Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Low-Intensity Guided Help Through Mindfulness (LIGHTMIND): Study protocol for a randomised controlled trial comparing supported Mindfulness-Based Cognitive Therapy self-help to supported Cognitive Behavioural Therapy self-help for adults experiencing depression

Clara Strauss (c.y.strauss@sussex.ac.uk)
University of Sussex https://orcid.org/0000-0002-0303-763X

Amy Arbon
Brighton and Sussex University Hospitals NHS Trust

Michael Barkham
The University of Sheffield

Sarah Byford
King's College London

Rebecca Crane
Bangor University

Richard de Visser
University of Sussex

Margaret Heslin
King's College London

Anna-Marie Jones
Sussex Partnership NHS Foundation Trust

Fergal Jones
Canterbury Christ Church University

Laura Lea
Sussex Partnership NHS Foundation Trust

Glenys Parry
The University of Sheffield

Claire Rosten
University of Brighton - Falmer Campus

Kate Cavanagh
University of Sussex

Study protocol

Keywords: depression, mindfulness, cognitive behavioural therapy, mindfulness-based cognitive therapy, self-help

Posted Date: February 27th, 2020

DOI: https://doi.org/10.21203/rs.2.24697/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Version of Record: A version of this preprint was published at Trials on May 4th, 2020. See the published version at https://doi.org/10.1186/s13063-020-04322-1.

Abstract

Background Depression has serious personal, family and economic consequences. It is estimated that it will cost £12.15 billion to the economy each year in England by 2026. Improving Access to Psychological Therapies (IAPT) is the National Health Service talking therapies service in England for adults experiencing anxiety or depression. Over 1 million people are referred to IAPT every year, over half experiencing depression. Where symptoms of depression are mild/moderate, people are typically offered Cognitive Behavioural Therapy (CBT) self-help supported by a psychological wellbeing practitioner (PWP). The problem is that over half of people who complete treatment for depression in IAPT remain depressed despite receiving National Institute of Health and Care Excellent (NICE) recommended treatment. Furthermore, less than half of IAPT service users complete treatment. This study seeks to investigate the effectiveness of an alternative to CBT self-help. Mindfulness-based cognitive therapy differs from CBT in focus, approach and practice and may be more effective with a higher number of treatment completions.

Methods/Design This is a definitive randomised controlled trial comparing supported mindfulness-based cognitive therapy self-help (MBCT-SH) with supported cognitive behavioural therapy self-help (CBT-SH) for adults experiencing mild/moderate depression being treated in IAPT services. Four hundred and ten participants experiencing mild/moderate depression will be recruited from IAPT services and randomised to receive either an MBCT-based self-help workbook or a CBT-based self-help workbook. Participants will be asked to complete their workbook within 16 weeks, with six support sessions with a PWP. The primary outcome is depression symptom severity upon treatment completion. Secondary outcomes are treatment completion rates and measures of generalized anxiety, wellbeing, functioning and mindfulness. An exploratory non-inferiority analysis will be conducted in the event the primary hypothesis is not supported. A semi-structured interview with participants will guide understanding of change processes.

Discussion If the findings from this randomised controlled trial demonstrate that MBCT-SH is more effective than CBT-SH for adults experiencing depression, this will provide evidence for policy makers and lead to changes to clinical practice in IAPT services, leading to greater choice of self-help treatment options and better outcomes for service users. If the exploratory non-inferiority analysis is conducted and this indicates non-inferiority of MBCT-SH in comparison to CBT-SH this will also be of interest to policy makers when seeking to increase service user choice of self-help treatment options for depression.

Background

Around 15% of adults in England experience clinically significant depression or anxiety in any week[1]. Improving Access to Psychological Therapies (IAPT) is an initiative launched in the National Health Service (NHS) in England In 2006 that aims to improve access to psychological therapies for people experiencing anxiety and depression with over 1.5 million people now referred to IAPT each year[2].

Depression is typically recurrent - following one episode of major depression 50% will relapse and after two episodes 80% relapse[3]. In addition to the impact on individuals and their families, depression is estimated to cost the economy in England £12.15 billion a year by 2026[4]. In order to meet the needs of people experiencing depression IAPT typically offers stepped-care[5] – supported self-help at what is called 'Step 2' followed by, where needed, face-to-face therapy at 'Step 3'. In line with National Institute of Health and Care Excellence (NICE)[6] guidelines, at Step 2 people are provided with cognitive behavioural therapy self-help (CBT-SH) materials supported by a trained Psychological Wellbeing Practitioner (PWP).

However, IAPT has shown modest treatment outcomes for CBT self-help - only 41% of people receiving book-based PWP-supported CBT self-help for depression met criteria for remission in the 2018-19 financial year[2]. In addition, this figure is for initial remission and does not consider sustained recovery[7]. Partial remission from depression is associated with greater risk of relapse[8]. A related problem in IAPT is high rates of treatment drop-out - only 36% of people referred to IAPT in 2018-19 completed a course of treatment[2]. Completing treatment is important because it is associated with better outcomes[9]. Moreover, costs for treatment non-completers surpass that of treatment completers in IAPT[10]. Yet, there is poor understanding of reasons for non-completion[11], and this evidence gap needs addressing. Improving remission rates for depression and increasing treatment completion require urgent attention.

Mindfulness is the capacity to pay attention, intentionally and non-judgmentally, to current experience. Mindfulness-based interventions (MBIs) teach the application of mindfulness in everyday life and work by reducing rumination and worry[12]. They address well-established mechanisms which trigger and maintain depression[13]. MBIs differ from CBT in important ways: (1) CBT includes evaluating the accuracy of difficult thoughts, MBIs encourage a self-compassionate, non-judgmental and accepting attitude towards experience, including unpleasant thoughts; (2) regular meditation practice (verbally guided attention towards present-moment experiences) is integral to MBIs but is not included in CBT-meditation is the training ground that enables participants to experience thoughts in the moment as transient mental events[14]; and (3) participant experience is different in terms of content and goals.

Mindfulness-based cognitive therapy (MBCT) is a group therapy recommended for relapse prevention for depression in the UK by the NICE[15] that includes elements of CBT for depression. Meta-analyses show MBCT reduces the relative risk of relapse for people with a history of multiple episodes of depression by 31%[16]. Mindfulness-based group interventions, in comparison to control conditions, lead to significant reductions in depression severity for people currently depressed[17]. Thus, MBCT groups are a good candidate for not only attaining initial symptom remission but also for achieving sustained recovery and preventing relapse. However, this evidence applies to formal face-to-face MBCT groups, delivered by highly trained MBCT therapists and we cannot assume this potential will generalise to a supported self-help intervention in a service such as IAPT.

MBCT self-help (MBCT-SH) delivered at Step 2 in IAPT services has the potential to reduce the cost of delivery and to widen access to people unable or unwilling to attend a group[18]. This protocol is for a

definitive RCT of clinical and cost effectiveness comparing MBCT-SH with CBT-SH for people experiencing mild to moderate depression. Our primary hypothesis is that supported MBCT-SH, in comparison to supported CBT-SH, will lead to greater reductions in depressive symptom severity from baseline to post-intervention.

Secondary hypotheses are:

- MBCT-SH in comparison to CBT-SH will lead to greater reduction in depressive symptom severity from baseline to six-months follow-up.
- A greater proportion of MBCT-SH participants will be in the non-clinical range for depressive symptoms than CBT-SH participants at post-intervention (i.e. remission) and six-months follow-up (i.e. recovery).
- MBCT-SH in comparison to CBT-SH will lead to greater improvements in mindfulness, generalised anxiety, work and social adjustment and wellbeing from baseline to post-intervention and from baseline to six-months follow-up.
- Treatment completion rates will be higher for MBCT-SH than CBT-SH.
- Depressive symptom severity outcomes will be mediated by treatment completion.
- MBCT-SH will be cost-effective in comparison to CBT-SH at follow-up.
- MBCT-SH will be a safe alternative to CBT-SH, with a similarly low incidence of serious adverse events during therapy and lasting negative effects of therapy.

In the event that the primary hypothesis of MBCT-SH superiority over CBT-SH on the primary outcome is not supported an additional exploratory analysis will be carried out to explore non-inferiority of MBCT-SH compared to CBT-SH.

A qualitative component will close the evidence gap concerning reasons for treatment non-completion in IAPT services by identifying facilitators and barriers to treatment completion in both arms. Qualitative interviews will be conducted using the Change Interview[19] to ascertain facilitators and barriers to treatment completion for each intervention. Questions were added to the end of interview following advice from the study's lived experience Public and Patient Involvement (PPI) consultation panel. These questions enquire about participants' experiences of their allocated intervention beyond depressive symptom change.

Methods/design

Design and sample size

This is a parallel-groups, superiority pragmatic RCT with 1:1 allocation to MBCT-SH or CBT-SH, with blinded assessments at all time points. Participants will be blind to the hypothesised direction of effects. Four hundred and ten people meeting eligibility criteria for major depressive disorder or mixed anxiety and depression will be randomly allocated to receive MBCT-SH or CBT-SH, along with six sessions of support

from a PWP. Participants will complete measures at baseline (Time 0), 16 weeks post-randomisation (post-intervention, Time 1) and 42 weeks post randomisation (6-months follow-up, Time 2). In addition, 24 participants will be interviewed about their experiences of both self-help interventions (12 participants per arm) at Time 1 with a focus on better understanding barriers and facilitators to engaging in self-help interventions in IAPT services and investigating any negative experiences or effects of treatments.

The sample size was based on detecting a between-group effect size of 0.36 based on the difference between the reported between-group effect of CBT-SH (0.42)[20] and the reported between-group effect of MBCT-SH (0.78)[21]. Recruiting 205 patients into each arm would provide 90% power to detect a between-group difference of 0.36 with a 5% alpha and a two-sided t-test whilst allowing for 20% attrition at post-intervention (as found in our pilot study). Therefore, a total sample size of 410 will be required.

The study design was informed through consultation with a PPI group chaired by a PPI co-applicant consultant (LL). Members of the PPI group had participated in a pilot study of the intervention or had lived experience of depression, mindfulness and/or CBT. The PPI group were instrumental in advising on a number of aspects of study design including the frequency and nature of support sessions and the study recruitment strategy and materials.

Participants

Participants will be recruited through ten IAPT services across England. A list of sites can be requested through the corresponding author.

Inclusion criteria are that participants: (1) be aged 18 years or over; (2) meet diagnostic criteria on the revised Clinical Interview Schedule (CIS-R)[22] for a primary diagnosis of a depressive episode, mixed anxiety and depression, or non-specified mild neurotic disorder; (3) score 10 or more on the PHQ-9[23] at their initial IAPT assessment (cut-off indicating a probable major depressive episode); and (4) have sufficient literacy skills to read and understand the self-help materials.

Exclusion criteria are that participants: (1) have severe symptoms of depression (a score 20 or more on the PHQ-9); (2) score of 4 on the CIS-R suicidality scale; and (3) express a strong preference (5/5) for one intervention over the other on the treatment preference question such that if randomised to the non-preferred intervention they would be likely to drop out of the intervention.

Measures

Demographics

A questionnaire will be completed to collect demographic information.

Diagnostic status

The Clinical Interview Schedule (CIS-R)[22] will be conducted at baseline (Time 0) to ascertain diagnostic status. The CIS-R is routinely used in primary care mental health and IAPT research[1] and has been

validated for telephone completion[24].

Primary Outcome Measure

Depression symptom severity (PHQ-9)[23]. The PHQ-9 is a 9-item self-report measure of depression symptom severity used in all IAPT services with good sensitivity and specificity. Items are rated on a four-point scale. Scores under 10 are considered sub-clinical, 10–14 mild, 15–19 moderate and 20 + severe. The PHQ-9 will be administered at Time 0, Time 1 and Time 2.

Secondary Outcome Measure

Generalised anxiety (GAD-7)[25]. This is a 7-item measure of generalised anxiety used in IAPT. Items are rated on a 4-point scale and the measure has excellent psychometric properties[25]. This will be administered at Time 0, Time 1 and Time 2.

Wellbeing (SWEMWS)[26]. The short version of the Warwick Edinburgh Mental Wellbeing Scale consists of 7 questions rated on a 5-point scale designed to measure wellbeing. The scale has good psychometric properties and is used widely[27]. This measure was added following advice from the Public and Patient Involvement (PPI) consultation panel. This will be administered at Time 0, Time 1 and Time 2.

Functioning (WSAS)[28]. The Work and Social Adjustment Scale (WSAS) is a 5-item measure of daily occupational and social functioning that is used routinely in IAPT. This will be administered at Time 0, Time 1 and Time 2.

Mindfulness (FFMQ-15)[29]. Mindfulness will be measured using 15-item version of the Five-Facet Mindfulness Questionnaire. This has excellent psychometric properties and is sensitive to change following MBCT[29]. This will be administered at Time 0, Time 1 and Time 2.

The Change Interview[19] will be used to guide the qualitative component of the study. This is a widely-used semi-structured interview designed to explore participants' experiences of psychological interventions and has been successfully used in previous studies by members our team. Questions about participants' experiences of the effects of their allocated intervention on personally-relevant outcomes (i.e. not necessarily restricted to depressive symptoms) have been added at the end of the interview following advice from the study's lived experience consultation panel. The Change Interview will be conducted by the PPI consultant co-applicant on the study (LL) with the expectation that this will facilitate participants to be open about their experiences of the study and interventions. This will be conducted at Time 1.

Health Economic Measures

Service use. An adapted version of the Adult Service Use Schedule (AD-SUS) will be used to measure individual-level all-cause hospital and community-based health and social care resource use. The AD-SUS was developed in previous research for use with people with common mental disorders[30, 31] and adapted for the purpose of this study. The baseline (Time 0) AD-SUS will cover the period 3 months prior

to randomisation. At the Time 1 and Time 2 follow-up interviews, the AD-SUS will cover the period since last interview.

Health-related quality of life (EQ-5D-5L)[32]. The EQ-5D is a five-dimension, five-level, generic, preference-based measure of health-related quality of life covering mobility, self-care, usual activities, pain/discomfort and anxiety/depression. We will use the recently developed five level version, to maximise sensitivity[33]. This measure will be administered at Time 0, Time 1 and Time 2.

Intervention Evaluation Measures and Tools

Intervention expectation form. This will be used to assess expectation of benefit and treatment credibility at Time 0.

Lasting negative effects questionnaire. This will be used to ask participants about any lasting negative effects of their allocated intervention at Time 2.

PWP rating scale. This will be used for participants to rate the quality/helpfulness of the sessions between the participant and their PWP at Time 1.

Weekly diaries. These record the extent to which participants are engaging with the self-help course each week during intervention delivery.

Engagement questionnaire (end of treatment). This records the extent to which participants engaged with the self-help course during the entire course of the intervention and will be administered at Time 1.

Engagement questionnaire (follow-up). This records the extent to which participants continued to engage with the self-help course following the end of the intervention and will be administered at Time 2.

Session attendance. Number of PWP sessions attended (0–6) and duration of each support session.

Treatment completion. This is defined as attending at least 50% of the PWP sessions (i.e. attending at least 3 sessions).

Procedure

See Fig. 1 for the SPIRIT Schedule of enrolment, interventions, and assessments. Patients with a diagnosis of depression will be sought through IAPT services. The study will also be advertised in General Practitioner surgeries and elsewhere. Self-referrers will be guided to the study via their local IAPT service. Informed consent will be obtained from each participant. Potential participants will be given a copy of the study participant information sheet and will have the opportunity to discuss the study in person with the research assistant (RA) before signing the consent form (a copy of which can be obtained from the corresponding author).

Once the participant has consented to participate in the trial, the participant will complete the full set of baseline measures with an RA present in person or by phone. Measures will be completed online or on

paper, depending on participant preference. Participants who do not meet eligibility criteria at the baseline assessment will be referred back to the person who conducted their initial assessment for usual care to be offered by the service.

At the end of the baseline assessment, eligible participants will be randomised to either the MBCT-SH or CBT-SH arm. Participants will then be given their allocated self-help workbook. Randomisation will be stratified by centre and PHQ-9 score (mild or moderate) using random block length. Eligible participants will be randomly allocated using the Sealed Envelope[34] online service. The study statistician will use Sealed Envelope to set up and test the randomisation procedure incorporating stratification by site and PHQ-9 severity category (mild or moderate) using random block length and 1:1 allocation. The statistician will not have any further involvement in the randomisation process. The RA will randomise participants by completing the online form with participant's details. This will immediately show whether the participant is assigned to the MBCT-SH or CBT-SH arm and participants will be given their self-help workbook. Participants will not be told the hypotheses in relation to the arm to which they have been randomised.

Participants will then guide themselves through their allocated intervention over the 8-week course with six PWP support sessions. A maximum of 16 weeks is given for the intervention period to allow participants to complete their allocated 8-week course to take account of breaks for holidays, sickness etc. PWP support sessions may be offered by phone or face-to-face, depending on usual practice in the service and participant preference. This mirrors the usual way in which self-help interventions are offered in IAPT – i.e. offering a self-help workbook alongside a limited number of PWP support sessions.

Participants will complete measures online (with a postal option) at 16 weeks post-randomisation (post-intervention, Time 1) and 42 weeks post-randomisation (6-month follow-up, Time 2). Participants will have the option to choose whether to complete the Time 1 and Time 2 measures with an RA present in person or by phone (who will be blind to group allocation) or on their own. In the event that an RA is required to be present during Time 1 or Time 2 assessments and becomes unblinded the assessment will be completed by another, blinded RA. Where Time 1 and Time 2 assessments are not completed, participants will be contacted at weekly intervals for up to one month to remind them to complete these assessments, unless participants have discontinued from the study.

Twenty-four participants will be invited to take part in the qualitative Change Interview after their post-intervention (Time 1) quantitative assessment is completed. Participants will be interviewed on a first come, first served basis with 12 participants interviewed in each of two groups: (1) MBCT-SH intervention completers, and (2) CBT-SH intervention completers.

Therapy Protocols

MBCT Self-Help

The MBCT-SH workbook ‘The Mindful Way Workbook'[35], written for clinical populations, presents MBCT as a self-help package. MBCT-SH participants will be given the workbook and will be asked to guide themselves through the self-help course within a 16-week time period (the time period determined in our pilot). As is routine at Step 2, participants will be offered six PWP sessions to answer questions and provide encouragement.

PWPs currently train in CBT-SH. To match training between arms we will offer PWP training in MBCT-SH. The training involves PWPs: (1) attending an MBCT group as a participant and guiding themselves through the MBCT-SH workbook, or completing the MBCT course using the workbook as a guide, and (2) attending a two-day experiential mindfulness skills workshop. As is standard in delivering MBIs, PWPs will be encouraged to maintain their own personal mindfulness practice throughout the study, and this will be recorded using the PWP Mindfulness Practice Record. Fortnightly MBCT-SH group supervision for PWPs will be provided.

CBT Self-help

The CBT-SH workbook 'Overcoming Low Mood and Depression'[36] has evidence demonstrating its effectiveness in reducing depression symptom severity[37]. This workbook is often used at Step 2 in IAPT.

Matched to the MBCT-SH condition, participants allocated to CBT-SH will be given a copy of their workbook and will be encouraged to guide themselves through within 16 weeks alongside six PWP sessions to answer questions and provide encouragement.

As in the MBCT-SH condition, fortnightly CBT-SH group supervision for PWPs will be provided.

Intervention Fidelity and Adherence

The same PWPs will deliver both interventions in order to minimise therapist effects, as some PWPs achieve substantially better outcomes than others. In order to minimise therapeutic drift and therapy contamination the PWP protocols are detailed and there will be fortnightly supervision of PWPs. PWPs will be asked to audio record at least one complete MBCT-SH case and at least one complete CBT-SH case. A random 10% sample of recordings from each PWP will be rated for fidelity to the therapy protocols by a clinical psychologist trained in CBT and MBCT and who is independent of the PWP training and supervision.

Participants will be prompted each week by the research assistant to complete weekly diaries (online/paper versions) to record the amount of workbook read and time spent engaged in intervention tasks.

(Serious) Adverse Events Monitoring

A protocol for identifying and independently assessing serious adverse events will ensure that such events are addressed in a timely fashion and responded to, including if a serious adverse event is

classified as potentially study-related. Serious adverse events and their classification will be reported to the Data Safety Monitoring Board (DSMB) and Trial Steering Committee (TSC) and action will be taken as deemed necessary.

Serious and other adverse events will be discussed in intervention supervision (with CS or FJ) and in service-based clinical supervision in the relevant IAPT service. Where deemed in the best interests of participants, the study intervention may be discontinued and other treatment options may be recommended by the IAPT service.

Planned Data Analysis

The primary analysis will be a quantitative analysis of the primary outcome at the primary endpoint (Time 1) using an intention-to-treat approach (ITT) where participants are analysed as per their randomisation allocation regardless of treatment received.

Secondary analyses will consist of ITT analyses of the primary outcome at the follow-up time point (Time 2) and all secondary outcomes. A per protocol analysis will also be carried out for those participants receiving an adequate dose of their allocated intervention, defined as attending at least 50% of the PWP sessions (i.e. at least 3 sessions).

A descriptive summary of all measures will be provided by group (MBCT-SH & CBT-SH) and time point (Time 0, Time 1 and Time 2) as appropriate. Comparisons between groups for all measures will be carried out using independent t-tests and Chi-square testing for continuous and categorical data, respectively. Unstandardised effect sizes for the primary outcome and secondary outcomes will be estimated using linear mixed models with treatment group (MBCT-SH vs CBT-SH), time and a treatment group by time interaction entered as fixed factors; site, baseline PHQ-9 and baseline value of the outcome will be entered as covariates. Individual participants will be included in the analysis as random effects. Contrasts will be used as appropriate to estimate effects at different time points. A non-significant group by time interaction will imply common treatment effects at each time point.

Standardised (Cohen's d) effect sizes for each outcome will be calculated by dividing the between-group unstandardized effect by the baseline pooled standard deviation.

95% confidence intervals will be calculated for all unstandardised estimates. Group differences in dichotomous outcomes at the different time points will be analysed in a similar way but using multilevel logistic regression models and baseline PHQ-9 scores. Baseline balance will be presented in the descriptive table broken down by study arm. No adjustment will be made for differences between co-variates at baseline. Outliers will be removed if and only if they look erroneous. Scores at the extreme will not be removed if they are deemed to be true. The suitability of the assumption of approximate normality will be explored by plotting the residuals from this model. If normality is violated then transformations and non-parametric testing will be employed. A sensitivity analysis will be carried out by carrying out the

final analysis on the primary outcome, with and without any individual cases what were involved in violations of the protocol.

Additional exploratory analysis

In the event that there is no evidence to support the primary hypothesis of MBCT-SH superiority over CBT-SH on our primary outcome, an additional exploratory analysis will be carried out to explore non-inferiority of MBCT-SH compared to CBT-SH. The analysis will be based on detecting a between-group non-inferiority margin of 2 points on the PHQ-9 with a one-sided $\alpha = 0.025$. To operationalise this, a two-sided 95% confidence interval will be created around the effect size (MBCT-SH – CBT-SH) and we will conclude non-inferiority if the upper limit of the CI is wholly below 2 PHQ-9 points for both the PP and ITT analyses. The non-inferiority limit was set through consultation with service users and clinicians and looking at the literature [38, 39]

Data entry accuracy and missing data

We aim to minimise missing data and data entry inaccuracies at the point of collection. The Qualtrics online survey software used to collect all data will automatically flag any unanswered questions, giving participants to chance to answer these. If a participant would prefer not to answer a question they can leave it unanswered for a second time and the software will proceed onto the next page. At the point of analysis data will be summarised to look at patterns of missingness. Missing data will be replaced using multiple imputation as appropriate. Missing data will be assessed and if more than 5% of data is missing multiple imputation will be carried out followed by a sensitivity analysis. The sensitivity analysis will compare the results for a complete case analysis to the imputed data analysis. Multiple imputation will be carried out under the assumption the data is missing at random (MAR). Anonymised data will be stored on the Qualtrics platform and on password-protected NHS and university computers. Personal data will be stored securely in locked filing cabinets in NHS research offices and on password protect NHS computers.

Planned interim analysis and stopping rules

No interim analysis has been planned. The trial will be paused or stopped if deemed necessary by the DSMB.

Multiple testing

There shall be no multiple testing.

Economic Evaluation

The economic evaluation will be conducted covering the period from Time 0 to Time 2 and will take the NHS/personal social services perspective preferred by NICE[40]. Resource use data from the AD-SUS will be combined with unit costs to calculate the total costs of the MBCT-SH and CBT-SH groups. The cost of the two interventions, MBCT-SH and CBT-SH, will be calculated using a micro-costing approach[41] based

on PWPs' salary, including relevant on-costs and overheads. Data on the number and duration of PWP contacts in the MBCT-SH and CBT-SH arms will be recorded using a proforma completed by PWPs. Data on indirect time, including preparation and supervision, will be collected directly from the PWPs. All other health and social care services will be costed using nationally applicable published unit costs, such as the NHS Reference Costs for hospital costs, the British National Formulary for medication and the PSSRU Unit Costs of Health and Social Care.

Costs and outcomes will be compared and presented in terms of mean differences and 95% confidence intervals obtained by non-parametric bootstrap regression to account for the non-normal distribution commonly found in economic data[42]. Cost -effectiveness will be assessed through the calculation of incremental cost-effectiveness ratios and will be explored in terms of quality-adjusted life years (QALYs) calculated from the EQ-5D-5L and using the area under the curve approach[43]. Uncertainty will be explored using cost-effectiveness planes and cost-effectiveness acceptability curves based on the net-benefit approach[44, 45]. These curves are an alternative to confidence intervals around ICERs and show the probability that one intervention is cost-effective compared to the other, for a range of values that a decision maker would be willing to pay for an additional unit of an outcome. All economic analyses will include relevant baseline variables to provide a more relevant treatment-effect estimate[46]. The primary analysis will include those with complete data needed to be included in the economic evaluation. Sensitivity analyses will explore the impact of missing data.

Qualitative Data Analysis

Qualitative data will be analysed using Thematic Analysis[47] in order to identify facilitators and barriers to treatment completion for each intervention arm. Analysis will be informed by the structure of the Change Interview[19], but it will also be able to identify inductively-derived themes reflecting participants' experiences.

Discussion

Cognitive Behavioural Therapy self-help (CBT-SH), supported by a psychological wellbeing practitioner (PWP), is the usual treatment offered in IAPT services to people with mild/moderate symptoms of depression. However, over half of people who complete this treatment remain depressed and, furthermore, less than half of IAPT service users complete treatment. This results in disappointing treatment outcomes for many service users and increasing costs for mental health services in primary care. Finding an alternative, more effective self-help treatment would lead to better outcomes for service users and a more efficient use of NHS resources.

MBCT-SH differs from CBT-SH in focus, approach and practice, but it may still be able to be delivered in IAPT services with support from PWPs. By teaching service-users the ability to intentionally pay attention, non-judgementally, to current experience, MBIs aim to reduce rumination and worry, key components of depression, by teaching the application of mindfulness in everyday life and work. MBCT-SH, therefore,

offers a potentially viable and more effective alternative to CBT-SH for improving both outcomes for service users and treatment completion rates.

This definitive randomised control trial directly compares MBCT-SH to CBT-SH with the primary aim of determining the clinical and cost effectiveness of MBCT-SH at reducing depression symptom severity compared to CBT-SH. There is also much less known about the effectiveness of supported self-help mindfulness-based interventions in comparison to their in-person group-based counterparts and so this trial will advance understanding in this area. If the primary superiority hypothesis is not supported, the exploratory non-inferiority analysis will help elucidate if MBCT-SH may be non-inferior to current best practice (i.e. CBT-SH) and therefore findings will be of clinical relevance. Findings from the Change Interview will highlight facilitators and barriers to engagement in both MBCT-SH and CBT-SH and will hopefully lead to recommendations for maximising engagement to both these interventions.

The results of this trial will provide valuable evidence to inform clinical practice and commissioners of services. This could enable a greater choice in effective treatment options for IAPT service users, help elucidate issues around why some people are unable to complete treatment and allow for a more efficient use of NHS resources. The results will also provide evidence more generally about mindfulness-based interventions, their clinical and cost effectiveness, and the mechanisms of change which underpin them.

Trial Status

At the time of manuscript submission, recruitment for this study was ongoing. Recruitment started on 1 December 2017 and is due to be completed on 31 January 2020.

Abbreviations

ADSUS	Adult Service Use Schedule
CBT	Cognitive Behavioural Therapy
CBT-SH	Cognitive Behavioural Therapy Self Help
CIS-R	Clinical Interview Schedule
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
DSMB	Data Safety Monitoring Board
FFMQ-15	Five-Facet Mindfulness Questionnaire 15
GAD-7	Generalised Anxiety Disorder 7
IAPT	Improving Access to Psychological Therapies
ICER	Incremental Cost-Effectiveness Ratios
LEAP	Lived Experience Advisory Panel
MBCT-SH	Mindfulness Based Cognitive Therapy Self Help
MBI	Mindfulness Based Intervention
PHQ-9	Patient Health Questionnaire 9
PPI	Patient and Public Involvement
PSSRU	Personal Social Services Research Unit
PWP	Psychological Wellbeing Practitioner
RA	Research Assistant
RCT	Randomised Controlled Trial
SWEMWS	Short Warwick-Edinburgh Mental Well-being Scale
TSC	Trial Steering Committee
WSAS	Work and Social Adjustment Scale

Declarations

Ethics approval and consent to participate

This study has received full ethical approval from the Health Research Authority (HRA) in the UK (Research Ethics Committee reference: 17/LO/0596) in the UK. Informed consent will be obtained from all participants through completion of a consent form. Important modifications to the trial protocol will be submitted for approval from the trial sponsor and HRA.

Confidentiality

Participants will be assigned a unique identification code which will be used to complete assessments and will be used for data files

Consent for publication

Participants will be asked to consent to their anonymised data to be used in research publications.

Availability of data and material

The datasets created for the current study will be available from the corresponding author on reasonable request.

Funding information

This paper presents independent research funded by the National Institute for Health Research (NIHR) under its Research for Patient Benefit (RfPB) Programme (Grant Reference Number PB-PG-0815-20056). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

Competing interests

CS is Research Lead for the Sussex Mindfulness Centre and has received NIHR and other funding for research trials evaluating mindfulness-based interventions. KC, FJ, LL, CR and SB have received research funding to evaluate mindfulness-based interventions. All other authors declare that they have no conflicts of interest.

Funding

This study was funded by the NIHR Research for Patient Benefit programme, reference number PB-PG-0815-20056. Data collection, data storage, data analysis, interpretation of findings and the decision to publish findings will be conducted independently of the funders.

Trial oversight

Brighton & Sussex Clinical Trials Unit will help to manage the study. The Trial Steering Committee (TSC) will compromise of an independent chair, two additional independent members and two lay members. The Chief Investigator (CS), Trial Manager (AA) and Trial Statistician (AMJ) will also attend the TSC. The role of the TSC will be to over the trial and ensuring that it is running in line with the HRA-approved protocol. The Data and Safety Monitoring Board (DSMB) will compromise of an independent chair and two additional independent members, and will comprise of separate membership to the TSC. The DSMB will be independent of the study sponsor. The Chief Investigator (CS), Trial Manager (AA) and Trial Statistician (AMJ) will also attend the TSMB meetings when requested to do so by the chair. The DSMB

will have sight of study data and will have the authority to pause or close the trial if it has concerns about participant safety or trial integrity. TSC reports will be shared with members of the DSMB and vice versa. Copies of the DSMB and TSC charters can be requested from the corresponding author. A Lived Experience Advisory Panel (LEAP) will comprise of PPI members and will be chaired by the study PPI Consultant and co-applicant (LL). The LEAP will meet on 7 occasions during the course of the study and their role will be to advise on recruitment and retention strategies, participant experience and they will contribute to dissemination of study findings to participants, patients and the public. The PPI Consultant on the study (LL) will attend weekly operational meetings to oversee the day-to-day running of the study from a PPI perspective and to act as bridge between the research team and LEAP.

Authors' contributions

CS led on study design with all authors contributing to the design of the study. CS and CR wrote the first draft of the manuscript with all authors contributing to subsequent drafts. All authors read and approved the final manuscript.

Dissemination

Findings will be written up regardless of outcome for publication in peer reviewed journals and an accessible summary of findings will be produced for participants and members of the public with the support of the Lived Experience Advisory Forum (LEAP).

Acknowledgements

We would like to thank the RfPB stream of NIHR for funding this study (PB-PG-0815-20056) and we would like to thank Brighton & Sussex Clinical Trials Unit for supporting delivery of the study.

This study would not be possible without the hard work and dedication of the study research assistants and we are very grateful to them: Ellie Ball, Peter Beadle, Chloe Burke, Marina Christoforou, Roxanne Denny, Guy Emery, Natalia Fagbemi, Luke Groom, Molly Heeger, Maggie Karanasiou and Amy Pound

We would like to thank the IAPT services for agreeing to take part in this study, the Principal Investigators (PIs) and clinical leads in these sites and the PWPs agreeing to contribute their time to the study. The IAPT services are: Brighton and Hove Wellbeing Service (PI: Juliet Couche, Step 2 Lead: Lizzie Gray), East Riding Emotional Wellbeing Service (PI and Step 2 link: Zoe Lane), Health in Mind in East Sussex (PI: Juliet Couche, Step 2 Lead, Jan Shepherd), Health in Mind in North-East Essex (PI: Maggie Rosairo, Step 2 Lead: John Birsall), italk in Hampshire, Lewisham IAPT service (PI: Janet Wingrove and Kate Rimes, Step 2 Lead: Jackie Ganley), South West Yorkshire Partnership NHS Foundation Trust (PI: Rick Stebbings), Talking Change in Portsmouth (PI: Mahdi Ghomi, Step 2 Lead: Charlotte Hodges), Talking Therapies Southwark (PI: Janet Wingrove and Kate Rimes, Step 2 Lead: Janet Wingrove) and Time to Talk in West Sussex (PI: Claire Taylor, Service Leads: Simon Winter and Siaeda Cullen).

We are extremely grateful to members of the PPI group who contributed to the design, who will support delivery of the study and will contribute to dissemination of findings.

References

1. McManus S, Meltzer H, Brugha TT, Bebbington PP, Jenkins R. Adult psychiatric morbidity in England, 2007 Results of a household survey. London: NHS Information Centre for Health and Social Care; 2009.
2. Health and Social Care Information Centre (HSCIC). Psychological Therapies, Annual Report on the use of IAPT services - England, 208-19 [Internet]. 2019. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/psychological-therapies-annual-reports-on-the-use-of-iapt-services/annual-report-2018-19
3. Burcusa SL, Iacono WG. Risk for recurrence in depression. Clin Psychol Rev [Internet]. 2007 [cited 2015 Jun 7];27:959–85. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2169519&tool=pmcentrez&rendertype=abstract
4. McCrone P, Dhanasiri S, Patel A, Knapp M, Lawton-Smith S. Paying the Price: The cost of mental health care in England to 2026. London, UK; 2008.
5. Bower P, Gilbody S. Stepped care in psychological therapies: access, effectiveness and efficiency. Br J Psychiatry. 2005;186.
6. National Institue of Health and Care Excellence [NICE]. Common Mental Health Disorders. 2011.
7. DeRubeis RJ, Siegle GJ, Hollon SD. Cognitive therapy versus medication for depression: treatment outcomes and neural mechanisms. Nat Rev Neurosci [Internet]. 2008 [cited 2015 Oct 7];9:788–96. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2748674&tool=pmcentrez&rendertype=abstract
8. Paykel ES. Partial remission, residual symptoms, and relapse in depression. Dialogues Clin Neurosci. 2008;10:431–7.
9. Cahill J, Barkham M, Hardy G, Rees A, Shapiro DA, Stiles WB, et al. Outcomes of patients completing and not completing cognitive therapy for depression. Br J Clin Psychol [Internet]. 2003 [cited 2015 Oct 16];42:133–43. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12828803
10. Radhakrishnan M, Hammond G, Jones PB, Watson A, McMillan-Shields F, Lafortune L. Cost of improving Access to Psychological Therapies (IAPT) programme: an analysis of cost of session, treatment and recovery in selected Primary Care Trusts in the East of England region. Behav Res Ther [Internet]. 2013 [cited 2015 Nov 16];51:37–45. Available from: http://www.sciencedirect.com/science/article/pii/S0005796712001556
11. Waller R, Gilbody S. Barriers to the uptake of computerized cognitive behavioural therapy: a systematic review of the quantitative and qualitative evidence. Psychol Med [Internet]. Cambridge University Press; 2009 [cited 2015 Nov 13];39:705–12. Available from: http://journals.cambridge.org/abstract_S0033291708004224

12. Gu J, Strauss C, Bond R, Cavanagh K. How do Mindfulness-Based Cognitive Therapy and Mindfulness-Based Stress Reduction Improve Mental Health and Wellbeing? A Systematic Review and Meta-Analysis of Mediation Studies. Clin Psychol Rev [Internet]. 2015 [cited 2015 Feb 2];37:1–12. Available from: http://www.sciencedirect.com/science/article/pii/S0272735815000197
13. Nolen-Hoeksema S, Wisco BE, Lyubomirsky S. Rethinking Rumination. Perspect Psychol Sci [Internet]. 2008;3:400–24. Available from: http://pps.sagepub.com/lookup/doi/10.1111/j.1745-6924.2008.00088.x
14. Teasdale JD. Metacognition, mindfulness and the modification of mood disorders. Clin Psychol Psychother. John Wiley & Sons, Ltd.; 1999;6:146–55.
15. National Institute of Health and Care Excellence [NICE]. Depression: the treatment and management of depression in adults (update). London; 2009.
16. Kuyken W, Warren FC, Taylor RS, Whalley B, Crane C, Bondolfi G, et al. Efficacy of Mindfulness-Based Cognitive Therapy in Prevention of Depressive Relapse. JAMA Psychiatry [Internet]. 2016 [cited 2017 Feb 9];73:565. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27119968
17. Strauss C, Cavanagh K, Oliver A, Pettman D. Mindfulness-Based Interventions for People Diagnosed with a Current Episode of an Anxiety or Depressive Disorder: A Meta-Analysis of Randomised Controlled Trials. Laks J, editor. PLoS One [Internet]. 2014 [cited 2014 Apr 25];9:e96110. Available from: http://dx.plos.org/10.1371/journal.pone.0096110
18. Cavanagh K, Strauss C, Forder L, Jones F. Can mindfulness and acceptance be learnt by self-help?: A systematic review and meta-analysis of mindfulness and acceptance-based self-help interventions. Clin Psychol Rev [Internet]. Elsevier Ltd; 2014 [cited 2014 Mar 20];34:118–29. Available from: http://www.sciencedirect.com/science/article/pii/S0272735814000026
19. Elliott R, Slatick E, Urman M. Qualitative change process research on psychotherapy: Alternative strategies. In: Frommer, J, Rennie DL, editor. Qual Psychother Res Methods Methodol. Lengerich, Germany: Pabst Science; 2001. p. 69–111.
20. Bower P, Kontopantelis E, Sutton A, Kendrick T, Richards DA, Gilbody S, et al. Influence of initial severity of depression on effectiveness of low intensity interventions : meta-analysis of individual patient data. 2013;540:1–11.
21. Boggs JM, Beck A, Felder JN, Dimidjian S, Metcalf CA, Segal Z V. Web-based intervention in mindfulness meditation for reducing residual depressive symptoms and relapse prophylaxis: a qualitative study. J Med Internet Res [Internet]. 2014 [cited 2014 Apr 29];16:e87. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3978551&tool=pmcentrez&rendertype=abstract
22. Lewis G, Pelosi AJ, Araya R, Dunn G. Measuring psychiatric disorder in the community: a standardized assessment for use by lay interviewers. Psychol Med [Internet]. Cambridge University Press; 2009 [cited 2015 Oct 16];22:465. Available from: http://journals.cambridge.org/abstract_S0033291700030415

23. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med [Internet]. 2001 [cited 2015 Feb 4];16:606–13. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1495268&tool=pmcentrez&rendertype=abstract
24. EVANS M, KESSLER D, LEWIS G, PETERS TJ, SHARP D. Assessing mental health in primary care research using standardized scales: can it be carried out over the telephone? Psychol Med [Internet]. Cambridge University Press; 2004 [cited 2017 Mar 9];34:S0033291703008055. Available from: http://www.journals.cambridge.org/abstract_S0033291703008055
25. Spitzer RL, Kroenke K, Williams JBW, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med [Internet]. 2006;166:1092–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16717171
26. NHS Health Scotland & University of Warwick & University of Edinburgh. Short Warwick-Edinburgh Mental Well-Being Scale. Edinburgh; 2007.
27. Stewart-Brown S, Platt S, Tennant A, Maheswaran H, Parkinson J, Weich S, et al. The Warwick-Edinburgh Mental Well-being Scale: A Valid and reliable tool for measuring mental well-being in diverse populations and projects. J Epidemilogy Community Heal. 2011;11.
28. MUNDT JC. The Work and Social Adjustment Scale: a simple measure of impairment in functioning. Br J Psychiatry [Internet]. 2002 [cited 2016 Feb 22];180:461–4. Available from: http://bjp.rcpsych.org/content/180/5/461.short
29. Gu J, Strauss C, Crane C, Barnhofer T, Karl A, Cavanagh K, et al. Examining the factor structure of the 39-item and 15-item versions of the five-facet mindfulness questionnaire before and after mindfulness-based cognitive therapy for people with recurrent depression. Psychol Assess [Internet]. 2016 [cited 2016 Dec 23];28:791–802. Available from: http://doi.apa.org/getdoi.cfm?doi=10.1037/pas0000263
30. Bower P, Byford S, Sibbald B, Ward E, King M, Lloyd M, et al. Randomised controlled trial of non-directive counselling, cognitive-behaviour therapy, and usual general practitioner care for patients with depression. II: Cost effectiveness. BMJ. 2000;321.
31. Kuyken W, Byford S, Taylor RS, Watkins E, Holden E, White K, et al. Mindfulness-based cognitive therapy to prevent relapse in recurrent depression. J Consult Clin Psychol. 2008;76:966–78.
32. Brooks R. EuroQol: the current state of play. Health Policy [Internet]. 1996 [cited 2015 Nov 24];37:53–72. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10158943
33. Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual Life Res [Internet]. 2011 [cited 2015 Oct 15];20:1727–36. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3220807&tool=pmcentrez&rendertype=abstract
34. Sealed Envelope Ltd. Sealed Envelope: Randomisation and online databases for clinical trials [Internet]. [cited 2016 Mar 23]. Available from: www.sealedenvelope.com

35. Teasdale JD, Williams JMG, Segal Z. The Mindful Way Workbook: An 8-Week Program to Free Yourself from Depression and Emotional Distress. London, UK: Guildford Press; 2014.
36. Williams C. Overcoming Depression and Low Mood, 3rd Edition: A Five Areas Approach [Paperback]. London: CRC Press; 2012.
37. Williams C, Wilson P, Morrison J, McMahon A, Andrew W, Allan L, et al. Guided self-help cognitive behavioural therapy for depression in primary care: a randomised controlled trial. PLoS One [Internet]. 2013 [cited 2014 Apr 26];8:e52735. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3543408&tool=pmcentrez&rendertype=abstract
38. Richards DA, Ekers D, McMillan D, Taylor RS, Byford S, Warren FC, et al. Cost and Outcome of Behavioural Activation versus Cognitive Behavioural Therapy for Depression (COBRA): a randomised, controlled, non-inferiority trial. Lancet [Internet]. Elsevier; 2016 [cited 2018 Mar 31];388:871–80. Available from: https://www.sciencedirect.com/science/article/pii/S0140673616311400
39. Saxon D, Ashley K, Bishop-Edwards L, Connell J, Harrison P, Ohlsen S, et al. A pragmatic randomised controlled trial assessing the non-inferiority of counselling for depression versus cognitive-behaviour therapy for patients in primary care meeting a diagnosis of moderate or severe depression (PRaCTICED): Study protocol for a rand. Trials. 2017;18:93.
40. National Institute of Health and Care Excellence [NICE]. Guide to the methods of technology appraisal. London: NICE; 2013.
41. Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. Methods for the economic evaluation of health care programmes. Oxford, UK: Oxford University Press; 2015.
42. Thompson SG, Barber JA. How should cost data in pragmatic randomised trials be analysed? Br Med J. 2000;320:1197–200.
43. Manca A, Hawkins N, Sculpher MJ. Estimating mean QALYs in trial-based cost-effectiveness analysis: the importance of controlling for baseline utility. Health Econ [Internet]. 2005 [cited 2020 Jan 18];14:487–96. Available from: http://doi.wiley.com/10.1002/hec.944
44. Briggs AH. A Bayesian approach to stochastic cost-effectiveness analysis. Health Econ [Internet]. 1999 [cited 2020 Jan 18];8:257–61. Available from: http://doi.wiley.com/10.1002/%28SICI%291099-1050%28199905%298%3A3%3C257%3A%3AAID-HEC427%3E3.0.CO%3B2-E
45. Fenwick E, Byford S. A guide to cost-effectiveness acceptability curves. Br. J. Psychiatry. 2005. p. 106–8.
46. Assmann SF, Pocock SJ, Enos LE, Kasten LE. Subgroup analysis and other (mis)uses of baseline data in clinical trials. Lancet. Elsevier Limited; 2000;355:1064–9.
47. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol [Internet]. 2006;3:77–101. Available from: http://www.tandfonline.com/doi/abs/10.1191/1478088706qp063oa

Figures

	Enrolment	Allocation	Intervention Period	Post-intervention	Follow-up and Close
TIMEPOINT		**Time 0**		**Time 1**	**Time 2**
ENROLMENT:					
Informed Consent	X				
Allocation		X			
INTERVENTIONS:					
MBCT-SH			X		
CBT-SH			X		
ASSESSMENTS:					
Baseline Assessment	X				
Post-intervention Assessment				X	
Follow-up Assessment					X

Figure 1

Schedule of enrollment, interventions, and assessments

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SPIRITChecklist.doc