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## The HARMONIC trial: Study protocol for a randomised controlled feasibility trial of Shaping Healthy Minds – a modular transdiagnostic intervention for mood, stressor-related and anxiety disorders in adults

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-024546
Article Type:	Protocol
Date Submitted by the Author:	31-May-2018
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Keywords:	Transdiagnostic, Depression, Anxiety, Posttraumatic Stress Disorder, Common Mental Health Problems

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The HARMONIC trial: Study protocol for a randomised controlled feasibility trial of *Shaping Healthy Minds* – a modular transdiagnostic intervention for mood, stress and anxiety disorders in adults

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Trial Registration: NCT03143634 (ClinicalTrials.gov)

Protocol Version: First, 31/05/2018

Funding: National Institute of Health Research, Research for Patient Benefit (RfPB: PB-PG-0214-33072)

Word count: 4482 words

## Abstract

**Introduction:** Anxiety, mood and trauma-related disorders are common, affecting up to 20% of adults. Many of these individuals will experience symptoms of more than one disorder as diagnostically defined. However, most psychological treatments focus on individual disorders and are less effective for those who experience comorbid disorders. The HARMONIC trial introduces a novel transdiagnostic intervention (*Shaping Healthy Minds*), which synthesises several evidence-based treatment techniques to address the gap in effective interventions for people with complex and comorbid difficulties. This early-phase trial aims to estimate the efficacy and feasibility of the transdiagnostic intervention in preparation for a later-phase randomised controlled trial, and to explore mechanisms of change.

**Methods/Analysis:** We outline a patient-level two-arm randomised controlled trial (HARMONIC) that compares *Shaping Healthy Minds* to treatment-as-usual (TAU) for individuals aged >18 years ( $N=50$ ) with co-morbid mood, anxiety, obsessive-compulsive or trauma/stressor disorder diagnoses, recruited from outpatient psychological services within the UK National Health Service. The co-primary outcomes will be 3-month follow-up scores on self-report measures of depressive symptoms, anxiety symptoms, and disability and functional impairment. Secondary outcomes include changes in symptoms linked to individual disorders. We will assess the feasibility and acceptability of *Shaping Healthy Minds*, the utility of proposed outcome measures, and refine the treatment manuals in preparation for a later-phase trial.

**Ethics and dissemination:** This trial protocol has been approved by the Health Research Authority of the National Health Service of the United Kingdom (East of England, Reference: 16/EE/0095). We anticipate that trial findings will inform future revisions of clinical guidelines for numerous forms of mood, anxiety, and stressor-related disorders. Findings will be disseminated broadly via peer-reviewed empirical journal articles, conference presentations, clinical workshops, and a trial website.

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5 **Key Words:** Transdiagnostic, Depression, Anxiety, Posttraumatic Stress Disorder, Common  
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7 Mental Health Problems  
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11 **Trial registration:** Clinicaltrials.gov identifier: NCT03143634. This trial protocol is written  
12  
13 in compliance with the Standard Protocol Items: Recommendations for Interventional Trials  
14  
15 (SPIRIT) guidelines.  
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### 18 19 20 **Strengths and limitations of this study**

- 21  
22 • The first study to investigate the potential efficacy of a flexibly-delivered modular  
23  
24 transdiagnostic treatment protocol in adults with unipolar mood, anxiety, and trauma-  
25  
26 related disorders.  
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- 28  
29 • Investigating the feasibility and procedural uncertainties associated with the  
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31 transdiagnostic intervention – *Shaping Healthy Minds* – in preparation for a scaled-up  
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33 clinical trial.  
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36 • Evaluation of *Shaping Healthy Minds* against treatment-as-usual (TAU) currently  
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38 provided by the NHS will determine the potential value of the new protocol.  
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41 • This trial aims to provide a point estimate of efficacy of the *Shaping Healthy Minds*  
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43 protocol, relative to TAU, in preparation for a later-stage trial, and to explore putative  
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45 mediators and moderators of treatment outcome.  
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3 The HARMONIC trial: Study protocol for a randomised controlled feasibility trial of *Shaping*  
4 *Healthy Minds* – a modular transdiagnostic intervention for mood, stressor-related and anxiety  
5 disorders in adults  
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9 Mood, stressor-related, obsessive-compulsive and anxiety disorders – so called  
10 common mental health problems (CMHP; NICE, 2011) – are one of the largest causes of  
11 disability in the world, with 16 – 20% of adults affected at any given time [1, 2]. Maximising  
12 our ability to treat CMHP in cost effective, efficient, and effective ways that can be widely  
13 disseminated is a priority [2]. At present, there is a range of complex psychological treatments  
14 with demonstrated efficacy in the treatment of CMHP, and in preventing recurrence.  
15  
16 Consequently, the National Institute of Health and Care Excellence (NICE) recommends  
17 psychological treatment at various points in the care pathway to all those suffering from such  
18 problems, although there are not specific recommendations for individuals experiencing more  
19 than one problem [3]. Between 40 – 80% of patients experiencing a CMHP also experience an  
20 additional comorbid CMHP [4, 5]. Even our best available psychological treatments only  
21 achieve clinical recovery for 40 – 70% of patients, depending on their primary CMHP, with  
22 people suffering complex co-morbid conditions faring significantly worse [6]. For the  
23 majority of patients who receive treatment, there remains a significant risk of future relapse  
24 [7, 8]. A key challenge therefore is how we can build on and extend beyond the current  
25 psychological treatments for CMHP to increase efficacy, and sustained recovery, particularly  
26 for those with co-morbid, recurrent, and complex presentations [9].  
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46 Over the past decade, there has been a major shift in the conceptualisation of CMHP,  
47 away from a single-diagnosis approach in favour of a transdiagnostic model [10, 11]. There is  
48 strong empirical and theoretical support for development of transdiagnostic treatment  
49 approaches, as many of the cognitive, emotional, behavioural, and interpersonal factors which  
50 drive symptomology are consistent across disorders [12, 13]. A transdiagnostic approach  
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3 thereby has the potential to improve the efficacy and efficiency of treatment for people with  
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5 anxiety, stress and depression.  
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8 There are potential limitations to the commonly-utilised single-disorder-focused  
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10 treatment approach. First, with the exception of a few existing programmes [14, 15], most  
11  
12 evidence-based treatment protocols are single-disorder-focused programs (e.g., depression  
13  
14 [16], generalised anxiety [17, 18], social anxiety [19], and post-traumatic stress disorder [20]).  
15  
16 Comorbid conditions and disorders are either ignored, or minimally treated within these  
17  
18 treatment packages. This leaves a mismatch between the available evidence base and the  
19  
20 clinical reality which clinicians face: the majority of people with any given CMHP have at  
21  
22 least one or more comorbid disorders to their primary diagnosis [4]. Second, in the attempt to  
23  
24 manualise treatments, most packages are inflexible ‘one-size-fits-all’ approaches, leaving  
25  
26 patients with a wide range of problems and presentations receiving the same treatment  
27  
28 package, regardless of their symptoms, goals, and concerns [14]. Third, in practice, many  
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30 clinicians already deliver evidence-based psychological treatments in a flexible manner in  
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32 order to address individual concerns and goals. Manualised treatments need to better reflect  
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34 the realities of service-user experiences and treatment delivery. This approach merits  
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36 improvement so that delivered treatments are more efficient, effective, and personalised to  
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38 individuals’ concerns.  
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42 Existing psychological treatments for CMHP share more similarities than differences  
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44 [21]. Despite differences in the theoretical foundation underlying available psychological  
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46 treatments, and the terms used to describe maintaining factors and treatment targets, there are  
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48 many common elements. For instance, psychoeducation, graded exposure, mindfulness  
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50 techniques, and behavioural activation form a key component of a variety of effective  
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52 treatments such as trauma-focused cognitive behavioural therapy, cognitive behavioural  
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54 therapy (CBT), acceptance and commitment therapy (ACT), Dialectical Behaviour Therapy  
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(DBT), exposure therapy and mindfulness-based cognitive therapy (MBCT). The widespread availability of so many treatment options has the potential to elicit considerable decision-making difficulties for the treating clinician. In both formulation and treatment planning, challenging decisions occur when selecting the order in which to treat multiple difficulties, in evaluating the most appropriate treatment approach, and working out which treatment option will be acceptable and effective for the client.

A recent equivalence RCT demonstrated that a transdiagnostic protocol (The *Unified Protocol for Transdiagnostic Treatment of Emotional Disorders* [22]) and single-disorder protocols produced statistically equivalent reduction in severity of principal anxiety disorder diagnosis, but that there was less attrition in the transdiagnostic group [23]. Promising results have also been found for other transdiagnostic treatment protocols, including Norton's Transdiagnostic Group Cognitive Behavioral Therapy for Anxiety [15], Gros's Transdiagnostic Behavior Therapy for affective disorders [24], and Schmidt's False Safety Behaviour Elimination Therapy for Anxiety Disorders [25]. In addition, our systematic review and meta-analysis supported the overall efficacy of transdiagnostic treatments [10]. The review called for more high-quality studies to resolve uncertainties surrounding the heterogeneity of treatment effects and to determine the best treatment approaches and designs. We aim to address these issues through evaluating a novel intervention which combines a number of evidence-based treatment strategies. In utilising a modular approach, this trial will contribute to identification and evaluation of effective treatment components and delivery method. The modular approach to treatment design incorporates self-contained functional units (therapy modules) that can operate independently and be delivered flexibly, but also refer to other modules if needed [22]. A complex, modular, tailored transdiagnostic intervention that targets common underlying processes maximises goodness of fit and has a

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3 direct focus on process rather than symptoms. The approach is thereby suitable for complexity  
4 and comorbidity as well as sub-syndromal and prodromal symptoms.  
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7 The transdiagnostic intervention we have developed – *Shaping Healthy Minds* –  
8 targets the processes and symptoms that are common to CMHPs and offers a number of  
9 advances in transdiagnostic treatment by incorporating the best available techniques from  
10 existing manual-based treatments into the one treatment package. A key aim of the  
11 programme is to encompass the treatment techniques that skilled psychologists and mental  
12 health clinicians already implement in standard practice for depressed, stressed and anxious  
13 patients with complex presentations [26]. The intervention also builds on the Unified Protocol  
14 for Transdiagnostic Treatment for Emotional Disorders described by Barlow et al. [14], by  
15 working towards a prescriptive approach for the delivery of treatment modules based on the  
16 formulation of the client's presenting difficulties [9]. Specifically, the treatment expands  
17 beyond interventions grounded in a sole treatment paradigm (e.g., CBT) towards a theory-  
18 driven approach that utilises efficacious techniques translated from basic science alongside  
19 components drawn from a wide range of evidence-based psychological treatments (e.g.,  
20 Mindfulness-based interventions, ACT, Behavioural Activation, and DBT).  
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37 The treatment protocol for *Shaping Healthy Minds* also changes the way that  
38 standardised manual-based treatments are delivered. Rather than using integral interventions  
39 (where all patients receive the same relatively fixed, complete protocol), the transdiagnostic  
40 intervention is a modular intervention, whereby the assessment of core problematic areas of  
41 emotional, cognitive, interpersonal, and behavioural processes informs the selection and  
42 sequence of treatment modules targeted at specific problem areas for patients [22]. This  
43 modular approach allows for standardised, yet flexible treatment that is personalised to the  
44 individual concerns, problems, and goals for the patient. Finally, it expands beyond  
45 interventions that typically focus on alleviating negative symptomatology (e.g., negative  
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3 thoughts, excessive negative emotions) and incorporates interventions designed to increase  
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5 positive emotions, capture strengths, and enhance resilience for sustained recovery.  
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7 We aim to examine the feasibility of *Shaping Healthy Minds* in reducing symptoms of  
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9 depression, anxiety, distress, disability and functional impairment through an early-stage  
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11 randomised clinical trial, in line with recommendations for the development of complex  
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13 interventions [27]. In particular, we will gather data on the extent to which *Shaping Healthy*  
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15 *Minds* performs comparably to TAU for a given service-user's primary diagnosed problem  
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17 [10, 28] as well as for other significant additional, secondary, and/or comorbid difficulties. In  
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19 addition, this trial will provide a preliminary evaluation of whether a modular transdiagnostic  
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21 treatment approach may be effective at reducing the distress and impairment associated with  
22  
23 CMHP [10]. The trial will also provide an indication of the feasibility and acceptability, of the  
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25 transdiagnostic intervention to service-users and clinicians by recruiting through post-primary  
26  
27 care UK NHS psychology services where complex comorbidity represents the modal clinical  
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29 presentation. In addition, the trial will provide initial estimates of cost-effectiveness in terms  
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31 of service-use and potential quality-adjusted life years added. We therefore present the  
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33 protocol for a feasibility trial with co-primary outcomes, examining the effect of *Shaping*  
34  
35 *Healthy Minds* on primary and comorbid diagnoses. The feasibility trial will provide a  
36  
37 plausible range of point estimates of the efficacy of *Shaping Healthy Minds* on standardised  
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39 continuous symptom measures for primary and secondary diagnoses to inform this key  
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41 question, refine the treatment manual and contribute to the design of future scaled-up trials  
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43 [27].  
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## 48 **Methods and Analysis**

### 49 **Study Design**

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51 The design is a parallel arm RCT comparing *Shaping Healthy Minds* to TAU.  
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55 Participants will be assessed three times - at baseline, at post-treatment, and at 3-month  
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3 follow-up. These three time points involve face-to-face assessments including the full battery  
4 of primary and additional outcomes and process measures, described below.  
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### 6 7 **Participants and recruitment**

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9 The proposed feasibility study will seek to recruit 50 people aged 18 and above with a  
10 primary diagnosis of a unipolar mood, anxiety, obsessive-compulsive, or trauma- and  
11 stressor-related disorder (CMHPs) with at least one additional comorbid diagnosis according  
12 to the Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition (DSM-5 [29]).  
13 Participants will be randomly allocated to one of two groups: (1) *Shaping Healthy Minds*, or  
14 (2) TAU. Diagnosis of CMHPs will be determined by trained research staff using the  
15 Structured Clinical Interview for the DSM-5 (SCID-5; [30]). To be eligible participants will  
16 also need to score > 10 on either the Patient Health Questionnaire (PHQ-9) or the Generalised  
17 Anxiety Disorder Questionnaire (GAD-7; see Study Measures below). Exclusion criteria are  
18 current/past psychosis or bipolar disorder, current diagnosis of alcohol or substance use  
19 disorder (all assessed via the Structured Clinical Interview for the DSM-5; SCID-5; [30]),  
20 organic brain damage, complex trauma history or recurrent self-injury requiring specialist  
21 services, or current suicidality that warrants immediate clinical attention and constitutes a  
22 current risk of harm to the individual (all assessed via participant report and the clinical care  
23 team). Participants may be engaged with the multi-disciplinary clinical care team, but those  
24 randomised to *Shaping Healthy Minds* will not be receiving other psychological services  
25 whilst participating in the trial. All other services (e.g., medication review with psychiatrist or  
26 general practitioner, occupational therapy, social support services) may be continued, and  
27 there are no medication exclusions.  
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50 Participants will be recruited through local NHS clinical psychology services,  
51 including the high intensity team of the Cambridge Psychological Wellbeing Service, and  
52 secondary care services with expertise in treatment of more complex and comorbid affective  
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3 disorders. The recruitment pathways will involve suitable service-users on a waitlist to receive  
4 treatment being identified by a member of the clinical service (including an Assistant  
5 Psychologist focusing primarily on recruitment into clinical research studies) who will  
6 provide them with a letter outlining the study. Service-users will then be able to contact the  
7 research team to opt into the study. Initial eligibility will be screened over the telephone, and  
8 suitable participants will be invited to complete the SCID, either at the clinical service or the  
9 research unit. At the beginning of this session, all participants will provide written informed  
10 consent (see supplementary materials for a sample Participant Information Sheet and Consent  
11 Form). No potential participants will be contacted by a member of the research team until  
12 they have given consent for such contact to a member of the clinical care team.  
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### 24 **Participant allocation**

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26 Following both baseline assessment sessions, eligible participants will be stratified  
27 according to depression (PHQ-9) and anxiety (GAD-7) severity scores and randomised to  
28 either *Shaping Healthy Minds* ( $n = 25$ ) or TAU ( $n = 25$ ). This will be achieved using  
29 computer generated, quasi-random numbers and will be conducted by the trial statistician  
30 (PW), blind to study objectives. Once generated, this information is passed to the project  
31 coordinator responsible for delivering the intervention. Once a participant begins treatment,  
32 he or she is free to discontinue participation at any time, in which case s/he will be referred  
33 back to the appropriate NHS clinical care team. Figure 1 summarises participant flow through  
34 the trial.  
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### 46 **Interventions**

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48 *Shaping Healthy Minds* (SHM) is a modular intervention, comprising 10 independent  
49 modules that will last up to 20 sessions. The content of the modules is drawn from a number  
50 of evidence-based psychological therapies, including CBT [31], ACT [32], DBT [33], MBCT  
51 [34], and behavioural activation [35, 36]. The programme aims to bring together the core and  
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3 unique therapeutic techniques from the best available disorder-focused treatment packages  
4 into the one transdiagnostic treatment package (e.g., behavioural experiments [37] and graded  
5 exposure [38] from CBT, values exercises and mindfulness strategies from ACT [39], activity  
6 scheduling from BA [35], emotion regulation strategies from DBT [33], and present-moment  
7 awareness exercises from MBCT [40]). The elements of *Shaping Healthy Minds* were drawn  
8 from recent meta-analyses supporting the effectiveness of these treatment strategies (e.g., [36,  
9 41-43]), and the manuals were written and reviewed by experienced clinical psychologists  
10 (TD, JN, AB, CH, and MB). In addition, experts in particular fields (e.g., WK for mindfulness  
11 and case formulation) were consulted on the content of specific modules. Further, we received  
12 service-user input on the content of the draft modules, and a part of this feasibility trial will be  
13 receiving feedback from participants on their experience of using the manuals.  
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27 The modular approach is standardised, yet can be flexibly delivered according to an  
28 individual's concerns, problems, and goals [22]. The treatment focuses both on alleviating  
29 negative symptoms and enhancing positive wellbeing, by teaching skills and techniques and  
30 enhancing positive emotions, harness and build on strengths, and maximise resilience over the  
31 longer-term. Choice, order, and length of modules (i.e., number of session over which they  
32 are completed) is tailored to the transdiagnostic difficulties of the individual using  
33 collaborative case formulation [44], although there are three core modules that everyone  
34 receives (outlined below). Treatment consists of weekly face-to-face one-hour sessions with  
35 the trial therapists. Sessions will involve collaboratively setting an agenda for the session  
36 based on the participants' ratings for their top 3 problems and top 3 strengths, the goals set for  
37 therapy, and the module in focus. Participants will complete homework exercises to  
38 consolidate and practice the skills learned during the specific modules and will be strongly  
39 encouraged to continue this practice following the end of one module and move to the next.  
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3 The ten SHM modules (core modules listed in bold) are: (1) **Getting Acquainted with**  
4 **SHM**, (2) **Understanding Emotions**, (3) Managing and Tolerating Emotions, (4)  
5 Behavioural Activation, (5) Tackling Avoidance, (6) Tackling Unhelpful Thoughts, (7)  
6 Tackling Unhelpful Habits, (8) Overcoming Repetitive Thinking, (9) Managing Upsetting  
7 Memories and Images, and (10) **Relapse Prevention and Future Orientation**. Additional  
8 information about the content of the modules can be found in the supplementary materials.

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11 **Treatment-as-usual (TAU)**. For TAU, clinical psychologists and high-intensity CBT  
12 Therapists in teams specialising in CMHPs will be asked to provide the course of  
13 psychological therapy that they deem appropriate, in addition to referral to other health/social  
14 services and medication management. Psychological treatment in the specialist teams  
15 delivering TAU will standardly consist of disorder-focused Cognitive Behavioural Therapy,  
16 Eye Movement Desensitisation Reprocessing, or Behavioural Activation. The delivered  
17 treatment will be documented to ensure systematic understanding of the duration, frequency,  
18 and type of treatment administered.

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21 **Treatment Integrity**. Therapists with experience in treating adult CMHPs will deliver  
22 the transdiagnostic intervention. Treatment fidelity and clinician adherence for the *Shaping*  
23 *Healthy Minds* group will be established using continued monitoring of completion of module  
24 components and through independent rating of specific treatment strategies by the supervising  
25 clinical psychologist. After every session, clinicians will complete a bespoke Treatment  
26 Fidelity Checklist which is a session-by-session self-report measure of compliance with the  
27 *Shaping Healthy Minds* approach, and these will be evaluated during weekly clinical  
28 supervision with the trial clinical supervisor. In addition, a randomly-selected 25% of the  
29 audio-taped treatment sessions will be rated for adherence to the manuals by an experienced  
30 clinician, independent of the trial. Homework completion will be monitored by trial therapists.

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3 This bespoke measure will be supplemented with The Cognitive Therapy Scale –  
4 Revised (CTS-R) – a standardised measure of competence within cognitive therapy,  
5 consisting of adherence to and skilful application of cognitive therapy methods and the  
6 therapeutic alliance [45]. The CTS-R has 13-items that are completed by an independent rater,  
7 assessing agenda setting, feedback, collaboration, pacing and efficient use of time,  
8 interpersonal effectiveness, charisma/flair, facilitation of emotional expression, guided  
9 discovery, conceptualisation, identifying key cognitions, application of cognitive change  
10 methods, application of behavioural techniques, use of homework.  
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## 20 **Measures**

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22 **Co-primary outcomes.** The co-primary outcome measures are self-reported  
23 symptoms of depression and anxiety, indexed by the PHQ-9 [46], and GAD-7 [47], as well as  
24 levels of disability and functional impairment, indexed by the Work and Social Adjustment  
25 Scale (WSAS [48]).  
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31 **Secondary outcomes.** Given the transdiagnostic focus of the study, self-reported  
32 symptoms on specific disorders that client's meet criteria for at trial baseline will be indexed  
33 by the IAPT Phobia Scales (social phobia, agoraphobia, specific phobia, [49]), the Social  
34 Phobia Inventory (SPIN, [50]), the Penn State Worry Questionnaire (generalised anxiety,  
35 PSWQ, [51]), the Obsessive-Compulsive Inventory (OCI, [52]), the Revised Impact of Event  
36 Scale (posttraumatic stress, IES-R, [53]), the Agoraphobia-Mobility Inventory (MI, [54]), the  
37 Fear Questionnaire (specific phobias, FQ, [55]), the Panic Disorder Severity Scale- self report  
38 version (PDSS-SR, [56]), the Health Anxiety Inventory – short version (SHAI, [57]), and the  
39 Sheehan Disability Scale (SDS, [58]). Participants will only complete a selection of these  
40 measures depending on their concerns and associated diagnoses. In addition to these disorder-  
41 specific measures, the Inventory of Depression and Anxiety Symptoms (IDAS-II) will capture  
42 both disorder-specific and transdiagnostic symptom dimensionality within a single measure  
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3 [59]. Selection of these measures will be determined following completion of the structured  
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5 clinical interview at the beginning of assessment.  
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7 **Process Measures.** We will also include a number of process-related measures which  
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9 will be administered at baseline, at post-intervention, and at 3-month follow-up to begin to  
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11 explore mechanisms of change and the feasibility of conducting embedded process outcome  
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13 research within this type of trial (see Table 1). To explore the value of the individual modules  
14  
15 administered within the transdiagnostic intervention, we will also administer module-relevant  
16  
17 measures (e.g., rumination, distress tolerance) before and after completion of the module.  
18  
19 Finally, participants' expectancy of treatment outcomes and measures of engagement and  
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21 compliance will be administered at pre and post-intervention to inform the further  
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23 development of the protocol.  
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26 **Health economics measures.** Data collection for the health economic evaluation will  
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28 take a patient-level perspective [74, 75], recording the cost-per-session of treatment and  
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30 productivity losses resulting from time off work as a consequence of their mental health  
31  
32 difficulties. Data will be collected using the Healthlines Resource Use Questionnaire [74, 75],  
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34 which is a measure of the participants use of health care services (including NHS, help at  
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36 home), occupational productivity (i.e., time off work) and cost of transdiagnostic treatment  
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38 delivery (e.g., direct and indirect time spent in service delivery). The Medical Outcomes  
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40 Study Questionnaire Short Form 36 Health Survey (SF-36) [76], a generic quality of life  
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42 questionnaire, will measure overall health and wellbeing, daily functioning, and general life  
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44 satisfaction across multiple domains. These measures allow calculation of the additional  
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46 number of quality of life years the treatment will yield. These data will allow preliminary  
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48 estimates of the potential cost-utility of the transdiagnostic intervention and also of the  
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50 feasibility of acquiring these data within the trial protocol.  
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## Methodological Aspects

**Power analysis and sample size.** Although a standard power calculation based on detecting treatment effects is the conventional approach to determining sample sizes for trials, the main aim of the current trial is to elucidate feasibility for a larger later-stage evaluation. We therefore sought at this stage only to provide a point-estimate of the effect of *Shaping Healthy Minds* to inform a power calculation for this putative fully powered later phase evaluation. Our previous experience with such early phase trial platforms indicates that 50 patients will provide sufficient numbers and diagnostic diversity to evaluate feasibility, acceptability, and procedural uncertainty for *Shaping Healthy Minds* and a plausible test of recruitment protocols. This will give 40 patients (20 per arm) at 3-month posttreatment follow up, assuming 20% attrition. This will provide a reasonable range of point estimates of effect on our set of candidate outcome measures sufficient to guide later phase trial work.

**Data collection and confidentiality.** Outcome data for all participants who are randomised will be collected via face-to-face interviews and written questionnaires at baseline, post-treatment, and 3-month follow-up. To maintain confidentiality all participants will be given a trial number so that personally identifying information is not linked to assessment or trial information. All data (including personally-identifiable information) will be stored on secure UK NHS databases, secure University of Cambridge servers and within locked filing cabinets under the management of the trial coordinator. Access will be limited to the immediate clinical research team.

**Blinding.** Outcome assessments will be conducted by independent raters who have no therapeutic relationship with the patients and are blind to treatment condition. Double blinding of patients and therapists is not possible due to the nature of the trial (i.e., a psychological intervention). Unblinding will not be necessary because participants and therapists are not blinded to intervention allocation.

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**Statistical analysis plan.** Initial analyses of the outcomes will be conducted by the trial statistician, blind to trial condition, following CONSORT standards (see Figure 2, supplementary materials). There are no planned interim analyses. Initial analyses will be conducted on an intention-to-treat basis, with subsequent analyses being per protocol. Mixed model analyses of variance (ANOVAs) will be used to compare groups on outcomes at the three assessment points – baseline, post-intervention, and 3-month follow-up. Baseline levels on relevant measures will be included as covariates, as appropriate. Both intent-to-treat and per-protocol exploratory analyses will be conducted with our range of outcome measures following CONSORT standards. Multiple imputation will be used to account for missing data. Intent-to-treat analysis will also be used for those lost to attrition. Exploratory moderation and mediation analyses to examine process variables will be conducted using the MacArthur approach [77]. For the health economic data, costs associated with service use will be calculated by attaching a unit cost to each instance of use, and data will be combined with quality-adjusted life years (QALYs, [72]) derived from the SF-36 to arrive at a preliminary estimate of the cost-utility of the transdiagnostic intervention.

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**Monitoring and data management.** The trial will take place at NHS sites and a research unit in the East of England. A Trial Management Group (TMG), will meet 1-2 times a year to: manage the protocol; monitor recruitment in relation to targets; deal with any adverse events; and co-ordinate the different stages of the project. The TMG consists of research clinical psychologists and assistant psychologists, a psychiatrist, a health economist, clinical psychology researchers, the trial statistician, a nurse practitioner, and a service user representative. Day-to-day project management will be the responsibility of a smaller trial team, meeting fortnightly to deal with administrative issues, troubleshooting, and recruitment flow. Clinical supervision will take place fortnightly. As this is a Phase I/II trial, a data-management committee was deemed unnecessary, and as such the trial team are responsible

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3 for monitoring and data management. Data will be monitored for completeness and  
4 consistency using spot checks and plausibility checks carried out by the trial statistician. The  
5 trial lead, trial coordinator, and statistician will have full access to the final trial dataset. The  
6  
7 study data will be reported in line with the current CONSORT recommendations.  
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11 **Safety aspects.** Adverse events are managed in line with UK MRC protocols and, in  
12 the unlikely case of an adverse event, will be documented appropriately. Precautions have  
13 been taken to reduce the likelihood of adverse events occurring; for example, patients who are  
14 acutely suicidal or at high risk of harm do not meet study inclusion criteria. The interventions  
15 are delivered by therapists experienced in the management of risk and in the treatment of  
16 psychological disorders. In the case of any adverse events as a result of the intervention that  
17 would interfere with participation, participation in the trial will be discontinued. Regular  
18 team meetings will be conducted to monitor any difficulties patients may be having and ways  
19 of best dealing with these difficulties. Serious adverse events will be reported to the Ethics  
20 Committee. The trial is underwritten by the University of Cambridge in the case that any  
21 individual suffers harm or requires post-trial care. Any adverse events will be reported in the  
22 trial paper.  
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37 **Ethical approval and protocol amendments.** This project has received ethical  
38 approval from the Health Research Authority of the UK National Health Service (East of  
39 England; REC reference: 16/EE/0095). The study will be conducted within appropriate UK  
40 MRC, National Health Service and professional ethical guidelines, ensuring that Good  
41 Clinical Practice procedures are adhered to at all times. Protocol amendments will be  
42 circulated to the ethics committee, and trial team, and published in the online registration of  
43 the trial, and in the trial paper.  
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52 **Dissemination policy.** There are no publication restrictions and findings will be  
53 disseminated broadly to participants, healthcare professionals, the public, and other relevant  
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1 groups. Academic outputs will take the form of peer-reviewed empirical journal articles,  
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3 commentary pieces, and conference presentations. Clinical outputs will be prioritised by the  
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5 research team in order to maximise the impact of the findings with practitioners and  
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7 commissioners. Outputs will comprise clinical conferences, workshops, service user groups,  
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9 and a study website that will make the intervention materials and related measures generally  
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11 available. We will send all participants a report describing the findings and their implications.  
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13 We will also make participants aware of the study website. We anticipate that trial findings  
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15 will inform future revisions of clinical guidelines for numerous forms of mood, anxiety, and  
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17 stress disorders, and the development of guidelines for comorbid conditions. Anonymised  
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19 data from the trial will be made publicly available on an open-access database.  
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## 24 Discussion

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26 A significant proportion of the cost of CMHPs is generated by adults suffering from  
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28 complex and comorbid depression, stress and anxiety, where treatment non-response, cross-  
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30 sector service-use across health, social care, and housing, and loss of productivity are greatest.  
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32 Providing effective interventions for these mental health problems therefore has the potential  
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34 to reduce both long-term treatment costs as well as prevent large productivity losses. At  
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36 present, most psychological interventions focus on specific diagnoses and many treatment  
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38 manuals take a 'one-size-fits-all' approach. Current evidence-based interventions only  
39  
40 achieve clinical recovery for 40-70% of patients, with people suffering complex co-morbid  
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42 conditions faring significantly worse. This randomised controlled feasibility trial aims to pave  
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44 the way for a scaled-up efficacy trial of a new transdiagnostic modular treatment for all  
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46 CMHPs – *Shaping Healthy Minds* – that enables the flexible delivery of evidence-based  
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48 techniques. This treatment approach may improve the effectiveness and dissemination of  
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50 evidence-based intervention for the many individuals for whom diagnosis-specific treatments  
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52 leave significant difficulties unaddressed. The results from this trial will provide a range of  
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3 estimates of effect sizes that can be used to power a later stage trial of treatment efficacy, to  
4 refine the treatment protocol, and to inform future evaluation of the mechanisms underlying  
5 any treatment effects. If effective, *Shaping Healthy Minds* has the potential to improve  
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7 outcome for those with complex presentations, through offering a cost-effective treatment  
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9 option to reduce chronic, transdiagnostic psychological difficulties.  
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16 **Trial Status:** This trial was registered at [clinicaltrials.gov](http://clinicaltrials.gov) on 4 May 2017 (NCT03143634).  
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18 This article was submitted on 31 May 2018. To date, 15 participants have met eligibility  
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20 criteria for the study and have been randomised to a condition. The trial opened on 31 July  
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22 2017, and data collection aims to be completed by September 2019.  
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## List of Abbreviations

DSM – Diagnostic and Statistical manual

IAPT – Improving Access to Psychological Therapies

HARMONIC – The Healthy and Resilient Mind Programme: Building Block for Mental Wellbeing

MRC – Medical Research Council

NHS – National Health Service

PTSD – Posttraumatic Stress Disorder

RCT – Randomised Controlled Trial

SCID-5 – Structured Clinical Interview for DSM-5 disorders

TAU – Treatment-as-usual

CMHP – Common Mental Health Problems

NICE – National Institute for Health and Care Excellence

CBT – Cognitive Behaviour Therapy

ACT – Acceptance and Commitment Therapy

DBT – Dialectical Behaviour Therapy

MBCT – Mindfulness Based Cognitive Therapy

### Authors' contributions

MB will manage the trial, deliver the intervention, co-develop the treatment manuals and helped to draft the manuscript; CH will assist with trial management and helped to draft the manuscript; AB advises on the delivery of the interventions and provided guidance on the protocol; JC provides practical and NHS service support for the trial; COL, RE and DJ provides support for the trial management; PW is the trial statistician responsible for the randomisation, advise on analysis strategy, and analysis of the data; LL provides support for the health economics component; SR provides service-user support for the trial; SG and WK advised on the treatment manual; JN co-developed and adapted the treatment manuals; TD designed the study, co-developed and adapted the treatment manuals, and helped to draft the manuscript. All authors read and approved the final manuscript.

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## Funding

This paper presents independent research funded by the National Institute of Health Research (NIHR) under its Research for Patient Benefit (RfPB) Programme (Grant Reference Number PB-PG-0214-33072) grant awarded to Tim Dalglish, Peter Watson, Jill Newby, Leonora Brosan, Rajini Ramana, Louise Lafortune, Sarah Rae, Simon Gilbody, Willem Kuyken, and Caitlin Hitchcock. Jill Newby is supported by a NHMRC/MRFF Fellowship (1145382).

Please note that the funding body does not have authority over the running of the trial – all decisions rest with the trial team. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

## Competing Interests

The authors have no competing interests.

## Patient consent

Obtained.

## Ethics approval

NHS National Research Ethics Committee (East of England, Reference: 16/EE/0095)

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Table 1.

*Additional Outcome and Process measures to assess changes in potential mechanisms of psychological distress and in response to specific transdiagnostic intervention modules.*

Measure	Focus area
The Treatment Credibility / Expectancy Questionnaire (CEQ) [60]	Expectancy about treatment outcome, as well as the credibility of the treatment.
Cognitive Emotion Regulation Questionnaire (CERQ) [61]	Ability to contextualize negative events within a wider frame of reference.
The Experiences Questionnaire (EQ) [62]	Ability to disengage from troublesome mental content and take a more accepting stance towards it, as well as the tendency to engage in rumination.
Differential Emotions Scale (DES [63])	Intensity with which they experience different emotions on a typical day to obtain summary scores for positive emotions, negative emotions, and denied emotions (the number of emotions <i>not</i> endorsed by the participant).
Levels of Personality Functioning Scale (LPFS) [64]	Personality functioning based on the DSM-5 Alternative Model of Personality Disorders. It has four subscales: Identity, Self-Direction, Empathy, and Intimacy.
Ruminative Responses Scale of the Response Styles Questionnaire (RRS) [65]	Rumination (Module 7 – Overcoming Repetitive Thinking)
Distress Tolerance Scale (DTS)[66]	Ability to tolerate distress (Module 3 – Managing and Tolerating Emotions)
Difficulties with Emotion Regulation Scale (DERS) [67]	Ability to label, perceive, and regulate emotions (Modules 2 – Understanding Emotions and 3 – Managing and Tolerating Emotions)
Dysfunctional Attitudes Scale (DAS) short form (version 1 and 2) [68]	Negative beliefs, thoughts and assumptions (Module 6 – Tackling Unhelpful Thoughts)

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3	Kentucky Inventory of	Mindful awareness (Module 2 – Understanding Emotions)
4	Mindfulness Skills (KIMS)	
5	[69]	
6		
7	Anxiety Sensitivity Index	Fear of physical anxiety sensations (Module 3 – Managing
8	(ASI) [70]	and Tolerating Emotions and Module 5 – Tackling
9		Avoidance)
10		
11	Posttraumatic cognitions	Trauma-related beliefs and maladaptive appraisals of
12	inventory – short version	intrusive symptoms (Module 9 – Managing Upsetting
13	(PTCI) [71]	Memories and Images)
14		
15	Skills of Cognitive Therapy	Implementation of cognitive therapy skills (Module 6 –
16	(SoCT) [72]	Tackling Unhelpful Thoughts)
17		
18	The Multidimensional	Avoidance of internal experiences including thoughts,
19	Experiential Avoidance	feelings, physical sensations (Module 5 – Tackling
20	Questionnaire [73]	Avoidance)
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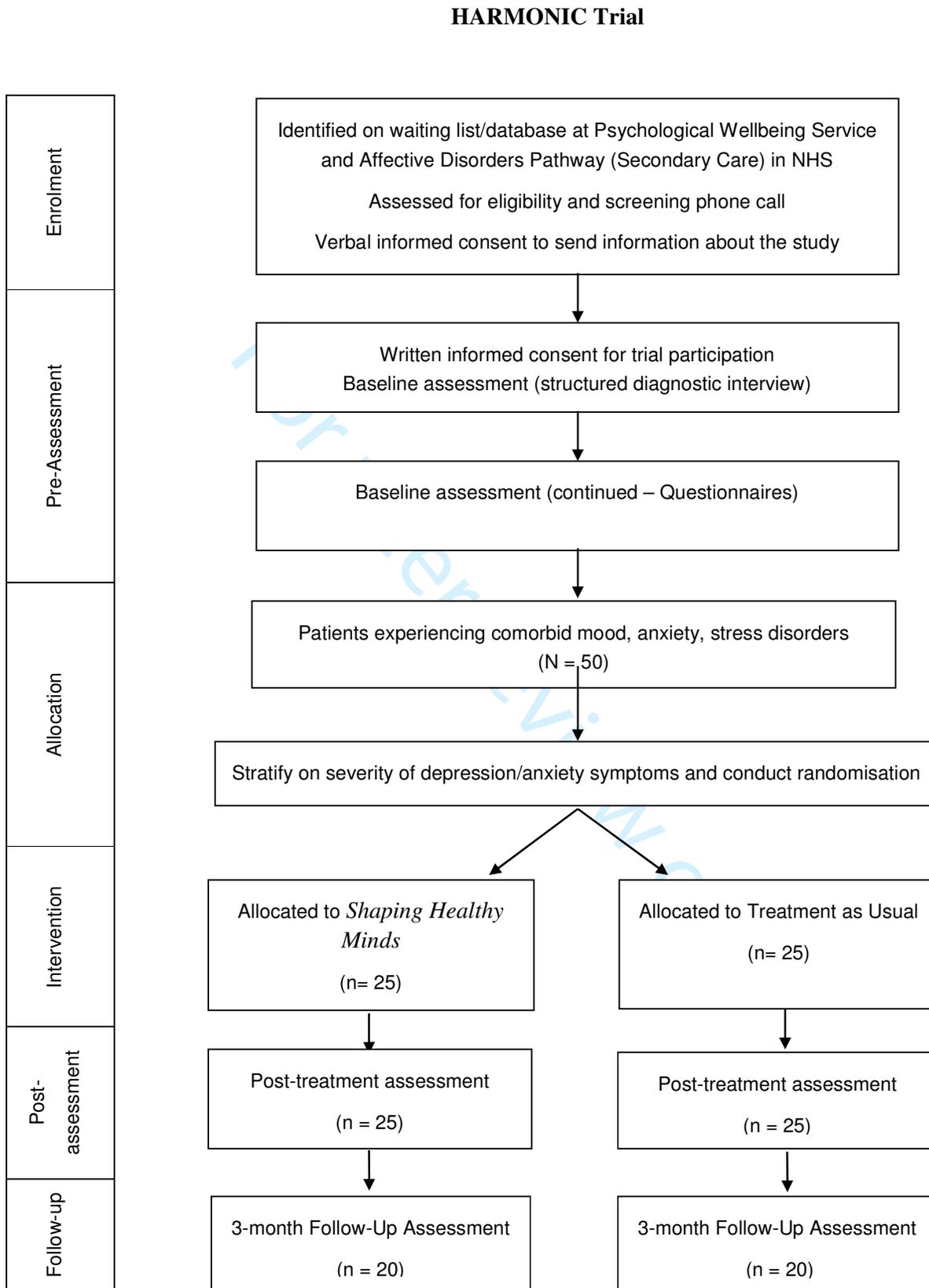


Figure 1. Participant flow diagram with anticipated participant numbers at each stage

## HARMONIC Trial (Healthy and Resilient Mind Programme: Building Blocks for Mental Wellbeing)

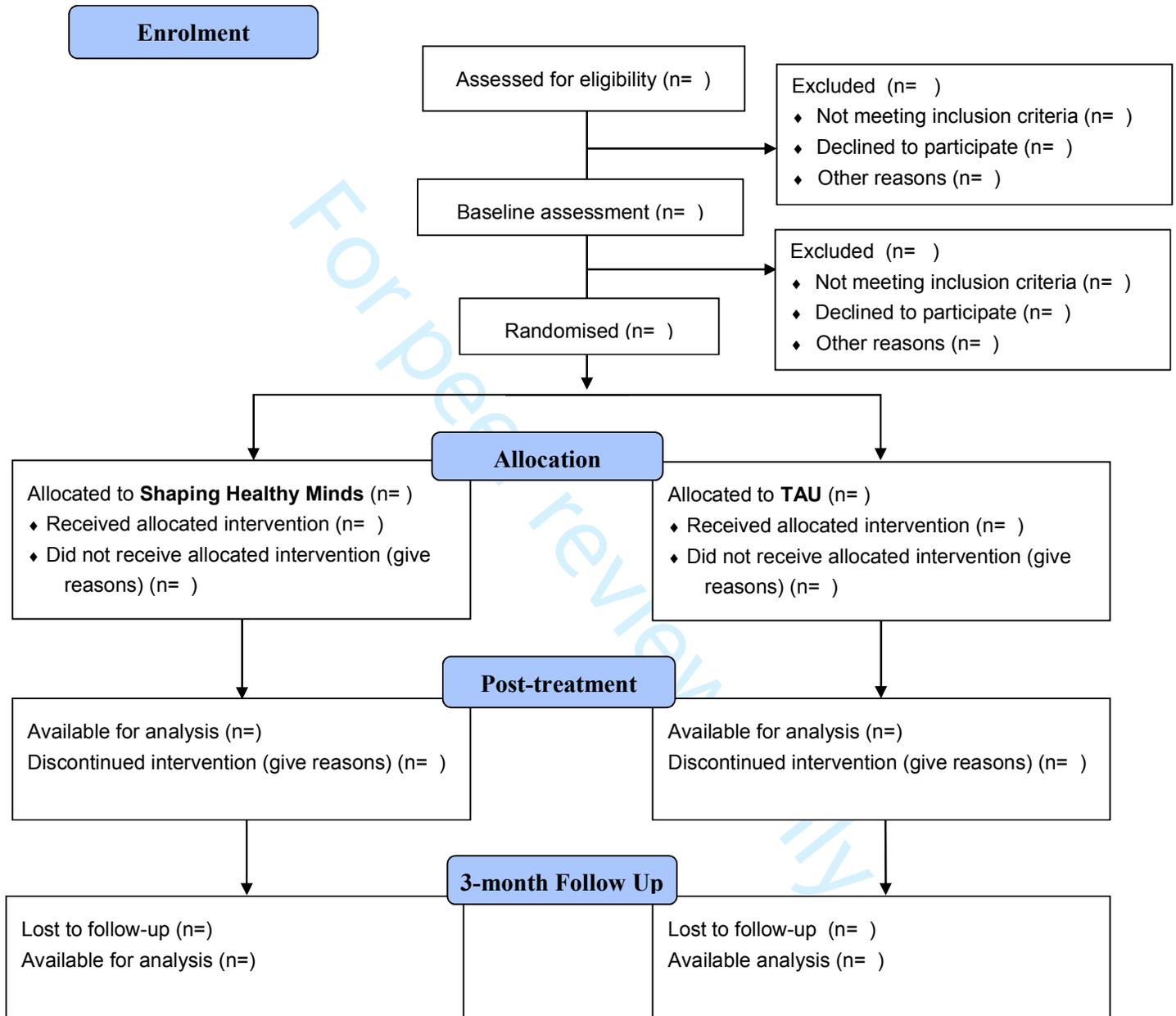


Figure 2. CONSolidated Standards of Reporting Trials (CONSORT) diagram

Table 1.

*Key treatment components of Shaping Healthy Minds Core and Optional Modules.*

#	Module Title	Sections of Module	Duration (sessions)
1	Getting Acquainted with <i>Shaping Healthy Minds Core Module</i>	<ul style="list-style-type: none"> <li>• Education about depression and anxiety, and about emotions (Including 5-part model of emotion episodes)</li> <li>• Orientation to treatment</li> <li>• Defining Top 3 Problems and Top 3 Strengths</li> <li>• Setting treatment goals and making plans</li> <li>• Enhancing motivation</li> </ul>	1-3
2	Understanding emotions <i>Core Module</i>	<ul style="list-style-type: none"> <li>• Education about emotions</li> <li>• Orientation to the emotion model</li> <li>• Self-monitoring of emotion episodes</li> <li>• Introduction to Mindful Awareness of Emotions</li> </ul>	1-2
3	Managing and Tolerating Emotions <i>Optional Module</i>	<ul style="list-style-type: none"> <li>• Education about emotion management toolbox</li> <li>• Relaxation</li> <li>• Exercise</li> <li>• Social Support</li> <li>• Distraction</li> <li>• Self-soothing</li> <li>• Accepting and Tolerating Feelings</li> </ul>	1-3
4	Behavioural Activation <i>Optional Module</i>	<ul style="list-style-type: none"> <li>• Education about low activity cycle</li> <li>• Activity Monitoring</li> <li>• Activity Scheduling and establishing positive routines</li> <li>• Savouring the good things</li> </ul>	1-2
5	Tackling Avoidance <i>Optional Module</i>	<ul style="list-style-type: none"> <li>• Education about avoidance</li> <li>• In vivo exposure</li> <li>• Interoceptive exposure</li> <li>• Emotion exposures</li> </ul>	1-3
6	Tackling unhelpful thoughts <i>Optional Module</i>	<ul style="list-style-type: none"> <li>• Education about thoughts</li> <li>• Thought monitoring</li> <li>• Thought questioning and cognitive flexibility</li> <li>• Behavioural experiments</li> <li>• Accepting and tolerating thoughts</li> </ul>	1-3
7	Tackling unhelpful habits	<ul style="list-style-type: none"> <li>• Education about habits</li> <li>• Self-monitoring of habits</li> </ul>	1-3

	<i>Optional Module</i>	<ul style="list-style-type: none"> <li>• Step-by-step habit change process</li> </ul>	
8	Overcoming Repetitive Thinking <i>Optional Module</i>	<ul style="list-style-type: none"> <li>• Education about rumination and worry</li> <li>• Self-monitoring of rumination and worry</li> <li>• Getting unstuck toolbox</li> <li>• Shifting thinking styles and perspective, directing attention</li> </ul>	1-4
9	Managing upsetting memories and images <i>Optional Module</i>	<ul style="list-style-type: none"> <li>• Education about memories and intrusive images</li> <li>• Monitoring of memories</li> <li>• Imaginal exposure</li> <li>• Rescripting memories</li> <li>• Reliving + rescripting memories</li> </ul>	2-4
10	Preventing relapse and building a positive future <i>Core Module</i>	<ul style="list-style-type: none"> <li>• Education about lapses and relapses</li> <li>• Evaluating treatment progress and consolidating learning</li> <li>• Creating a therapy blueprint (relapse prevention plan)</li> <li>• Setting goals and making future plans</li> </ul>	1



**Participant Information Sheet**  
**Study title: *Shaping Healthy Minds***

We invite you to participate in a study investigating a new modular treatment for mental health difficulties. Please read this information sheet if you wish to hear about the study in more detail. Your participation is *entirely voluntary*. Your treatment through the NHS will not be affected if you decide not to participate in this research.

This treatment – *Shaping Healthy Minds* (SHM) – treats symptoms that are common across depression and multiple anxiety disorders. The treatment consists of components of the best available evidence-based psychological treatments (e.g., mindfulness-based interventions, Acceptance and Commitment Therapy, Cognitive Behavioural Therapy, Behavioural Activation, and Dialectical Behaviour Therapy). Through using components of different types of therapy, the SHM aims to not only treat the principle problem that each individual is experiencing (e.g., depression or anxiety) but to target other psychological symptoms the individual is experiencing at the same time. In this way, someone who is experiencing both depression and anxiety will receive treatment for both of these issues, in contrast to the usual approach of treating one problem first, using only one type of therapy.

***Purpose of the study***

The purpose of this study is test whether the SHM is an effective treatment for people experiencing multiple psychological difficulties. We are interested in whether SHM will reduce symptoms of multiple mental health issues in those who are suffering from both depression and one or more anxiety disorders.

***What's involved?***

If you decide to take part, you would be asked to attend a 'screening' session to determine whether you are eligible to participate in this study. It will take 60-90 minutes and involves interviews and questionnaires focusing on emotions and mental health.

If you are eligible to participate in the trial you will then be randomly allocated to one of two groups:

- (i) 15-20 sessions of the *Shaping Healthy Minds* (SHM) programme,
- (ii) Treatment you would usually receive from the NHS (Treatment-as-Usual)

You will not be able to choose which of these groups you are allocated to, as the allocation is random and decided by a computer.

In the SHM programme, you will complete individual sessions with a clinical psychologist. The exact therapy components that you complete will be selected in consultation with you and based on the particular symptoms you are experiencing. That is, the treatment will be shaped for you. You will also receive the regular NHS care that you normally receive except for any psychological therapy.

In Treatment-as-Usual, you will receive all of the regular NHS services you would normally receive including any psychological therapy.

In addition to receiving treatment sessions, you will be asked to attend five assessment sessions where you will be asked to complete some questionnaires, some computer-based tasks that ask about your memories and emotions, including a task that involves pleasant and unpleasant images. In addition, there is an **optional** neuroimaging task, involving two functional magnetic resonance imaging scans (before and after treatment).

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1 You can choose not to complete the imaging sessions and still participate in the study.

2  
3 Prior to completing the treatment sessions (SHM or Treatment-as-Usual) which form the main part of the study, you will  
4 be asked to complete one assessment session which involves interviews and questionnaires, and one assessment  
5 session with computer tasks and the optional imaging session. You would then repeat these two assessment sessions  
6 after completing the treatment, followed by one final assessment session 3 months following the completion of  
7 treatment. Each assessment session will take approximately one and a half hours, which includes a break if  
8 needed. With your consent, some sessions will be audio-recorded to allow checks on the quality of the  
9 treatment you are receiving.

### 11 ***Why have I been invited to take part?***

12 All individuals currently receiving NHS services for depression or anxiety in the Cambridge area are being  
13 invited to participate in this study.

### 15 ***Do you have to take part?***

16 No, it is up to you to decide. We will describe the study and go through this information sheet, which we will  
17 then give to you. If you do want to join in we'll ask you to sign a consent form, a copy of which you can keep  
18 along with this information sheet. You are free to withdraw from the study at any point *without giving us a*  
19 *reason*. You will not be treated any differently by any NHS service if you choose not to participate in this study  
20 or if you decide to withdraw.

### 23 ***Will I be reimbursed?***

24 You will be reimbursed for the assessment sessions at a rate of £6 per hour for your time. It is anticipated that  
25 the one screening session and four assessment sessions will not exceed a total of ten hours, for which you  
26 would receive a minimum of £45, plus travel costs. If you choose to do the neuroimaging sessions as well, you  
27 will receive £20 per imaging session, so you would receive a total of £85. You will not be reimbursed for the  
28 therapy sessions as you will be receiving therapy free of charge by qualified clinical psychologists.

### 31 ***Are there any risks or benefits associated with taking part?***

32 All of the tasks, interviews, and questionnaires we will ask you to complete have been used safely in previous  
33 research. As with any research involving emotional material, there is a chance that you will experience some  
34 upset when you discuss personal memories and difficulties. In our experience this is usually very mild and  
35 short-lived with no lasting ill effects. After participation you will receive a complete and thorough explanation  
36 of the study and you will be encouraged to express your feelings about your experience, if you wish.  
37 Additionally, you will be able to contact a member of the research team (a qualified clinical psychologist) after  
38 any session should you feel you are experiencing distress as a result of taking part in the study.

### 41 ***What are the possible benefits of taking part?***

42 We hope that the findings from this research will lead to improvement in treatment options for people  
43 experiencing multiple mental health disorders. We also hope that completing the SHM, if you are randomly  
44 allocated to that treatment, will have a beneficial impact on your psychological difficulties. We cannot  
45 guarantee that this will be the case for everybody who takes part, but you will have an opportunity to  
46 experience a range of therapeutic strategies and techniques.

### 48 ***What if there is a problem?***

49 For any complaint about the way you have been dealt with during the study or any possible harm you may  
50 have suffered you can contact the Patient Advice and Liaison Service on 01223 726 774,  
51 <http://www.cpft.nhs.uk/about-us/pals.htm>

### 54 ***Further Information & Contact Details:***

55 If you would like any further information about this project please contact the research coordinator **Dr**  
56 **Melissa Black** at the MRC Cognition and Brain Sciences Unit (Tel: **01223 273 739**; Email: [melissa.black@mrc-](mailto:melissa.black@mrc-cbu.cam.ac.uk)  
57 [cbu.cam.ac.uk](mailto:melissa.black@mrc-cbu.cam.ac.uk))

59 **Thank you for reading this information sheet**

60 For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>



Trial record **1 of 23** for: mood anxiety disorders | United Kingdom

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### The Modular Protocol for Mental Health (MPMH) (MPMH)

ClinicalTrials.gov Identifier: **NCT03143634**

 The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our [disclaimer](#) for details.

[Recruitment Status](#) ⓘ: Enrolling by invitation

[First Posted](#) ⓘ: May 8, 2017

[Last Update Posted](#) ⓘ: August 11, 2017

**Sponsor:**

Medical Research Council Cognition and Brain Sciences Unit

**Collaborator:**

Cambridgeshire and Peterborough NHS Foundation Trust

**Information provided by (Responsible Party):**

Medical Research Council Cognition and Brain Sciences Unit

[Study Details](#)

[Tabular View](#)

[No Results Posted](#)

[Disclaimer](#)

[How to Read a Study Record](#)

#### Tracking Information

**First Submitted Date**  
ICMJE April 27, 2017

1 2 3 4 5 6 7 8	<b>First Posted Date</b> <small>ICMJE</small>	May 8, 2017
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23	<b>Last Update Posted Date</b>	August 11, 2017
24 25 26 27 28	<b>Actual Study Start Date</b> <small>ICMJE</small>	July 18, 2017
29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46	<b>Estimated Primary Completion Date</b>	March 31, 2019 (Final data collection date for primary outcome measure)
	<b>Current Primary Outcome Measures</b> <small>ICMJE</small> (submitted: May 4, 2017)	<ul style="list-style-type: none"> <li>• Change in Depression symptoms [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session, three-months following final treatment session ] Patient Health Questionnaire - 9-item version (PHQ-9; Kroenke &amp; Spitzer, 2002)</li> <li>• Change in Anxiety symptoms [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session, three-months following final treatment session ] General Anxiety Disorder Questionnaire - 7-item version (GAD-7; Spitzer, Kroenke, Williams, &amp; Lowe, 2006)</li> <li>• Change in Level of disability and functional impairment [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session, three-months following final treatment session ] Work and Social Adjustment Scale (WSAS; Mundt, J.C. et al., 2002)</li> </ul>
	<b>Original Primary Outcome Measures</b> <small>ICMJE</small>	<i>Same as current</i>
	<b>Change History</b>	<a href="#">Complete list of historical versions of study NCT03143634 on ClinicalTrials.gov Archive Site</a>
	<b>Current Secondary Outcome Measures</b> <small>ICMJE</small> (submitted: May 4, 2017)	<ul style="list-style-type: none"> <li>• Change in symptoms of social phobia, agoraphobia and specific phobia [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session, three-months following final treatment session ] IAPT Phobia Scales (Department of Health/IAPT, 2011). This measure will only be completed by participants with symptoms of social phobia, agoraphobia or specific phobia.</li> <li>• Change in symptoms of social anxiety [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session, three-months following final treatment session ] The Social Phobia Inventory (SPIN; Connor, Davidson, Churchill, Sherwood, Foa, &amp; Weisler, 2000). This measure will only be completed by participants with symptoms of social anxiety.</li> <li>• Change in symptoms of generalised anxiety [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session, three-months following final treatment session ]</li> </ul>

The Penn State Worry Questionnaire (PSWQ; Meyer, Miller, Metzger, & Borkovec, 1990). This measure will only be completed by participants with symptoms of generalised anxiety disorder.

- Change in symptoms of obsessive-compulsive disorder [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session, three-months following final treatment session ]

The Obsessive-Compulsive Inventory (OCI; Foa, Kozak, Salkovskis, Coles, & Amir, 1998). This measure will only be completed by participants with symptoms of obsessive-compulsive disorder.

- Change in symptoms of post-traumatic stress disorder [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session, three-months following final treatment session ]

The Revised Impact of Event Scale (IES-R; Weiss, 2007). This measure will only be completed by participants with symptoms of PTSD.

- Change in symptoms of agoraphobia [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session, three-months following final treatment session ]

The Agoraphobia-Mobility Inventory (MI; Chambless, Caputo, Jasin, Gracely, & Williams, 1985). This measure will only be completed by participants with symptoms of agoraphobia.

- Change in symptoms of specific phobias [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session, three-months following final treatment session ]

The Fear Questionnaire (FQ; Marks & Mathews, 1979). This measure will only be completed by participants with symptoms of specific phobia.

- Change in symptoms of panic disorder [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session, three-months following final treatment session ]

The Panic Disorder Severity Scale - self report version (PDSS-SR; Shear, Brown, Barlow, Money, Holomskas, Woods, Gorman, & Papp, 1997). This measure will only be completed by participants with symptoms of panic disorder.

- Change in symptoms of illness anxiety [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session, three-months following final treatment session ]

The Health Anxiety Inventory - short version (SHAI; Salkovskis, Rimes, Warwick, & Clark, 2002). This measure will only be completed by participants with symptoms of illness anxiety.

- Change in level of disability and functional impairment [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session, three-months following final treatment session ]

Sheehan Disability Scale (SDS; Sheehan, 1983)

- Change in expectancy about treatment outcome, as well as the credibility of the treatment [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session, three-months following final treatment session ]

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	<p>The Treatment Credibility / Expectancy Questionnaire (CEQ; Devilly &amp; Borkovec, 2000)</p> <ul style="list-style-type: none"> <li>• Change in ability to contextualize negative events within a wider frame of reference [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session, three-months following final treatment session ]</li> </ul> <p>Cognitive Emotion Regulation Questionnaire (CERQ; Garnefski, Kraaij &amp; Spinhoven, 2000)</p> <ul style="list-style-type: none"> <li>• Change in disengagement from and acceptance of troublesome mental content, rumination [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session, three-months following final treatment session ]</li> </ul> <p>Experiences Questionnaire (EQ; Fresco et al., 2007)</p> <ul style="list-style-type: none"> <li>• Intensity with which participants experience 36 different emotions on a typical day [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session, three-months following final treatment session ]</li> </ul> <p>Differential Emotions Scale (DES; Izard, 1993)</p> <ul style="list-style-type: none"> <li>• Change in personality functioning on four subscales: Identity, Self-Direction, Empathy, and Intimacy [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session, three-months following final treatment session ]</li> </ul> <p>Levels of Personality Functioning Scale (LPFS; Morey et al., 2017)</p> <ul style="list-style-type: none"> <li>• Change in use of NHS services, other mental health services or activities, help at home, and time off work/lost income [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session, three-months following final treatment session ]</li> </ul> <p>Healthlines Resource Use Questionnaire (Salisbury, O’Cathain, Edwards, Thomas, Gaunt, Hollinghurst, et al., 2016)</p> <ul style="list-style-type: none"> <li>• Change in quality of life assessment of health and wellbeing, daily functioning, and general life satisfaction across multiple domains [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session, three-months following final treatment session ]</li> </ul> <p>World Health Organisation (WHO) Quality of Life Inventory (WHOQOL; World Health Organisation, 1998)</p>
<p><b>Original Secondary Outcome Measures</b> <small>ICMJE</small></p>	<p><i>Same as current</i></p>
<p><b>Current Other Outcome Measures</b> <small>ICMJE</small> (submitted: May 4, 2017)</p>	<ul style="list-style-type: none"> <li>• Change in measure of memory specificity [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session ]</li> </ul> <p>Autobiographical Memory Test (Williams &amp; Broadbent, 1986).</p> <ul style="list-style-type: none"> <li>• Change in cognitive flexibility for emotional information [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session ]</li> </ul> <p>Affective Card Sorting Task (Barcelo, 2003; Deveney &amp; Deldin, 2006)</p>

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- Change in immediate recall and working memory for neutral information [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session ]  
Digit Span Task (Wechsler, 2008)
- Change in brief measure of premorbid intelligence [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session ]  
National Adult Reading Test (Nelson & Wilson, 1991)
- Change in emotional structure (awareness and differentiation) [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session ]  
Levels of Emotional Awareness Scale (Lane et al., 1990)
- Change in potential neurobiomarkers that may account for risk of disorders and/or predict treatment response (optional component of participation) [ Time Frame: Baseline (within two weeks of first treatment session), within one week of the final treatment session ]  
Functional connectivity during resting state MRI
- Change in levels of rumination [ Time Frame: Within one-week pre-delivery of relevant treatment module; within one-week post-delivery of relevant treatment module (varied time-frame) ]  
Ruminative Responses Scale of the Response Styles Questionnaire (RRS; Treynor, Gonzalez, Nolen-Hoeksema, 2003)
- Change in ability to tolerate distress [ Time Frame: Within one-week pre-delivery of relevant treatment module; within one-week post-delivery of relevant treatment module (varied time-frame) ]  
Distress Tolerance Scale (DTS; Simons & Gaher, 2005)
- Change in ability to label, perceive, and regulate emotions [ Time Frame: Within one-week pre-delivery of relevant treatment module; within one-week post-delivery of relevant treatment module (varied time-frame) ]  
Difficulties with Emotion Regulation Scale (DERS; Gratz & Roemer, 2004)
- Change in negative beliefs, thoughts and assumptions [ Time Frame: Within one-week pre-delivery of relevant treatment module; within one-week post-delivery of relevant treatment module (varied time-frame) ]  
Dysfunctional Attitudes Scale (DAS; Weissman, 1979)
- Change in mindful awareness [ Time Frame: Within one-week pre-delivery of relevant treatment module; within one-week post-delivery of relevant treatment module (varied time-frame) ]  
Kentucky Inventory of Mindfulness Skills (KIMS; Baer, Smith, & Allen, 2004)

- Change in fear of physical anxiety sensations [ Time Frame: Within one-week pre-delivery of relevant treatment module; within one-week post-delivery of relevant treatment module (varied time-frame) ]  
Anxiety Sensitivity Index (ASI; Reiss, Peterson, Gursky, & McNally 1986)
- Change in trauma-related beliefs and maladaptive appraisals of intrusive symptoms [ Time Frame: Within one-week pre-delivery of relevant treatment module; within one-week post-delivery of relevant treatment module (varied time-frame) ]  
Posttraumatic cognitions inventory - short version (PTCI; Foa, Ehlers, Clark, Tolin, Orsillo, 1999)
- Change in implementation of cognitive therapy skills [ Time Frame: Within one-week pre-delivery of relevant treatment module; within one-week post-delivery of relevant treatment module (varied time-frame) ]  
Skills of Cognitive Therapy (SoCT; Jarrett, 2010)
- Change in avoidance of internal experiences including thoughts, feelings, physical sensations. [ Time Frame: Within one-week pre-delivery of relevant treatment module; within one-week post-delivery of relevant treatment module (varied time-frame) ]  
The Multidimensional Experiential Avoidance Questionnaire (Gamez, Chmielewski, Kotov, Ruggero & Watson, 2011)

**Original Other Outcome Measures** ICMJE

*Same as current*

**Descriptive Information**

**Brief Title** ICMJE

The Modular Protocol for Mental Health (MPMH)

**Official Title** ICMJE

The Modular Protocol for Mental Health (MPMH): A Pilot Randomised Clinical Trial of a Transdiagnostic Psychological Treatment for **Mood** and **Anxiety Disorders** in Adults

**Brief Summary**

Currently, our best psychological treatments for anxiety and mood disorders only focus on individual diagnoses. So, there are separate treatments for Panic Disorder, or Depressive Disorder, or Social Anxiety, etc. These 'diagnosis-specific' treatments work well for people whose problems fit neatly into a single diagnosis. However, they work far less well for people with complex problems involving multiple diagnoses, and 50% of patients fail to respond well to these existing treatments.

The purpose of this study is to test a new psychological treatment for anxiety and mood problems (the Modular Protocol for Mental Health [MPMH]). Instead of focusing on any single diagnosis, MPMH combines the best treatment techniques into 10 modules to target problems common across all of the different mood and anxiety diagnoses (e.g., intense emotions, negative thinking, upsetting memories, distressing habits). MPMH should therefore be a better treatment for the large numbers of individuals whose problems do not fit neatly into a single diagnosis and for whom any treatments targeting a single diagnosis would leave significant difficulties unaddressed.

BMJ Open: first published as 10.1136/bmjopen-2018-024546 on 18 August 2018. Downloaded from <http://bmjopen.bmj.com/> on December 18, 2020 by guest. Protected by copyright.

Detailed Description	<i>Not Provided</i>
Study Type <sup>ICMJE</sup>	Interventional
Study Phase	Phase 1 Phase 2
Study Design <sup>ICMJE</sup>	<p>Allocation: Randomized  Intervention Model: Parallel Assignment  Masking: Single (Outcomes Assessor)  Masking Description:  Only the outcome assessor will be masked, as this is a psychological intervention it is not possible to mask the participant, care provider or investigator.  Primary Purpose: Treatment</p>
Condition <sup>ICMJE</sup>	<ul style="list-style-type: none"> <li>• Major Depressive <b>Disorder</b></li> <li>• Generalized <b>Anxiety Disorder</b></li> <li>• Posttraumatic Stress <b>Disorder</b></li> <li>• Social <b>Anxiety Disorder</b></li> <li>• Panic <b>Disorder</b></li> <li>• Agoraphobia</li> <li>• Obsessive-Compulsive <b>Disorder</b></li> <li>• Illness <b>Anxiety Disorder</b></li> </ul>
Intervention <sup>ICMJE</sup>	<ul style="list-style-type: none"> <li>• Behavioral: The Modular Protocol for Mental Health  This intervention is based on evidence-based cognitive-behavioural approaches to psychological disorders and offers a flexible approach to treatment delivery that targets the maladaptive processes common to mood and anxiety disorders.</li> <li>• Behavioral: Treatment-as-usual  This intervention will consist of psychological therapies delivered by high-intensity therapists or clinical psychologists.</li> </ul>
Study Arms	<ul style="list-style-type: none"> <li>• Experimental: The Modular Protocol for Mental Health  The Modular Protocol for Mental Health (Psychological Therapy) will last up to 18 regular weekly face-to-face sessions. Treatment follows a standard structured treatment session as per Cognitive Behavioural Therapy. The MPMH Treatment Manual was written by clinical</li> </ul> <p>For peer review only - <a href="http://bmjopen.bmj.com/site/about/guidelines.xhtml">http://bmjopen.bmj.com/site/about/guidelines.xhtml</a></p>

psychologists. The selection and ordering of the modules for treatment will be delivered and determined by the Trial Clinical Psychologist in collaboration with the service-user. The treatment modules include:

M1. Getting Acquainted M2. Understanding Emotions M3. Managing and Tolerating Emotions M4. Behavioural activation M5. Tackling Avoidance M6. Tackling Unhelpful Thoughts M7. Tackling Unhelpful Habits M8. Overcoming Repetitive Thinking M9. Managing Upsetting Memories and Images M10. Relapse Prevention and Future Orientation

Intervention: Behavioral: The Modular Protocol for Mental Health

- Placebo Comparator: Treatment-as-usual

For Treatment-as-usual (Psychological Therapy), clinicians will be asked to provide whatever treatment they deem appropriate, including psychological services, medication and referral to other services. TAU will be delivered by high-intensity therapists or clinical psychologists.

Intervention: Behavioral: Treatment-as-usual

#### Publications \*

- First MB, Williams JBW, Karg RS, Spitzer RL: Structured Clinical Interview for DSM-5—Research Version (SCID-5 for DSM-5, Research Version; SCID-5-RV). Arlington, VA, American Psychiatric Association, 2015
- [Newby JM, McKinnon A, Kuyken W, Gilbody S, Dalgleish T. Systematic review and meta-analysis of transdiagnostic psychological treatments for anxiety and depressive disorders in adulthood. Clin Psychol Rev. 2015 Aug;40:91-110. doi: 10.1016/j.cpr.2015.06.002. Epub 2015 Jun 6. Review.](#)
- Kroenke, K.; Spitzer, R.L. The PHQ-9: A new depression diagnostic and severity measure. *Psychiatric Annals*, Vol 32(9), Sep 2002, 509-515. <http://dx.doi.org/10.3928/0048-5713-20020901-06>
- [Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006 May 22;166\(10\):1092-7.](#)
- [Mundt JC, Marks IM, Shear MK, Greist JH. The Work and Social Adjustment Scale: a simple measure of impairment in functioning. Br J Psychiatry. 2002 May;180:461-4.](#)
- IAPT/Department of Health, The IAPT data handbook version 2.0.1. 2011: Published to Department of Health Website, in electronic PDF format only
- [Connor KM, Davidson JR, Churchill LE, Sherwood A, Foa E, Weisler RH. Psychometric properties of the Social Phobia Inventory \(SPIN\). New self-rating scale. Br J Psychiatry. 2000 Apr;176:379-86.](#)
- [Meyer TJ, Miller ML, Metzger RL, Borkovec TD. Development and validation of the Penn State Worry Questionnaire. Behav Res Ther. 1990;28\(6\):487-95.](#)
- Foa, E.B., Kozak, M.J., Salkovskis, P.M., Coles, M.E., and Amir, N. (1998). The validation of a new obsessive-compulsive disorder scale: The Obsessive-Compulsive Inventory. *Psychological Assessment*, 10(3), 206-214.

- 1 • Weiss, D.S., The Impact of Event Scale: Revised, in Cross-cultural assessment of psychological trauma and PTSD, J.P. Wilson and C.S. Tang,  
2 Editors. 2007, Springer: New York. p. 219-238.
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- 4 • [Marks IM, Mathews AM. Brief standard self-rating for phobic patients. Behav Res Ther. 1979;17\(3\):263-7.](#)
- 5 • [Shear MK, Brown TA, Barlow DH, Money R, Sholomskas DE, Woods SW, Gorman JM, Papp LA. Multicenter collaborative panic disorder severity  
6 scale. Am J Psychiatry. 1997 Nov;154\(11\):1571-5.](#)
- 7 • [Salkovskis PM, Rimes KA, Warwick HM, Clark DM. The Health Anxiety Inventory: development and validation of scales for the measurement of  
8 health anxiety and hypochondriasis. Psychol Med. 2002 Jul;32\(5\):843-53.](#)
- 9 • Sheehan, D.V., The Anxiety Disease. 1983, New York: Charles Scribner and Sons.
- 10 • [Devilley GJ, Borkovec TD. Psychometric properties of the credibility/expectancy questionnaire. J Behav Ther Exp Psychiatry. 2000 Jun;31\(2\):73-86.](#)
- 11 • [Garnefski N, Rieffe C, Jellesma F, Terwogt MM, Kraaij V. Cognitive emotion regulation strategies and emotional problems in 9 - 11-year-old  
12 children: the development of an instrument. Eur Child Adolesc Psychiatry. 2007 Feb;16\(1\):1-9. Epub 2006 Jun 21.](#)
- 13 • [Fresco DM, Moore MT, van Dulmen MH, Segal ZV, Ma SH, Teasdale JD, Williams JM. Initial psychometric properties of the experiences  
14 questionnaire: validation of a self-report measure of decentering. Behav Ther. 2007 Sep;38\(3\):234-44. Epub 2007 Apr 24.](#)
- 15 • [Izard CE, Libero DZ, Putnam P, Haynes OM. Stability of emotion experiences and their relations to traits of personality. J Pers Soc Psychol. 1993  
16 May;64\(5\):847-60.](#)
- 17 • [Morey LC. Development and initial evaluation of a self-report form of the DSM-5 Level of Personality Functioning Scale. Psychol Assess. 2017  
18 Oct;29\(10\):1302-1308. doi: 10.1037/pas0000450. Epub 2017 Feb 27.](#)
- 19 • [Development of the World Health Organization WHOQOL-BREF quality of life assessment. The WHOQOL Group. Psychol Med. 1998  
20 May;28\(3\):551-8.](#)
- 21 • [Salisbury C, O'Cathain A, Edwards L, Thomas C, Gaunt D, Hollinghurst S, Nicholl J, Large S, Yardley L, Lewis G, Foster A, Garner K, Horspool K,  
22 Man MS, Rogers A, Pope C, Dixon P, Montgomery AA. Effectiveness of an integrated telehealth service for patients with depression: a pragmatic  
23 randomised controlled trial of a complex intervention. Lancet Psychiatry. 2016 Jun;3\(6\):515-25. doi: 10.1016/S2215-0366\(16\)00083-3. Epub 2016  
24 Apr 27.](#)
- 25 • Treynor, W., R. Gonzalez, and S. Nolen-Hoeksema, Rumination Reconsidered: A Psychometric Analysis. Cognitive Therapy and Research 2003.  
26 27(3): p. 247-259.
- 27 • Simons, J.S. and R.M. Gaher, The Distress Tolerance Scale: Development and Validation of a Self-Report Measure. Motivation and Emotion,  
28 2005. 29(2): p. 83-102.
- 29 • Gratz, K.L. & Roemer, L. Journal of Psychopathology and Behavioral Assessment (2004) 26: 41. doi:10.1023/B:JOBA.0000007455.08539.94

- Weissman, A.N., The Dysfunctional Attitude Scale: A Validation Study. 1979, University of Pennsylvania.
- [Baer RA, Smith GT, Allen KB. Assessment of mindfulness by self-report: the Kentucky inventory of mindfulness skills. Assessment. 2004 Sep;11\(3\):191-206.](#)
- [Reiss S, Peterson RA, Gursky DM, McNally RJ. Anxiety sensitivity, anxiety frequency and the prediction of fearfulness. Behav Res Ther. 1986;24\(1\):1-8.](#)
- Foa, E.B., Ehlers, A., Clark, D.M., Tolin, D.F., Orsillo, S.M., The Posttraumatic Cognitions Inventory (PTCI): Development and validation. Psychological Assessment, 1999. 11(3): p. 303-314.
- [Jarrett RB, Vittengl JR, Clark LA, Thase ME. Skills of Cognitive Therapy \(SoCT\): a new measure of patients' comprehension and use. Psychol Assess. 2011 Sep;23\(3\):578-86. doi: 10.1037/a0022485.](#)
- [Gámez W, Chmielewski M, Kotov R, Ruggero C, Watson D. Development of a measure of experiential avoidance: the Multidimensional Experiential Avoidance Questionnaire. Psychol Assess. 2011 Sep;23\(3\):692-713. doi: 10.1037/a0023442.](#)
- [Williams JM, Broadbent K. Autobiographical memory in suicide attempters. J Abnorm Psychol. 1986 May;95\(2\):144-9.](#)
- [Deveney CM, Deldin PJ. A preliminary investigation of cognitive flexibility for emotional information in major depressive disorder and non-psychiatric controls. Emotion. 2006 Aug;6\(3\):429-37.](#)
- [Barceló F. The Madrid card sorting test \(MCST\): a task switching paradigm to study executive attention with event-related potentials. Brain Res Brain Res Protoc. 2003 Mar;11\(1\):27-37.](#)
- Wechsler, D. (2008). Wechsler Adult Intelligence Scale—Fourth Edition. San Antonio, TX: Pearson.
- Nelson HE, Wilson J (1991) National Adult Reading Test (NART), NFER-Nelson, Windsor, UK.
- [Lane RD, Quinlan DM, Schwartz GE, Walker PA, Zeitlin SB. The Levels of Emotional Awareness Scale: a cognitive-developmental measure of emotion. J Pers Assess. 1990 Fall;55\(1-2\):124-34.](#)

\* Includes publications given by the data provider as well as publications identified by ClinicalTrials.gov Identifier (NCT Number) in Medline.

### Recruitment Information

<b>Recruitment Status</b> <small>ICMJE</small>	Enrolling by invitation
<b>Estimated Enrollment</b> <small>ICMJE</small> (submitted: May 4, 2017)	50

1	<b>Original Estimated Enrollment</b> <small>ICMJE</small>	<i>Same as current</i>
2	<b>Estimated Study Completion Date</b>	March 31, 2019
3	<b>Estimated Primary Completion Date</b>	March 31, 2019 (Final data collection date for primary outcome measure)
4	<b>Eligibility Criteria</b> <small>ICMJE</small>	<p>Inclusion Criteria:</p> <ul style="list-style-type: none"> <li>• Patients with a primary diagnosis of a unipolar mood, anxiety, stress or obsessive-compulsive disorder with at least one additional comorbid diagnosis according to the DSM-5. The criteria for diagnosis will be based on the Structured Clinical Interview for the DSM (SCID) which assesses disorders according to DSM-5 diagnostic criteria.</li> <li>• To be eligible participants will also need to score &gt;10 on either the Patient Health Questionnaire (PHQ-9) or Generalised Anxiety Disorder -7 item scale, GAD-7 (see Study Measures above).</li> </ul> <p>Exclusion Criteria:</p> <ul style="list-style-type: none"> <li>• Current/past psychosis or bipolar disorder</li> <li>• Current full diagnosis of substance use disorder</li> <li>• Organic brain damage</li> <li>• Complex trauma history or recurrent self-injury requiring specialist services (as deemed by the NHS Clinical Care team)</li> <li>• Current suicidality that warrants immediate clinical attention and constitutes a current risk of harm to the individual.</li> </ul>
5	<b>Sex/Gender</b>	Sexes Eligible for Study: All
6	<b>Ages</b>	18 Years to 65 Years (Adult)
7	<b>Accepts Healthy Volunteers</b>	No
8	<b>Contacts</b> <small>ICMJE</small>	<i>Contact information is only displayed when the study is recruiting subjects</i>
9	<b>Listed Location Countries</b> <small>ICMJE</small>	<b>United Kingdom</b>
10	<b>Removed Location Countries</b>	

## Administrative Information

<b>NCT Number</b> <small>ICMJE</small>	NCT03143634
<b>Other Study ID Numbers</b> <small>ICMJE</small>	MP:MH RfPB PB-PG-0214-33072
<b>Has Data Monitoring Committee</b>	No
<b>U.S. FDA-regulated Product</b>	Studies a U.S. FDA-regulated Drug Product: No Studies a U.S. FDA-regulated Device Product: No
<b>IPD Sharing Statement</b>	Plan to Share IPD: Undecided
<b>Responsible Party</b>	Medical Research Council Cognition and Brain Sciences Unit
<b>Study Sponsor</b> <small>ICMJE</small>	Medical Research Council Cognition and Brain Sciences Unit
<b>Collaborators</b> <small>ICMJE</small>	Cambridgeshire and Peterborough NHS Foundation Trust
<b>Investigators</b> <small>ICMJE</small>	Principal Investigator: Tim Dagleish, PhD Medical Research Council Cognition and Brain Sciences Unit
<b>PRS Account</b>	Medical Research Council Cognition and Brain Sciences Unit
<b>Verification Date</b>	August 2017
<small>ICMJE</small>	Data element required by the <a href="#">International Committee of Medical Journal Editors</a> and the <a href="#">World Health Organization ICTRP</a>



SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents\*

Section/item	Item No	Description	Page/Line Reference
<b>Administrative information</b>			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	p. 1, line 1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	p. 1, line 28
	2b	All items from the World Health Organization Trial Registration Data Set	See attached
Protocol version	3	Date and version identifier	p. 1, line 29
Funding	4	Sources and types of financial, material, and other support	p. 1, line 30
			p. 22, line 1
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	p. 1, line 4
	5b	Name and contact information for the trial sponsor	p. 22, line 20
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	p. 22, line 1
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	p. 16, line 16
<b>Introduction</b>			

1	Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	p. 4, line 4
2				
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7		6b	Explanation for choice of comparators	p. 8, line 6
8	Objectives	7	Specific objectives or hypotheses	p. 8, line 9
9				
10	Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	p. 8, line 23
11				
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14				
15				
16	<b>Methods: Participants, interventions, and outcomes</b>			
17				
18	Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	p. 9, line 23
19				
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22				
23	Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	p. 9, line 4 p. 9, line 12 p. 12, line 15
24				
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29	Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	p. 10, line 21
30				
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32				
33		11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	p. 10, line 17
34				
35				
36				
37				
38		11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	p. 12, line 15 p. 17, line 5
39				
40				
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42				
43		11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	p. 9, line 20
44				
45	Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	p. 13, line 9
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1	Participant	13	Time schedule of enrolment, interventions (including any	p. 9, line 23
2	timeline		run-ins and washouts), assessments, and visits for	Figure 1
3			participants. A schematic diagram is highly	
4			recommended (see Figure)	
5				
6				
7	Sample size	14	Estimated number of participants needed to achieve	p. 15, line 2
8			study objectives and how it was determined, including	
9			clinical and statistical assumptions supporting any	
10			sample size calculations	
11				
12	Recruitment	15	Strategies for achieving adequate participant enrolment	p. 9, line 23
13			to reach target sample size	
14				

### Methods: Assignment of interventions (for controlled trials)

#### Allocation:

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17				
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19	Sequenc	16a	Method of generating the allocation sequence (eg,	p. 10, line 10
20	e		computer-generated random numbers), and list of any	
21	generatio		factors for stratification. To reduce predictability of a	
22	n		random sequence, details of any planned restriction (eg,	
23			blocking) should be provided in a separate document	
24			that is unavailable to those who enrol participants or	
25			assign interventions	
26				
27				
28	Allocatio	16b	Mechanism of implementing the allocation sequence (eg,	p. 10, line 10
29	n		central telephone; sequentially numbered, opaque,	
30	concealm		sealed envelopes), describing any steps to conceal the	
31	ent		sequence until interventions are assigned	
32	mechanis			
33	m			
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36	Impleme	16c	Who will generate the allocation sequence, who will	p. 10, line 14
37	ntation		enrol participants, and who will assign participants to	
38			interventions	
39				
40	Blinding	17a	Who will be blinded after assignment to interventions	p. 15, line 20
41	(masking)		(eg, trial participants, care providers, outcome	
42			assessors, data analysts), and how	
43				
44		17b	If blinded, circumstances under which unblinding is	p. 15, line 20
45			permissible, and procedure for revealing a participant's	
46			allocated intervention during the trial	
47				

### Methods: Data collection, management, and analysis

1				
2	Data	18a	Plans for assessment and collection of outcome,	p. 13, line 8
3	collection		baseline, and other trial data, including any related	p. 15, line 13
4	methods		processes to promote data quality (eg, duplicate	
5			measurements, training of assessors) and a description	
6			of study instruments (eg, questionnaires, laboratory	
7			tests) along with their reliability and validity, if known.	
8			Reference to where data collection forms can be found,	
9			if not in the protocol	
10				
11		18b	Plans to promote participant retention and complete	p. 16, line 16
12			follow-up, including list of any outcome data to be	
13			collected for participants who discontinue or deviate from	
14			intervention protocols	
15				
16				
17	Data	19	Plans for data entry, coding, security, and storage,	p. 15, line 17
18	manageme		including any related processes to promote data quality	p. 16, line 16
19	nt		(eg, double data entry; range checks for data values).	
20			Reference to where details of data management	
21			procedures can be found, if not in the protocol	
22				
23	Statistical	20a	Statistical methods for analysing primary and secondary	p. 16, line 1
24	methods		outcomes. Reference to where other details of the	
25			statistical analysis plan can be found, if not in the	
26			protocol	
27				
28		20b	Methods for any additional analyses (eg, subgroup and	p. 16, line 10
29			adjusted analyses)	
30				
31		20c	Definition of analysis population relating to protocol non-	p. 16, line 9
32			adherence (eg, as randomised analysis), and any	
33			statistical methods to handle missing data (eg, multiple	
34			imputation)	
35				
36				
37	<b>Methods: Monitoring</b>			
38				
39	Data	21a	Composition of data monitoring committee (DMC);	p. 16, line 16
40	monitoring		summary of its role and reporting structure; statement of	
41			whether it is independent from the sponsor and	
42			competing interests; and reference to where further	
43			details about its charter can be found, if not in the	
44			protocol. Alternatively, an explanation of why a DMC is	
45			not needed	
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48		21b	Description of any interim analyses and stopping	p. 16, line 3
49			guidelines, including who will have access to these	
50			interim results and make the final decision to terminate	
51			the trial	
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1	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	p. 17, line 5
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7	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	p. 16, line 17
8				
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11	<b>Ethics and dissemination</b>			
12				
13	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	p. 17, line 17
14				
15				
16				
17	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	p. 16, line 16 p. 17, line 21
18				
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24	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	p. 10, line 7
25				
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28		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
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32	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	p. 15, line 13
33				
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38	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	p. 22, line 11
39				
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41	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	p. 17, line 2
42				
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45	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	p. 17, line 14
46				
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49	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	p. 17, line 24
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1		31b	Authorship eligibility guidelines and any intended use of professional writers	p. 21, line 1
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4		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	p. 17, line 24
5				
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## Appendices

8				
9				
10				
11	Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Supplementary materials
12				
13				
14				
15	Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A
16				
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\*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](https://creativecommons.org/licenses/by-nc-nd/3.0/)" license.

# BMJ Open

## The HARMONIC trial: Study protocol for a randomised controlled feasibility trial of Shaping Healthy Minds – a modular transdiagnostic intervention for mood, stressor-related and anxiety disorders in adults

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-024546.R1
Article Type:	Protocol
Date Submitted by the Author:	15-Jun-2018
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<b>Primary Subject Heading</b>:	Mental health
Secondary Subject Heading:	Research methods
Keywords:	Transdiagnostic, Depression, Anxiety, Posttraumatic Stress Disorder, Common Mental Health Problems

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The HARMONIC trial: Study protocol for a randomised controlled feasibility trial of *Shaping Healthy Minds* – a modular transdiagnostic intervention for mood, stressor-related and anxiety disorders in adults

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Trial Registration: NCT03143634 (ClinicalTrials.gov)

Protocol Version: First, 31/05/2018

Funding: National Institute of Health Research, Research for Patient Benefit (RfPB: PB-PG-0214-33072)

Word count: 4652 words

## Abstract

**Introduction:** Anxiety, mood and trauma-related disorders are common, affecting up to 20% of adults. Many of these individuals will experience symptoms of more than one disorder as diagnostically defined. However, most psychological treatments focus on individual disorders and are less effective for those who experience comorbid disorders. The HARMONIC trial introduces a novel transdiagnostic intervention (*Shaping Healthy Minds*), which synthesises several evidence-based treatment techniques to address the gap in effective interventions for people with complex and comorbid difficulties. This early-phase trial aims to estimate the efficacy and feasibility of the transdiagnostic intervention in preparation for a later-phase randomised controlled trial, and to explore mechanisms of change.

**Methods/Analysis:** We outline a patient-level two-arm randomised controlled trial (HARMONIC) that compares *Shaping Healthy Minds* to treatment-as-usual (TAU) for individuals aged >18 years ( $N=50$ ) with co-morbid mood, anxiety, obsessive-compulsive or trauma/stressor disorder diagnoses, recruited from outpatient psychological services within the UK National Health Service. The co-primary outcomes will be 3-month follow-up scores on self-report measures of depressive symptoms, anxiety symptoms, and disability and functional impairment. Secondary outcomes include changes in symptoms linked to individual disorders. We will assess the feasibility and acceptability of *Shaping Healthy Minds*, the utility of proposed outcome measures, and refine the treatment manuals in preparation for a later-phase trial.

**Ethics and dissemination:** This trial protocol has been approved by the Health Research Authority of the National Health Service of the United Kingdom (East of England, Reference: 16/EE/0095). We anticipate that trial findings will inform future revisions of clinical guidelines for numerous forms of mood, anxiety, and stressor-related disorders. Findings will be disseminated broadly via peer-reviewed empirical journal articles, conference presentations, clinical workshops, and a trial website.

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5 **Key Words:** Transdiagnostic, Depression, Anxiety, Posttraumatic Stress Disorder, Common  
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7 Mental Health Problems  
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11 **Trial registration:** Clinicaltrials.gov identifier: NCT03143634.  
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### 14 **Strengths and limitations of this study**

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18 • The first study to investigate the feasibility and procedural uncertainties of a flexibly-  
19 delivered modular transdiagnostic treatment protocol – *Shaping Healthy Minds* – in  
20 adults with unipolar mood, anxiety, and trauma-related disorders.  
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24 • This trial will provide a point estimate of efficacy of the *Shaping Healthy Minds*  
25 protocol, relative to TAU, in preparation for a later-stage trial, and explore putative  
26 mediators and moderators of treatment outcome.  
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- 29  
30 • Comparison of *Shaping Healthy Minds* against treatment-as-usual (TAU) currently  
31 provided by the NHS will provide a rigorous evaluation of treatment potential  
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35 • Administering self-report questionnaires that are specific to each service-user's  
36 secondary diagnoses may limit the ability to draw group-based conclusions  
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3 The HARMONIC trial: Study protocol for a randomised controlled feasibility trial of *Shaping*  
4 *Healthy Minds* – a modular transdiagnostic intervention for mood, stressor-related and anxiety  
5 disorders in adults  
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9 Mood, stressor-related, obsessive-compulsive and anxiety disorders – so called  
10 common mental health problems (CMHP; NICE, 2011) – are one of the largest causes of  
11 disability in the world, with 16 – 20% of adults affected at any given time [1, 2]. Maximising  
12 our ability to treat CMHP in cost effective, efficient, and effective ways that can be widely  
13 disseminated is a priority [2]. At present, there is a range of complex psychological treatments  
14 with demonstrated efficacy in the treatment of CMHP, and in preventing recurrence.  
15  
16 Consequently, the National Institute of Health and Care Excellence (NICE) recommends  
17 psychological treatment at various points in the care pathway to all those suffering from such  
18 problems, although there are not specific recommendations for individuals experiencing more  
19 than one problem [3]. Between 40 – 80% of patients experiencing a CMHP also experience an  
20 additional comorbid CMHP [4, 5]. Even our best available psychological treatments only  
21 achieve clinical recovery for 40 – 70% of patients, depending on their primary CMHP, with  
22 people suffering complex co-morbid conditions faring significantly worse [6]. For the  
23 majority of patients who receive treatment, there remains a significant risk of future relapse  
24 [7, 8]. A key challenge therefore is how we can build on and extend beyond the current  
25 psychological treatments for CMHP to increase efficacy, and sustained recovery, particularly  
26 for those with co-morbid, recurrent, and complex presentations [9].  
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46 Over the past decade, there has been a major shift in the conceptualisation of CMHP,  
47 away from a single-diagnosis approach in favour of a transdiagnostic model [10, 11]. There is  
48 strong empirical and theoretical support for development of transdiagnostic treatment  
49 approaches, as many of the cognitive, emotional, behavioural, and interpersonal factors which  
50 drive symptomology are consistent across disorders [12, 13]. A transdiagnostic approach  
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3 thereby has the potential to improve the efficacy and efficiency of treatment for people with  
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5 anxiety, stress and depression.

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7 There are potential limitations to the commonly-utilised single-disorder-focused  
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9 treatment approach. First, with the exception of a few existing programmes [14, 15], most  
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11 evidence-based treatment protocols are single-disorder-focused programs (e.g., depression  
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13 [16], generalised anxiety [17, 18], social anxiety [19], and post-traumatic stress disorder [20]).  
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15 Comorbid conditions and disorders are either ignored, or minimally treated within these  
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17 treatment packages. This leaves a mismatch between the available evidence base and the  
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19 clinical reality which clinicians face: the majority of people with any given CMHP have at  
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21 least one or more comorbid disorders to their primary diagnosis [4]. Second, in the attempt to  
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23 manualise treatments, most packages are inflexible ‘one-size-fits-all’ approaches, leaving  
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25 patients with a wide range of problems and presentations receiving the same treatment  
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27 package, regardless of their symptoms, goals, and concerns [14]. Third, in practice, many  
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29 clinicians already deliver evidence-based psychological treatments in a flexible manner in  
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31 order to address individual concerns and goals. Manualised treatments need to better reflect  
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33 the realities of service-user experiences and treatment delivery. This approach merits  
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35 improvement so that delivered treatments are more efficient, effective, and personalised to  
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37 individuals’ concerns.  
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42 Existing psychological treatments for CMHP share more similarities than differences  
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44 [21]. Despite differences in the theoretical foundation underlying available psychological  
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46 treatments, and the terms used to describe maintaining factors and treatment targets, there are  
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48 many common elements. For instance, psychoeducation, graded exposure, mindfulness  
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50 techniques, and behavioural activation form a key component of a variety of effective  
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52 treatments such as trauma-focused cognitive behavioural therapy, cognitive behavioural  
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54 therapy (CBT), acceptance and commitment therapy (ACT), Dialectical Behaviour Therapy  
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3 (DBT), exposure therapy and mindfulness-based cognitive therapy (MBCT). The widespread  
4 availability of so many treatment options has the potential to elicit considerable decision-  
5 making difficulties for the treating clinician. In both formulation and treatment planning,  
6 challenging decisions occur when selecting the order in which to treat multiple difficulties, in  
7 evaluating the most appropriate treatment approach, and working out which treatment option  
8 will be acceptable and effective for the client.  
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16 A recent equivalence RCT demonstrated that a transdiagnostic protocol (The *Unified*  
17 *Protocol for Transdiagnostic Treatment of Emotional Disorders* [22]) and single-disorder  
18 protocols produced statistically equivalent reduction in severity of principal anxiety disorder  
19 diagnosis, but that there was less attrition in the transdiagnostic group [23]. Promising results  
20 have also been found for other transdiagnostic treatment protocols, including Norton's  
21 Transdiagnostic Group Cognitive Behavioral Therapy for Anxiety [15], Gros's  
22 Transdiagnostic Behavior Therapy for affective disorders [24], and Schmidt's False Safety  
23 Behaviour Elimination Therapy for Anxiety Disorders [25]. In addition, our systematic review  
24 and meta-analysis supported the overall efficacy of transdiagnostic treatments [10]. The  
25 review called for more high-quality studies to resolve uncertainties surrounding the  
26 heterogeneity of treatment effects and to determine the best treatment approaches and designs.  
27 We aim to address these issues through evaluating a novel intervention which combines a  
28 number of evidence-based treatment strategies. In utilising a modular approach, this trial will  
29 contribute to identification and evaluation of effective treatment components and delivery  
30 method. The modular approach to treatment design incorporates self-contained functional  
31 units (therapy modules) that can operate independently and be delivered flexibly, but also  
32 refer to other modules if needed [22]. A complex, modular, tailored transdiagnostic  
33 intervention that targets common underlying processes maximises goodness of fit and has a  
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3 direct focus on process rather than symptoms. The approach is thereby suitable for complexity  
4 and comorbidity as well as sub-syndromal and prodromal symptoms.  
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7 The transdiagnostic intervention we have developed – *Shaping Healthy Minds* –  
8 targets the processes and symptoms that are common to CMHPs and offers a number of  
9 advances in transdiagnostic treatment by incorporating the best available techniques from  
10 existing manual-based treatments into the one treatment package. A key aim of the  
11 programme is to encompass the treatment techniques that skilled psychologists and mental  
12 health clinicians already implement in standard practice for depressed, stressed and anxious  
13 patients with complex presentations [26]. The intervention also builds on the Unified Protocol  
14 for Transdiagnostic Treatment for Emotional Disorders described by Barlow et al. [14], by  
15 working towards a prescriptive approach for the delivery of treatment modules based on the  
16 formulation of the client's presenting difficulties [9]. Specifically, the treatment expands  
17 beyond interventions grounded in a sole treatment paradigm (e.g., CBT) towards a theory-  
18 driven approach that utilises efficacious techniques translated from basic science alongside  
19 components drawn from a wide range of evidence-based psychological treatments (e.g.,  
20 Mindfulness-based interventions, ACT, Behavioural Activation, and DBT).  
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37 The treatment protocol for *Shaping Healthy Minds* also changes the way that  
38 standardised manual-based treatments are delivered. Rather than using integral interventions  
39 (where all patients receive the same relatively fixed, complete protocol), the transdiagnostic  
40 intervention is a modular intervention, whereby the assessment of core problematic areas of  
41 emotional, cognitive, interpersonal, and behavioural processes informs the selection and  
42 sequence of treatment modules targeted at specific problem areas for patients [22]. This  
43 modular approach allows for standardised, yet flexible treatment that is personalised to the  
44 individual concerns, problems, and goals for the patient. Finally, it expands beyond  
45 interventions that typically focus on alleviating negative symptomatology (e.g., negative  
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3 thoughts, excessive negative emotions) and incorporates interventions designed to increase  
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5 positive emotions, capture strengths, and enhance resilience for sustained recovery.  
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7 We aim to examine the feasibility of *Shaping Healthy Minds* in reducing symptoms of  
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9 depression, anxiety, distress, disability and functional impairment through an early-stage  
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11 randomised clinical trial, in line with recommendations for the development of complex  
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13 interventions [27]. In particular, we will gather data on the extent to which *Shaping Healthy*  
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15 *Minds* performs comparably to TAU for a given service-user's primary diagnosed problem  
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17 [10, 28] as well as for other significant additional, secondary, and/or comorbid difficulties. In  
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19 addition, this trial will provide a preliminary evaluation of whether a modular transdiagnostic  
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21 treatment approach may be effective at reducing the distress and impairment associated with  
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23 CMHP [10]. The trial will also provide an indication of the feasibility and acceptability, of the  
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25 transdiagnostic intervention to service-users and clinicians by recruiting through post-primary  
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27 care UK NHS psychology services where complex comorbidity represents the modal clinical  
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29 presentation. In addition, the trial will provide initial estimates of cost-effectiveness in terms  
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31 of service-use and potential quality-adjusted life years added. We therefore present the  
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33 protocol for a feasibility trial with co-primary outcomes, examining the effect of *Shaping*  
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35 *Healthy Minds* on primary and comorbid diagnoses. The feasibility trial will provide a  
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37 plausible range of point estimates of the efficacy of *Shaping Healthy Minds* on standardised  
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39 continuous symptom measures for primary and secondary diagnoses to inform this key  
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41 question, refine the treatment manual and contribute to the design of future scaled-up trials  
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46 [27].  
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## 48 **Methods and Analysis**

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50 This trial protocol is written in compliance with the Standard Protocol Items:  
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52 Recommendations for Interventional Trials (SPIRIT) guidelines.  
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## Study Design

The design is a parallel arm RCT comparing *Shaping Healthy Minds* to TAU. Participants will be assessed three times - at baseline, at post-treatment, and at 3-month follow-up. These three time points involve face-to-face assessments including the full battery of primary and additional outcomes and process measures, described below.

## Participants and recruitment

The proposed feasibility study will seek to recruit 50 people aged 18 and above with a primary diagnosis of a unipolar mood, anxiety, obsessive-compulsive, or trauma- and stressor-related disorder (CMHPs) with at least one additional comorbid diagnosis according to the Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition (DSM-5 [29]). Participants will be randomly allocated to one of two groups: (1) *Shaping Healthy Minds*, or (2) TAU. Diagnosis of CMHPs will be determined by trained research staff using the Structured Clinical Interview for the DSM-5 (SCID-5; [30]). To be eligible participants will also need to score > 10 on either the Patient Health Questionnaire (PHQ-9) or the Generalised Anxiety Disorder Questionnaire (GAD-7; see Study Measures below). Exclusion criteria are current/past psychosis or bipolar disorder, current diagnosis of alcohol or substance use disorder (all assessed via the Structured Clinical Interview for the DSM-5; SCID-5; [30]), organic brain damage, complex trauma history or recurrent self-injury requiring specialist services, or current suicidality that warrants immediate clinical attention and constitutes a current risk of harm to the individual (all assessed via participant report and the clinical care team). Participants may be engaged with the multi-disciplinary clinical care team, but those randomised to *Shaping Healthy Minds* will not be receiving other psychological services whilst participating in the trial. All other services (e.g., medication review with psychiatrist or general practitioner, occupational therapy, social support services) may be continued, and there are no medication exclusions.

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3 Participants will be recruited through local NHS clinical psychology services,  
4 including the high intensity team of the Cambridge Psychological Wellbeing Service, and  
5 secondary care services with expertise in treatment of more complex and comorbid affective  
6 disorders. The recruitment pathways will involve suitable service-users on a waitlist to receive  
7 treatment being identified by a member of the clinical service (including an Assistant  
8 Psychologist focusing primarily on recruitment into clinical research studies) who will  
9 provide them with a letter outlining the study. Service-users will then be able to contact the  
10 research team to opt into the study. Initial eligibility will be screened over the telephone, and  
11 suitable participants will be invited to complete the SCID, either at the clinical service or the  
12 research unit. At the beginning of this session, all participants will provide written informed  
13 consent (see supplementary materials for a sample Participant Information Sheet and Consent  
14 Form, Supplementary File 1). No potential participants will be contacted by a member of the  
15 research team until they have given consent for such contact to a member of the clinical care  
16 team.

### 32 33 **Participant allocation**

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35 Following both baseline assessment sessions, eligible participants will be stratified  
36 according to depression (PHQ-9) and anxiety (GAD-7) severity scores and randomised to  
37 either *Shaping Healthy Minds* ( $n = 25$ ) or TAU ( $n = 25$ ). This will be achieved using  
38 computer generated, quasi-random numbers and will be conducted by the trial statistician  
39 (PW), blind to study objectives. Once generated, this information is passed to the project  
40 coordinator responsible for delivering the intervention. Once a participant begins treatment,  
41 he or she is free to discontinue participation at any time, in which case s/he will be referred  
42 back to the appropriate NHS clinical care team. Figure 1 summarises participant flow through  
43 the trial.

## Interventions

*Shaping Healthy Minds* (SHM) is a modular intervention, comprising 10 independent modules that will last up to 20 sessions. The content of the modules is drawn from a number of evidence-based psychological therapies, including CBT [31], ACT [32], DBT [33], MBCT [34], and behavioural activation [35, 36]. The programme aims to bring together the core and unique therapeutic techniques from the best available disorder-focused treatment packages into the one transdiagnostic treatment package (e.g., behavioural experiments [37] and graded exposure [38] from CBT, values exercises and mindfulness strategies from ACT [39], activity scheduling from BA [35], emotion regulation strategies from DBT [33], and present-moment awareness exercises from MBCT [40]). The elements of *Shaping Healthy Minds* were drawn from recent meta-analyses supporting the effectiveness of these treatment strategies (e.g., [36, 41-43]), and the manuals were written and reviewed by experienced clinical psychologists (TD, JN, AB, CH, and MB). In addition, experts in particular fields (e.g., WK for mindfulness and case formulation) were consulted on the content of specific modules.

The modular approach is standardised, yet can be flexibly delivered according to an individual's concerns, problems, and goals [22]. The treatment focuses both on alleviating negative symptoms and enhancing positive wellbeing, by teaching skills and techniques and enhancing positive emotions, harness and build on strengths, and maximise resilience over the longer-term. Choice, order, and length of modules (i.e., number of session over which they are completed) is tailored to the transdiagnostic difficulties of the individual using collaborative case formulation [44], although there are three core modules that everyone receives (outlined below). Treatment consists of weekly face-to-face one-hour sessions with the trial therapists. Sessions will involve collaboratively setting an agenda for the session based on the participants' ratings for their top 3 problems and top 3 strengths, the goals set for

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3 therapy, and the module in focus. Participants will complete homework exercises to  
4 consolidate and practice the skills learned during the specific modules and will be strongly  
5 encouraged to continue this practice following the end of one module and move to the next.  
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9 The ten SHM modules (core modules listed in bold) are: (1) **Getting Acquainted with**  
10 **SHM**, (2) **Understanding Emotions**, (3) Managing and Tolerating Emotions, (4)  
11 **Behavioural Activation**, (5) Tackling Avoidance, (6) Tackling Unhelpful Thoughts, (7)  
12 Tackling Unhelpful Habits, (8) Overcoming Repetitive Thinking, (9) Managing Upsetting  
13 Memories and Images, and (10) **Relapse Prevention and Future Orientation**. Additional  
14 information about the content of the modules can be found in the supplementary materials  
15 (Supplementary Table 1).  
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24 **Treatment-as-usual (TAU)**. For TAU, clinical psychologists and high-intensity CBT  
25 Therapists in teams specialising in CMHPs will be asked to provide the course of  
26 psychological therapy that they deem appropriate, in addition to referral to other health/social  
27 services and medication management. Psychological treatment in the specialist teams  
28 delivering TAU will standardly consist of disorder-focused Cognitive Behavioural Therapy,  
29 Eye Movement Desensitisation Reprocessing, or Behavioural Activation. The delivered  
30 treatment will be documented to ensure systematic understanding of the duration, frequency,  
31 and type of treatment administered.  
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41 **Treatment Integrity**. Therapists with experience in treating adult CMHPs will deliver  
42 the transdiagnostic intervention. Treatment fidelity and clinician adherence for the *Shaping*  
43 *Healthy Minds* group will be established using continued monitoring of completion of module  
44 components and through independent rating of specific treatment strategies by the supervising  
45 clinical psychologist. After every session, clinicians will complete a bespoke Treatment  
46 Fidelity Checklist which is a session-by-session self-report measure of compliance with the  
47 *Shaping Healthy Minds* approach, and these will be evaluated during weekly clinical  
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3 supervision with the trial clinical supervisor. In addition, a randomly-selected 25% of the  
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5 audio-taped treatment sessions will be rated for adherence to the manuals by an experienced  
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7 clinician, independent of the trial. Homework completion will be monitored by trial therapists.  
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10 This bespoke measure will be supplemented with The Cognitive Therapy Scale –  
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12 Revised (CTS-R) – a standardised measure of competence within cognitive therapy,  
13  
14 consisting of adherence to and skilful application of cognitive therapy methods and the  
15  
16 therapeutic alliance [45]. The CTS-R has 13-items that are completed by an independent rater,  
17  
18 assessing agenda setting, feedback, collaboration, pacing and efficient use of time,  
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20 interpersonal effectiveness, charisma/flair, facilitation of emotional expression, guided  
21  
22 discovery, conceptualisation, identifying key cognitions, application of cognitive change  
23  
24 methods, application of behavioural techniques, use of homework.  
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## 26 27 **Measures**

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29 **Co-primary outcomes.** The co-primary outcome measures are self-reported  
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31 symptoms of depression and anxiety, indexed by the PHQ-9 [46], and GAD-7 [47], as well as  
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33 levels of disability and functional impairment, indexed by the Work and Social Adjustment  
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35 Scale (WSAS [48]).  
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38 **Secondary outcomes.** Given the transdiagnostic focus of the study, self-reported  
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40 symptoms on specific disorders that client's meet criteria for at trial baseline will be indexed  
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42 by the IAPT Phobia Scales (social phobia, agoraphobia, specific phobia, [49]), the Social  
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44 Phobia Inventory (SPIN, [50]), the Penn State Worry Questionnaire (generalised anxiety,  
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46 PSWQ, [51]), the Obsessive-Compulsive Inventory (OCI, [52]), the Revised Impact of Event  
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48 Scale (posttraumatic stress, IES-R, [53]), the Agoraphobia-Mobility Inventory (MI, [54]), the  
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50 Fear Questionnaire (specific phobias, FQ, [55]), the Panic Disorder Severity Scale- self report  
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52 version (PDSS-SR, [56]), the Health Anxiety Inventory – short version (SHAI, [57]), and the  
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54 Sheehan Disability Scale (SDS, [58]). Participants will only complete a selection of these  
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measures depending on their concerns and associated diagnoses. In addition to these disorder-specific measures, the Inventory of Depression and Anxiety Symptoms (IDAS-II) will capture both disorder-specific and transdiagnostic symptom dimensionality within a single measure [59]. Selection of these measures will be determined following completion of the structured clinical interview at the beginning of assessment.

**Process Measures.** We will also include a number of process-related measures which will be administered at baseline, at post-intervention, and at 3-month follow-up to begin to explore mechanisms of change and the feasibility of conducting embedded process outcome research within this type of trial (see Table 1). To explore the value of the individual modules administered within the transdiagnostic intervention, we will also administer module-relevant measures (e.g., rumination, distress tolerance) before and after completion of the module. Finally, participants' expectancy of treatment outcomes and measures of engagement and compliance will be administered at pre and post-intervention to inform the further development of the protocol.

**Health economics measures.** Data collection for the health economic evaluation will take a patient-level perspective [60, 61], recording the cost-per-session of treatment and productivity losses resulting from time off work as a consequence of their mental health difficulties. Data will be collected using the Healthlines Resource Use Questionnaire [60, 61], which is a measure of the participants use of health care services (including NHS, help at home), occupational productivity (i.e., time off work) and cost of transdiagnostic treatment delivery (e.g., direct and indirect time spent in service delivery). The Medical Outcomes Study Questionnaire Short Form 36 Health Survey (SF-36) [62], a generic quality of life questionnaire, will measure overall health and wellbeing, daily functioning, and general life satisfaction across multiple domains. These measures allow calculation of the additional number of quality of life years the treatment will yield. These data will allow preliminary

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3 estimates of the potential cost-utility of the transdiagnostic intervention and also of the  
4 feasibility of acquiring these data within the trial protocol.  
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### 7 **Methodological Aspects**

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9 **Power analysis and sample size.** Although a standard power calculation based on  
10 detecting treatment effects is the conventional approach to determining sample sizes for trials,  
11 the main aim of the current trial is to elucidate feasibility for a larger later-stage evaluation.  
12 We therefore sought at this stage only to provide a point-estimate of the effect of *Shaping*  
13 *Healthy Minds* to inform a power calculation for this putative fully powered later phase  
14 evaluation. Our previous experience with such early phase trial platforms indicates that 50  
15 patients will provide sufficient numbers and diagnostic diversity to evaluate feasibility,  
16 acceptability, and procedural uncertainty for *Shaping Healthy Minds* and a plausible test of  
17 recruitment protocols. This will give 40 patients (20 per arm) at 3-month posttreatment follow  
18 up, assuming 20% attrition. This will provide a reasonable range of point estimates of effect  
19 on our set of candidate outcome measures sufficient to guide later phase trial work.  
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33 **Data collection and confidentiality.** Outcome data for all participants who are  
34 randomised will be collected via face-to-face interviews and written questionnaires at  
35 baseline, post-treatment, and 3-month follow-up. To maintain confidentiality all participants  
36 will be given a trial number so that personally identifying information is not linked to  
37 assessment or trial information. All data (including personally-identifiable information) will  
38 be stored on secure UK NHS databases, secure University of Cambridge servers and within  
39 locked filing cabinets under the management of the trial coordinator. Access will be limited to  
40 the immediate clinical research team.  
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50 **Blinding.** Outcome assessments will be conducted by independent raters who have no  
51 therapeutic relationship with the patients and are blind to treatment condition. Double  
52 blinding of patients and therapists is not possible due to the nature of the trial (i.e., a  
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3 psychological intervention). Unblinding will not be necessary because participants and  
4  
5 therapists are not blinded to intervention allocation.  
6

7 **Statistical analysis plan.** Initial analyses of the outcomes will be conducted by the  
8  
9 trial statistician, blind to trial condition, following CONSORT standards (see Supplementary  
10  
11 Figure File 2). There are no planned interim analyses. Initial analyses will be conducted on an  
12  
13 intention-to-treat basis, with subsequent analyses being per protocol. Mixed model analyses of  
14  
15 variance (ANOVAs) will be used to compare groups on outcomes at the three assessment  
16  
17 points – baseline, post-intervention, and 3-month follow-up. Baseline levels on relevant  
18  
19 measures will be included as covariates, as appropriate. Both intent-to-treat and per-protocol  
20  
21 exploratory analyses will be conducted with our range of outcome measures following  
22  
23 CONSORT standards. Multiple imputation will be used to account for missing data. Intent-to-  
24  
25 treat analysis will also be used for those lost to attrition. Exploratory moderation and  
26  
27 mediation analyses to examine process variables will be conducted using the MacArthur  
28  
29 approach [63]. For the health economic data, costs associated with service use will be  
30  
31 calculated by attaching a unit cost to each instance of use, and data will be combined with  
32  
33 quality-adjusted life years (QALYs, [62]) derived from the SF-36 to arrive at a preliminary  
34  
35 estimate of the cost-utility of the transdiagnostic intervention.  
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39 **Monitoring and data management.** The trial will take place at NHS sites and a  
40  
41 research unit in the East of England. A Trial Management Group (TMG), will meet 1-2 times  
42  
43 a year to: manage the protocol; monitor recruitment in relation to targets; deal with any  
44  
45 adverse events; and co-ordinate the different stages of the project. The TMG consists of  
46  
47 research clinical psychologists and assistant psychologists, a psychiatrist, a health economist,  
48  
49 clinical psychology researchers, the trial statistician, a nurse practitioner, and a service user  
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51 representative. Day-to-day project management will be the responsibility of a smaller trial  
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53 team, meeting fortnightly to deal with administrative issues, troubleshooting, and recruitment  
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3 flow. Clinical supervision will take place fortnightly. As this is a Phase I/II trial, a data-  
4  
5 management committee was deemed unnecessary, and as such the trial team are responsible  
6  
7 for monitoring and data management. Data will be monitored for completeness and  
8  
9 consistency using spot checks and plausibility checks carried out by the trial statistician. The  
10  
11 trial lead, trial coordinator, and statistician will have full access to the final trial dataset. The  
12  
13 study data will be reported in line with the current CONSORT recommendations.  
14

### 15 16 **Patient and Public Involvement**

17  
18 Most broadly, the driving force behind the development of *Shaping Healthy Minds* has  
19  
20 been feedback from many hundreds of service users in clinical settings, specifically related to  
21  
22 the suitability of treatments for complex and comorbid CMHPs. A Lived Experience Group  
23  
24 comprising service users and carers hosted by the Cambridge Centre for Affective Disorders  
25  
26 discussed the details of the current study at its meeting on 12 November 2013. This group  
27  
28 provided useful feedback to the research team in terms of the materials for service-users (e.g.,  
29  
30 consent forms), the clinical setting for the intervention, and optimal forms of PPI involvement  
31  
32 (specifically, the use of service-user researchers to conduct qualitative interviews with service  
33  
34 users). Further, we received service-user input on the content of the draft treatment modules,  
35  
36 and a part of this feasibility trial will be receiving feedback from participants on their  
37  
38 experience of participating in the trial and using the manuals. We will send all participants a  
39  
40 report describing the findings and their implications. We will also make participants aware of  
41  
42 the study website. There will be a number of roles following completion of recruitment  
43  
44 including the refinement and revision of the treatment manual along with involvement in the  
45  
46 academic output preparation.  
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### 50 51 **Ethics and Dissemination**

52  
53 **Ethical approval and protocol amendments.** This project has received ethical  
54  
55 approval from the Health Research Authority of the UK National Health Service (East of  
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3 England; REC reference: 16/EE/0095). The study will be conducted within appropriate UK  
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5 MRC, National Health Service and professional ethical guidelines, ensuring that Good  
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7 Clinical Practice procedures are adhered to at all times. Protocol amendments will be  
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9 circulated to the ethics committee, and trial team, and published in the online registration of  
10  
11 the trial, and in the trial paper.  
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13  
14 **Safety aspects.** Adverse events are managed in line with UK MRC protocols and, in  
15  
16 the unlikely case of an adverse event, will be documented appropriately. Precautions have  
17  
18 been taken to reduce the likelihood of adverse events occurring; for example, patients who are  
19  
20 acutely suicidal or at high risk of harm do not meet study inclusion criteria. The interventions  
21  
22 are delivered by therapists experienced in the management of risk and in the treatment of  
23  
24 psychological disorders. In the case of any adverse events as a result of the intervention that  
25  
26 would interfere with participation, participation in the trial will be discontinued. Regular  
27  
28 team meetings will be conducted to monitor any difficulties patients may be having and ways  
29  
30 of best dealing with these difficulties. Serious adverse events will be reported to the Ethics  
31  
32 Committee. The trial is underwritten by the University of Cambridge in the case that any  
33  
34 individual suffers harm or requires post-trial care. Any adverse events will be reported in the  
35  
36 trial paper.  
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40 **Dissemination policy.** There are no publication restrictions and findings will be  
41  
42 disseminated broadly to participants, healthcare professionals, the public, and other relevant  
43  
44 groups. Academic outputs will take the form of peer-reviewed empirical journal articles,  
45  
46 commentary pieces, and conference presentations. Clinical outputs will be prioritised by the  
47  
48 research team in order to maximise the impact of the findings with practitioners and  
49  
50 commissioners. Outputs will comprise clinical conferences, workshops, service user groups,  
51  
52 and a study website that will make the intervention materials and related measures generally  
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54 available. We will send all participants a report describing the findings and their implications.  
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3 We will also make participants aware of the study website. We anticipate that trial findings  
4 will inform future revisions of clinical guidelines for numerous forms of mood, anxiety, and  
5 stress disorders, and the development of guidelines for comorbid conditions. Anonymised  
6 data from the trial will be made publicly available on an open-access database.  
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## 10 11 Discussion

12  
13 A significant proportion of the cost of CMHPs is generated by adults suffering from  
14 complex and comorbid depression, stress and anxiety, where treatment non-response, cross-  
15 sector service-use across health, social care, and housing, and loss of productivity are greatest.  
16 Providing effective interventions for these mental health problems therefore has the potential  
17 to reduce both long-term treatment costs as well as prevent large productivity losses. At  
18 present, most psychological interventions focus on specific diagnoses and many treatment  
19 manuals take a 'one-size-fits-all' approach. Current evidence-based interventions only  
20 achieve clinical recovery for 40-70% of patients, with people suffering complex co-morbid  
21 conditions faring significantly worse. This randomised controlled feasibility trial aims to pave  
22 the way for a scaled-up efficacy trial of a new transdiagnostic modular treatment for all  
23 CMHPs – *Shaping Healthy Minds* – that enables the flexible delivery of evidence-based  
24 techniques. This treatment approach may improve the effectiveness and dissemination of  
25 evidence-based intervention for the many individuals for whom diagnosis-specific treatments  
26 leave significant difficulties unaddressed. The results from this trial will provide a range of  
27 estimates of effect sizes that can be used to power a later stage trial of treatment efficacy, to  
28 refine the treatment protocol, and to inform future evaluation of the mechanisms underlying  
29 any treatment effects. If effective, *Shaping Healthy Minds* has the potential to improve  
30 outcome for those with complex presentations, through offering a cost-effective treatment  
31 option to reduce chronic, transdiagnostic psychological difficulties.  
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3 **Trial Status:** This trial was registered at [clinicaltrials.gov](http://clinicaltrials.gov) on 4 May 2017 (NCT03143634).

4 This article was submitted on 31 May 2018. To date, 15 participants have met eligibility

5 criteria for the study and have been randomised to a condition. The trial opened on 31 July

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2017, and data collection aims to be completed by September 2019.

**Figure 1.** Participant flow diagram for the HARMONIC Trial with anticipated participant

numbers at each stage

## List of Abbreviations

DSM – Diagnostic and Statistical manual

IAPT – Improving Access to Psychological Therapies

HARMONIC – The Healthy and Resilient Mind Programme: Building Block for Mental Wellbeing

MRC – Medical Research Council

NHS – National Health Service

PTSD – Posttraumatic Stress Disorder

RCT – Randomised Controlled Trial

SCID-5 – Structured Clinical Interview for DSM-5 disorders

TAU – Treatment-as-usual

CMHP – Common Mental Health Problems

NICE – National Institute for Health and Care Excellence

CBT – Cognitive Behaviour Therapy

ACT – Acceptance and Commitment Therapy

DBT – Dialectical Behaviour Therapy

MBCT – Mindfulness Based Cognitive Therapy

### Authors' contributions

MB will manage the trial, deliver the intervention, co-develop the treatment manuals and helped to draft the manuscript; CH will assist with trial management and helped to draft the manuscript; AB advises on the delivery of the interventions and provided guidance on the protocol; JC provides practical and NHS service support for the trial; COL, RE and DJ provides support for the trial management; PW is the trial statistician responsible for the randomisation, advise on analysis strategy, and analysis of the data; LL provides support for the health economics component; SR provides service-user support for the trial; SG and WK advised on the treatment manual; JN co-developed and adapted the treatment manuals; TD designed the study, co-developed and adapted the treatment manuals, and helped to draft the manuscript. All authors read and approved the final manuscript.

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## Funding

This paper presents independent research funded by the National Institute of Health Research (NIHR) under its Research for Patient Benefit (RfPB) Programme (Grant Reference Number PB-PG-0214-33072) grant awarded to Tim Dalglish, Peter Watson, Jill Newby, Leonora Brosan, Rajini Ramana, Louise Lafortune, Sarah Rae, Simon Gilbody, Willem Kuyken, and Caitlin Hitchcock. Jill Newby is supported by a NHMRC/MRFF Fellowship (1145382).

Please note that the funding body does not have authority over the running of the trial – all decisions rest with the trial team. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

## Competing Interests

The authors have no competing interests.

## Patient consent

Obtained.

## Ethics approval

NHS National Research Ethics Committee (East of England, Reference: 16/EE/0095)

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Table 1.

*Additional Outcome and Process measures to assess changes in potential mechanisms of psychological distress and in response to specific transdiagnostic intervention modules.*

Measure	Focus area
The Treatment Credibility / Expectancy Questionnaire (CEQ) [64]	Expectancy about treatment outcome, as well as the credibility of the treatment.
Cognitive Emotion Regulation Questionnaire (CERQ) [65]	Ability to contextualize negative events within a wider frame of reference.
The Experiences Questionnaire (EQ) [66]	Ability to disengage from troublesome mental content and take a more accepting stance towards it, as well as the tendency to engage in rumination.
Differential Emotions Scale (DES [67])	Intensity with which they experience different emotions on a typical day to obtain summary scores for positive emotions, negative emotions, and denied emotions (the number of emotions <i>not</i> endorsed by the participant).
Levels of Personality Functioning Scale (LPFS) [68]	Personality functioning based on the DSM-5 Alternative Model of Personality Disorders. It has four subscales: Identity, Self-Direction, Empathy, and Intimacy.
Ruminative Responses Scale of the Response Styles Questionnaire (RRS) [69]	Rumination (Module 7 – Overcoming Repetitive Thinking)
Distress Tolerance Scale (DTS)[70]	Ability to tolerate distress (Module 3 – Managing and Tolerating Emotions)
Difficulties with Emotion Regulation Scale (DERS) [71]	Ability to label, perceive, and regulate emotions (Modules 2 – Understanding Emotions and 3 – Managing and Tolerating Emotions)
Dysfunctional Attitudes Scale (DAS) short form (version 1 and 2) [72]	Negative beliefs, thoughts and assumptions (Module 6 – Tackling Unhelpful Thoughts)

1		
2		
3	Kentucky Inventory of	Mindful awareness (Module 2 – Understanding Emotions)
4	Mindfulness Skills (KIMS)	
5	[73]	
6		
7	Anxiety Sensitivity Index	Fear of physical anxiety sensations (Module 3 – Managing
8	(ASI) [74]	and Tolerating Emotions and Module 5 – Tackling
9		Avoidance)
10		
11	Posttraumatic cognitions	Trauma-related beliefs and maladaptive appraisals of
12	inventory – short version	intrusive symptoms (Module 9 – Managing Upsetting
13	(PTCI) [75]	Memories and Images)
14		
15	Skills of Cognitive Therapy	Implementation of cognitive therapy skills (Module 6 –
16	(SoCT) [76]	Tackling Unhelpful Thoughts)
17		
18	The Multidimensional	Avoidance of internal experiences including thoughts,
19	Experiential Avoidance	feelings, physical sensations (Module 5 – Tackling
20	Questionnaire [77]	Avoidance)
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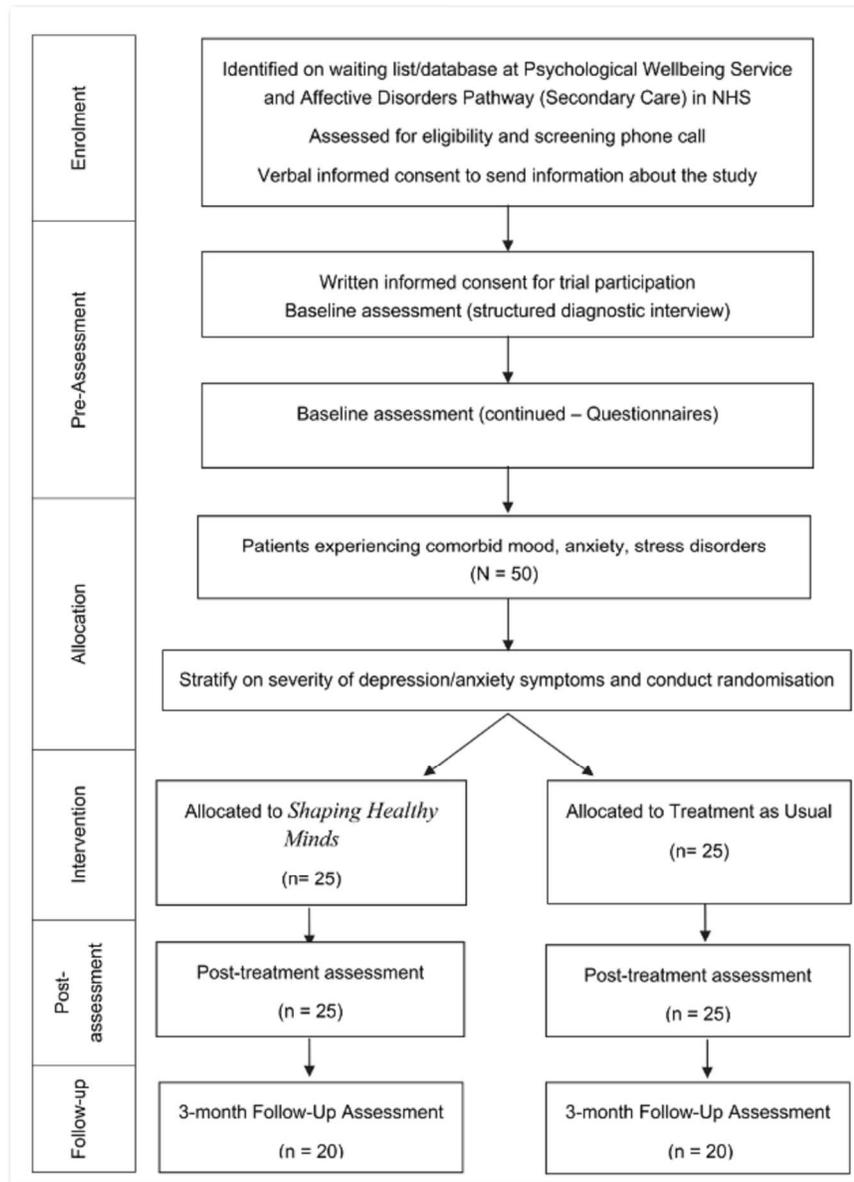


Figure 1. Participant flow diagram for the HARMONIC Trial with anticipated participant numbers at each stage



**Participant Information Sheet**  
**Study title: *Shaping Healthy Minds***

We invite you to participate in a study investigating a new modular treatment for mental health difficulties. Please read this information sheet if you wish to hear about the study in more detail. Your participation is *entirely voluntary*. Your treatment through the NHS will not be affected if you decide not to participate in this research.

This treatment – *Shaping Healthy Minds* (SHM) – treats symptoms that are common across depression and multiple anxiety disorders. The treatment consists of components of the best available evidence-based psychological treatments (e.g., mindfulness-based interventions, Acceptance and Commitment Therapy, Cognitive Behavioural Therapy, Behavioural Activation, and Dialectical Behaviour Therapy). Through using components of different types of therapy, the SHM aims to not only treat the principle problem that each individual is experiencing (e.g., depression or anxiety) but to target other psychological symptoms the individual is experiencing at the same time. In this way, someone who is experiencing both depression and anxiety will receive treatment for both of these issues, in contrast to the usual approach of treating one problem first, using only one type of therapy.

***Purpose of the study***

The purpose of this study is test whether the SHM is an effective treatment for people experiencing multiple psychological difficulties. We are interested in whether SHM will reduce symptoms of multiple mental health issues in those who are suffering from both depression and one or more anxiety disorders.

***What's involved?***

If you decide to take part, you would be asked to attend a 'screening' session to determine whether you are eligible to participate in this study. It will take 60-90 minutes and involves interviews and questionnaires focusing on emotions and mental health.

If you are eligible to participate in the trial you will then be randomly allocated to one of two groups:

- (i) 15-20 sessions of the *Shaping Healthy Minds* (SHM) programme,
- (ii) Treatment you would usually receive from the NHS (Treatment-as-Usual)

You will not be able to choose which of these groups you are allocated to, as the allocation is random and decided by a computer.

In the SHM programme, you will complete individual sessions with a clinical psychologist. The exact therapy components that you complete will be selected in consultation with you and based on the particular symptoms you are experiencing. That is, the treatment will be shaped for you. You will also receive the regular NHS care that you normally receive except for any psychological therapy.

In Treatment-as-Usual, you will receive all of the regular NHS services you would normally receive including any psychological therapy.

In addition to receiving treatment sessions, you will be asked to attend five assessment sessions where you will be asked to complete some questionnaires, some computer-based tasks that ask about your memories and emotions, including a task that involves pleasant and unpleasant images. In addition, there is an **optional** neuroimaging task, involving two functional magnetic resonance imaging scans (before and after treatment).

1 You can choose not to complete the imaging sessions and still participate in the study.

2  
3 Prior to completing the treatment sessions (SHM or Treatment-as-Usual) which form the main part of the study, you will  
4 be asked to complete one assessment session which involves interviews and questionnaires, and one assessment  
5 session with computer tasks and the optional imaging session. You would then repeat these two assessment sessions  
6 after completing the treatment, followed by one final assessment session 3 months following the completion of  
7 treatment. Each assessment session will take approximately one and a half hours, which includes a break if  
8 needed. With your consent, some sessions will be audio-recorded to allow checks on the quality of the  
9 treatment you are receiving.

### 12 ***Why have I been invited to take part?***

13 All individuals currently receiving NHS services for depression or anxiety in the Cambridge area are being  
14 invited to participate in this study.

### 17 ***Do you have to take part?***

18 No, it is up to you to decide. We will describe the study and go through this information sheet, which we will  
19 then give to you. If you do want to join in we'll ask you to sign a consent form, a copy of which you can keep  
20 along with this information sheet. You are free to withdraw from the study at any point *without giving us a*  
21 *reason*. You will not be treated any differently by any NHS service if you choose not to participate in this study  
22 or if you decide to withdraw.

### 25 ***Will I be reimbursed?***

26 You will be reimbursed for the assessment sessions at a rate of £6 per hour for your time. It is anticipated that  
27 the one screening session and four assessment sessions will not exceed a total of ten hours, for which you  
28 would receive a minimum of £45, plus travel costs. If you choose to do the neuroimaging sessions as well, you  
29 will receive £20 per imaging session, so you would receive a total of £85. You will not be reimbursed for the  
30 therapy sessions as you will be receiving therapy free of charge by qualified clinical psychologists.

### 33 ***Are there any risks or benefits associated with taking part?***

34 All of the tasks, interviews, and questionnaires we will ask you to complete have been used safely in previous  
35 research. As with any research involving emotional material, there is a chance that you will experience some  
36 upset when you discuss personal memories and difficulties. In our experience this is usually very mild and  
37 short-lived with no lasting ill effects. After participation you will receive a complete and thorough explanation  
38 of the study and you will be encouraged to express your feelings about your experience, if you wish.  
39 Additionally, you will be able to contact a member of the research team (a qualified clinical psychologist) after  
40 any session should you feel you are experiencing distress as a result of taking part in the study.

### 43 ***What are the possible benefits of taking part?***

44 We hope that the findings from this research will lead to improvement in treatment options for people  
45 experiencing multiple mental health disorders. We also hope that completing the SHM, if you are randomly  
46 allocated to that treatment, will have a beneficial impact on your psychological difficulties. We cannot  
47 guarantee that this will be the case for everybody who takes part, but you will have an opportunity to  
48 experience a range of therapeutic strategies and techniques.

### 51 ***What if there is a problem?***

52 For any complaint about the way you have been dealt with during the study or any possible harm you may  
53 have suffered you can contact the Patient Advice and Liaison Service on 01223 726 774,  
54 <http://www.cpft.nhs.uk/about-us/pals.htm>

### 57 ***Further Information & Contact Details:***

58 If you would like any further information about this project please contact the research coordinator **Dr**  
59 **Melissa Black** at the MRC Cognition and Brain Sciences Unit (Tel: **01223 273 739**; Email: [melissa.black@mrc-](mailto:melissa.black@mrc-cbu.cam.ac.uk)  
60 [cbu.cam.ac.uk](mailto:melissa.black@mrc-cbu.cam.ac.uk))

**Thank you for reading this information sheet**

For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>



Participant ID Number:

**Participant Consent Form (Version 2.2, April 2018)**

**Title of the project:** Shaping Healthy Minds

**Name of project coordinator:** Dr Melissa Black

Please initial box:

1. I confirm that I have read and understood the Information Sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without my medical care or legal rights being affected.

3. I understand that data (including audio recordings) collected from me during the study may be looked at by individuals from the research team where it is relevant to my taking part in this research. I give permission for these individuals to have access to these data.

4. I understand that my GP will be informed of my participation in this study if s/he is not already aware of it.

5. I agree to take part in the above study.

6. I agree to a researcher contacting me after the end of this study about possible future research (optional).

.....  
Name of Participant

.....  
Date

.....  
Signature

.....  
Name of Person taking consent

.....  
Date

.....  
Signature

**(When the form is completed, 1 copy is for the participant and 1 is for the study files)**

**HARMONIC Trial (Healthy and Resilient Mind Programme: Building Blocks for Mental Wellbeing)**

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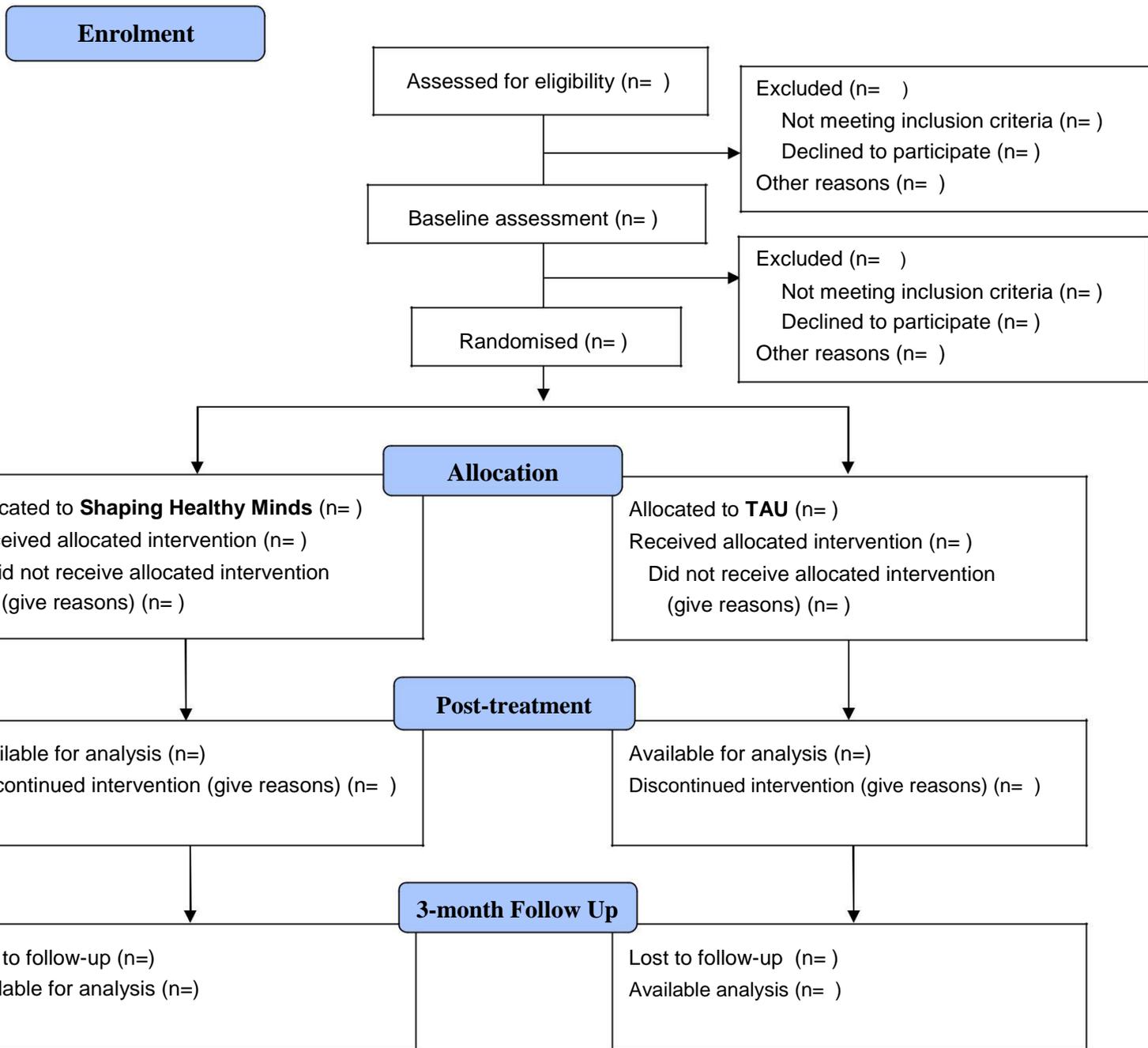


Figure 1. CONSolidated Standards of Reporting Trials (CONSORT) diagram

Supplementary Table 1.

*Key treatment components of Shaping Healthy Minds Core and Optional Modules.*

#	Module Title	Sections of Module	Duration (sessions)
1	Getting Acquainted with <i>Shaping Healthy Minds Core Module</i>	<ul style="list-style-type: none"> <li>• Education about depression and anxiety, and about emotions (Including 5-part model of emotion episodes)</li> <li>• Orientation to treatment</li> <li>• Defining Top 3 Problems and Top 3 Strengths</li> <li>• Setting treatment goals and making plans</li> <li>• Enhancing motivation</li> </ul>	1-3
2	Understanding emotions <i>Core Module</i>	<ul style="list-style-type: none"> <li>• Education about emotions</li> <li>• Orientation to the emotion model</li> <li>• Self-monitoring of emotion episodes</li> <li>• Introduction to Mindful Awareness of Emotions</li> </ul>	1-2
3	Managing and Tolerating Emotions <i>Optional Module</i>	<ul style="list-style-type: none"> <li>• Education about emotion management toolbox</li> <li>• Relaxation</li> <li>• Exercise</li> <li>• Social Support</li> <li>• Distraction</li> <li>• Self-soothing</li> <li>• Accepting and Tolerating Feelings</li> </ul>	1-3
4	Behavioural Activation <i>Optional Module</i>	<ul style="list-style-type: none"> <li>• Education about low activity cycle</li> <li>• Activity Monitoring</li> <li>• Activity Scheduling and establishing positive routines</li> <li>• Savouring the good things</li> </ul>	1-2
5	Tackling Avoidance <i>Optional Module</i>	<ul style="list-style-type: none"> <li>• Education about avoidance</li> <li>• In vivo exposure</li> <li>• Interoceptive exposure</li> <li>• Emotion exposures</li> </ul>	1-3
6	Tackling unhelpful thoughts <i>Optional Module</i>	<ul style="list-style-type: none"> <li>• Education about thoughts</li> <li>• Thought monitoring</li> <li>• Thought questioning and cognitive flexibility</li> <li>• Behavioural experiments</li> <li>• Accepting and tolerating thoughts</li> </ul>	1-3

1			
2			
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4	7	Tackling	• Education about habits
5		unhelpful habits	• Self-monitoring of habits
6		<i>Optional Module</i>	• Step-by-step habit change process
7			
8	8	Overcoming	• Education about rumination and worry
9		Repetitive	• Self-monitoring of rumination and worry
10		Thinking	• Getting unstuck toolbox
11		<i>Optional Module</i>	• Shifting thinking styles and perspective, directing attention
12			
13			
14			
15	9	Managing	• Education about memories and intrusive images
16		upsetting	• Monitoring of memories
17		memories and	• Imaginal exposure
18		images	• Rescripting memories
19		<i>Optional Module</i>	• Reliving + rescripting memories
20			
21			
22	10	Preventing	• Education about lapses and relapses
23		relapse and	• Evaluating treatment progress and consolidating learning
24		building a	• Creating a therapy blueprint (relapse prevention plan)
25		positive future	• Setting goals and making future plans
26		<i>Core Module</i>	
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SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents\*

Section/item	Item No	Description	Page/Line Reference
<b>Administrative information</b>			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	p. 1, line 1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	p. 1, line 28
	2b	All items from the World Health Organization Trial Registration Data Set	See attached
Protocol version	3	Date and version identifier	p. 1, line 29
Funding	4	Sources and types of financial, material, and other support	p. 1, line 30
			p. 22, line 1
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	p. 1, line 4
	5b	Name and contact information for the trial sponsor	p. 22, line 20
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	p. 22, line 1
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	p. 16, line 16
<b>Introduction</b>			

1	Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	p. 4, line 4
2				
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7		6b	Explanation for choice of comparators	p. 8, line 6
8	Objectives	7	Specific objectives or hypotheses	p. 8, line 9
9				
10	Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	p. 8, line 23
11				
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16	<b>Methods: Participants, interventions, and outcomes</b>			
17				
18	Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	p. 9, line 23
19				
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23	Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	p. 9, line 4 p. 9, line 12 p. 12, line 15
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29	Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	p. 10, line 21
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33		11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	p. 10, line 17
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38		11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	p. 12, line 15 p. 17, line 5
39				
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42		11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	p. 9, line 20
43				
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45	Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	p. 13, line 9
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1	Participant	13	Time schedule of enrolment, interventions (including any	p. 9, line 23
2	timeline		run-ins and washouts), assessments, and visits for	Figure 1
3			participants. A schematic diagram is highly	
4			recommended (see Figure)	
5				
6				
7	Sample size	14	Estimated number of participants needed to achieve	p. 15, line 2
8			study objectives and how it was determined, including	
9			clinical and statistical assumptions supporting any	
10			sample size calculations	
11				
12	Recruitment	15	Strategies for achieving adequate participant enrolment	p. 9, line 23
13			to reach target sample size	
14				

### Methods: Assignment of interventions (for controlled trials)

#### Allocation:

17				
18				
19	Sequenc	16a	Method of generating the allocation sequence (eg,	p. 10, line 10
20	e		computer-generated random numbers), and list of any	
21	generatio		factors for stratification. To reduce predictability of a	
22	n		random sequence, details of any planned restriction (eg,	
23			blocking) should be provided in a separate document	
24			that is unavailable to those who enrol participants or	
25			assign interventions	
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28	Allocatio	16b	Mechanism of implementing the allocation sequence (eg,	p. 10, line 10
29	n		central telephone; sequentially numbered, opaque,	
30	concealm		sealed envelopes), describing any steps to conceal the	
31	ent		sequence until interventions are assigned	
32	mechanis			
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35	Impleme	16c	Who will generate the allocation sequence, who will	p. 10, line 14
36	ntation		enrol participants, and who will assign participants to	
37			interventions	
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40	Blinding	17a	Who will be blinded after assignment to interventions	p. 15, line 20
41	(masking)		(eg, trial participants, care providers, outcome	
42			assessors, data analysts), and how	
43				
44		17b	If blinded, circumstances under which unblinding is	p. 15, line 20
45			permissible, and procedure for revealing a participant's	
46			allocated intervention during the trial	
47				

### Methods: Data collection, management, and analysis

1 2 3 4 5 6 7 8 9 10	Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	p. 13, line 8 p. 15, line 13
11 12 13 14 15 16		18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	p. 16, line 16
17 18 19 20 21 22	Data managemen t	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	p. 15, line 17 p. 16, line 16
23 24 25 26 27 28	Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	p. 16, line 1
29 30 31		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	p. 16, line 10
32 33 34 35 36		20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	p. 16, line 9
37 38	<b>Methods: Monitoring</b>			
39 40 41 42 43 44 45 46 47	Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	p. 16, line 16
48 49 50 51 52 53 54 55 56 57 58 59 60		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	p. 16, line 3

1	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	p. 17, line 5
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7	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	p. 16, line 17
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11	<b>Ethics and dissemination</b>			
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13	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	p. 17, line 17
14				
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17	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	p. 16, line 16 p. 17, line 21
18				
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24	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	p. 10, line 7
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28		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
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32	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	p. 15, line 13
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38	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	p. 22, line 11
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41	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	p. 17, line 2
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45	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	p. 17, line 14
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49	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	p. 17, line 24
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1		31b	Authorship eligibility guidelines and any intended use of professional writers	p. 21, line 1
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4		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	p. 17, line 24
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## Appendices

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11	Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Supplementary materials
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15	Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A
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\*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](https://creativecommons.org/licenses/by-nc-nd/3.0/)" license.