ISRCTN17755571 https://doi.org/10.1186/ISRCTN17755571

Mindfulness-based cognitive therapy for non-responders to IAPT (Improving Access to Psychological Therapies) treatment

Submission date
21/01/2021

Recruitment status
No longer recruiting

Registration date
02/03/2021

Overall study status
Completed

Last Edited
19/05/2025

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
If not treated sufficiently, Major Depression tends to take a recurrent or chronic lifetime course that is associated with a significantly increased risk for physical and neurodegenerative disorders. IAPT services provide evidence-based treatment for patients with common mental disorder with an access rate intended to rise to 25% of this population by 2021. However, about 50% of the depressed patients who come to the end of this pathway, have not responded sufficiently.

Our research will investigate whether Mindfulness-Based Cognitive Therapy (MBCT), a group-based treatment combining intensive training in mindfulness meditation and cognitive therapy, can effectively reduce symptoms and lead to sustained recovery in patients suffering from Major Depressive Disorder who have not sufficiently responded to high-intensity evidence-based therapy and have thus come to the end of the Increasing Access to Psychological Therapies (IAPT) care pathway. It will also test whether the introduction of this treatment can reduce subsequent service use.

Who can participate?
Adults aged18 - 65 years, who have not responded to a minimal effective dose of high-intensity treatment in IAPT (at least 12 sessions)

What does the study involve?
Patients who have not sufficiently responded to IAPT high-intensity therapy will be randomly allocated to take part either in MBCT, delivered via videoconferencing, or to continue with TAU in a three-centre (London, Exeter, Sussex) RCT.
Potential participants will be invited to one of the research sites to determine eligibility using clinical interviews and questionnaires. Eligible participants either receive an eight-week course of MBCT or continue with their treatment as usual. Follow-up assessments will be conducted remotely using online questionnaires.

What are the possible benefits and risks of participating?
Those who are randomly allocated to MBCT will have the opportunity to receive this treatment. However, to date, there is only preliminary evidence for its effectiveness in people who are currently suffering from symptoms. We do not anticipate that this research study will place participants at any more risk than they would face if attending other treatment programmes.

Where is the study run from?
University of Surrey (UK)

When is the study starting and how long is it expected to run for?
January 2021 to October 2023

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
Prof. Thorsten Barnhofer, t.barnhofer@surrey.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Thorsten Barnhofer

ORCID ID
https://orcid.org/0000-0003-2984-8454

Contact details
School of Psychology
University of Surrey
Guildford
United Kingdom
GU2 7XH
+44(0)1483686485
t.barnhofer@surrey.ac.uk

Additional identifiers

ClinicalTrials.gov (NCT)
NCT05236959

Integrated Research Application System (IRAS)
281532

Central Portfolio Management System (CPMS)
47796

Study information

Scientific Title
A randomised controlled trial to investigate the clinical effectiveness and cost-effectiveness of Mindfulness-Based Cognitive Therapy (MBCT) for depressed non-responders to Increasing Access to Psychological Therapies (IAPT) high intensity therapies

Acronym
RESPOND

Study objectives
1. Participants who receive Mindfulness-Based Cognitive Therapy (MBCT) will show significantly stronger reductions in depressive symptomatology than participants who receive TAU both at 10 weeks post-randomisation (post-treatment; secondary outcome) and at 34 weeks post-randomisation (primary outcome)
2. The MBCT intervention will be cost-effective either in terms of reductions in costs elsewhere in the health system or in improvements in outcomes

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 18/01/2021, West of Scotland REC 4 (Research Ethics, Ward 11, Dykebar Hospital, Grahamston Road, Paisley, PA2 7DE, UK; +44(0)141 314 0213; WoSREC4@ggc.scot.nhs.uk), ref: 20/WS/0177

Primary study design
Interventional

Study design
Interventional randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Depression

Interventions
Current intervention as of 03/10/2022:
Design
We will randomise 234 patients who have not responded to high-intensity IAPT interventions for depression, but do not meet eligibility criteria for secondary care services, in a 2-arm trial to take part in either MBCT or to continue with TAU, a comparator that is reflective of the current state of care (and in most cases will entail continued use of antidepressant medication). We will measure outcomes at baseline, 10-week and 34-week follow-up postrandomisation. Economic analyses will investigate effects of the interventions on subsequent service use.

Intervention
Participants will be allocated to receive either MBCT or TAU.
MBCT combines mindfulness training with elements from cognitive therapy. We will follow the treatment manual with minor adaptations to address the fact that patients are suffering from

current symptoms of depression following practice from our previous research (Barnhofer et al., 2009). The intervention will be delivered by trained MBCT therapists together with an assistant to groups of 13 patients using videoconferencing on a secure online platform. All three sites have prior experience with delivering MBCT in this format and will follow shared internal guidelines for videoconferencing delivery. All therapists will meet qualification in line with Good Practice Guidelines and competency level 'proficient' on the MBCT Therapy Pathway. Therapists will be selected based on ratings on the MBI-TAC and receive a one-day workshop fo familiarise them with the modifications of the program necessary for use with currently depressed patients. Manual adherence and treatment fidelity will be monitored using methods established in our previous trials (Williams et al., 2014; Barnhofer et al., 2009). MBCT consists of eight weekly group-based sessions and participants are asked to engage in home practice of mindfulness meditation for about an hour per day using guided meditation audio recordings, with attendance and practice monitored following previously established practices.

Participants in the TAU condition will be asked to continue with their usual care and follow the regimes suggested by their GP or mental health professional, which in most cases will consist of continuing use of antidepressant medication. Following previous practice in our trials (Williams et al., 2014), TAU participants will be invited to an interview to prevent tendencies towards ‘resentful demoralisation' and highlight the importance of their contribution. As the pre-class interview for the MBCT courses, this interview will be conducted via videoconferencing. Following suggestions from our patient representatives, all participants will be offered access to online mindfulness resources after the end of the study.

Baseline survey
Participant characteristics assessed as part of the SCID interview will allow us to make comparisons between eligible patients who declined to participate, and those patients who participated in the trial.

Economic evaluation
The economic evaluation, led by Dr Barbara Barrett, will take a health and social care perspective, as required for evidence presented to NICE. In addition, the cost perspective will be broadened to include the costs of time off productivity losses, since these are known to be relevant and important in those attending IAPT services. Costs will be calculated by collecting service use information using the Adult Service Use Schedule (AD-SUS), as self-report measure developed by the team at King’s and used in previous trials of MBCT, modified for use online, to which routine unit costs will be applied. We will collect data on all service use not just use related to mental health conditions, because there is evidence that successful treatment in IAPT can reduce use of all healthcare services. In addition, comparison via randomised groups will ensure that any differences in cost are due to the impact of the MBCT intervention. Information on TAU will be collected via the AD-SUS, modified to ensure that all relevant services are included. Data on the use of the MBCT intervention will be collected via therapist records and costs estimated using the standard approach set out by Curtis (2008), acknowledging the challenges of costing group-based interventions. Outcomes for the economic evaluation will be QALYs, calculated using health utilities derived from the EQ-5D, either the 5L or the 3L will be used depending on the most recent advice from NICE. Costs and outcomes will be combined in a cost-utility analysis providing information on whether or not MBCT is worthwhile in terms of costs savings elsewhere or improvements in outcomes, and information will be provided to decision makers with statistical analysis of differences in costs, cost-effectiveness planes and cost effectiveness acceptability curves.

Qualitative analyses
Qualitative analyses, led by Prof Barney Dunn, will be used to explore patient experience of the

intervention and to understand how the treatment might best benefit patients in the IAPT pathway. Previous trials have shown considerable variation in the degree to which patients engage in mindfulness practice and a major focus of the qualitative analyses will therefore be on factors influencing such engagement and its relation with dynamics of change. For this purpose, we will investigate:
1. Patients' views on acceptability of MBCT and mindfulness practice, and the experience of participating in the course remotely
2. Patients' views of the changes they experience and their utilization of mindfulness skills
3. Patients' views of the broader impact of MBCT on their lives

A subsample of participants in the MBCT arm, estimated to be 24 (or until data saturation has been reached), will be invited to a qualitative telephone interview conducted by trained research assistants. Recruitment will be purposive, including patients across all sites, and seeking to achieve maximum variation in relation to:
1. Completion/non-completion of treatment
2. Response/non-response to treatment
3. Recruitment site (to examine contextual factors)

Written feedback provided in the protocol sheets that MBCT participants receive on a weekly basis will be used to inform subsampling and will also provide us with the opportunity to explore any unanticipated experiences and effects in more depth.

In collaboration with service users, we will develop, and pilot test, a semi-structured topic guide based on the above aims. Interviews will be audio-recorded, transcribed verbatim, and anonymized. Thematic analysis of interview transcripts will be conducted using a Framework approach, involving the coding and sorting of textual units according to both deductive and inductively-derived categories, and the use of matrices to review the coded data, investigate commonalities and differences and search for patterns. Coding and data management will be facilitated by NVivo software.

Randomisation
We will allocate individual participants to either MBCT or TAU at a ratio of 1:1 through remote randomisation at the UKCRC-registered Exeter Clinical Trials Unit (ExeCTU), following informed consent, completion of baseline assessment and enrolment in the trial. Randomisation will use minimisation on depression severity (PHQ-9<19 versus ≥19), antidepressant use at baseline and recruitment site.

Data collection methods
At baseline, trained research assistants will administer clinical interviews and self-report questionnaires at each of the sites. Post-treatment and follow-up assessments will be conducted remotely by asking participants to complete self-report questionnaires on a dedicated webpage via secure online portal.

Blinding
As baseline assessment of participants is carried out prior to randomisation, there is no risk of disclosure of treatment allocation to the assessor at the time. Use of remote assessments, initiated through automated email, will rule out any potential effects of assessors on assessments of outcomes. The statisticians will remain blind to treatment allocation throughout the analysis.

_____

Previous intervention:
Design
We will randomise 234 patients who have not responded to high-intensity IAPT interventions for depression, but do not meet eligibility criteria for secondary care services, in a 2-arm trial to take part in either MBCT or to continue with TAU, a comparator that is reflective of the current state of care (and in most cases will entail continued use of antidepressant medication). We will measure outcomes at baseline, 10-week and 34-week follow-up postrandomisation. Economic analyses will investigate effects of the interventions on subsequent service use.

Intervention
Participants will be allocated to receive either MBCT or TAU.
MBCT combines mindfulness training with elements from cognitive therapy. We will follow the treatment manual with minor adaptations to address the fact that patients are suffering from current symptoms of depression following practice from our previous research (Barnhofer et al., 2009). The intervention will be delivered by trained MBCT therapists together with an assistant to groups of 13 patients using videoconferencing on a secure online platform. All three sites have prior experience with delivering MBCT in this format and will follow shared internal guidelines for videoconferencing delivery. All therapists will meet qualification in line with Good Practice Guidelines and competency level 'proficient' on the MBCT Therapy Pathway. Therapists will be selected based on ratings on the MBI-TAC and
receive a one-day workshop fo familiarise them with the modifications of the program necessary for use with currently depressed patients. Manual adherence and treatment fidelity will be monitored using methods established in our previous trials (Williams et al., 2014; Barnhofer et al., 2009). MBCT consists of eight weekly group-based sessions and participants are asked to engage in home practice of mindfulness meditation for about an hour per day using guided meditation audio recordings, with attendance and practice monitored following previously established practices.

Participants in the TAU condition will be asked to continue with their usual care and follow the regimes suggested by their GP or mental health professional, which in most cases will consist of continuing use of antidepressant medication. Following previous practice in our trials (Williams et al., 2014), TAU participants will be invited to an interview to prevent tendencies towards ‘resentful demoralisation' and highlight the importance of their contribution. As the pre-class interview for the MBCT courses, this interview will be conducted via videoconferencing. Following suggestions from our patient representatives, all participants will be offered access to online mindfulness resources after the end of the study.

Baseline survey
Participant characteristics assessed as part of the SCID interview will allow us to make comparisons between eligible patients who declined to participate, and those patients who participated in the trial.

Economic evaluation
The economic evaluation, led by Dr Barbara Barrett, will take a health and social care perspective, as required for evidence presented to NICE. In addition, the cost perspective will be broadened to include the costs of time off productivity losses, since these are known to be relevant and important in those attending IAPT services. Costs will be calculated by collecting service use information using the Adult Service Use Schedule (AD-SUS), as self-report measure developed by the team at King’s and used in previous trials of MBCT, modified for use online, to which routine unit costs will be applied. We will collect data on all service use not just use related to mental health conditions, because there is evidence that successful treatment in IAPT can reduce use of all healthcare services. In addition, comparison via randomised groups will

ensure that any differences in cost are due to the impact of the MBCT intervention. Information on TAU will be collected via the AD-SUS, modified to ensure that all relevant services are included. Data on the use of the MBCT intervention will be collected via therapist records and costs estimated using the standard approach set out by Curtis (2008), acknowledging the challenges of costing group-based interventions. Outcomes for the economic evaluation will be QALYs, calculated using health utilities derived from the EQ-5D, either the 5L or the 3L will be used depending on the most recent advice from NICE. Costs and outcomes will be combined in a cost-utility analysis providing information on whether or not MBCT is worthwhile in terms of costs savings elsewhere or improvements in outcomes, and information will be provided to decision makers with statistical analysis of differences in costs, cost-effectiveness planes and cost effectiveness acceptability curves.

Qualitative analyses

Qualitative analyses, led by Prof Barney Dunn, will be used to explore patient experience of the intervention and to understand how the treatment might best benefit patients in the IAPT pathway. Previous trials have shown considerable variation in the degree to which patients engage in mindfulness practice (10)and a major focus of the qualitative analyses will therefore be on factors influencing such engagement and its relation with dynamics of change. For this purpose, we will investigate:

1) patients' views on acceptability of MBCT and mindfulness practice, and the experience of participating in the course remotely,
2) patients' views of the changes they experience and their utilization of mindfulness skills, and
3) patients' views of the broader impact of MBCT on their lives.

A subsample of participants in the MBCT arm, estimated to be 24 (or until data saturation has been reached), will be invited to a qualitative telephone interview conducted by trained research assistants. Recruitment will be purposive, including patients across all sites, and seeking to achieve maximum variation in relation to:

1) completion/non-completion of treatment,
2) response/non-response to treatment, and
3) recruitment site (to examine contextual factors).

Written feedback provided in the protocol sheets that MBCT participants receive on a weekly basis will be used to inform subsampling and will also provide us with the opportunity to explore any unanticipated experiences and effects in more depth.

In collaboration with service users, we will develop, and pilot test, a semi-structured topic guide based on the above aims. Interviews will be audio-recorded, transcribed verbatim, and anonymized. Thematic analysis of interview transcripts will be conducted using a Framework approach, involving the coding and sorting of textual units according to both deductive and inductively-derived categories, and the use of matrices to review the coded data, investigate commonalities and differences and search for patterns. Coding and data management will be facilitated by NVivo software.

Timeline for delivery

In each site, we will recruit 3 cohorts of 26 participants with an initial recruitment phase of 3 months and at least 1-month intervals between treatment phases. Anticipated total duration is 24 months including 3 months for set-up, 7 months for final follow-up and assessment of the last cohort, and 4 months for data analysis and write-up.

Randomisation

We will allocate individual participants to either MBCT or TAU at a ratio of 1:1 through remote

randomisation at the UKCRC-registered Exeter Clinical Trials Unit (ExeCTU), following informed consent, completion of baseline assessment and enrolment in the trial. Randomisation will use minimisation on depression severity (PHQ-9<19 versus ≥19), antidepressant use at baseline and recruitment site.

Data collection methods
At baseline, trained research assistants will administer clinical interviews and self-report questionnaires at each of the sites. Post-treatment and follow-up assessments will be conducted remotely by asking participants to complete self-report questionnaires on a dedicated webpage via secure online portal.

Blinding
As baseline assessment of participants is carried out prior to randomisation, there is no risk of disclosure of treatment allocation to the assessor at the time. Use of remote assessments, initiated through automated email, will rule out any potential effects of assessors on assessments of outcomes. The statisticians will remain blind to treatment allocation throughout the analysis.

Intervention Type
Behavioural

Primary outcome(s)
Depressive symptomatology as assessed using the PHQ-9 at baseline and 34 weeks post-randomisation

Key secondary outcome(s)
1. Depressive symptomatology as assessed using the PHQ-9 at baseline and 10 weeks post-randomisation
2. Service-use information will be collected using the Adults Service Use Schedule throughout the study

Completion date
23/10/2023

Eligibility

Key inclusion criteria
Current inclusion criteria as of 04/01/2022:
1. Non-response to a minimal effective dose of high-intensity treatment in IAPT (at least 12 sessions, in line with NICE draft guideline suggestions) defined in line with the caseness threshold adopted by IAPT as a Patient Health Questionnaire-9 (PHQ-9) score of 10 or higher
2. Meeting criteria for a current episode of Major Depression according to DSM-5 as assessed through the Mini International Neuropsychiatric Interview for DSM-5 (MINI)
3. Aged 18 years or older
4. Access to a working internet connection to participate in video conferencing assessments and interventions. According to the IAPT database, the majority of patients who receive high-intensity psychological treatment will also have received treatment with antidepressant medication, and most of these patients will therefore meet consensus criteria for treatment resistance

———

Previous inclusion criteria:
1. Non-response to a minimal effective dose of high-intensity treatment in IAPT (at least 12 sessions, in line with NICE draft guideline suggestions) defined in line with the caseness threshold adopted by IAPT as a Patient Health Questionnaire-9 (PHQ-9) score of 10 or higher
2. Meeting criteria for a current episode of Major Depression according to DSM-5 as assessed through the Mini International Neuropsychiatric Interview for DSM-5 (MINI)
3. Age between 18 and 65 years
4. Access to a working internet connection to participate in video conferencing assessments and interventions. According to the IAPT database, the majority of patients who receive high-intensity psychological treatment will also have received treatment with antidepressant medication, and most of these patients will therefore meet consensus criteria for treatment resistance

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
259

Key exclusion criteria
Current exclusion criteria as of 04/01/2022:
1. Based on the judgment of their IAPT therapist they are eligible for secondary care specialist services
2. Receiving individual psychotherapy or counselling from other sources than the NHS at a frequency of more than once a month
3. They present with a level of risk to self or others that cannot be safely managed in a primary care service context (i.e. active suicidal plans), a history of psychosis or psychotic symptoms, a current episode of mania, alcohol or substance abuse or dependence within the past 3 months, current post-traumatic stress disorder, obsessive-compulsive disorder or eating disorder
4. They suffer from any other significant disease or disorder that may either put the participant at risk because of participation in the trial, or may influence the result of the trial, or the participant's ability to participate in the trial
5. Have an insufficient ability to understand or read English
6. Patients who are currently taking antidepressant medication will be allowed into the trial and medication use will be documented for statistical analysis

———

Previous exclusion criteria:
1. Based on the judgment of their IAPT therapist they are eligible for secondary care specialist services
2. Receiving individual psychotherapy or counselling from other sources than the NHS at a frequency ofmore than once a month
3. Report the presence of active suicidal plans, a history of psychosis or psychotic symptoms, a current episode of mania, alcohol or substance abuse or dependence within the past 3 months
4. Suffer from severe medical illness
5. Have an insufficient ability to understand or read English. Patients who are currently taking antidepressant medication will be allowed into the trial and medication use will be documented for statistical analysis

Date of first enrolment
09/06/2021

Date of final enrolment
24/01/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Sussex Partnership NHS Foundation Trust Assessment and Treatment Centre
Chapel Street
Chichester
United Kingdom
PO19 1BX

Study participating centre
Devon Partnership NHS Trust
Research and Development Team
Wonford House
Dryden Road
Exeter
United Kingdom
EX2 5AF

Study participating centre
Institute of Psychiatry, Psychology & Neuroscience
South London and Maudsley NHS Foundation Trust

Research and Development Office
King’s College London
Denmark Hill Campus
16 De Crespigny Park
London
United Kingdom
SE5 8AF

Sponsor information

Organisation
Sussex Partnership NHS Foundation Trust

ROR
https://ror.org/05fmrjg27

Funder(s)

Funder type
Government

Funder Name
NIHR Central Commissioning Facility (CCF); Grant Codes: NIHR200750

Funder Name
National Institute for Health Research (NIHR) (UK)

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the trial will be stored in a non-publicly available repository at Sussex Partnership NHS Foundation Trust upon publication of main study results. Anonymised data may be accessed and analysed by members of the project team and by researchers collaborating with members of the project team on the analysis of these data. Data sharing will be enabled using a controlled access model in line with Good Practice Principles for Sharing Individual Participant Data from Publicly Funded Clinical Trials from the UK Medical Research Council. Scientists seeking to access the data for use in future projects must do so via request to the CI and projects using the data must have been approved in accordance with contemporary UK ethical and regulatory processes pertaining to the release of anonymised data under these circumstances. We will follow current recommendations on anonymizing and curating trial data for sharing.

Research data with personal information removed and replaced through a code and original research records, including video recordings of assessment interviews and therapy sessions, will be retained for 10 years, before being destroyed and retained in electronic form. The electronic records will be kept for 10 years after the end of the study. Publications will not contain any patient-identifiable information.

(added 05/01/2022)
The datasets generated during and/or analysed during the current study are/will be available upon request from the CI, Thorsten Barnhofer (t.barnhofer@surrey.ac.uk) . Projects using the data must have been approved in accordance with contemporary UK ethical and regulatory processes pertaining to the release of anonymised data under these circumstances. We will follow current recommendations on anonymizing and curating trial data for sharing. Consent for data sharing has been obtained from participants and anonymised data will be retained for 10 years.

IPD sharing plan summary

Stored in non-publicly available repository, Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		19/05/2025	19/05/2025	Yes	No
Protocol article		19/01/2023	23/01/2023	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	version v01.2	21/01/2021	02/03/2021	No	Yes
Participant information sheet	version 1.3	21/04/2021	03/10/2022	No	Yes
Participant information sheet	version 1.4	11/05/2021	03/10/2022	No	Yes
Participant information sheet	version 1.5	28/07/2021	03/10/2022	No	Yes
Participant information sheet	version 1.6	07/11/2021	03/10/2022	No	Yes
Protocol file	version v01.3	11/02/2021	02/03/2021	No	No
Protocol file	version 1.4	21/04/2021	03/10/2022	No	No

Protocol file	version 1.5	12/05/2021	03/10/2022	No	No
Protocol file	version 1.6	17/08/2021	03/10/2022	No	No
Protocol file	version 2.0	11/11/2021	03/10/2022	No	No
Protocol file	version 2.1	03/07/2022	03/10/2022	No	No
Statistical Analysis Plan	version 1.0		14/07/2023	No	No