leaflets and discuss the study opportunistically with AS&Rs who access the services. All participant-facing documentation will have the necessary approvals from a Research Ethics Committee.

The research team will also use social media to promote the study to potential participants, including posting the trial flyer and providing updates on recruitment figures and introductions to team members.

Potential participants will be made known to the research team via one of the following methods:

- By contacting the research team directly via telephone or email;
- By agreeing to their details being given to the research team (via a participant recommendation form, completed by the PIA with the AS&R, and returned to the research team by the PIA);
- By attending a researcher-attended drop-in session at collaborating NGOs on a specific date/time, advertised by posters/leaflets/verbally

Following identification of a potential participant, the researcher will arrange a meeting to give more information about the trial and, if possible, obtain informed consent as described in the section below.

5.2 Informed Consent

Informed consent is a process initiated prior to an individual agreeing to participate in a trial and continues throughout the individual's participation. Written informed consent is required for all those participating in LCTC coordinated trials. In obtaining and documenting informed consent, the researcher will comply with applicable regulatory requirements and will adhere to the ethical principles that have their origin in the Declaration of Helsinki.

[10] http://urgentcare24.com/
[11] https://www.merseycare.nhs.uk/our-services/physical-health-services/social-inclusion-team/
[12] http://www.maryseacolehouse.com/liverpool-community-development-services
[13] https://www.serco.com/uk/sector-expertise/immigration/community-accommodation-and-support

The PROSPER Participant Information Sheet and Consent form (PISC), describing in detail the implications of participation with reference to the intervention, and potential benefits and risks, will be approved by an independent Research Ethics Committee (REC). The PISC will also include a contact point where further information about the trial may be obtained.

5.2.1 Prospective Consent Process

The researcher, based in Department of Health Services Research at University of Liverpool, will contact the potential participant to arrange a face-to-face meeting. This meeting will be arranged at the convenience of the AS&R where possible and can be attended by an interpreter if required. The meeting will take place at a convenient location which could include one of the NGO centres, a community centre, a counselling centre, NHS premises and University of Liverpool.

Objectives, risks and inconveniences of the trial and the conditions under which it is to be conducted will be provided by a research team member experienced in informed consent discussions who has been delegated this duty. All potential participants will be given the opportunity to ask any questions that may arise, will have the opportunity to discuss the study with others and be given time to consider the information prior to agreeing to participate. It will be made clear to the participant that an eligibility assessment will be conducted once consent is given and that if the participant is found to be ineligible for any reason that they will be unable to participate.

The potential participant will be asked to read and review the PISC. Upon reviewing the document, the researcher will explain the research study to the potential participant. The PISC and the discussion with the participant will emphasise that participation in the trial is voluntary and that the participant may withdraw from the trial at any time and for any reason. Consideration will also be given to the sensitive nature of the research topic to minimise any distress caused to potential participants as a result of the discussions.

If the asylum seeker or refugee decides that they would like to participate, he or she will then personally sign and date the informed consent document. The document should then be signed and dated by the person obtaining consent. A copy of the informed consent document will be given to the potential participant for their records. The original document will be maintained by the research team separate from any personal identifiable information collected for any participants. A further copy will be sent to the LCTC via secure methods if the participant is eligible for full trial participation (this will be sent separately from any participant data subsequently collected).

If the potential participant requires more time to consider involvement in the trial a further meeting can be arranged at the discretion of the researcher.

If the individual does not wish to take part, their reason for not providing consent will be recorded on the PROSPER Screening Log.

Once consent has been given the asylum seeker or refugee may, without being subject to any resulting detriment, withdraw from the trial at any time by revoking the informed consent. Details of the procedures to follow in case of participant withdrawal are described in section 5.6.

5.3 Eligibility and Baseline

5.3.1 Eligibility Assessment

Once written informed consent has been obtained, the potential participant can be assessed for eligibility, as per the criteria detailed in Section 3.

Eligibility assessment should follow a staged process. The researcher will review responses at the end of each stage, and if the potential participant is found to be ineligible there will be no requirement for completion of the next stage.

Firstly, through discussion with the potential participant, the researcher will complete sociodemographic questions.

The researcher will then assess the following exclusion criteria: complex mental disorder (bipolar disorder/manic depression, or schizophrenia); cognitive impairment (moderate/severe intellectual disability, any dementia); substance misuse; currently receiving a formal psychological therapy.

If the potential participant remains eligible, they will be asked to self-complete the HADS, WHODAS and PHQ-9 questionnaires within the Eligibility Questionnaire Booklet. The researcher will review the completed PHQ-9 questionnaire to assess whether the potential participant is at imminent risk of suicide. If there are any concerns regarding suicide risk, the researcher should follow the procedure outlined in the Suicidal Ideation Guidance Document (refer to Section 6, Safety Reporting).

If the potential participant is eligible following this process, the researcher will proceed to conduct the baseline assessments outlined in the following section. This will allow consistency for outcome measurement completion, and also reduce the need for attendance at additional meetings.

If the researcher has any concerns or uncertainties from the non-clinical eligibility assessment above, they should contact the CI or nominated deputy to discuss the case.

AS&Rs who are assessed as ineligible can be reconsidered for participation at a later date if circumstances change e.g. if they are able to register with a GP. If this is more than two weeks after consent has been obtained, the consent process will need to be repeated.

5.3.2 Baseline Assessments

Following the completion of the Eligibility Assessment outlined in the previous section, the researcher will ask the eligible participant to self-complete the Baseline Questionnaire Booklet, which incorporates the remaining baseline assessments: the WHO-5, PSYCHLOPS and PCL-5 questionnaires. The CSRI Form, which has been adapted for PROSPER, will be completed by the researcher through discussion with the participant.

5.3.3 Eligibility Confirmation

If the AS&R is not eligible to participate, the Eligibility and Baseline CRF and Eligibility Questionnaire Booklet will not be returned to LCTC. If these have been partially or fully completed then they will be stored, separately from the consent form, in the Department of Health Services Research. The reason for the AS&R's ineligibility will be recording on the PROSPER Screening Log.

For a potential participant who completes the eligibility assessment process and is deemed eligible to participate in PROSPER Pilot, and where there has been no concern or uncertainty that necessitated the researcher contacting the CI or nominated deputy, the researcher will complete the Eligibility and Baseline CRF. The researcher will be required to confirm that they have no safeguarding concerns based on the potential participant's responses. The researcher will then sign and date the Eligibility and Baseline CRF.

For a potential participant who completes the eligibility assessment process and is deemed eligible to participate in PROSPER Pilot, but where there was concern or uncertainty that necessitated the researcher contacting the CI or nominated deputy, the CI or nominated deputy will review the information provided by the participant against the eligibility criteria defined in Section 3 to allow completion of the Eligibility and Baseline CRF. The CI or nominated deputy will be required to confirm that they have no safeguarding concerns based on the potential participant's responses. The CI or nominated deputy will then sign and date the Eligibility and Baseline CRF.

The Eligibility and Baseline CRF must be completed, signed and dated before randomisation can occur.

5.4 Randomisation Procedures

Participants will be randomised to receive either arm A (individual PM+ intervention), arm B (group PM+ intervention), or arm C (the control) (in a ratio of 1:1:1) once:

a. Fully informed written consent has been obtained;
b. Eligibility criteria have been fulfilled and full eligibility confirmed;
c. Baseline assessments have been completed.

Participants will be randomised using a secure (24-hour) web-based randomisation program controlled centrally by the LCTC. A personal login username and password, provided by the LCTC, will be required to access the randomisation system. Designated research staff will be issued with their personal login and password upon completion of training in the use of the system.

When the system requirements are confirmed the participant treatment allocation and a unique study number (randomisation number) will be displayed on a secure webpage and an automated email confirmation will be sent to prosper.study@liverpool.ac.uk

Randomisation: web access https://ctrc.liv.ac.uk/Randomisation/PROSPER

*If there are any problems with the randomisation systems contact the LCTC on **0151 795 8782** or via email on **prosper.study@liverpool.ac.uk***

In the event of a randomisation system failure, the researcher should contact the coordinating team in LCTC (Monday to Friday between 9:00 to 17:00 excluding bank holidays and University Closed days) to try to resolve the problem. If the problem cannot be resolved the LCTC will perform central randomisation and randomise the participant using the back-up randomisation system. The back-up randomisation system is an exact replica of the live system but is based on a standalone PC at LCTC.

The researcher will update the PROSPER Screening Log when a participant has been randomised.

The researcher will be responsible for notifying the participant of their allocation. In the event that a participant is randomised to arm A or arm B, the researcher will inform the PSS Lead. Intervention delivery will be coordinated by PSS.

Further information about the intervention is provided in section 4.

The research team will notify the participant's GP by letter of their enrolment into the trial and to what treatment arm they have been allocated.

5.5 Schedule for Assessments and Follow-up

All assessments and follow up are to be conducted in line with the Schedule of Assessments below.

Schedule of Assessments

	Screening and Baseline	**Randomisation**	**13 week follow up**	**26 week follow up**
Timepoint (weeks)	0	0	13±2	26±2
Procedures:				
Consent, Eligibility screening and confirmation				
Written and Informed Consent	X			
Assessment of Eligibility	X			
Confirmation of Eligibility	X			
Randomisation		X		
Confirm Consent		X	X	X
Data Collection				
HADS	X		X	X
WHODAS	X		X	X
PHQ-9	X		X	X
PSYCHLOPS	X		X	X
PCL-5	X		X	X
WHO-5	X		X	X
CSRI	X		X	X
Adverse Events				
Assessment of AEs	X		X	X

In the case of premature discontinuation/withdrawal, there are no additional assessments for participants.

All specified outcomes will be measured at 13 and 26 weeks post-baseline (13 ± 2 weeks (11-15 weeks) and 26 ± 2 weeks (24-28 weeks)). 13 weeks will be the primary end point: this is consistent with previous trials (Rahman et al, 2016). It allows time for intervention delivery and often corresponds to the time for first decision on leave to remain for asylum seekers.

26 weeks post-baseline for the second follow-up is as a balance between long-term outcome and participant attrition; it also commonly corresponds to the second decision on leave to remain after appeal.

Follow Up Visit 1 – 13 week follow up

This should be a face-to-face appointment at 13 weeks ± 2 weeks from baseline. The following activities should occur:

- Verbal confirmation of continued consent;
- The participant will complete the following questionnaires within the Follow Up Questionnaire Booklet: HADS, WHODAS, PHQ-9, WHO-5, PSYCHLOPS, PCL-5;
- If suicidal ideation is disclosed or suspected, the researcher will follow the steps outlined in the Suicidal Ideation Guidance document;
- Recording of any adverse event information (see Section 6 for more information)
- Researcher-led completion of the adapted CSRI;
- Completion of Follow Up CRF

Follow Up Visit 2 – 26 week follow up

This should be a face-to-face appointment at 26 weeks ± 2 weeks from baseline and should follow the same process as the follow up appointment at 13 weeks.

All follow up appointments will be coordinated and conducted by a trained researcher. They will conduct a preliminary review of the data collected to screen for missing data or any responses that may need further follow up or clinical discussion.

Follow up appointments are expected to take around 1 hour which should allow for completion of all data collection and review of any adverse events.

N.B. If a face-to-face appointment cannot be arranged during the follow up window then the visit can be conducted by telephone if possible. As a last resort, all questionnaires could be posted to the participant and returned by post. Participant responses **must** be completed during the appropriate visit window, evidenced by completion of the “Date Completed” field at the front of the booklet.

5.5.1 Assessment of Efficacy

Efficacy will be assessed using a group-wise comparison of the primary outcome: severity of combined anxiety and depressive symptoms at 13 weeks post-baseline measured using the Hospital Anxiety and Depression Scale (HADS, Zigmond 1983). HADS is a well-established 14-item scale consisting of 2 subscales: HADS-A (anxiety; 7 items; possible score range, 0-21) and HADS-D (depression; 7 items; possible score range, 0-21). Higher scores indicate more anxiety and/or depression. HADS has been widely used across cultures; it is sensitive to change over time and has good reliability and validity (Herrmann 1997).

Efficacy Parameter	Assessment Tool	Further Information
Severity of combined anxiety and depressive symptoms	Hospital Anxiety and Depression Scale (HADS)	HADS is a well-established 14-item scale consisting of 2 subscales: HADS-A (anxiety; 7 items; possible score range, 0-21) and HADS-D (depression; 7 items; possible score range, 0-21). Higher scores indicate more anxiety and/or depression. HADS has been widely used across cultures; it is sensitive to change over time and has good reliability and validity (Herrmann 1997).
Subjective wellbeing	WHO-5 Wellbeing Index	Validated in international studies for both clinical and psychometric properties and available in many languages (Topp 2015).
Functional impairment	WHO Disability Assessment Schedule (WHODAS)	Applicable across all health states including mental disorders. WHODAS has shown good validity in terms of internal consistency, test-retest reliability, and agreement with other measures of disability across countries.
Progress with problems for which participant has sought help	Psychological Outcomes Profile (PSYCHLOPS)	Covers 3 domains: problems (2 questions), functioning (1 question), and well-being (1 question). PSYCHLOPS has internal consistency, convergent validity with measures of emotional distress, and is sensitive to change.
Post-traumatic Stress Disorder (PTSD)	Post-traumatic Stress Disorder Checklist for DSM-5 (PCL-5)	Has good psychometric properties for diagnostic accuracy and internal consistency.
Depressive Disorder	9-item Patient Health Questionnaire (PHQ-9)	Based on DSM-IV depression diagnostic criteria. Total severity score ranges from 0 to 27, with 10 as conventional cut-off to diagnose depressive disorder

5.5.2 Assessment of Cost Efficacy

Socio-demographic data, and use of services and supports will be captured by an adapted Client Service Receipt Inventory (CSRI, Beecham 1992). This data can be used for a wide range of applications, including estimating the costs of service receipt and societal costs.

5.5.3 Assessment of Safety

Safety assessments will be based on information disclosed by the participant throughout trial duration and by those who have knowledge of their welfare, including GPs, other health professional and NGO members. The Chief Investigator and other research staff are responsible for monitoring and reporting all adverse events (see Section 6 for more information).

Safety information will be independently monitored by an Independent Data and Safety Monitoring Committee.

5.5.4 Process Evaluation and Feasibility Assessment

Relevance and acceptability of proposed outcomes will be tested, with a view to their incorporation or refinement for a definitive trial. These will include:

- Effectiveness of PM+, based on the primary outcome of combined HADS scores;
- Cost-effectiveness of PM+ from an NHS perspective, based on the primary outcome of combined HADS scores (Drummond 2015; NICE 2012).
- Cost benefit from a societal perspective, given that costs and potential benefits will extend beyond the NHS to local government and voluntary sectors (McIntosh 2010; Pearce et al 2006; Sugden and Williams 1978).
- Impact on health inequalities using the NIHR CLAHRC NWC Health Inequalities Assessment Toolkit (www.hiat.org.uk): first, within AS&R communities in relation to age, gender, nationality, education, prior occupation and asylum status; and second, between AS&Rs and national populations, comparing mental health status (anxiety, depression PTSD and wellbeing) with UK population norms, with reference to published psychiatric morbidity data (McManus et al, 2016).

The feasibility of the 13- and 26-week time points will be assessed, with specific reference to rates of participant attrition.

Researchers will undertake a systems-based *process evaluation* (Moore 2015), beginning three months into the PROSPER Pilot, to: understand service provider and participant experiences and perspectives on acceptability, efficiency, implementation and development of PM+; understand service-users' perceptions and experiences of accessing and participating in PM+; explore how PM+ fits into existing health/social care systems; and understand change process dynamics including barriers and facilitators to implementing PM+. An ethnographic method will be adopted including observation of PM+ implementation, interviews and focus group discussions. Heterogeneity within the population will be considered and whether the intervention's feasibility and effectiveness may differ by demography or asylum status, and how this may influence the choice of target population for our proposed definitive trial. A topic guide will be developed.

Analysis will be based on narrative synthesis, combining data tabulation and narrative techniques. This will involve iterative review and refinement in order to reach agreement on a set of general propositions in relation to the data.

The perspectives of Normalisation Process Theory (Murray et al, 2010; Finch et al, 2013) will be used to assess the potential for implementing a full randomised controlled trial, focussing on the progression criteria set out above.

5.6 Intervention Discontinuation and Participant Discontinuation/Withdrawal

In consenting to the trial, participants agree to all trial activities including administration of trial intervention and follow-up assessments / visits and data collection. Every effort should be made to facilitate the completion of these for every recruited participant. If it is not possible to complete these activities (or it is deemed inappropriate) the reasons why should be documented. The following sub-sections describe the different levels of discontinuation/ withdrawal.

5.6.1 Premature Discontinuation of Trial Intervention

Participants may discontinue the study intervention for reasons including, but not limited to:

- Participant-led i.e. request by the participant
- Researcher/Clinician/Lay therapist-led:
    - Any change in the participant's condition that justifies the discontinuation of the intervention in the researcher/clinician/lay therapist's opinion;
    - Reasons of non-adherence or non-compliance with study intervention or other trial procedures e.g. unable to complete course of PM+;
    - Participant meets an exclusion criterion (either newly developed or not previously recognised).

Discontinuation from PM+ does not mean discontinuation of the study altogether, and the remaining study procedures i.e. 13- and 26-week follow up visits and data collection, and process evaluation, should be completed as indicated in the protocol (unless consent is specifically withdrawn).

5.6.2 Participant Withdrawal from Follow Up

Participants are free to withdraw from follow up at any time without providing a reason, though a reason should be recorded if one is given. Those who wish to withdraw from further follow-up will have the data collected up to the point of that withdrawal included in the analyses. The participant will not contribute further data to the study and the LCTC should be informed, via email to the LCTC and via completion of a Withdrawal CRF to be returned to the LCTC within 24 hours.

Death of a participant would be recorded on a Withdrawal CRF and a Death CRF.

5.6.3 Participant Transfer

For participants moving from the area, every effort will be made for the participant to be followed-up and to complete their remaining study appointment(s) remotely.

5.6.4 Loss to Follow-up

A participant will be considered lost to follow up if s/he fails to return for any scheduled visits and is not contactable by the site research team.

If a participant fails to attend/facilitate a required study visit the following actions must be taken:

- The researcher will attempt to contact the participant and reschedule the missed visit (be conscious of acceptable windows for collecting valid data) and advise the participant on the importance of maintaining the assigned visit schedule.
- Before a participant is deemed to be lost to follow up, the research team will make reasonable effort to regain contact with the participant.
- If the participant continues to be unreachable they should be considered withdrawn from the study with a primary reason of lost to follow up and this should be recorded on the Withdrawal CRF.

5.7 End of Trial

The end of the trial is defined to be the date on which data for all participants is locked and data entry privileges are withdrawn from the trial database. However, the trial may be closed prematurely by the Trial Steering Committee (TSC), on the recommendation of the Independent Data and Safety Monitoring Committee (IDSMC).

5.7.1 Study Discontinuation

As this is a pilot trial with a 12-month window for recruitment, intervention and follow up, study discontinuation is not a relevant concern. All participants to the pilot will be offered per-protocol intervention (i.e. five sessions of individual PM+, five sessions of group PM+, or support from local NGO).

6 SAFETY REPORTING

Safety reporting in research aims to ensure both the safety of trial participants and the safety of current and future participants. Effective safety reporting facilitates an ongoing assessment of risk-benefit ratio. Emerging safety data allows the sponsor to safely manage the trial by introducing amendments to the protocol, provide updated information to research team members and participants where necessary and determine whether it is safe to continue to conduct the trial or make changes to the protocol.

Definitions and responsibilities relating to safety reporting in non-CTIMP trials are provided by the Research Ethics Committee. Serious Adverse Events (SAEs) reportable to the REC are those that are:

- **related** to the study (i.e. they resulted from administration of any of the research procedures) and
- **unexpected** (as determined by CI or nominated deputy)

Further details of the specific safety and adverse event reporting for PROSPER are detailed under specific headings within this section.

6.1 Notes Regarding Adverse Events

As PROSPER is a non-CTIMP psychological intervention trial within a distressed AS&R population, it is expected that there could be a worsening of depression/anxiety symptoms that will be unrelated to the intervention but instead may be related to the ongoing adversity faced by participants. As such, only reportable adverse events listed in section 6.1.1 will be assessed by the CI for assignment of causality.

Due to the sensitive nature of the adverse events of interest, it is advised that direct questions about the occurrence of these should be avoided. Disclosure of any adverse events should be at the discretion of the participant. If, during any contact with participants, a researcher or lay therapist has any safeguarding concerns or becomes aware of any adverse event this should be dealt with promptly and appropriately as per the procedures detailed within this section.

6.1.1 Reportable Adverse Events

No adverse events are expected to be related to the intervention.

However, it is recognised that the recruited population is vulnerable and the expected incidence of mental health symptoms associated with the levels of adversity they are exposed to is high. As such, any occurrence of the following adverse events will be recorded:

- Suicidal ideation
- Self-harm
- Suicide attempts
- Any worsening of mental health condition
- Diagnosis of new mental health condition

The CI will assess any of the above adverse events for relatedness. If any are considered possibly, probably or almost certainly related, and serious, these will be reported to the REC.

6.1.2 Non-Reportable Adverse Events

Because the intervention is psychological, it can be reasonably assumed that no physical adverse events will be related to the intervention.

This includes (but is not limited to) any adverse event that could be described as one of the following:

- Development of new physical health condition e.g., influenza, newly diagnosed heart condition, stroke etc.
- Accident/injury
- Pregnancy
- Medical or surgical procedures

6.1.3 Other Notable Events

Data collection will also involve collection of information, via the CSRI form, regarding interaction with the judicial system which may have a detrimental impact on participant wellbeing (e.g. court summons and detention) and which will be reported to oversight committees as notable events.

6.1.4 Notification of deaths

If any member of the research team becomes aware of the death of a participant, they should complete a Withdrawal CRF and a Death CRF and return these to the LCTC within 24 hours.

6.2 Definitions used in Adverse Event Reporting

Adverse events listed in 6.1.1 will be categorised according to the following classifications:

6.2.1 Seriousness

In PROSPER Pilot, an adverse event will be classed as ‘serious’ if it:

- Results in death
- Is life threatening, or places the participant at immediate risk of death from the event as it occurred
- Requires or prolongs hospitalisation
- Causes persistent or significant disability or incapacity
- Is another condition which investigators judge to represent significant hazards

It is expected that a non-clinical researcher should be able to make an assessment of seriousness for reportable adverse events within PROSPER. Where there is any uncertainty or queries, the researcher should escalate the AE to the CI for clinical review and determination of seriousness (see flow chart in section 6.3.3).

All suicide attempts will be classed as “serious”.

If suicidal ideation is suspected or noted at baseline or follow up appointments, the researcher will administer the P4 screener (for further details and guidance please refer to Suicidal Ideation Guidance document). Suicidal ideation will only meet the criteria of "serious" if responses to the P4 screener indicate a 'moderate' or 'high' risk.

All reportable serious adverse events should be notified to the CI immediately – within 24 hours (refer to Section 6.3.2 for specific details).

If a participant dies as a result of a non-reportable serious adverse event (i.e. not listed in 6.1.1) this should be recorded on a Withdrawal CRF and a Death CRF.

6.2.2 Relationship to Trial Intervention

All AEs will be assessed by the CI for relatedness to the study intervention. An AE whose causal relationship to the intervention is assessed by the CI as "possible", "probable", or "almost certain" is a Related Adverse Event. The assignment of the causality will be made using the definitions in the following table:

Relationship	Description
Unrelated	There is no evidence of any causal relationship. N.B. An alternative cause for the AE will be given
Unlikely	There is little evidence to suggest there is a causal relationship (e.g. the event did not occur within a reasonable time after a trial intervention session). There is another reasonable explanation for the event (e.g. the participant's clinical condition, other concomitant treatment).
Possibly	There is some evidence to suggest a causal relationship (e.g. because the event occurs within a reasonable time after a trial intervention session). However, the influence of other factors may have contributed to the event (e.g. the participant's clinical condition, other concomitant treatments).
Probably	There is evidence to suggest a causal relationship and the influence of other factors is unlikely.
Almost certainly	There is clear evidence to suggest a causal relationship and other possible contributing factors can be ruled out.

6.2.3 Expectedness

The individual and group PM+ manuals do not list any particular adverse events that are expected as a direct result of the intervention. Therefore, all reportable adverse events which are considered by the CI to be related to the trial intervention will be classed as unexpected.

Related adverse events will be monitored on an ongoing basis.

Any related serious adverse events will be reported as per section 6.3.2.

6.2.4 Severity of Adverse Events

If applicable, the assignment of the severity/grading will be made by the CI or nominated deputy using the definitions below.

Regardless of the classification of an AE as serious or not, its severity must be assessed according to medical criteria alone using the following categories:

Mild: does not interfere with routine activities
Moderate: interferes with routine activities
Severe: impossible to perform routine activities

A distinction is drawn between serious and severe AEs. Severity is a measure of intensity (see above) whereas seriousness is defined using the criteria in section 6.2.1, hence, a severe AE need not necessarily be a Serious Adverse Event.

6.3 Reporting Procedures

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

6.3.1 Non serious AEs

All reportable events (refer to 6.1.1) occurring between baseline and the final follow up visit (approximately 26 weeks), whether related or not, will be recorded on an Adverse Event Form.

The researcher or PSS wellbeing mentor must contact the CI with details of the Adverse Event as soon as they become aware of it. The CI will provide an assessment by email of whether or not the Adverse Event is related to the intervention (the email must not contain any identifiable information), and the site must print this email and store it in their ISF. The site should return a copy of the completed Adverse Event Form to LCTC within seven days of becoming aware of the Adverse Event, and retain the original form in the ISF.

6.3.2 Serious AEs

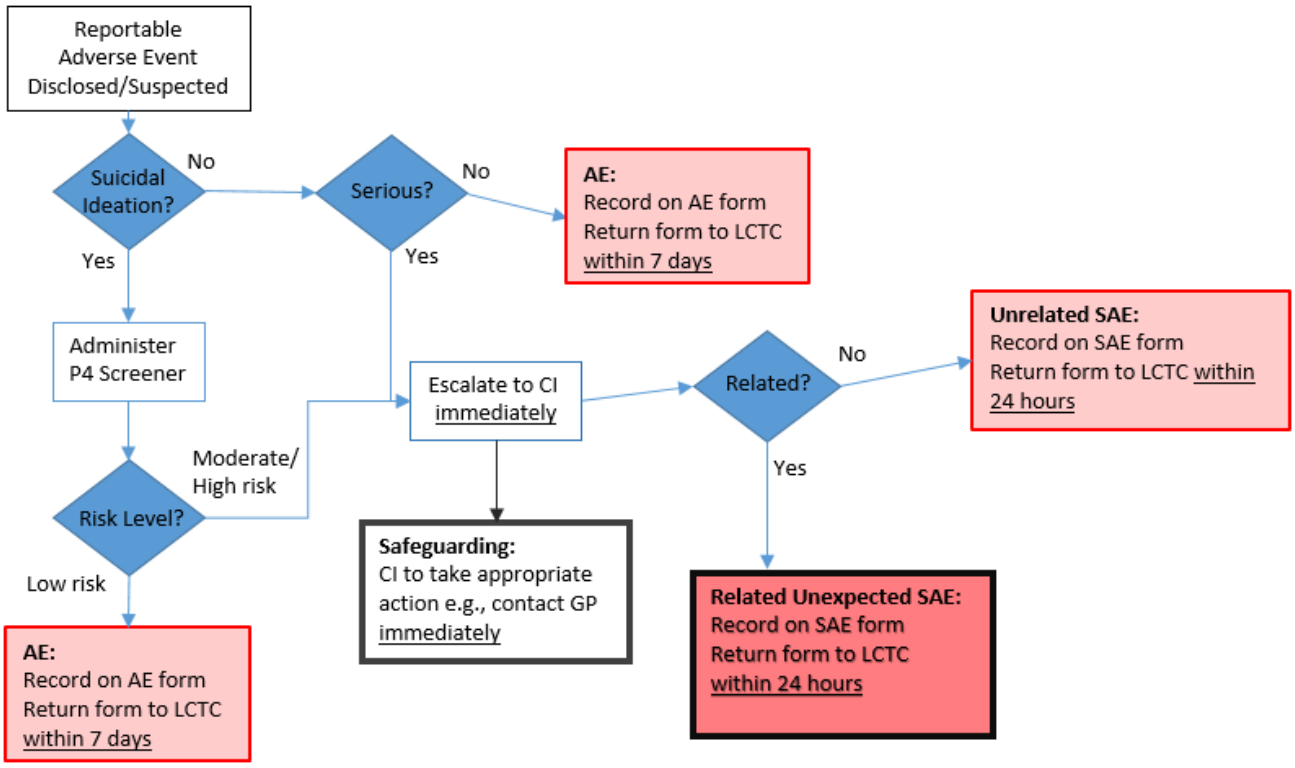
All reportable adverse events (refer to 6.1.1) that meet the definition of serious should be notified to the CI as soon as possible and within 24 hours. The CI should complete the Serious Safety Event Report Form which includes the nature of event, date of onset, severity, any action taken, outcome and causality (where applicable dependent on the nature of the event) and send to the LCTC within 24 hours of becoming aware. Any available additional information should be sent within 5 days if the event has not resolved at the time of reporting. For further details of CI's reporting responsibilities, refer to section 6.6.

An Adverse Event Form should also be completed.

The LCTC will notify the REC of all RUSAEs occurring during the study within 15 days.

For additional information in cases of suicidal ideation refer to the Suicidal Ideation Guidance Document.

6.3.3 Flowchart for Reporting Requirements of Adverse Events



6.4 Lay Therapist & Supervisor Responsibilities

If a lay therapist has any concerns regarding participant safety they should follow the standard procedure of their employing organisation (PSS) to assess/escalate this so it can be processed accordingly.

Lay therapist responsibilities:

- Notify the wellbeing mentor as soon as any red flags become apparent;
- Discuss any non-serious general concerns over participant wellbeing with wellbeing mentor during weekly supervision sessions.

Wellbeing mentor responsibilities:

- Respond immediately to lay therapist concerns by reviewing, assessing and collecting any other required information;
- If still concerned or action is required, discuss immediately with PSS Clinical Lead;
- If no further action is required, complete an Adverse Event form following the procedure detailed in section 6.3.1 and send a copy to LCTC within seven days of becoming aware of the adverse event.

PSS Clinical Lead responsibilities:

- Any adverse event meeting the criteria of ‘serious’, or where classification of ‘serious’ is subjective, should be immediately escalated to the Chief Investigator;
- Follow PSS standard procedures with regard to notifying participant’s GP / signposting to alternative therapies or support;
- Notify the CI of any additional action taken.

If a trial participant becomes distressed as a result of experiencing a flashback during an intervention session, PSS staff will adhere to the following procedure:

- The lay therapist will immediately suspend the session and explain the need to contact one of the wellbeing mentors to ensure the participant is looked after safely;
- The lay therapist will sit with the participant until the wellbeing mentor arrives;
- The wellbeing mentor will conduct an assessment and, if further support is required, will discuss immediately with the PSS Clinical Lead.
- If needed, the PSS Clinical Lead would then notify the participant's GP and signpost to alternative therapies or support, for example, PSS's Spinning World service (an NHS-funded counselling service for young refugees and asylum seekers who have experienced or witnessed human rights abuses.
- One week later, the wellbeing mentor will make a follow-up telephone call to the participant, to check that appropriate support has been arranged.

6.5 Researcher Responsibilities

Once participants are enrolled, researchers are only expected to only have contact with participants at 13- and 26-week follow up visits. By this point in the study, it is anticipated that those participants randomised to receive the intervention will have completed the programme. However, it is possible that the researcher will become aware of or have concerns about safeguarding the participants due to self-reported or suspected self-harm or suicidal ideation. In these circumstances, an assessment of seriousness (as per criteria in section 6.2.1) should be made and the appropriate action taken:

Not serious:
Any AE not meeting criteria of 'serious' should be recorded on an Adverse Event form, following the procedure detailed in section 6.3.1.

Serious/Not Sure:
Any AE meeting the criteria of 'serious', or where classification of 'serious' is subjective, should be immediately escalated to the Chief Investigator. An Adverse Event Form should also be completed.

6.6 Chief Investigator Responsibilities

The CI should review all non-serious reportable adverse events for relatedness, in line with the procedure detailed in section 6.3.1.

When an adverse event meets the criteria of 'serious', or where classification of 'serious' is subjective, it will be escalated to the CI or nominated deputy. They must first re-assess the seriousness of the adverse event (as per criteria in 6.2.1). In cases where the researcher or PSS Clinical Lead has previously categorised the event as serious, the CI will be asked to review and confirm the classification. Where the researcher or PSS Clinical Lead was unable to make the assessment, the CI will record their assessment. If the CI does not consider the AE to be serious, this will be discussed further with the researcher or PSS Clinical Lead. If an agreement on seriousness cannot be reached, the CI will document this on the Serious Safety Event Report Form and the adverse event will be classed as serious for reporting purposes.

All SAEs should then be categorised by the CI in relation to:

- Relatedness (see 6.2.2)
- Severity (see 6.2.4)

All SAEs should be categorised as above within 24 hours of the CI being notified of the event and all relevant information recorded on a Serious Safety Event Report Form.

Once all available information is recorded on the Serious Safety Event Report Form, the CI should follow the steps below:

1. send the Serious Safety Event Report Form by secure email to the LCTC
2. where possible telephone the LCTC /trial coordinator to alert them to the email
3. provide any further information as soon as it becomes available

NB. The participant must not be identifiable.

In the case of some SAEs, further action may be required such as: notification of participant's GP; signposting to alternative therapies/help/support; or withdrawal of participant. Any further action should be added to the Serious Safety Event Report Form as soon as it is available and an updated Serious Safety Event Report Form provided to the LCTC.

The initial report shall be followed by more detailed reports as appropriate if more information becomes available.

6.7 LCTC Responsibilities

Upon receipt of an initial Serious Safety Event Report Form complete with the minimum information required the LCTC are responsible for further reporting as delegated by the trial Sponsor, University of Liverpool.

6.7.1 Onward Reporting

The LCTC is undertaking reporting of RUSAEs to the Research Ethics Committee as follows:

- All RUSAEs must be reported within 15 days of the LCTC first becoming aware of the event.
- A list of all reportable SAEs must be reported annually.

The following issues will also be reported in an expedited fashion:

- An increase in the rate of occurrence or a qualitative change of an expected serious adverse event, which is judged to be clinically important;
- Post-study RUSAEs that occur after the participant has completed a clinical trial and are notified by the participant to any member of the research team;
- New events related to the conduct of the trial or the development of the interventions and likely to affect the safety of the participants, such as:
    a. A SAE which could be associated with the trial procedures and which could modify the conduct of the trial;
    b. Any anticipated end or temporary halt of a trial for safety reasons and conducted with the same intervention in another country;
- Recommendations of the IDSMC, if any, where relevant for the safety of the participants.

6.7.2 Safety Reports

Safety reports will be generated during the course of the trial which allows for monitoring of SAE reporting. The LCTC will send annual progress reports containing a list of all SAEs to the REC.
The LCTC will notify the IDSMC of all reportable (refer to section 6.1.1) SAEs within 2 weeks of becoming aware, and the LCTC will include the number of non-serious reportable AEs in routine IDSMC reports. Any concerns raised by the IDSMC or inconsistencies noted during the reporting process may prompt additional training for the research staff. Additional training will also be provided if unacceptable delay in safety reporting timelines. If any safety reports identify issues that have implications for the safety of trial participants, all relevant stakeholders participating in the trial will be notified.

6.8 Time Period for Safety Reporting

AEs will be recorded during the study from the point of randomisation until the end of a participant's involvement in the trial at the 26-week follow up appointment. Any RUSAEs that are recorded during this time period will be reported to the REC.

Intervention delivery is likely to have been completed during the first 12 weeks of a participant's involvement in the trial so there are not likely to be any related safety events after 26 weeks. However, members of the research team are expected to report any AE that they become aware of after the reporting time period stated.

6.9 Follow-up After Adverse Events

All participants will have their own GPs who retain responsibility for their clinical care. In cases where a member of the research team becomes aware of suicidal ideation at any time, they will follow the suicidal ideation guidance and the CI will notify the participant's GP.

When reporting SAEs and RUSAEs the Chief Investigator will apply the following criteria where possible to provide information relating to event outcomes: resolved; resolved with sequelae (specifying with additional narrative); not resolved/ongoing; ongoing at final follow-up; fatal or unknown.

6.10 Contact Details and Out-of-hours Medical Cover

Out-of-hours support may be offered by local NGOs or NHS services as standard of care for this population. Participant information sheets will contain contact telephone numbers of local NGOs who provide support services for AS&Rs, and contact telephone numbers to use in the event of a health emergency.

The research team will not be responsible for providing emergency/out-of-hours care for participants.

7 STATISTICAL CONSIDERATIONS

7.1 Introduction

A full and detailed statistical analysis plan (SAP), following ICH E9 and the CONSORT guidelines, will be developed prior to the first comparative monitoring report to be presented to the IDSMC. The main features of these planned statistical analyses, which refer specifically to the PROSPER pilot, are detailed below.

7.2 Method of Randomisation

Participants will be randomised using a secure (24-hour) web-based randomisation program controlled centrally by the LCTC. Randomisation lists will be generated in a 1:1:1 ratio, to individual PM+, group PM+ and control, using block randomisation with random variable block sizes, (see section 5.4 for back-up randomisation method). The randomisation list will be generated by a statistician at the LCTC (independent to the PROSPER trial).

7.3 Sample Size Calculation

The aim is to recruit 105 participants, 35 to each of three arms - individual PM+, group PM+ and control. Individual sessions will be offered as gender- and language-specific[14]. At least four groups will be offered for the group intervention, each with up to 8 or 9 participants, each gender-specific[15].

The sample size needs to be sufficient to estimate retention levels in a definitive trial. With an expectation of 80% retention, samples of 35 participants for each of the individual, group and control arm will provide an accurate estimate of retention +/- 13% (67% to 93%).

Retention rates will be assessed in each arm separately, as there may be systematic differences between them; for example, those randomised to the control arm may be less likely to remain engaged than those randomised to the individual or group arms, while those randomised to the group arm may be demotivated if faced with a lengthy wait for their group to begin.

7.3.1 Interim Monitoring and Analyses

No formal interim analysis is planned, but there will be regular monitoring by the Independent Data and Safety Monitoring Committee (IDMSC), who will meet at least annually. After each meeting, the IDSMC will provide a recommendation to the TSC on the continuation of the trial.

[14] The lay therapist and the study participant will be the same gender and will both be comfortable in a common language.
[15] Participants will all be the same gender; lay therapists may be mixed gender.

7.4 Analysis Plan

Analysis will be by the intention-to-treat principle as far as is practically possible. All analyses will be descriptive, focussed on assessing the criteria for deciding whether to progress to a full trial. All estimates of proportions will be presented with 95% confidence intervals. Rates of recruitment and attrition will be presented both for lay therapists and trial participants, along with the proportion of interventions which are successfully delivered per protocol. The proportion of missing data in the proposed trial outcome measures will be assessed.

No formal testing of intervention effect will be carried out, but estimates of between group differences between the test groups and the control in outcome measures will be presented, with 95% confidence intervals, to assess whether a clinically important improvement in outcome would be plausible in a full trial. The effect of clustering by intervention provider on outcomes in the two PM+ groups will be investigated, to inform design of a full trial with a partially nested design.

8 REGULATORY AND ETHICAL APPROVALS

8.1 Statement of Compliance

The study will be carried out in accordance with:

- LCTC Liverpool Clinical Trials Centre Standard Operating Procedures
- The template content is structured consistent with the SPIRIT (Standard Protocol Item: Recommendations for Interventional Trials 2013)
- UK Policy Framework

8.2 Regulatory Approval

PROSPER does not require any regulatory approval.

8.3 Ethical Considerations

General risks to trial participants and lay therapists, and their mitigations, are discussed in 1.3.1 above.

The fact that participants will not be able to choose their own treatment is specified and explained in the Participant Information Sheet, and will be discussed with participants by the researcher during the process of gaining informed consent.

The trial will involve additional visits for participants, with researcher and lay therapists, over their usual activities. These are set out in the Participant Information Sheet. Every effort will be made by researcher and lay therapists to schedule these contacts to avoid disruption to participants' current schedules. Participants' expenses for attending research and therapy meetings will be covered.

8.3.1 Ethical Approval

The trial protocol and other trial-specific documentation has received the favourable opinion of the North West – Liverpool Central Research Ethics Committee (Ref: 19/NW/0345).

9 DATA MANAGEMENT AND TRIAL MONITORING

Details of the monitoring to be carried out for the PROSPER study are included in the PROSPER Trial Monitoring Plan.

Trial Oversight Committees related to the monitoring of the trial are detailed on page 15.

9.1 Source Documents

In order to resolve possible discrepancies between information appearing in the case report form (CRF) and any other participant related documents, the CRF will be considered the source document for data where no prior record exists and which is recorded directly in the CRF. A PROSPER source document list will be produced for reference and will be stored in the TMF.

9.2 Data Capture Methods

The study case report form (CRF) is the primary data collection instrument for the study. All data requested on the CRF must be recorded. All missing data must be explained. If a space on the CRF is left blank because the procedure was not done or the question was not asked, “N/D” will be written. If the item is not applicable to the individual case, “N/A” will be written. Or if the data item is unknown, “NK” will be written. If a data item has not been recorded on source data then “NR” will be written’. All entries will be printed legibly in black ink. If any entry error has been made, to correct such an error, a single straight line will be drawn through the incorrect entry and the correct data entered above it. All such changes will be initialled and dated. Errors will not be erased or whited out. For clarification of illegible or uncertain entries, the clarification will be printed above the item, then initialled and dated.

Questionnaires utilised for PROSPER are a source document and the researcher will photocopy them in order to retain a copy at site before providing originals to LCTC. All documents sent by sites will be sent separately to the consent form as this has participant identifiable data on it.

9.3 Monitoring

9.3.1 Central Monitoring

Data stored at LCTC will be checked for missing or unusual values (range checks) and checked for consistency within participants over time. Any suspect data will be returned to the site in the form of data queries. Data query forms will be produced at the LCTC from the trial database and sent either electronically or through the post to a named individual (as listed on the site delegation log). Sites will respond to the queries providing an explanation/resolution to the discrepancies and return the data query forms to LCTC. The forms will then be filed along with the appropriate CRFs and the appropriate corrections made on the database. There are a number of monitoring features in place at the LCTC to ensure reliability and validity of the trial data, to be detailed in the trial monitoring plan.

9.3.2 Clinical Site Monitoring

In order to perform their role effectively, the trial coordinator (or monitor) and persons involved in Quality Assurance and Inspection may need direct access to primary data, e.g. participant records, laboratory reports, appointment books, etc. Since this affects the participant's confidentiality, this fact is included on the Participant Information Sheet and Informed Consent Form.

9.4 Confidentiality

Case report forms will be labelled with the participant's initials and unique trial screening and/or randomisation number. Medical information may be given to the participant's medical team and all appropriate medical personnel responsible for the participant's welfare.

Individual participant information obtained as a result of this study is considered confidential and disclosure to third parties is prohibited with the exceptions noted below.

- Disclosure in case of safeguarding others
- Disclosure in case of suspected/reported suicidal ideation

The LCTC will be undertaking activities requiring the transfer of identifiable data. Verification that appropriate informed consent is obtained will be enabled by the provision of copies of participant's signed informed consent forms being supplied to the LCTC by the Department of Health Services Research, which requires that name data will be transferred to the LCTC.

This transfer of identifiable data is disclosed in the PISC. The LCTC will preserve the confidentiality of participants taking part in the study and The University of Liverpool is registered as a Data Controller with the Information Commissioners Office. Bangor University is also a Data Controller. Other trial documents will not be posted in the same envelope as the consent form as there is a risk to participant confidentiality.

9.5 Quality Assurance and Control

- The Trial Coordinator at the LCTC will verify appropriate approvals are in place prior to initiation of the site and the relevant personnel have attended trial specific training. A greenlight checklist will verify all approvals are in place prior to trial initiation at LCTC and the individual site.
- The PMG will determine the minimum key staff required to be recorded on the delegation log in order for the site to be eligible to be initiated.
- Data will be evaluated for compliance with protocol and accuracy in relation to source documents
- The study will be conducted in accordance with procedures identified in the protocol.
- Independent oversight of the trial will be provided by the Independent Data and Safety Monitoring Committee and independent members of the Trial Steering Committee.
- The types of materials to be reviewed, who is responsible, and the schedule for reviews may be specified or referenced in other documents
- Types and mechanisms of training of staff for the study will be specified.
- The CI and other key staff will attend site initiation training, coordinated by the LCTC, which will incorporate elements of trial-specific training necessary to fulfil the requirements of the protocol;
- The Project Management Group is to monitor screening, randomisation and consent rates between centres.
- The process for consent, recruitment and randomisation will be evaluated for compliance with the protocol.

- Data quality checks and monitoring procedures will be undertaken in line with the trial Data Management Plan;
- Independent oversight of the trial will be provided by the Independent Data and Safety Monitoring Committee and independent members of the Trial Steering Committee.

9.6 Records Retention

The PI at each site will make arrangements to store the essential trial documents (as defined in Essential Documents for the Conduct of a Clinical Trial (ICH E6, Guideline for Good Clinical Practice)), including the Investigator Site File, until the LCTC informs the investigator that the documents are no longer to be retained, or for a minimum period of 10 years (whichever is soonest).

The PI is responsible for archiving of all relevant source documents so that the trial data can be compared against source data after completion of the trial (e.g. in case of inspection from authorities).

The PI will ensure the continued storage of the documents, even if the investigator, for example, leaves the organisation or retires before the end of required storage period. Delegation must be documented in writing.

The LCTC undertakes to store originally completed CRFs for the same period, except for source documents pertaining to the individual investigational site, which are kept by the investigator only. The LCTC will archive the documents in compliance with GCP guidelines. All electronic CRFs and trial data will be archived onto an appropriate media for long term accessible storage. Hard copies of data will be boxed and transferred to secure premises where unique reference numbers are applied to enable confidentiality, tracking and retrieval.

10 INDEMNITY

PROSPER is sponsored by the University of Liverpool and co-ordinated by the LCTC in the University of Liverpool. The University of Liverpool holds insurance against claims for compensation for injury caused by participation in a clinical trial. The conduct of the trial as described in this protocol is covered under the University of Liverpool's Clinical Trials insurance policy.

11 PUBLICATION AND DISSEMINATION

11.1 Publication Policy

Refer to PROSPER publication strategy.

11.2 Dissemination to Key Stakeholders

Refer to PROSPER publication strategy.

Information for trial participants is available on a trial website: www.prosper-trial.org.uk

A newsletter for trial participants will also be set up.

11.3 Data Sharing

At the end of the trial, after the primary results have been published, the anonymised individual participant data (IPD) and associated documentation (e.g., protocol, statistical analysis plan, annotated blank CRF) may be prepared in order to be shared with external researchers. All requests for access to the IPD will be reviewed by an internal committee at the LCTC and discussed with the Chief Investigator in accordance with the LCTC policy on data sharing.

12 CHRONOLOGY OF PROTOCOL AMENDMENTS

Version 1.0 (01/04/2019) Version for internal review process – not approved

Version 2.0 (03/05/2019) Original version submitted for REC review

Version 3.0 (01/07/2019) Original approved version.

Summary of Amendments from Protocol V2.0 to Protocol V3.0		
Protocol Section Number	**Protocol Section Title**	**Summary of Changes**
4.2	Training and supervision	• Additional information provided about qualifications and experience of Wellbeing Mentors, and observations/supervision by Master Trainer.
4.4	Venue for delivery of intervention	• Amended to state that all sessions will be delivered within organisations which have on-site staff with experience and training in managing emotional distress.
6.4	Lay Therapist & Supervisor Responsibilities	• Information added regarding procedure that PSS staff will adhere to if a trial participant becomes distressed as a result of experiencing a flashback during an intervention session.

Version 4.0 (07/08/2019)

Summary of Amendments from Protocol V3.0 to Protocol V4.0		
Protocol Section Number	**Protocol Section Title**	**Summary of Changes**
N/A	Title page	• Sponsor reference updated – the previous reference was for the feasibility study.
N/A	Protocol Summary	• Inclusion criterion d changed to: Have conversational English.
3.1	Eligibility Criteria	• Inclusion criterion d changed to: Have conversational English.
5.3	Eligibility and Baseline	• Minor changes for purpose of clarification; terminology corrections (no procedural changes).
5.6.2	Participant Withdrawal from Follow Up	• Death of a participant will be classed as a Withdrawal (previously Death was listed under 5.6.1, Premature Discontinuation of Trial Intervention); • Withdrawal CRF will be returned to the LCTC within 24 hours rather than within 7 days.
6	Safety Reporting	• Addition of relevant timelines for clarification and consistency purposes; • Changes to terminology to refer to Serious Safety Event Report Form rather than SAE Form.
6.1.1	Reportable Adverse Events	• Clarification of what adverse events will be reported.
6.1.4	Notification of deaths	• Clarification of how participant death should be recorded.
6.2.1	Seriousness	• Clarification of procedure that will be followed in the event of suicidal ideation.

6.2.3	Expectedness	• Clarification that all reportable related adverse events will be considered unexpected (and therefore will not be assessed for expectedness).
6.3.1	Non Serious AEs	• Clarification of the procedure by which AEs will be assessed for relatedness to the intervention.
6.3.3	Flowchart for Reporting Requirements of Adverse Events	• Updated for purpose of consistency / clarification.
6.4	Lay Therapist & Supervisor Responsibilities	• Change to timescale for PSS reporting of Adverse Events, to be consistent with the timescale for researcher reporting of Adverse Events.
6.6	Chief Investigator Responsibilities	• Clarification over what would happen if there is uncertainty over whether an AE is serious or not.
N/A	N/A	• References to Clinical Trials Research Centre (CTRC) changed to Liverpool Clinical Trials Centre (LCTC) following recent institutional change.
N/A	N/A	• Other minor typographical errors, corrections and clarifications in order to ensure consistency made throughout.

Version 5.0 (11/12/2019)

Summary of Amendments from Protocol V4.0 to Protocol V5.0		
Protocol Section Number	**Protocol Section Title**	**Summary of Changes**
N/A	Title page	• Addition of trial ISRCTN number.
5.1	Participant Identification	• Clarification regarding organisations that may be involved in participant identification. • Addition of paragraph regarding use of social media in participant recruitment.
9.6	Records Retention	• Corrections and clarifications
10	Indemnity	• Correction to indemnity statement
11	Publication and Dissemination	• Addition of trial website information
N/A	N/A	• Other minor typographical errors, corrections and clarifications in order to ensure consistency made throughout.

13 REFERENCES

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14 DOCUMENTS SUPPLEMENTARY TO THE PROTOCOL

Participant information sheet and consent form
GP Letter
Study instruments (including CRFs / data collection booklets as detailed in the protocol)
Suicidal Ideation Guidance Document
PROSPER publication strategy
Participant Recommendation Form
PROSPER Leaflet/Poster
Source Document Checklist

Any of the above documents that are subject to ethical review will be submitted as a separate document to avoid making unnecessary protocol amendments.