The University of Manchester

Remote Approaches to Psychosocial Intervention Delivery

STUDY PROTOCOL

Title:	Remote Approaches to Psychosocial Intervention Delivery (RAPID): a multi-arm, multi-stage Randomised Controlled Trial
Version Number:	**9.0 07/JUN/2024**
ISRCTN:	**ISRCTN33079589**
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Funders:	National Institute for Health Research – Health Technology Agency (NIHR 132690)
Sponsor:	The University of Manchester
Sponsor Reference:	TBC
Chief Investigator:	Professor Anthony P Morrison

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The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirement.

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

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

For and on behalf of the Study Sponsor:

Signature: Date:

Name (please print):

Position:

Chief Investigator:

Signature: Date: 7th June 2024

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Abbreviations

Term	Description
ACT	Acceptance and Commitment Therapy
AE	Adverse Event
AP	Assistant Psychologist
CBT	Cognitive Behaviour Therapy
CRN	Clinical Research Network
DBT	Dialectical Behaviour Therapy
HBTT	Home Based Treatment Team
HTA	Health Technology Assessment
ICJME	International Committee of Medical Journal Editors
NHS	National Health Service
NIHR	National Institute for Health Research
PPI	Patient and Public Involvement
RCT	Randomised Controlled Trial
SAE	Serious Adverse Event
SMHP	Serious Mental Health Problem
UK	United Kingdom

Summary of protocol amendments

All changes summarise below have been approved by the funder (National Institute for Health Research, Health Technology Assessment), the sponsor, and the relevant regulatory bodies required for the amendment.

Category	Summary	Protocol version and date	Amendment type and number
Inclusion criteria	In response to feedback from NHS crisis services that patients can be discharged within a short time frame from referral to the crisis service, the inclusion criteria was changed from '*Receiving care from a HBTT (referrals to HBTT Team are associated with increased risk of a psychiatric hospital admission in the near future)'* to *'Currently receiving care from a Home-Based Treatment Team/ Crisis team or have done so within the last 14 days, since referrals to HBTT/Crisis Team are associated with increased risk of a psychiatric hospital admission in the near future'*.	Version 4.0 06/OCT/2023	Substantial amendment 02
Blinding	Sentence regarding blinding changed from *"Blinding of the allocation code will be maintained for Research Assistants (RAs) until all outcome measures for all subjects have been collected"* to *"Blinding of the allocation code of a subject will be maintained for Research Assistants (Ras) until all outcomes for that subject have been collected."*	Version 5.0 06/MAR/2023	Non-substantial amendment 03
Study design	Study design changed from a four-arm trial to a three-arm trial following removal of the BrighterSide mobile app intervention arm. This decision was based on unpublished efficacy data from a large Australian randomised controlled trial of the BrighterSide app which had a primary outcome of suicidal ideation, in conjunction with early engagement data from the RAPID trial, which showed low levels of use of the app by	Version 6.0 02/MAY/2023	Substantial amendment 3

	participants. As such the following changes were made to the randomisation ratio, sample size and number required for the interim anlaysis: (i) Randomisation ratio changed from 2:1:1:1 favouring TAU to 3:2:2 favouring TAU. (ii) Sample size required for planned interim analysis changed from *after first 559* participants to *after first 452 participants*. (iii) Total sample size changed from 1235 to 1064 (not inclusive of the 54 participants randomised to BrighterSide at the time of dropping this arm)		
Inclusion criteria	Broadening of inclusion criteria based on feedback from consultant psychiatrists at some of the study sites and a review of referral data to include Post Traumatic Stress Disorder (PTSD) and complex PTSD (cPTSD).	Version 6.0 02/MAY/2023	Substantial amendment 3
Exclusion criteria	Following removal of the BrighterSide app, the exclusion criteria were updated by removal of the following criterion, *"visual impairment, severe enough to prevent engagement with the BrighterSide app as provision would be impossible on both financial and logistical ground"*.	Version 6.0 02/MAY/2023	Substantial amendment 3
Provision of mobile phone and data	Protocol updated to reflect removal of the automatic offer of a mobile phone and data package to participants, but option to retain offer if there	Version 7.0 18/AUG/2023	Non-substantial amendment 04

package to participants	was no alternative option for the participant to engage in the study. This was based on feedback from study participants that the usage of mobile phones and data packages provided was low.		
Monthly recruitment target	Following review of the internal pilot recruitment data by the funder the monthly recruitment target has been reduced from 50 to 35 from 01/JUN/2023.	Version 8.0 27/NOV/2023	Non-substantial amendment 05
Interim analysis	Following agreement from the funder, the interim analysis will take place after 385 participants provide 6-month outcome data, which will be 31/MAR/2024 and provide 92% power.	Version 8.0 27/NOV/2023	Non-substantial amendment 05
Health Economic analysis	Due to the unfeasible nature of accessing and extracting service use from electronic patient records, the trial will switch to collect only psychiatric inpatient admissions from hospital record data (these are likely a key driver of costs in this population). With the rest being taken from the self-report questionnaire, as this is being collected during interview, there is the opportunity to limit missing data as the research team can prompt and explain questions to participants.	Version 8.0 27/NOV/2023	Non-substantial amendment 05
Concomitant psychiatric medications	Concomitant psychiatric medication data will not be collected at baseline, 3 or 6-months due to the unfeasible nature of accessing and extracting cross-sectional data on concomitant psychiatric medications from the electronic patient records. Collection of concomitant psychiatric medications was not in the original funded protocol as this data is not required for either clinical or cost-effectiveness anlaysis. This was added on requested of the MHRA as a requirement of a clinical trial of a medical device. As of	Version 8.0 27/NOV/2023	Non-substantial amendment 05

	23/NOV/2023 the RAPID trial ceased to be a clinical trial of a medical device and it is deemed that collection and retention of data that will not be required for either the clinical or cost-effectiveness analysis is unethical.		
Study design	Following the planned interim analysis the study design has changed from a three-arm trial to a two-arm trial with the removal of the PREVAIL intervention arm. The planned interim analysis showed that PREVAIL exceeded the threshold for futility (one-sided p-value >= 0.4) as per the statistical analysis plan. Both the DMC and TSC made the recommendation to the funder to drop this intervention arm. This decision was ratified by the funder on 7th June 2024. As such the following changes were made to the randomisation ratio, sample size and project timescales: (i) Randomisation ratio changed from 3:2:2 favouring TAU to 1:1. (ii) Total sample size changed from 1064 (not inclusive of the 54 participants randomised to BrighterSide) to 937 (not inclusive of the 54 participants randomised to BrighterSide). This gives a study total sample size of 991 when including the 54 BrighterSide participants. (iii) Recruitment will end 31st May 2025 with the final follow-up being completed by 30th	Version 9.0 07/JUN/2024	Substantial amendment 4

	November 2025 and overall study end date, as defined by submission of report to the funder of 31st January 2026.		

Abstract

People with serious mental health problems (SMHP) are more likely to be admitted to psychiatric hospital following contact with crisis services. Admissions can have significant personal costs and be traumatic and are the most expensive form of mental health care. In the context of COVID-19, admitting someone to hospital can be additionally problematic, since people with SMHP are potentially vulnerable to COVID-19 due to an increased risk of underlying physical health problems and taking medications. There is an urgent need for treatments to reduce suicidal thoughts and behaviours and, therefore, reduce avoidable hospital admissions.

RAPID is a large, multi-site 3 arm, 2 stage randomised controlled trial to determine the clinical and cost effectiveness of two brief and remotely delivered psychosocial treatments, compared to treatment as usual, for people with SMHP who have had recent suicidal thoughts or behaviours. Recruitment is at Glasgow, Manchester, Oxford and London (East and North East).

Our primary outcome is psychiatric hospital admissions over a 6-month period. We also assess the impact on suicidal thoughts and behaviour, hope, recovery, anxiety and depression. The remote treatments delivered over 3 months are: structured peer support (PREVAIL), which includes suicide prevention strategies based on cognitive behaviour therapy (CBT), delivered by peer support workers via telephone or videoconferencing and a safety planning approach delivered over the telephone by assistant psychologists (SAFETEL). The initial phase of the trial was a four-arm trial with a mobile-app (BrighterSide) intervention arm, that was removed following the release of unpublished efficacy data from a large Australian randomised controlled trial of the BrighterSide app which had a primary outcome of suicidal ideation, in conjunction with early engagement data from the RAPID trial, which showed low levels of use of the app by participants. This change was not planned as part of the adaptive design. At the time the BrighterSide app was removed a total of 54 participants had been allocated to this intervention. We initially ran an internal pilot with clear progression criteria and a recruitment target of 200 people over 4 months. In Stage 1, we randomised participants in the ratio 2:2:3 in favour of TAU using an independent remote web-based randomisation system using permuted blocks of random size stratified by site. An interim analysis was performed using data from the first 385 PREVAIL, SAFETEL and TAU participants with outcome data at 6 months which resulted in the PREVAIL intervention arm being dropped for lack of benefit on the primary outcome in Stage 2. For the second stage of the trial the design is two-arms (SAFTEL + TAU and TAU alone) with a randomisation allocation ratio of 1:1. The expected total sample size is 991 participants, inclusive of the 54 BrighterSide participants.

Background

What is the problem?

The majority of first psychiatric hospital admissions (admissions) are due to suicidality (1). In the UK, compulsory admission under the Mental Health Act is mandatory in cases of considerable danger to self, including suicidal ideation; the rate of compulsory admissions has increased fourfold from 1984 to 2016 (2). The Five Year Forward View for Mental Health (FYFVMH) highlights the number of people being detained and calls for intervention to prevent compulsory admissions, especially in men of African and Caribbean heritage, who are up to 6.6 times more likely to be admitted (3). People with SMHP, such as psychosis, bipolar and Emotionally Unstable Personality Disorder, are the diagnostic groups most likely to have an admission following contact with home-based treatment teams (HBTT) (4). FYFVMH requires increased "access to high quality care, that prevents avoidable admissions and supports recovery for people of all ages who have SMHPs and significant risk or safety issues in the least restrictive setting" (3). Admissions can have significant personal costs and are the most expensive form of mental health care (5). Many acute wards are not always safe, therapeutic or conducive to recovery (3, 6). Admissions are more problematic since COVID-19, with potential to transmit COVID-19 to ward environments or put someone at risk of infection if COVID-19 is present on the ward (7), particularly given the high rates of physical health comorbidities (cardiovascular and metabolic

problems) found in people with SMHPs (8). Mental Health Trusts in England have a target of reducing bed occupancy to 80% to allow infection prevention and control.

HBTTs are part of a UK strategy to provide community care to people with SMHPs who are in crisis, including suicidality, with the aim of reducing admissions (9). However, more than half of users of HBTTs have an admission within a year of discharge from hospital (10). Systematic reviews and meta-analyses of interventions to reduce admissions for people with SMHPs reveal a lack of evidence for effective interventions. There is an urgent need to identify interventions that reduce both admissions and pressure on HBTTs by addressing suicidality in people with SMHPs.

How does the existing literature support this proposal?

A systematic review of interventions to reduce early readmissions (11) identified 15 RCTs; a large proportion of these were delivered remotely via telephone calls and two studies included Peer Support (PS) as the intervention. Findings were encouraging, but studies had limitations including clinical heterogeneity, small sample sizes and low statistical power. A recent systematic review of interventions to reduce admissions (12) identified 19 RCTs and concluded that crisis planning, self-management, relapse prevention and monitoring show some efficacy; however, the limited number of studies and the heterogeneity of interventions suggest further research is required. A recent systematic review of self-management strategies for people with SMHP found that self-management had a significant effect at follow-up on the mean number of readmissions, with effects on length of admission at end of treatment and at follow-up; whilst these findings suggest that self-management approaches may be effective in reducing readmissions and length of stay, the authors recommend a high-quality trial of self-management strategies with admissions as the primary outcome (13). Our feasibility RCT showed that a self-management approach for patients admitted to UK general hospitals following a suicide attempt, which combined a safety plan (with identification of warning signs, distraction techniques and social/professional support sources) with follow-up telephone support (SAFETEL (14)) was feasible and acceptable.

Peer support is highly valued by service users, forming part of the vision for the future of mental health services (3). Employing people with lived experiences of SMHPs and recovery to work as Peer Support Workers (PSWs) is a preferred means of realising recovery principles in MH services (18). A systematic review and meta-analysis of PS found evidence that PS was associated with positive effects on measures of hope (19), which protects against suicidal ideation (20). The findings from this meta-analysis suggest a role for PS as an intervention to reduce suicidal ideation. Whilst the review found no effect of PS on hospitalisation, there were only two studies of PS which reported hospitalization as an outcome. Since the review, a RCT of a PS self-management program for people discharged from a crisis team found that a significant reduction in readmission to acute care (21). Our recent feasibility study of a structured PS intervention for suicidality, PREVAIL (Peers for Valued Living) (22) demonstrated feasibility and acceptability for PS specialists to engage patients at high risk for suicide in a supportive peer relationship.

Digital interventions have been proposed as a way to improve existing interventions for suicidality, extending the scalability and accessibility and allowing tailoring of the intervention to individuals based on their data (15). A recent systematic review of the effectiveness of digital interventions in reducing suicidality found, across four RCTs, an effect for psychological factors associated with suicidality (depression, distress, self-harm, coping and self-efficacy), but no direct effects for the reduction of suicidality.

A recent review of self-guided digital interventions for suicidality (16) explored the effectiveness of both direct (targeting suicidality) and indirect (targeting depression) interventions for suicide, identifying ten direct and six indirect web/app-based interventions for suicidality. Meta-analysis showed that direct self-guided digital interventions significantly reduced suicidal ideation post-intervention. The magnitude of effects was similar to the effect sizes identified in meta-analyses of face-to-face interventions for those at risk of suicide.

We have shown in an RCT that an online self-help program for adults designed to help reduce suicidal ideation (Living with Suicidal Thoughts: LwST) is successful in reducing suicidal thinking (17). This has been repurposed with considerable input from the lived experience community from a web-based intervention into a mobile app version to improve access (BrighterSide mobile app).

Existing systematic reviews and meta-analyses of interventions to reduce admission indicate that there is a need for high quality research. Given the heterogeneity in the clinical interventions offered across studies, a head-to-head comparison of promising psychosocial interventions, shown to be feasible and acceptable, would be an efficient and cost-effective approach to research in the area.

Initial evidence from systematic reviews indicated a number of candidate interventions to reduce admission via the target mechanism of suicidality, including PS, self-management strategies and direct digital interventions. The RAPID trial initially incorporated all three of these candidate interventions in the study design, which was a 4-armed multi-arm, multi-stage randomised controlled trial with three interventions: PREVAIL (peer support), SAFETEL (delivered by Assistant Psychologists) and the BrighterSide mobile app. A decision, ratified by the funder, our independent oversight committees (TSC and DMC) and the PPI group, was made in April 2023 to submit an amendment to remove the BrighterSide mobile app (class 1 medical device) arm. This decision was based on unpublished efficacy data from a large Australian randomised controlled trial which had a primary outcome of suicidal ideation, in conjunction with early engagement data from the RAPID trial, which showed low levels of use of the app by participants.

This protocol reflects RAPID as a 3-armed multi-arm, multi-stage randomised controlled trial with two interventions PREVAIL (peer support) and SAFETEL (delivered by Assistant Psychologists). RAPID will remain a clinical trial of a medical device until the last participant randomised to receive the BrighterSide app finishes in the 6-month intervention window and has been off-boarded from the app. Following this time, the RAPID trial will no longer include the BrighterSide mobile app (class 1 medical device) and as such, will not require regulation by the Medicines and Healthcare products Regulatory Authority. Processes outlined in study protocol v 5.0 06/MAR/2023 shall continue be adhered to for participants randomised prior to the switch to a 3-armed multi-arm, multi-stage randomised controlled trial, until the last participant randomised to receive the BrighterSide app finishes in the 6-month intervention window and has been off-boarded from the app.

Why is this research need now?

Admissions can have significant costs for the individual and their families including loss of relationships, employment and housing, stigma and traumatisation (5, 23), as well as financial costs for the NHS. Admission is often seen as unacceptable to many service users because it represents a restriction on personal freedom. Reducing admissions and suicide rates is a government priority, with a target for improving access to high quality care that prevents admissions for people with SMHPs (3). Psychiatric inpatients with SMHP are among the most vulnerable to COVID-19 due to a greater risk of transmission in ward settings and existing physical health comorbidities (7). There is already a large mortality gap, with people with psychosis living 15 years less on average (24).

There is a need for evidence-based interventions to reduce admission, via reduction of suicidality. Our focus on remote delivery of established brief psychosocial interventions, utilisation of different modalities of delivery that can provide sustainable and scalable solutions, that are also suitable for a pandemic context, will significantly advance treatment options.

Clinical trials in mental health have been criticised for being too small and not using efficient trial designs (25). Our proposal is for a large, multi-arm multi-stage (MAMS) design to answer a minimum of 3 clinically important hypotheses using the fewest number of participants, thereby maximising the use of resources and value for money.

Aims and objectives

Our primary aim is to answer the question of which brief, remote psychosocial intervention for people with SMHPs who report recent suicidal ideation, or a suicide attempt is most clinically effective and cost-effective in preventing avoidable admissions in comparison to treatment as usual (TAU), and to determine the safety of the interventions.

Specific hypotheses: compared to TAU, our brief, remote interventions plus TAU will lead to:

1) reduction in psychiatric hospital admissions over 6 months (primary outcome)
2) reduction in psychiatric hospital admissions over 3 months
3) reduction in suicidal ideation over 3 and 6 months
4) improvement in user-defined recovery and quality of life over 3 and 6 months

We also hypothesise that our interventions will be cost-effective over 6 months in comparison to TAU.

Research methods

We will conduct a 3-arm 2-stage trial, with blinded outcome assessment. It will compare TAU to two active comparators: TAU plus PREVAIL (Peers for Valued Living) and TAU plus SAFETEL. We will recruit adults with a SMHP diagnosis and current suicidal ideation from HBTTs across 4 UK cities with high levels of diversity and social adversity. Each intervention will be delivered remotely over a 3-month treatment window. All participants will receive TAU from HBTTs. Assessments will be conducted at baseline, 3 months (end of treatment) and 6 months (primary endpoint). The primary outcome is any psychiatric hospital admission over 6 months.

The multi-arm, multi-stage (MAMS) design enables early identification, and subsequent removal, of the least effective novel intervention, thereby increasing trial efficiency. In Stage 1, we will randomise participants in the ratio 2:2:3in favour of TAU using an independent remote web-based randomisation system (at King's CTU) using permuted blocks of random size stratified by site. An interim analysis will be performed using data from the first 385 participants with outcome data at 6 months. This will result in one or both arms being dropped for lack of benefit in Stage 2, with subsequent change to the allocation ratio of future participants to 1:1. Stage 1 will include an internal pilot (n=200) to test recruitment and other trial parameters, with progression criteria based on these (developed with the Trial Steering Committee and ratified by the funder) (26).

Internal pilot study progression criteria

Proposed length of internal pilot: 10 months (4 months recruitment and 6 months follow-up)

% Threshold*	Red	Amber	Green
Trial recruitment	<60%	60-99%	100%
Recruitment rate/ site/ month	0-5	6-9	At least 10
Number of sites opened	1-3	4	5
Total number of participants recruited	<120	120-199	200
Proportion receiving allocated intervention	<60%	60-79%	>=80%
Proportion with complete primary outcome data	<90%	90-94%	>=95%

Theoretical/conceptual framework

Admissions in people with SMHPs are commonly triggered by suicidal ideation and behaviour. Therefore, our interventions seek to reduce admissions by reduction of suicidal ideation. Each of these interventions is theory-informed, and they target established psychosocial risk factors for suicide such as entrapment and social connectedness. Predominant theories of suicide adopt an ideation-to-action framework which recognises that to reduce suicide, it is important to address the factors that lead to suicidal ideation, as well as those that increase the likelihood that an individual acts on their thoughts. For example, safety planning fits with the integrated motivational-volitional model of suicide (27), which has identified key volitional factors

governing the transition from suicidal thoughts and acts. Safety planning, which comprises 6 evidence-based steps, has potential to be effective because as well as targeting the escalation of suicidal thoughts it also reduces the likelihood that someone attempts suicide when they experience a suicidal crisis. PREVAIL is informed by the interpersonal theory of suicide (28), in which thwarted belongingness is a key process.

The intervention components broadly fall under four categories: building trusting relationships, bridging and engaging social connection, safety planning, and facilitating access to internal and external coping. Proposed mediators of change (reduction in suicidal ideation leading to reduction in admissions) can include: (1) access to a therapeutic relationship (including with a peer) (2) role-modelling of recovery and living well with SMHPs (3) reduction in entrapment (4) increased hope (5) access to social support (6) development of internal and external coping for suicidal thoughts. Intermediate outcomes include reduced admissions, reduced suicidal ideation, perceived burdensomeness and entrapment and improved social support and experience of compassion. Longer term benefits include service user benefit (improved recovery and quality of life) and service improvement (skilled workforce and a replicable model capable of implementation at pace and scale) and empowerment. The specific components and mediators involved in each intervention are outlined below:

Intervention	Trusting relationship	Role-modelling recovery	Social connectedness	Safety planning	Reduced entrapment	Increased hope	Internal and external coping
SAFETEL	X		X	X	X	X	X
PREVAIL	X	X	X	X	X	X	X

Sample size and design characteristics

We will randomise a maximum of 991 participants inclusive of 54 participants allocated to the BrighterSide arm of the study at the rate of 30 per month. We power for an expected difference in proportion of admission rates between arms of 7.5%, and an expected admission rate within 6 months in the TAU group of 15% (based on extensive audit data from our NHS Trusts).

The design follows the methods outlined for MAMS designs with binary outcomes (29) calculated using -nstagebin- in Stata. It uses the same outcome at both Stages and has a primary endpoint of 6 months after recruitment. The accrual rate was initially assumed to be 50 per month. The internal pilot ended on 31/05/2023 and following review of the internal pilot recruitment on 14/08/2023 by the funder, the monthly recruitment target was reduced to 35 per month with effect from 01/06/2023 in each stage and the loss-to-follow-up rate is 5%. One-sided significance levels of 30% and 2.5% and powers of 92% and 90% are used in the 1st and 2nd stages respectively. We will use a 2:2:3 allocation in favour of TAU and both comparator arms can continue to the 2nd Stage of the trial. Recruitment for stage 1 will continue whilst the interim analysis is being conducted and we will move seamlessly into stage 2 without a pause in recruitment between stage 1 and 2. In Stage 2, we will have keep the existing allocation or switch to 1:1 allocation if there is only one active intervention arm.

The interim analysis was scheduled after 452 participants provide 6-month outcome data. Following agreement from the funder, the interim analysis will take place after 385 participants provide 6-month outcome data, which will be in May 2024and provide 92% power. This was an unplanned change to the adaptive design. The interim analysis may result in one or both interventions being removed from the trial at stage 1 (power=92%, one-sided alpha=0.3). The final analysis has 90% power and a one-sided alpha = 0.025. The overall family-wise error rate (FWER) is 0.0397. There is no need to account for multiple testing in a multi-arm trial with independent comparators (30). We have allowed for a 5% missing data in the primary outcome (this is routinely available in electronic medical records, so we should have less than 5% attrition).

The total sample size of 991 represents the maximum possible sample size under the 2-stage MAMS trial design; the minimum sample size if both arms are dropped for futility at the interim analysis would be 684. We do not intend to suspend recruitment whilst the formal interim analysis is undertaken and results disclosed; due to the expected lag of 7 months (6-month data follow-up plus 1 month for data transfer, checking and interim analysis), approximately 175 further participants will have been recruited by the time of the interim decision-making.

Target population:

People experiencing a Serious Mental Health Problem (SMHP) who are at increased risk of psychiatric hospital admission (PHAs) due to suicidal thinking or behaviour.

Inclusion criteria

1. Currently receiving care from a Home-Based Treatment Team/ Crisis team or have done so within the last 14 days, since referrals to HBTT/Crisis team are associated with increased risk of a psychiatric hospital admission in the near future.
2. Aged 16+
3. Meet criteria for a diagnosis of SMHP (schizophrenia spectrum, bipolar, major depressive disorder, EUPD, PTSD or cPTSD) since these diagnoses account for the majority of PHAs for mental health difficulties
4. Experienced suicidal ideation or attempt within the last month / current crisis episode, as operationalised by answering 'yes' to items 1 or 2 of the Columbia-Suicide Severity Rating Scale.
5. Able to provide informed consent.
6. Receiving care from a Community Mental Health Team or Early Intervention Service, to ensure ongoing specialist mental health support following discharge from HBTT.

Exclusion criteria

1. Organic impairment, as this could be the cause of mental health symptoms rather than a SMHP.
2. Non-English speaking, since two of the interventions are remotely delivered talking therapies and one of the interventions is a smartphone app which has only been developed in English. Provision for non-English speakers would be impossible on both financial and logistical grounds.
3. Primary diagnosis of a drug or alcohol dependence, as this could be the cause of mental health symptoms rather than a SMHP.
4. Moderate to severe learning disability as confirmed by the participants responsible clinician in their care team
5. Immediate risk to others, for ethical and safety reasons
6. Currently receiving psychiatric inpatient care (since people in recent contact with crisis teams may have already been admitted to hospital)

Recruitment method and consent process

We will utilise multiple recruitment methods to ensure our recruitment strategy has maximum engagement of clinical services and reach to all potentially eligible service users. The initial recruitment approach will be as follows: (1) an engagement event with relevant teams (HBTT, liaison psychiatry etc.) and staff at each site to raise awareness of the study and (2) prior to the start of the study Principal Investigators and the trial manager will establish contact with the individual HBTT with initial presentations slots for the study start. The Principal Investigators will support initial liaisons to ensure maximum support and engagement between the study and clinical teams. The approach throughout the recruitment phase will focus on continued awareness and engagement with relevant services. We will achieve this by: (1) establishing regular contact between the Research Assistants (RA)/ Research Delivery Team (RDT) staff and services and where possible we will agree attendance at the service referral meetings and/or physically locate the RA at the service base. Continued

presence and awareness of the study will ensure fair access to all potential participants throughout the lifetime of recruitment by ensuring the HBTT have confidence in the study design and team. Where agreements are not in place to regularly attend the referral meeting, we will approach service staff to organise individual case load reviews to identify all eligible participants. We will work closely with the RDT at each site and utilise their expertise and knowledge of engaging these services. Where in place, we will utilise local NHS Trust Standard Operating procedures (SOP) for delegation of screening and first contact from service staff to the RDT. We will provide all relevant staff members with a study leaflet, poster and access to a brief animation to outline the study. We have successfully utilised these approaches on our other NIHR funded studies (FOCUS; MAPS; SAFETEL).

Verbal consent to contact will be sought by the potential participant's clinician in the HBTT. To aid this initial discussion all potential participants will be provided with access to a study leaflet and access to a brief animation that explains the study rationale and some of the design elements that may be unfamiliar e.g., randomisation. Use of an animation will provide maximum reach to those who may find spoken word and visual presentation more accessible than written word. Prior to taking written informed consent, all potential participants will be provided with a Participant Information Sheet (PIS). To ensure the information sheet is accessible and written in the least technical language we will produce the information materials with Patient and Public Input (PPI). Participants will be given at least 24 hours to consider the information before providing written informed consent. During the COVID-19 pandemic this will be either emailed to the potential participant or sent to them in the post. We will utilise existing approaches to taking consent remotely approved by the sponsor including audio recording the consent visit and obtaining written consent when it is possible to meet with the participant face-to-face. Audio recording will be done in line with the sites NHS policy and procedures. Audio recording of consent will follow the sites local NHS Trust policies and procedures. Audio recordings will be transferred to a secure NHS drive and will only be accessible by members of the research team with delegated responsibility to access, as per the study delegation log.

Type and content of participant information materials

With input from service users who have lived experience of a SMHP and a suicidal ideation /suicidal attempt we will produce a study leaflet, an informational animation and a Participant Information Sheet (PIS). Work with our panel of service users will include identifying key questions they have about the study to ensure these are addressed within our informational material. We will seek guidance on how to appropriately and sensitively address potentially distressing topics such as suicidal ideation/ intent. To ensure we develop easy to read materials we will explain in lay terminology research concepts i.e., information about the research blind, randomisation and the interventions. Where possible, the information materials will utilise pictures/infographics. The content of the PIS will comply with the requirements set out in ICH-GCP Topic E6 R1. On request we will provide the written material in other accessible formats such as large print or coloured paper or in audio-recorded format for people with visual impairments.

Overview of research methods to capture data from participants and their frequency

We will offer choice regarding the methods of data collection i.e., face-to-face or remote delivery. If a service user is unable to participate due to lack of a telephone/ mobile phone, then we would provide them with a mobile phone. For ethical reasons, if we provide a participant with a mobile phone we will allow them to keep it after they exit the trial in order to prevent reinstating digital exclusion and digital poverty for those that required a phone. Public and Patient Involvement (PPI) consultation highlighted the ethical importance of not reinstating digital exclusion and digital poverty by removing the mobile phone from a participant who clearly required one for participation. The frequency of data collection is three time points: baseline, 3 months and 6 months. We have carefully selected the research assessment time points to ensure we can address the research question whilst balancing this with minimising participant burden. For participants who request data collection via face-to-face methods we will use an assertive outreach approach to data collection that will be flexible, pragmatic and driven by service-user choice. We will agree with participants preferred methods for reminding them of appointments for research assessments including text and letter prompts. We provide more details in the section titled "Risks and Anticipated Benefits".

Study participant support

We will utilise protocols for study participant support from our previous NIHR funded trials to minimise drop-out. These approaches centre on minimising burden and ensuring appropriate support throughout the assessment process. Our research staff (RAs, Assistant Psychologists and Peer Support Workers) will have training in person-centred support and have access to regular supervision with trained psychologists/ therapists to ensure any distress that may arise throughout the assessments or interventions is appropriately addressed. The following approaches will be taken offer of a supportive follow-up call with a RA within 48 hours of a research assessment (remote or face-to-face) to discuss any issues that may have arisen for them after completing the measures, (2) offer of a 'Helpline Numbers' card that will detail national and local helpline numbers; and (3) ordering of outcome measures in priority and reminders regarding choice to decline questions/ measures and take breaks whenever required. We provide more details in the section titled 'Risks and Anticipated Benefits'.

Methods for sharing study progress and findings with study participants

We will provide participants who take part in Stage 1 with a summary of the internal pilot and feasibility results. Findings from the end of Stage 2 will be provided to all participants including those who took part in Stage 1. PPI will be integral to producing summaries of the research finding to ensure accessibility as outlined above and where possible we will employ infographics to summarise the main findings. To ensure maximum connection to the study participants we will disseminate the results via multiple modalities. Throughout the lifetime of the study, we will host regular updates regarding the study progress on the project website and provide all study participants with a link to ensure continued engagement with progress.

Payments, rewards and recognition for study participants.

Participants will receive a token of appreciation of £10 per research assessment (£30 in total).

Equality, Diversity and Inclusion for study participants

Every person eligible to take part in research will be offered the same opportunity of taking part in that research regardless of protected characteristics. We will inspect data from each site to indicate the population characteristics of people with SMHP presenting to services with suicidal ideation/ intent. We will monitor recruitment in relation to the population characteristics of the study sample with our Trial Steering Committee and independent Data Monitoring and Ethics Committee. We will ensure that our SURG has appropriate representation of the study population. As there may be geographic variation and specific issues relating to the local population, we will also establish local expert advisory panels (LEAP). Our SURG and LEAPs will be established prior to the start of the study to ensure they can make specific recommendations on potential barriers and facilitators to engagement in advance of the recruitment starting. In particular, recommendations for our informational materials, recruitment approaches and staff cultural competence will be reviewed. Whilst participants will require sufficient command of English to complete written informed consent, assessment measures and engage with the interventions, this does not exclude people with English as a second language and we take every measure possible within the protocol and funding arrangements to engage a potential participant who does not have English as a first language; for example, where spoken word is more accessible than written we will provide materials in spoken word. If a participant is unable to take part in the study because they do not have access to a telephone/ mobile phone then they will be offered a mobile phone and data plan to ensure no person is excluded from the project on the basis of digital poverty. For ethical reasons, based on the feedback of our PPI consultation, participants who are provided with a mobile phone will be allowed to keep the mobile phone after they exit the trial to prevent reinstating digital exclusion and poverty by removing the mobile phone.. We will seek guidance from our SURG and LEAP regarding staff training and ensuring a culturally competent research team. Racism and structural discrimination towards people from Black and other minority ethnic communities may act as a barrier to engaging in the study due to understandable mistrust; we will review equality and diversity issues regularly within our SURG and local LEAPs.

Health technologies to be assessed

SAFETEL

SAFETEL is a brief, innovative evidence-based clinical intervention. It is telephone-delivered (although can include use of video-conferencing software) and is implemented by assistant psychologists (APs). In the initial phase of delivery, a safety plan is developed collaboratively. It has six components: i) identifying warning signs of an impending suicidal crisis; ii) utilising internal coping strategies; iii) engaging social contacts & social settings to distract from suicidal thoughts; iv) contacting social supports for assistance in resolving the suicidal crisis; v) contacting mental health professionals; vi) minimising access to lethal means.). The suitability and likelihood of employing these strategies during a suicidal crisis is explored, as well as examples of such strategies being provided. Follow-up contacts are provided over a period of 12 weeks. The follow-up calls comprise three components: 1) suicide risk assessment and mood check; 2) review of the participant's safety plan, with revisions made if required; 3) supporting treatment engagement through exploration of barriers to engagement, motivational enhancement, problem-solving and support.

The core element of SAFETEL is the collaborative development of the Safety Plan (within the 1st session). This is a prioritised list of coping strategies and supports that individuals can use during or preceding suicidal crises. It has been developed to also address challenges in continuity of care across vulnerable transitions. SAFETEL incorporates telephone follow-up in order to conduct periodic risk assessment and mood checks. This allows for the continuous review of the Safety Plan and provides opportunities to problem-solve obstacles to treatment and help with linkage to services, if necessary. It actively incorporates evidence-based suicide prevention strategies, including facilitation of problem solving and coping skills, identification and use of social supports and emergency contacts, lethal means restriction, service linkage, and motivational enhancement to promote community treatment engagement.

APs will deliver the intervention and will be trained by Professor Rory O'Connor based on training developed in the United States. They will receive refresher training once during the intervention delivery period. Fidelity to delivery will be checked in an ongoing way and feedback given to staff with opportunities for further refresher training if required. With participants' consent, all sessions will be audio-recorded. Audio recording will be done in line with the sites NHS policy and procedures. Audio recording of consent will follow the sites local NHS Trust policies and procedures. Audio recordings will be transferred to a secure NHS drive and will only be accessible by members of the research team with delegated responsibility to access, as per the study delegation log. Fidelity of intervention delivery will be checked in different ways for the initial safety planning sessions and follow-up sessions. For the initial sessions, 20% of the recordings will be randomly selected to check fidelity against a standardised rating scale of fidelity for the Safety Planning Intervention. These will be double coded by another team member and tested using Cronbach's α to test inter-rater reliability. A standardised checklist for the follow-up support calls will be completed by the research team to enhance intervention fidelity and the results will be reported descriptively. Adherence will be defined as attending the initial safety planning session and at least one follow-up call.

PREVAIL (Peers for Valued Living)

Up to 12 remotely delivered sessions of PREVAIL over 12 weeks (choice of telephone or video-conferencing delivery will be offered). It is delivered in three phases: i) assessment and getting to know you ii) active involvement and iii) ending and consolidation. The intervention utilises common elements of PS, including supportive listening and sharing of one's own recovery story; such activities are adapted to working with people at high risk for suicide. In addition to adherence to principles and values of PS (shared lived experience; reciprocity and mutuality; validating experiential knowledge; choice and control; discovering strengths and making connections), semi-structured conversations incorporate suicide prevention strategies derived from cognitive behavioural therapy (CBT) and motivational interviewing, including goal setting, distress tolerance, and increasing optimism and social connectedness. These conversations use a standardised format including the steps of Invite, Learn, Share, and Motivate (ILSM). In the Invite step, permission is sought from the

participant to have a conversation about a hope or belongingness-related topic. During the Learn step, information regarding what the participant has already tried and what the participant thinks might be helpful or relevant to their situation is elicited. During the Share step, helpful suggestions are made on the basis of the PSW's personal experience or knowledge. Finally, the Motivate step engages the participant in "change talk," including how taking action might be helpful to them and how they might implement changes (31).

These sessions also involve safely addressing suicidal crises; to detect and address acute suicide risk, PSWs ask about suicidal thoughts or behaviours at each encounter. If endorsed, the PSWs use a scripted risk assessment algorithm to gather additional information regarding any recent suicidal behaviours, whether suicidal ideation has worsened since the thoughts were last discussed with a clinician and the person's level of intent to act upon their thoughts. If any of these risk factors are present, the PSW would then immediately contact the mental health clinician on-call for the study to review the assessment with the patient still present, and it would be the clinician's responsibility to determine the necessary next steps to ensure safety.

It is expected that the final phase, focusing on endings, consolidation and future directions (including future access to peer support) will span sessions 11-12 (approximately), although endings and the time-limited nature of PREVAIL will be regularly discussed throughout all phases. The PSW may transition to a step-down phase at session 10 by moving to fortnightly contact. The aim of the final sessions is to consolidate learning, review what has been helpful and develop a plan to maintain gains. The format of this work will be flexible.

It is expected that peer relationships will offer emotional and instrumental support and promote hope through role modelling. PSWs will offer validation of the person's suicidal experiences and concerns by showing understanding through their own experiences and enabling the participant to engage in talking about their experiences and concerns relating to suicide and hopes for the future. These principles will be reflected in the fidelity checklist to ensure principles are adhered to; fidelity will be monitored using both PSW reports regarding session content and audio-recordings of sessions. Audio recording will be done in line with the sites NHS policies and procedures. Audio recording of consent will follow the sites local NHS Trust policies and procedures. Audio recordings will be transferred to a secure NHS drive and will only be accessible by members of the research team with delegated responsibility to access, as per the study delegation log. Adherence to the intervention will be defined as attending at least two peer support sessions.

We have experience from policy and practice development (Scottish Recovery Network), previous RCTs delivering peer support, including telephone-delivered, (32, 33) and from local NHS peer support implementation (at GMMH) in developing and delivering training to PSWs. We also have access to the PREVAIL training that was developed in the US. The pace and timing of the training will ensure sufficient time to skill-up the PSWs. Training will be principles-based as outlined above and will also focus on the suicide prevention specific strategies available in the PREVAIL toolkit. Gillard, Kotecha-Hazzard, Pyle, Peel and Pfeiffer will deliver a rolling programme of training throughout the trial. This will allow reflective learning, guidance and further development and will ensure continued fidelity to the manual. All PSWs in participating centres will receive weekly supervision and we will facilitate peer to peer meetings to ensure connection and support across centres for the PSWs.

The PSWs will be NHS employees with NHS mandatory training on safeguarding vulnerable adults. Recruitment of peers will be informed by a body of guidance from the ImROC programme (Implementing Recovery through Organisational Change), commissioned by the Department of Health, which has worked with 29 NHS mental health service providers and their partners. Following current recommendations we will make the purpose and function of the role clear through the recruitment process, and the selection process will include assessment of the applicant's readiness to cope with the demands of the post properly assessed as part of selection (34). We will require a minimum of at least one-year experience as a PSW. Each site has been selected as they are NHS Trusts which have demonstrated an existing commitment to PSW roles.

Comparator

The control condition is TAU, consisting of multi-disciplinary care delivered by HBTTs. Different psychosocial interventions are recommended in NICE guidelines for the different diagnostic groups, so there is no single active comparator that would be suitable. We will not ask referrers to withhold any treatment. All routine or additional treatments will be monitored.

Randomisation

Following informed and written consent, eligible participants will be randomised within 2 working days. King's Clinical Trials Unit (KCTU) will support the development of the randomisation system, which we have used successfully in several multisite trials with the same trial statistician (Professor Emsley). In Stage 1, randomisation will be in the ratio 2:2:3 to the groups and will be stratified by site. Randomisation (at the individual level) will be independent and concealed, using randomised-permuted blocks of random size , which will be administered via a study-specific web-based portal developed by KCTU. The allocation is made known to the Trial Manager (in order to monitor adherence to the randomisation algorithm), the Trial Administrator and APs/PSWs by email. The allocation is also made known to the participant by letter and phone call. Blinding of the allocation code of a subject will be maintained for Research Assistants (RAs) until all outcome measures for that subject have been collected. In Stage 2, we will retain 2:2:3 allocation in favour of TAU if both interventions continue or switch to 1:1 if only one intervention carries forward into Stage 2. We will prepare two randomisation systems so we can switch seamlessly to the new system without pausing recruitment following the interim analysis.

Protection against bias

Our primary outcome is objective (admission to hospital (yes/no), so should not be subject to rater bias. Assessors will be blind to treatment condition. Blindness will be maintained using a wide range of measures which we have implemented successfully in many of our single blind trials. These include separate offices for the PSWs/APs and RAs, protocols for answering telephones including reminders for clinicians, participants and family members about the blind, protocols for message taking and secretarial support, separate diaries and pigeonholes and data file security, using passwords and encryption of randomisation information. We will develop a standard operating procedure (SOP) for maintaining, recording and managing blinding, which will outline all of these procedures. This SOP will be reviewed by, and agreed with, our oversight committees. Each researcher will sign this SOP to confirm they understand and will comply with the blinding procedures. All blind breaks will be recorded by the Trial Manager and reviewed by the Chief Investigator for patterns in unblindings. There is only one follow-up scheduled during the intervention window (at 3 months, after end of treatment). This will reduce the risk of blind breaks occurring because of APs/PSWs and RAs crossing paths for visits, and it will reduce the opportunity for unblinding to occur because of communication with participants to arrange visits. Maintaining rater blindness to treatment allocation is crucial, and the DMC and TSC will regularly monitor unblindings by each centre and implement corrective action if necessary. All letters to participants and clinicians will contain a standardised statement about the need to maintain the single blinding process. Where possible, we will identify an independent assessor with whom the blind has not been broken to complete subsequent follow-ups, subject to any threats to participant engagement with follow-up.

Minimising attrition

Our primary outcome of admissions is collected from routine electronic care records and so we expect almost no missing data. We allow for a small amount of consent withdrawal and other factors at a conservative level of 5%. For the secondary clinical measures, a 20% loss to follow up is approaching the upper limit beyond which the validity of trial findings would be jeopardised. Our research group is very experienced in psychosocial intervention, SMHP and suicide prevention trials and we have achieved loss to follow up rates considerably less than 20% - for example, the FOCUS trial (with the same chief investigator and trial manager – now co-CI - combination) randomised 487 participants with psychosis over 5 sites and had attrition rates of approximately 10% at both end of treatment and final 21-month follow-up. We are, therefore, confident that we can achieve an attrition rate less than 20% for our secondary outcomes, and as indicated we will use a variety of evidence based strategies (including compensation of participants – we are requesting a working

budget of £30/head or £37050 to provide the participants with cash or vouchers following a systematic review of what improves retention in clinical trials (35).

Setting/context

The study will be conducted in HBTTs within secondary care MH services at 5 UK centres (Glasgow; Manchester; Oxford; London East and London Northeast).

Data collection and analysis

Acceptability of treatment will be measured using treatment drop-out rates. Treatment effectiveness will be assessed in terms of reduction in hospital admission. Therapeutic improvement will also be assessed using rate and degree of suicidal ideation, recovery from psychosis, hope and overall health status and utility. Assessors, who will be blind and independent to treatment group, will conduct all assessments at baseline, 3 months (end of treatment) and 6 months post-randomisation (primary endpoint).

Assessment schedule, administration, staff training, reliability and validity

All outcome measures will be administered at baseline and subsequently at 3 months (end of treatment) and 6 months (follow-up) by RAs who will have been trained in the use of all the instruments and scales, to achieve a satisfactory level of inter-rater reliability. Regular training sessions including the use of video and role play will be conducted with all RAs in order to maintain reliability and prevent rater drift. Participants will be offered choices regarding length of assessments, including the option of breaks and multiple occasions. Assessment measures will be clearly prioritised so that the most important will be collected first to minimise missing data. We will have a standard protocol for managing any distress that is associated with the completion of measures, which we have successfully utilised in several trials and has been developed in collaboration with service users; this includes telephone contact within 48 hours of assessments in order to check on participant well-being. Following consultation with our PPI group we offer participants a thank you card for completion of each research assessment timepoint.

Statistical analysis

A detailed statistical analysis plan for the primary and secondary outcomes, including the economic analysis, will be approved by the DMEC and TSC before first interim analysis of unblinded data. Interim and final analysis of the primary outcome (admissions) will be carried out blind to treatment arm allocation and independently by two trial statisticians.

We will report data in line with the CONSORT-SPI and CONSORT-multi arm statements showing numbers analysed at each follow-up stage, attrition rates and loss to follow-up. All analyses will be carried out using the intention to treat principle, incorporating data from all participants. Every effort will be made to follow up all participants in all arms for research assessments, including the arm which is dropped at Stage 1.

Analyses will be conducted in Stata version 16 or later. Descriptive statistics within each randomised group will be presented for baseline values. These will include counts and percentages for binary and categorical variables, and means and standard deviations, or medians with lower and upper quartiles, for continuous variables, along with minimum and maximum values and counts of missing values. There will be no tests of statistical significance or confidence intervals for differences between randomised groups on any baseline variable.

Stage 1 interim analysis: At stage 1, at least 153 participants will be analysed in the control arm and at least 102 in each experimental arm. We use the significance level as the critical value for the p-value of the observed treatment effect as this controls the type I error rate at the nominal level regardless of the true control event rate (36). Recruitment will continue to the experimental arms whose treatment effect estimate is significant at the one-sided 30% level, otherwise consideration is given for ceasing further randomisations to it. Between-group evaluation of secondary outcomes will be focused on Stage 2 analysis only.

Stage 2 analysis: A pairwise comparison of all experimental arms to control arm will be made, including the arm dropped for further randomisations in Stage 1. If the treatment effect estimate on the primary outcome is significant at the 2.5% one-sided level in the final analysis, then the experimental arm will be declared superior to the control arm. Under the design operating characteristics, the one-sided pairwise error rate is calculated to be 0.0213, and the family-wise error rate (FWER) is 0.0403.

The primary outcome (any admission at 6 months) will be analysed using a generalised linear model that includes fixed effects for treatment, diagnosis and site. For each pairwise comparison with TAU, we will report the difference in proportion of admissions as the estimate of treatment effect, as this is estimand driving the sample size calculation.

Secondary outcomes with repeated measures at 3 and 6 months will be analysed with generalised linear mixed models appropriate for the distribution of the outcome. Fixed effects will be treatment, diagnosis, site, time and time*group interactions, with a random effect for participant. Treatment effect estimates will be reported separately as adjusted mean differences in outcomes between the groups with 2-sided 95% confidence intervals and 1-sided p-values. We will check for differential predictors of missing outcomes by comparing responders to non-responders on key baseline variables. Any significant predictors will be included in the analysis models. This accounts for missing outcome data under a missing at random assumption, conditional on the covariates included in the model.

Health economic analysis

A within trial economic analysis will compare the net costs and health benefits of the included interventions plus TAU to TAU alone over the 6m trial follow-up, from the NHS and Social Care (costs) and patient (health benefits) perspective. The primary measure of health benefit will be quality-adjusted life-years (QALYs) estimated from the EQ-5D-5L and the utility tariffs recommended by NICE at the time of the analysis.

Health and social care service use (self-report supplemented by electronic medical record review for psychiatric hospital admission data) and EQ-5D-5L data will be collected for each participant at baseline, 3 months, and 6 months. Service use data will include face-to-face as well as telephone and remote contacts.

Primary care, secondary care and community service use will be collected via self-report using an economic patient questionnaire (EPQ) developed and used by the applicants in previous trials and adapted for this study. The UK literature recognises that issues with electronic routine data sources may result in self-reported data being the preferred option (41). Due to the unfeasible nature of accessing and extracting service use from routine electronic data sources, the trial will collect only psychiatric inpatient admissions from hospital record data (these are likely a key driver of costs in this population). With the rest being taken from the self-report questionnaire (EPQ), as this is being collected during interview, there is the opportunity to limit missing data as the research team can prompt and explain questions to participants. Research Assistants will be reminded of the importance of this data and encouraged to speak directly to the health economics team whenever they have queries. Items of resource use will be multiplied by published national health and social care costs (Department of Health Reference Costs; Unit Costs of Health and Social Care, PSSRU). The EPQ will be discussed and piloted with the SURG prior to being finalised for the start of the trial.

Multiple imputation will be used to impute missing observations. The analyses will control for key baseline covariates or characteristics (demographic, socio-economic and clinical measures) identified from the published literature and supplemented with analysis of pooled baseline data.

The cost and outcome effects will be bootstrapped to generate incremental cost-effectiveness ratios, cost-effectiveness acceptability curves and net benefit statistics. Cost-effectiveness acceptability curves (CEACs) will be plotted to summarise uncertainty associated with the ICER. To derive CEACs, the incremental cost and QALY (effect) estimates from the regression analyses will be bootstrapped to simulate the sample data of costs and QALY. The bootstrapped estimates of net QALYs will be revalued, using a range of ceiling ratios or

willingness to pay thresholds (WTPT) to gain 1 QALY. For each WTPT, a net benefit statistic (NB) will be estimated as:

NB = E * WTP – C

Where E = incremental QALY gained by intervention, WTP = willingness to pay to gain 1 QALY, C = incremental cost of intervention.

In the UK there is no universally agreed cost-effectiveness threshold value. One commonly reported threshold is from NICE in England of approximately £20,000 to £30,000 per QALY (37). However, there is a lack of consensus around the appropriate threshold (38, 39). Therefore, the monetary value of simulated QALYs will be varied from £0 to £30,000 to reflect a range of hypothetical willingness to pay thresholds.

As the analysis is comparing multiple options, a sensitivity analysis will adopt a fully incremental approach. Sensitivity analyses will also assess the choice of health benefit measure (QALYs calculated using ReQOL-10 as an alternative measure, suicidal thoughts, etc) and the impact of missing data (as statistical analysis).

All economic analyses will be pre-specified in an Economic Analysis Plan to be agreed with the TSC and IDMC. Reporting will be in line with the CHEERS statement (40).

Outcomes

Primary Outcome

The primary outcome measure will be any psychiatric hospital admission over 6 months (treated as a dichotomous variable) which will be taken from participant electronic medical records.

Secondary outcomes

Secondary outcomes include suicidal ideation and behaviour, NHS and social care use, hope, entrapment, user-defined recovery, quality of life, health status, anxiety, depression, death and safety (adverse and serious adverse event profile of the interventions).

1. Suicidal thoughts and behaviours using The Columbia–Suicide Severity Rating Scale (42), which is an interviewer rated measure that can be administered face-to-face or remotely.
2. Recovery will be assessed using a service-user defined self-report measure of recovery, The Process of Recovery Questionnaire (43)
3. Health status will be evaluated using the EQ-5D-5L, which is a generic and validated health status questionnaire shown to have acceptable validity in people with schizophrenia in European countries (44).
4. The Recovering Quality of Life (ReQoL-10) measure focuses on aspects of recovery and quality of life and was designed for use in a broad range of mental health conditions (45). It was collaboratively developed with service users and clinicians.
5. Wider NHS and social care use will be assessed by an economic patient questionnaire which will be adapted from questionnaires used in similar populations (46)
6. Anxiety will be measured using the GAD-7 (47).
7. Depression will be measured using the PHQ-9 (48).
8. Hope will be measured using the Adult HOPE Scale (AHS) (49), which is an 8-item self-report questionnaire.
9. Entrapment will be measured using the 4-item self-report Entrapment Scale Short-Form (50).
10. Adverse effects measures on exit from the study at 6-month assessment (51)

Adverse events (including death) and intervention related adverse effects will be monitored.

Withdrawal Criteria

A participant is free to withdraw from the trial if they wish to do so, without giving a reason and without it affecting their care.

A participant who chooses to withdraw from an intervention arm may continue with the research assessments if they wish. A participant who chooses to withdraw from the intervention arm plus research assessments will be asked for permission to check their medical records for the primary outcome data of hospitalizations for the period of time they would be involved in the trial (six-month period). Where agreement is provided to check medical records for the primary outcome data of hospitalisations, this agreement shall be documented in the participants medical records to evidence the discussion and agreement.

The researcher taking the withdrawal information should complete the RAPID trial withdrawal form and provide this to the site lead and trial manager to update participant records.

Participants who withdraw will not be replaced.

The sponsor may suspend or prematurely terminate the clinical investigation at an individual investigation site or the entire clinical investigation for significant and documented reasons, such as when recommended by the iDMC.

If suspicion of an unacceptable risk, including serious health threat to subjects, arises during the clinical investigation, or when so instructed by the EC or regulatory authorities, the sponsor shall suspend the clinical investigation while the risk is assessed. The sponsor shall terminate the clinical investigation if an unacceptable risk which cannot be controlled is confirmed. The sponsor shall consider terminating or suspending the participation of a particular investigation site or investigator in the clinical investigation if monitoring or auditing identifies serious or repeated deviations on the part of an investigator. If suspension or premature termination occurs, the terminating party shall justify its decision in writing and promptly inform the other parties with whom they are in direct communication. If, for any reason, the sponsor suspends or prematurely terminates the investigation at an individual investigation site, the sponsor shall inform the responsible regulatory authority as appropriate and ensure that the EC is notified, either by the principal investigator or by the sponsor. If the suspension or premature termination was in the interest of safety the sponsor shall inform all other principal investigators.

Access to or breaking the blinding code in the case of suspension or premature termination would be decided by the independent iDMC.

End of trial

The end of recruitment will be 31st May 2025. The last visit for follow-up will be 30 November 2025. The end of trial is defined by completion of data analysis and the final funder report submitted, which will be 31st January 2026.

Project timetables including recruitment rate

A Gantt chart is provided as an appendix.

Prior to the start of the study: This phase covered paperwork for ethics, HRA and NHS Capacity and Capability (C&C) approvals. site engagement with senior managers, clinicians and service users in the services participating in the study to raise awareness of the study before recruitment commences and to ensure sign off from senior managers. The first Service User Reference Group (SURG) before month zero to inform the development of study materials (information sheet, leaflets, and advertisement materials) and pilot the full assessment pack. Formation of our panel of additional local volunteer advisors at each site to ensure diversity of perspectives and service user experience, their expertise will be utilised to develop localised user-led information and resources. Tecruitment process for PSWs before month 1 to ensure that PSW are in post for month 1. Based on previous experience (32), we projected that this time will be required to ensure that the

necessary checks are in place i.e. DBS and Occupational Health checks. To facilitate the process, we approached the NHS Trusts to identify existing peer members of staff who have substantive contracts and can take on the role as a personal development opportunity. Ensuring these processes began before month 1 allowed room for any delays in staff recruitment and ensured timely start to the internal pilot.

Months 1-3 (study set-up): this phase covered: ethics, HRA and local NHS Capacity and Capability approvals, establishing the TSC and IDMC, harmonising the interventions for our context and finalising the treatment manuals for the adaptions of PREVAIL and SAFETEL, finalising the adaptation and site testing of the Brighter Future app, staff training for APs, PSWs and RAs by the end of month 3 with an extended PSW training period across months 1-3, to accommodate part-time staff working patterns and ensure sufficient time for both local and trial training. Site initiation meetings in month 3. The study web-based randomisation platform, data collection and data entry system and website will be in month 3. We will develop a film to explain the study to service users and staff.

Months 4-7 (Internal pilot recruitment): this phase covered the recruitment for the internal pilot in months 4-7, providing a total of 4 months to recruit (total n=200, which equates to a minimum of 10 per month per site).

Months 8-27: Stage 1 recruitment started after the internal pilot in month 8 and will be completed by approximately end of month 27 (end of June 2024). Stage 1 recruitment includes the pilot participants. In month 26 (May 2024), an interim analysis was conducted after 385 participants recruited to PREVAIL, SAFETEL and TAU who have reached and provided the 6-month endpoint, progression criteria data was presented to oversight committees for review and recommendations (6-month outcome data available on pilot participants); red-amber-green progression criteria reviewed. Recruitment target amended to 35 per month from 01/06/2023 following progression criteria review by the funder and oversight committees. Stage 2 recruitment reduced from 35 to 30 per month following review by the funder in June 2024.

Months 28-38: At the time of producing v9.0 of this adaptive design protocol, we expect Stage 2 recruitment to commence in month 28 (approximately 1st July 2024) and be completed by month 38 (31st May 2025) with trial recruitment at 30 per month. Final total sample size will be a 991 (inclusive of 54 participants allocated to BrighterSide).

Months 4-41: Intervention delivery for the internal pilot and definitive trial

Months 7-41: end treatment assessments for the internal pilot and main trial.

Months 10–44: 6-month follow-up assessments.

Months 45-46: Statistical analysis and write-up of main trial paper and monograph.

A summary of the project plan can be seen in Appendix 1.

Research Expertise in our Team

Morrison has been CI of numerous NIHR multisite RCTs examining CBT for psychosis. Pyle has managed these RCTs and is CI of a RCT of Peer Support (PS) for psychosis. Gillard is CI of a NIHR RCT of PS. Freeman, Gumley and Bucci have led NIHR studies of interventions for psychosis. Wood is CI of a RCT for crisis intervention in psychosis. Bradstreet has expertise in PS. O'Connor, Simpson, Christensen and Pfeiffer have expertise in suicide prevention, including development and preliminary evaluation of the candidate interventions. Bucci, Gumley, Kotecha-Hazzard, Allan and Christensen have expertise in digital intervention trials of smartphone apps for SMHPs. Emsley has expertise in trial design and analysis, as well as leading CTU involvement. Shields has expertise in health economics evaluations of mental health interventions. Allan, Longden and Peel have personal experience of SMHPs in addition to experience of involvement deign and conduct of SMHP-related clinical trials. Freeman, Emsley and Bucci are previous or current NIHR Research Professors. Davies (health

economics), Haddock (suicide prevention in psychosis) and Kapur (suicidal behaviour) will provide consultative expertise as named collaborators.

Applicant Roles in the Trial

Morrison and Pyle will be Chief Investigator and Trial Manager. Freeman, Gumley, Gillard, Morrison and Wood will lead the sites. Shields will conduct health economics analyses and Emsley will be the Trial Statistician. Bucci will be responsible for ensuring good practice and compliance with frameworks for digital interventions. Kotecha-Hazzard will coordinate the peer support training and supervision and be responsible for fidelity of peer support. O'Connor will provide consultancy and advice regarding the SAFETEL intervention and lead the training of staff to deliver the safety planning intervention. Simpson led the process evaluation of the SAFETEL intervention and will advise on implementation and assessment of fidelity across the interventions. Pfeiffer will lead the PREVAIL training and fidelity. Christensen has provided access and support for the BrighterSide app under the previous trial protocols. Allan, Longden and Peel will provide lived experience expertise to the trial management structures and lead PPI activities including SURG and local LEAPs.

Patient and Public Involvement

We have been developing our work on suicide prevention and peer support in collaboration with users and carers for many years. This proposal was developed in consultation with our existing SURG (10 people with psychosis) and 3 service user applicants. We have obtained feedback from PSWs working with people with SMHPs regarding process and content of peer support.

Management of the trial will include 3 service user applicants, plus governance through PPI members of the TSC. The trial will be further developed and implemented in collaboration with service users using a study specific SURG, which will consist of service user applicants and ten service users with experience of SMHP from each site. SURG will provide input at all phases of the research and dissemination. SURG will purposively recruit members from BAME communities to ensure the diversity of the population is represented. We will also have local LEAPs at each site.

Clinical Trials Unit Involvement

The trial will be run under the processes of the King's Clinical Trials Unit (KCTU; UKCRC registration number 53). KCTU has internationally recognised expertise in the design, conduct, analysis and reporting of multicentre mental health trials. Professor Emsley will take responsibility for the conduct of the trial processes and has been fully engaged with the CI throughout the planning stage to ensure the optimal scientific design, with the best and most appropriate analysis and suitable methods of managing and conducting the trial. The statistician will take responsibility for all aspects of the statistical analysis This will adequately support the trial's statistical needs (including specification of the randomisation system, liaison with database managers, preparation of the Statistical Analysis Plan, creation and delivery of progress reports to the TSC and IDMC, assist in enhancing the quality of the trial data by monitoring of accumulating data, and conducting all statistical analyses for the final data set). The development of MAMS studies in mental health is a goal of Emsley's NIHR Research Professorship and the KCTU.

Paper source data worksheets will be completed at sites and transferred to a web based electronic data capture system backed by an electronic data management system (InferMed MACRO version 4; KCTU) that will be hosted on a dedicated server within KCL. The system is compliant with Good Clinical Practice. The web-based system will be available for access 24 hours a day to authorised users. Roles will be assigned to users, giving the ability to enter data relating to participants or to view data and raise discrepancies. A full audit trail of data entry and any subsequent changes to entered data will be automatically date and time stamped, alongside information about the user making the entry/changes within the system. No data will be entered onto the system unless a participant has signed a consent form to participate in the trial. The system is programmed to perform validation checks, such as range checks to prevent data entry errors. Missing data

codes are routinely programmed into all fields, for ease of analysis. The system is also programmed to flag up when a missing data code is entered, to aid monitoring. A standard feature of InferMed MACRO data entry system is the built-in audit trail on all data fields, the automatic saving of data as you leave a form, and the ability to maintain a record of 'source data verification' checks. No data will be amended independently of the study site responsible for entering the data. Data entered from paper source worksheets completed at sites will be checked against the electronic data for accuracy. Accuracy will be checked for 100% of the primary outcome on the post-baseline timepoints across all sites. If the error rate is greater than 1% accuracy checks for all data will be triggered.

Project Management

The University of Manchester will be the primary sponsor. In accordance with high standards of research governance we would ensure researchers receive training in the International Conference on Harmonisation (ICH) Guidelines - Good Clinical Practice before recruitment commences. We will set up a Trial Steering Committee (TSC) and an Independent Data Monitoring and Ethics Committee (IDMC) prior to the start of the study. The TSC will comprise representatives from the research team, independent clinicians and statistician, a representative of the HTA, and a service user, and will have an independent chair. It will meet annually and initially before the trial begins for approval of the protocol and standard operating procedures. The TSC will monitor and supervise progress, consider reports and recommendations, including the Stage 1 to Stage 2 decisions.

An IDMC will also be established to monitor (1) recruitment of study participants, (2) ethical issues of consent, (3) quality of data (including missing data), (4) interim analysis of Stage 1 results (5) the incidence of adverse events, and (6) any other factors that might compromise the progress and satisfactory completion of the trial. This will also have an independent chairman and include an independent statistician with expertise in MAMS designs. It will meet on a 6-monthly basis.

The sponsor will support development of the monitoring plan and assist with the monitoring as and when needed. However, the data accuracy checks and day-to-day requirements around monitoring will be delegated from by the sponsor to the trial team including central and remote monitoring of sites.

Communication within and between sites: Each site will have a weekly team meeting to ensure regular communication and interaction between site leads, local clinicians and research assistants (measures will be followed to avoid blind breaks). There will be monthly Trial Management Group meetings with all applicants via video conference, with 6 monthly extended face-to-face meetings. The Trial Manager will conduct weekly telephone supervision with all RAs that will focus on inter-rater reliability of the interview measure, recruitment, liaison with referrers, compliance to follow-ups, and specific scoring queries. In addition, they will chair a fortnightly teleconference that focuses on recruitment and engagement to share best practice. The PSWs and APs will receive weekly supervision from a central supervisor based in Manchester, which will be focused on fidelity and adherence to the protocol and model. Supervision from site leads or their delegated representatives, focussed on problem solving, personal wellbeing, risk management and local issues will supplement this. We have used these processes successfully in several previous multisite RCTs of psychosocial interventions (33, 51, 53).

Data management

Each study participant will be assigned a unique trial identification number at the start of the assessment process. This number will be written on all clinical assessment forms/datasheets and databases used to record data on study participants. A hard copy of a record sheet linking patient identity and trial identification number for all participants will be kept at each site. It will be placed securely in a locked filling cabinet separate from datasheets. This will be also stored in an electronic database, which will be accessible to authorised users at the sites via the study web portal hosted at The Kings Clinical Trials Unit, Kings College London (it will be password protected and secure). The local study co-ordinator will enter the data on to an electronic database,

and all such data will be checked for errors before being transferred to the statistical package. All data will be kept secure at all times and maintained in accordance with the requirements of GDPR and archived according to GCP regulations.

In accordance with The University of Manchester Information Governance Office Records Retention, the retention periods are as follows:

- Informed consent form will be retained for 7 years after the end of study.
- Research data will be retained for 5 years after the primary publication.
- Research management documents for 6 years after the end of the study

Data will be archived in line with The University of Manchester's Research Data Management Policy.

Ethics

National Research Ethics Committee and HRA approval will be obtained prior to the start of data collection. Only those who agree to provide written informed consent will be included in the study. Potential participants will receive a PIS that includes a contact number for the study team.

Peer review

As a National Institute for Health Research (NIHR), Health Technology Assessment (HTA) funded study the scientific quality of the research has been assessed throughout the funding review process through both peer review of experts in the field and through the NIHR HTA funding panel. The protocol has been reviewed by the study sponsor, and the ethics committee.

Risks and anticipated benefits for trial participants

This study will add to the evidence base for the range of psychosocial interventions that should be provided to improve outcomes for people with SMHPs, who remain among the most socially excluded groups in society. If our brief remote interventions were found to be significantly superior to TAU in reducing hospital admissions and suicidality, without an adverse effect burden, this could have implications for the future evidence-based management of similar patients within secondary care mental health services. A potential risk is that some participants might find the research assessment process distressing. Participants' will be offered choice regarding the timing, modality (remote or face-to-face) and length of the assessments, including the option of breaks and assessments spread across multiple occasions (to minimise burden at any one time). We have a standardised protocol for managing distress, which has been developed with service users; this includes offering telephone contact within 48 hours of assessments in order to check on participant wellbeing. The research assistant will gain advice from their supervisor and take any appropriate action to minimise the participant's distress. The participant will be able to freely withdraw from the study at any point, which will not affect their statutory care.

Adverse effects

Adverse events (including death) and intervention related adverse effects will be monitored.

Definitions

Adverse Event

An adverse event will be defined as any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons whether or not related to the research procedures or intervention . This definition includes events related to the study interventions and events related to the procedures involved.

Serious Adverse Event

A Serious Adverse Event, will be defined as an adverse event that

a) results in death
b) is life-threatening.
c) requires hospitalisation or prolongation of existing hospitalisation.
d) results in persistent or significant disability or incapacity, or
e) consists of a congenital anomaly or birth defect.
f) other important medical event if determined to be serious based on medical judgement.

NB: Planned hospitalisation for a pre-existing condition, without a serious deterioration in health, is not considered a serious adverse event.

NB: Life threatening in the definition of an SAE refers to an event in which the subject was at risk of death at the time of the event; it does not refer to an event that hypothetically might have caused death if it were more severe. Clinical judgement should be exercised in deciding whether an SAE is serious in other situations. Important: AE's that are not immediately life-threatening or do not result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one or the other outcomes listed, should be considered serious.

Reporting

All serious adverse events will be reported to the sponsor no later than 3 calendar days from awareness of the event at the site.

For the avoidance of doubt, ALL AE/SAEs should be collected for all trial subjects from the time of their enrolment into the study. The time of enrolment is defined as the time at which, following recruitment, a subject sign and dates the informed consent form.

Initially all adverse events should be recorded on the Adverse Events Report Form by whoever has identified the event. This form should then be shared with the Chief Investigator, or a delegated individual, who makes an assessment as to whether the event is defined as serious in consultation with both the definitions in the Protocol.

An SAE occurring to a research participant will be reported to the main Research Ethics Committee where in the opinion of the Chief Investigator (CI) the event was: **related** – that is, it resulted from administration of any of the research procedures, **and unexpected** – that is, the type of event is not listed in the protocol as an expected occurrence.

Foreseeable adverse events include worsening of symptoms defined as an increase in severe suicidal thoughts within the past 12-weeks or a suicide attempt within the past 12-weeks. This study will recruit a cohort of participants who have experienced recent suicidal ideation, amongst whom recurrent thoughts of suicide are common. An analysis of a previous online trial for suicidal ideation found two consistent trajectories of suicidal ideation (Batterham et al., 2019): a majority group who experienced a decrease in the severity of suicidal ideation over time and a minority group who experience persistent severe suicidal ideation over a 12-month period. Adverse events related to severe suicidal ideation are therefore not considered unexpected. Thoughts of suicide are associated with increased rates of suicide (Large, Corderoy, and McHugh, 2020) and amongst those with suicidal ideation, between 25% and 58% will make a suicide attempt (Kessler, Borges, and Walters, 1999). Serious adverse events related to suicide attempts are therefore not considered unexpected.

The Sponsor (or the delegated responsible party/CI) must report SAEs to the Health Research Authority (HRA) according to the following timescales:

- **Reportable events which indicate a risk of imminent death, serious injury, or serious illness, and require prompt remedial action for other participants must be reported immediately and no later than 2 calendar days from Sponsor awareness of the event.**

- **SAEs which are both related and unexpected must be reported immediately and no later than 15 calendar days from Sponsor or CI awareness of the event.**

Causality and expectedness of AEs will be assessed, in a timely manner in consideration of the regulatory reporting requirements.

In order to ensure independent scrutiny of SAEs, the iDMC will monitor the occurrence of SAEs. This approach has been utilized in our other trials including the HTA funded FOCUS and MAPS trials. The Independent Data Monitoring and Ethics Committee (IDMC) will monitor SAEs for any patterns.

We will administer a measure of potential adverse effects from trial involvement at point of exit (50).

We plan to scrutinise any instances of participants being admitted to psychiatric hospital in the period of the trial. These events are likely to come to the attention of the APs or PSWs or assessors; however, we will also check medical records. The responsible clinical team, the Trial Management Group and IDMC will be informed of adverse events. The response to an adverse event will be determined on a case-by-case basis and in line with HRA guidance.

Obtaining informed consent

Written informed consent will be obtained from each subject prior to their inclusion in this study in line with the Information Sheets and Consent Forms, Guidance for Researchers and Reviewers, Version 3.2 May 2007 (National Research Ethics Service: NRES). Participants will be given least 24 hours to consider the information before providing written informed consent. During the COVID-19 pandemic this will be either emailed to the potential participant or sent to them in the post.

We will prioritise recording informed consent in writing via a wet-ink signature from the participant and the researcher taking informed consent. However, it may not be feasible at present to seek written consent on paper forms from a participant where covid-19 restrictions apply, for example where a participant is extremely clinically vulnerable and where the risks of meeting in-person are significant. In instances where informed consent is taken via a remote method (telephone or MS Teams) we shall adhere to the following approach, which has been agreed with the study sponsor:

1. The consent visit will be audio recorded as evidence of informed consent process and the participants consent to the study, we outlined in the PIS that in the case of remote consent we will require an audio recording of the participants consent.
2. The researcher shall initial each box on the consent form on behalf of the participant.
3. The researcher shall sign the consent form as evidence of their taking consent.
4. Where possible, written consent shall be sought at a later date subject to covid-19 restrictions.

Audio recording of consent will follow the sites local NHS Trust policies and procedures. Audio recordings will be transferred to a secure NHS drive and will only be accessible by members of the research team with delegated responsibility to access, as per the study delegation log.

Amendments to the Protocol

Minor revisions shall be used to indicate where small changes have been made to the protocol such as formatting, spelling or grammar corrections, or where changes have been made that do not require further approval or acknowledgement. Minor revisions shall be indicated by making increments to the decimal place of the version number e.g., V 1.2; V 1.3; V1.4.

Major revisions shall be used where changes to the protocol are significant and require re-approval. Major revisions shall be indicated by making increments to the whole number of the version e.g., V 1.0; V 2.0; V 3.0.

Amendments to the protocol will not be initiated until approval has been sought from the sponsor and where relevant the Research Ethics Committee and the Health Research Authority.

Access to the final trial dataset

The statistical support staff at the Kings Clinical Trials Unit will have access to the final trial dataset and this will include Professor Richard Emsley. The Health Economist and health economist support staff at The University of Manchester will have access to the final trial dataset. After the main publication the Chief Investigator, co-investigators and trial manager will have access to the final dataset.

Dissemination

Dissemination Policy

On completion of the trial the data will be analysed, and a final trial report prepared for the National Institute for Health Research (NIHR) to be published in Health Technology Assessment here: https://www.journalslibrary.nihr.ac.uk/hta/#/ . The Draft Final Report is due 14 days after the end date of the study.

All written and oral research outputs should acknowledge the NIHR funding, and support from the Clinical Research Network, independent Data Monitoring and Ethics Committee, Trial Steering Committee and Patient and Public Involvement groups.

We will provide participants who take part in Stage 1 with a summary of the internal pilot and feasibility results. Findings from the end of Stage 2 will be provided to all participants including those who took part in Stage 1 after the final trial report and main publication report has been published. PPI will be integral to producing summaries of the research finding to ensure accessibility as outlined above and where possible we will employ infographics to summarise the main findings. To ensure maximum connection to the study participants we will disseminate the results via multiple modalities. Throughout the lifetime of the study, we will host regular updates regarding the study progress on the project website and provide all study participants with a link to ensure continued engagement with progress.

A number of high-quality peer-reviewed open access publications are expected from the body of research. Participating investigators will have right to publish trial data with permission from the Chief Investigator.

This definitive research will provide evidence from a single study regarding clinical and cost effectiveness of a range of interventions that are brief and accessible. This output will address a number of unmet needs including improving the efficacy and accessibility of psychosocial interventions, developing the workforce and responding to the Five Year Forward View's aim of preventing avoidable hospital admissions. We will produce materials in diverse formats (written, audio and video) to engage our stakeholders (HBTT staff, service users and carers, commissioners, policy makers) throughout the trial and to communicate our findings on completion. We will also develop guidance and policy briefings for policy makers and commissioners. A core component of this research is the training and skilling-up of the workforce involved in the research through our training package. The training materials and intervention manuals will be made freely available via a web portal for APs and PSWs to utilise.

We will generate quantitative data that may be of interest to researchers examining the efficacy of psychosocial interventions, e.g., for systematic review and meta-analyses, individual patient data analysis. The database will be made freely available to researchers with the approval of the Chief Investigator.

Authorship eligibility guidelines

Authorship will be reviewed on a publication-by-publication basis. We will follow the International Committee of Medical Journal Editors (ICJME) recommendations for authorship and review these for each individual publication. Prior to commencing a publication, the Chief Investigator and trial manager/s will review the list of research team members to consider who would meet the ICJME criteria.

Indemnity

The University of Manchester has insurance available in respect of research involving human subjects that provides cover for legal liabilities arising from its actions or those of its staff or supervised students. The University of Manchester also has insurance available that provides compensation for non-negligent harm to research subjects occasioned in circumstances that are under the control of the University of Manchester.

References

1. Øiesvold T, Bakkejord T, Hansen V, Nivison M, Sørgaard KW. Suicidality related to first-time admissions to psychiatric hospital. Social psychiatry and psychiatric epidemiology. 2012;47(3):419-25.
2. Thompson A, Shaw M, Harrison G, Ho D, Gunnell D, Verne J. Patterns of hospital admission for adult psychiatric illness in England: analysis of Hospital Episode Statistics data. British Journal of Psychiatry. 2004;185(4):334-41.
3. Taskforce MH. The Five Year Forward View for Mental Health: A report from the independent Mental Health Taskforce to the NHS in England. NHS England; February 2016.
4. Hasselberg N, Gråwe RW, Johnson S, Šaltytė-Benth J, Ruud T. Psychiatric admissions from crisis resolution teams in Norway: a prospective multicentre study. BMC psychiatry. 2013;13:117-.
5. Bowers L, Chaplin R, Quirk A, Lelliott P. A conceptual model of the aims and functions of acute inpatient psychiatry. Journal of Mental Health. 2009;18(4):316-25.
6. Akther SF, Molyneaux E, Stuart R, Johnson S, Simpson A, Oram S. Patients' experiences of assessment and detention under mental health legislation: systematic review and qualitative meta-synthesis. BJPsych Open. 2019;5(3):e37.
7. Shinn AK, Viron M. Perspectives on the COVID-19 Pandemic and Individuals With Serious Mental Illness. J Clin Psychiatry. 2020;81(3).
8. Correll CU, Solmi M, Veronese N, Bortolato B, Rosson S, Santonastaso P, et al. Prevalence, incidence and mortality from cardiovascular disease in patients with pooled and specific severe mental illness: a large-scale meta-analysis of 3,211,768 patients and 113,383,368 controls. World Psychiatry. 2017;16(2):163-80.
9. Johnson S. Crisis resolution and home treatment teams: an evolving model. Advances in Psychiatric Treatment. 2013;19(2):115-23.
10. Werbeloff N, Chang CK, Broadbent M, Hayes JF, Stewart R, Osborn DPJ. Admission to acute mental health services after contact with crisis resolution and home treatment teams: an investigation in two large mental health-care providers. Lancet Psychiatry. 2017;4(1):49-56.
11. Vigod SN, Kurdyak PA, Dennis CL, Leszcz T, Taylor VH, Blumberger DM, et al. Transitional interventions to reduce early psychiatric readmissions in adults: systematic review. Br J Psychiatry. 2013;202(3):187-94.
12. Bone JK, McCloud T, Scott HR, Machin K, Markham S, Persaud K, et al. Psychosocial Interventions to Reduce Compulsory Psychiatric Admissions: A Rapid Evidence Synthesis. EClinicalMedicine. 2019;10:58-67.
13. Lean M, Fornells-Ambrojo M, Milton A, Lloyd-Evans B, Harrison-Stewart B, Yesufu-Udechuku A, et al. Self-management interventions for people with severe mental illness: systematic review and meta-analysis. Br J Psychiatry. 2019;214(5):260-8.
14. O'Connor RC, Lundy JM, Stewart C, Smillie S, McClelland H, Syrett S, et al. SAFETEL randomised controlled feasibility trial of a safety planning intervention with follow-up telephone contact to reduce suicidal behaviour: study protocol. BMJ Open. 2019;9(2):e025591.

15. Melia R, Francis K, Hickey E, Bogue J, Duggan J, O'Sullivan M, et al. Mobile Health Technology Interventions for Suicide Prevention: Systematic Review. JMIR mHealth and uHealth. 2020;8(1):e12516.
16. Torok M, Calear AL, Smart A, Nicolopoulos A, Wong Q. Preventing adolescent suicide: A systematic review of the effectiveness and change mechanisms of suicide prevention gatekeeping training programs for teachers and parents. J Adolesc. 2019;73:100-12.
17. van Spijker BA, Werner-Seidler A, Batterham PJ, Mackinnon A, Calear AL, Gosling JA, et al. Effectiveness of a Web-Based Self-Help Program for Suicidal Thinking in an Australian Community Sample: Randomized Controlled Trial. J Med Internet Res. 2018;20(2):e15-e.
18. Bradstreet S. Harnessing the lived experience: Formalising peer support approaches to promote recovery. The Mental Health Review. 2006;11(2):33-7.
19. Lloyd-Evans B, Mayo-Wilson E, Harrison B, Istead H, Brown E, Pilling S, et al. A systematic review and meta-analysis of randomised controlled trials of peer support for people with severe mental illness. BMC Psychiatry. 2014;14(1):39.
20. Tucker RP, Hagan CR, Hill RM, Slish ML, Bagge CL, Joiner TE, Jr., et al. Empirical extension of the interpersonal theory of suicide: Investigating the role of interpersonal hopelessness. Psychiatry Res. 2018;259:427-32.
21. Johnson S, Lamb D, Marston L, Osborn D, Mason O, Henderson C, et al. Peer-supported self-management for people discharged from a mental health crisis team: a randomised controlled trial. The Lancet. 2018;392(10145):409-18.
22. Pfeiffer PN, King C, Ilgen M, Ganoczy D, Clive R, Garlick J, et al. Development and pilot study of a suicide prevention intervention delivered by peer support specialists. Psychological Services. 2019;16(3):360-71.
23. Morrison APBSCPD, Bowe SBS, Larkin WBS, Nothard SBS. The Psychological Impact of Psychiatric Admission: Some Preliminary Findings. [Report]. Journal of Nervous & Mental Disease April 1999;187(4):250-253. 1999.
24. Hjorthøj C, Stürup AE, McGrath JJ, Nordentoft M. Years of potential life lost and life expectancy in schizophrenia: a systematic review and meta-analysis. The Lancet Psychiatry. 2017;4(4):295-301.
25. Holmes EA, Ghaderi A, Harmer CJ, Ramchandani PG, Cuijpers P, Morrison AP, et al. The Lancet Psychiatry Commission on psychological treatments research in tomorrow's science. The Lancet Psychiatry. 2018;5(3):237-86.
26. Avery KNL, Williamson PR, Gamble C, O'Connell Francischetto E, Metcalfe C, Davidson P, et al. Informing efficient randomised controlled trials: exploration of challenges in developing progression criteria for internal pilot studies. BMJ Open. 2017;7(2).
27. O'Connor RC, Kirtley OJ. The integrated motivational-volitional model of suicidal behaviour. Philos Trans R Soc Lond B Biol Sci. 2018;373(1754):20170268.
28. Van Orden KA, Witte TK, Cukrowicz KC, Braithwaite SR, Selby EA, Joiner TE, Jr. The interpersonal theory of suicide. Psychol Rev. 2010;117(2):575-600.
29. Bratton D, Phillips P, Parmar M. A multi-arm multi-stage clinical trial design for binary outcomes with application to tuberculosis. BMC medical research methodology. 2013;13:139.
30. Freidlin B, Korn EL, Gray R, Martin A. Multi-arm clinical trials of new agents: some design considerations. Clinical cancer research : an official journal of the American Association for Cancer Research. 2008;14(14):4368-71.
31. Gillard S, Foster R, Gibson S, Goldsmith L, Marks J, White S. Describing a principles-based approach to developing and evaluating peer worker roles as peer support moves into mainstream mental health services. Mental Health and Social Inclusion. 2017;21(3):133-43.
32. Gillard S, Bremner S, Foster R, Gibson SL, Goldsmith L, Healey A, et al. Peer support for discharge from inpatient to community mental health services: Study protocol clinical trial (SPIRIT Compliant). Medicine. 2020;99(10).
33. Gumley A, Bradstreet S, Ainsworth J, Allan S, Alvarez-Jimenez M, Beattie L, et al. Early Signs Monitoring to Prevent Relapse in Psychosis and Promote Well-Being, Engagement, and Recovery: Protocol for a Feasibility Cluster Randomized Controlled Trial Harnessing Mobile Phone Technology Blended With Peer Support. JMIR research protocols. 2020;9(1):e15058.

34. Gillard SG, Edwards C, Gibson SL, Owen K, Wright C. Introducing peer worker roles into UK mental health service teams: a qualitative analysis of the organisational benefits and challenges. BMC Health Services Research. 2013;13(1):188.
35. Edwards PJ, Roberts I, Clarke MJ, DiGuiseppi C, Wentz R, Kwan I, et al. Methods to increase response to postal and electronic questionnaires. Cochrane Database of Systematic Reviews. 2009(3):MR000008.
36. Bratton DJ, Phillips PPJ, Parmar MKB. A multi-arm multi-stage clinical trial design for binary outcomes with application to tuberculosis. BMC Medical Research Methodology. 2013;13(1):139.
37. Dillon A. Carrying NICE over the threshold. https://wwwniceorguk/news/blog/carrying-nice-over-the-threshold (accessed 18 Jun 2019). 2015.
38. Claxton K, Martin S, Soares M, Rice N, Spackman E, Hinde S, et al. Methods for the Estimation of the NICE Cost Effectiveness Threshold. Health Technology Assessment. 2015;19(14).
39. McCabe C, Claxton K, Culyer AJ. The NICE cost-effectiveness threshold: what it is and what that means. Pharmacoeconomics. 2008;26(9):733-44.
40. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, et al. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. BMJ : British Medical Journal. 2013;346:f1049.
41. Franklin, M., Thorn, J. Self-reported and routinely collected electronic healthcare resource-use data for trial-based economic evaluations: the current state of play in England and considerations for the future. BMC Med Res Methodol 19, 8 (2019). https://doi.org/10.1186/s12874-018-0649-9
42. Posner K, Brown GK, Stanley B, Brent DA, Yershova KV, Oquendo MA, et al. The Columbia-Suicide Severity Rating Scale: initial validity and internal consistency findings from three multisite studies with adolescents and adults. Am J Psychiatry. 2011;168(12):1266-77.
43. Law H, Neil ST, Dunn G, Morrison AP. Psychometric properties of the Questionnaire about the Process of Recovery (QPR). Schizophrenia Research. 2014;156(2):184-9.
44. Janssen MF, Pickard AS, Golicki D, Gudex C, Niewada M, Scalone L, et al. Measurement properties of the EQ-5D-5L compared to the EQ-5D-3L across eight patient groups: a multi-country study. Quality of Life Research. 2013;22(7):1717-27.
45. Keetharuth AD, Brazier J, Connell J, Bjorner JB, Carlton J, Taylor Buck E, et al. Recovering Quality of Life (ReQoL): a new generic self-reported outcome measure for use with people experiencing mental health difficulties. The British Journal of Psychiatry. 2018;212(1):42-9.
46. Davies LM, Barnes TRE, Jones PB, Lewis S, Gaughran F, Hayhurst K, et al. A Randomized Controlled Trial of the Cost-Utility of Second-Generation Antipsychotics in People with Psychosis and Eligible for Clozapine. Value in Health. 2008;11(4):549-62.
47. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006;166(10):1092-7.
48. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001;16(9):606-13.
49. Snyder CR, Harris C, Anderson JR, Holleran SA, Irving LM, Sigmon ST, et al. The will and the ways: development and validation of an individual-differences measure of hope. Journal of personality and social psychology. 1991;60(4):570-85.
50. De Beurs D, Cleare S, Wetherall K, Eschle-Byrne S, Ferguson E, B O'Connor D, et al. Entrapment and suicide risk: The development of the 4-item Entrapment Scale Short-Form (E-SF). Psychiatry Research. 2020;284:112765.
51. Morrison AP, Pyle M, Gumley AI, Schwannauer M, Turkington D, Maclennan G, et al. Cognitive behavioural therapy for clozapine resistant schizophrenia: the FOCUS RCT. Health Technology Assessment. 2018;in press.
52. Bradstreet S, Allan S, Gumley A. Adverse event monitoring in mHealth for psychosis interventions provides an important opportunity for learning. Journal of Mental Health. 2019;28(5):461-6.
53. Morrison AP, Law H, Carter L, Sellers R, Emsley R, Pyle M, et al. Comparing antipsychotic medication to cognitive behavioural therapy to a combination of both in people with psychosis: a pilot and feasibility randomised controlled trial. Lancet Psychiatry. 2018;5(5):411-23.

54. Bower P, Brueton V, Gamble C, Treweek S, Smith CT, Young B, et al. Interventions to improve recruitment and retention in clinical trials: a survey and workshop to assess current practice and future priorities. Trials. 2014;15:399.

Appendix 1

Year 1												
#month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Calendar month	**Apr' 22**	**May' 22**	**Jun' 22**	**Jul' 22**	**Aug'22**	**Sep'22**	**Oct'22**	**Nov'22**	**Dec'22**	**Jan'23**	**Feb'23**	**Mar'23**
Finalization of approvals (MHRA, REC/HRA, NHS)												
Finalize treatment manuals												
Systems (randomisation/ database, website)												
Staff training												
Site initiation meetings												
Internal pilot/ Stage 1 Recruitment (n=640)												
Intervention delivery												
3-month assessments												
6-month assessments												
Year 2												
#month	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**	**23**	**24**
Calendar month	**Aprl' 23**	**May' 23**	**Jun' 23**	**Jul' 23**	**Aug'23**	**Sep'23**	**Oct'23**	**Nov'23**	**Dec'23**	**Jan'24**	**Feb'24**	**Mar'24**
Stage 1 Recruitment												
Progression criteria data review												
Intervention delivery												
3-month assessments												
6-month assessments												
Year 3												
#month	**25**	**26**	**27**	**28**	**29**	**30**	**31**	**32**	**33**	**34**	**35**	**36**
Calendar month	**Aprl' 24**	**May' 24**	**Jun' 24**	**Jul' 24**	**Aug'24**	**Sep'24**	**Oct'24**	**Nov'24**	**Dec'24**	**Jan'25**	**Feb'25**	**Mar'25**
Interim analysis (n in PREVAIL, SAFETEL and TAU for interim analysis with 6-month data = 385)												
Stage 1 Recruitment (n=640)												
Stage 2 Recruitment (n=351)												
Intervention delivery												
3-month assessments												
6-month assessments												
Year 4												
#month	**37**	**38**	**39**	**40**	**41**	**42**	**43**	**44**	**45**	**46**		
Calendar month	**Aprl' 25**	**May' 25**	**Jun' 25**	**Jul' 25**	**Aug'25**	**Sep'25**	**Oct'25**	**Nov'25**	**Dec'25**	**Jan'26**		
Stage 2 Recruitment (n=351)												
Intervention delivery												
3-month assessments												
6-month assessments												
Data cleaning and analysis												