Mindfulness-based programmes for mental health promotion in adults in non-clinical settings: protocol of an individual participant data meta-analysis of randomised controlled trials

Authors:

1. Julieta Galante (**corresponding author**), Department of Psychiatry, University of Cambridge, Douglas House, 18b Trumpington Road, Cambridge, CB2 8AH, United Kingdom (second affiliation: National Institute for Health Research (NIHR) Applied Research Collaboration East of England). Email: mjg231@cam.ac.uk
2. Claire Friedrich, Department of Psychiatry, University of Cambridge, Cambridge, United Kingdom.
3. Tim Dalgleish, MRC Cognition and Brain Sciences Unit, University of Cambridge, Cambridge, United Kingdom (second affiliation: Cambridgeshire and Peterborough NHS Foundation Trust)
4. Ian R White, MRC Clinical Trials Unit, University College London, London, United Kingdom.
5. Peter B Jones, Department of Psychiatry, University of Cambridge, Cambridge, United Kingdom (second affiliation: NIHR Applied Research Collaboration East of England)

ABSTRACT

Introduction

With mental ill health listed as a top cause of global disease burden, there is an urgent need to prioritise mental health promotion programmes. Mindfulness-based programmes (MBPs) are being widely implemented to reduce stress in non-clinical settings. In a recent aggregate-level meta-analysis we found that, compared with no intervention, these MBPs reduce average psychological distress. However, heterogeneity between studies impedes generalisation of effects across every setting. Study-level moderators were insufficient to reduce heterogeneity; studying individual-level moderators is warranted. This requires individual participant data (IPD) and larger samples than those found in existing individual trials.

Methods and analysis

We propose an IPD meta-analysis. Our primary aim is to see if, and how, baseline psychological distress, gender, age, education, and dispositional mindfulness moderate the effect of MBPs on distress. We will search 13 databases for good-quality randomised controlled trials (RCTs) comparing in-person, expert-defined MBPs in non-clinical settings with passive controls. Two researchers will independently select, extract, and appraise trials using the revised Cochrane Risk-of-Bias Tool (RoB2). Anonymised IPD of eligible trials will be sought from authors, who will be invited to collaborate.

The primary outcome will be psychological distress measured using psychometrically-validated questionnaires at 1 to 6 months after programme completion. Pairwise random-effects two-stage IPD meta-analyses will be conducted. Moderator analyses will follow a “deft” approach. We will estimate subgroup-specific intervention effects. Secondary outcomes and sensitivity analyses are pre-specified. Multiple imputation strategies will be applied to missing data.

Ethics and dissemination

The findings will refine our knowledge on the effectiveness of MBPs and help improve the targeting of MBPs in non-clinical settings. They will be shared in accessible formats with a range of stakeholders. Public and professional stakeholders are being involved in the planning, conduct and dissemination of this project.

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STRENGTHS AND LIMITATIONS OF THIS STUDY

1. This is, to our knowledge, the first individual-participant-data (IPD) meta-analysis assessing the effectiveness of mindfulness-based programmes to reduce psychological distress among adults in non-clinical settings, and how it varies as a function of individual differences.
2. Preceded by a comprehensive systematic review, this IPD meta-analysis will have greater statistical power to detect effect moderators than any of the individual trials.
3. This IPD meta-analysis can overcome some, but not all, of the existing trials' methodological shortcomings.
4. As a secondary-data analysis, this study depends on trial data being shared; this factor can limit the validity and generalisability of the findings.
5. The outcomes and moderators that can be assessed are limited to those that the existing trials have measured, and how they have measured them.

INTRODUCTION

Common mental health disorders such as depression are among the top worldwide causes of morbidity, generating a very significant burden on societies ¹. The COVID-19 pandemic, a global natural stressor, is increasing this burden ². The last decade has seen an expansion of mental health prevention and promotion programmes in workplaces, educational establishments, and other community settings ³. They usually target psychological distress, a concept encompassing a range of disturbing or unpleasant mental or emotional experiences which, if unaddressed, can result in mental and physical health disorders ⁴.

Frequently promoted as a universal tool to reduce stress ⁵, mindfulness-based programmes (MBPs) are among the most commonly implemented preventive activities ⁶. In the United States of America, mindfulness training is present at 79% of medical schools ⁷, and offered by 22% of employers ⁸. MBPs typically define mindfulness as “the awareness that emerges through paying attention on purpose, in the present moment, and nonjudgmentally to the unfolding of experience moment by moment” ⁹. Their core elements are an emphasis on teaching mindfulness meditation and mindful activities, scientific approaches to managing health, suitability for delivery in public institutions across a range of settings and cultures, and class-based experiences of collective and individual inquiry with a qualified teacher in a participatory learning process ¹⁰.

We recently completed a systematic review and aggregate-level meta-analysis of randomised controlled trials (RCTs) assessing MBPs for mental health promotion in adults in non-clinical settings (from now on referred to as our previous review)¹¹. We found that, compared with no intervention, MBPs of the included studies, on average, reduced psychological distress (our most measured and robust outcome). However, given the heterogeneity between studies, the findings did not support generalisation of MBP effects across every setting. We investigated study-level factors that could moderate the effect of the MBPs on psychological distress, such as programme characteristics or type of population being targeted, but these were not able to fully explain the seen heterogeneity. Participant-level moderators of effect, such as participants’ prior mental health, may be at play.

Individual-participant-data (IPD) meta-analyses are the only practical choice for exploring how MBP effectiveness varies as a function of individual differences ¹²⁻¹⁴. In IPD meta-analyses, rather than extracting summary data from trial publications, the original individual-level trial data are sought directly from trial authors. Aggregate-level meta-analyses (the most common ones) may give misleading individual-level moderator results because of study-level confounding ¹⁴. Conducting further RCTs to perform sub-group analyses is expensive and impractical due to the large sample sizes required, particularly to find small-to-moderate effect sizes in low-risk populations. It is notoriously difficult to identify genuine predictors of differential response from single trials, as there is high potential for type I and type II errors ¹⁴. IPD meta-analyses can obtain results for specific sub-groups of participants across studies, and differential effects can be assessed across individuals, which can help reduce between-study heterogeneity¹⁵. Other advantages of this approach are that data can be checked and re-analysed, and missing data can be accounted for at the individual level ¹⁶. Finally, they can act as a stimulus for international collaboration, debate and consensus, and form the basis for further data sharing and open research.

The role of individual differences in MBPs

Preliminary evidence strongly suggests that the effectiveness of MBPs vary as a function of individual differences¹⁷. There have been several calls to study MBP effect modification more extensively, and small sample sizes have frequently been cited as a limiting factor^{12 13 18-21}.

Individuals with worse mental health to begin with may be the most likely to benefit because there is more room to what can be learnt. There is evidence that MBPs targeted at stressed groups^{11 22}, those with anxiety or mood disorders²³, those with higher symptom severity^{24 25}, or those experiencing stressful times²⁶ have larger effects. An IPD meta-analysis of mindfulness-based cognitive therapy (MBCT) to prevent recurrent depression relapse found a significant relative reduction in effect with better baseline status²⁷. Most findings thus suggest that higher baseline distress levels strengthen intervention effects, although some have found no evidence of interaction²⁸.

A meta-analysis of workplace MBPs found a significant moderating effect of gender on well-being and life satisfaction²⁹. This finding adds to previous evidence suggesting that MBP effects on men are smaller than those on women^{20 30 31}. It has been posited that women tend to internalise their distress more, which may make techniques such as mindfulness work more favourably, while an externalising coping style, more frequently associated with men, may limit the effectiveness of MBPs²⁰. Others proposed that neuroticism and conscientiousness, personality factors more common among women, may amplify MBP effects^{20 30 31}. Some studies exploring gender as a moderator, including the MBCT IPD meta-analysis, have found no moderating effects^{22 27}.

Meta-analytic evidence suggests that MBPs for children and adolescents³² and university students³³, have larger effects than those for adults¹¹. While some studies reported no moderating effects of age, one study found age to moderate intervention effects on levels of anxiety, with older adults reporting smaller reductions in anxiety over time compared to their younger counterparts³⁴. At play may be cognitive and cultural factors that are intrinsic to age such as plasticity and curiosity, or confounders such as education (e.g. young people belong to university student samples). However, age was not a moderator in the MBCT IPD meta-analysis and other studies^{27 35}.

Education levels are known to moderate the effectiveness of some psychological interventions³⁶. Concerns have been voiced that current MBPs may not be inclusive of diverse education backgrounds because of their language and cultural references³⁷. A recent meta-analysis has reported significant moderating effects of level of education in workplace MBPs, finding a larger improvement in well-being among more highly educated participants²⁹. However, education was not a moderator in the MBCT IPD meta-analysis²⁷.

Baseline levels of dispositional mindfulness, a multidimensional construct reflecting an individual's focus and quality of their attention³⁸, may moderate MBP effects, but the evidence is inconsistent and shows a complex picture³⁹. For example, Shapiro et al. report that participants with higher trait mindfulness at baseline experienced greater and long-lasting improvements in well-being and distress⁴⁰, while Greeson et al. found that baseline dispositional mindfulness did not moderate the effect of an MBP on depressive symptoms³⁵. A higher level of dispositional mindfulness may be needed to engage with MBPs, but this may also limit the amount that is to be learnt.

With the proliferation of mindfulness provision in recent times, understanding what works, for whom and in what circumstances becomes a pressing issue. This information is essential to tailor interventions, maximising effectiveness, cost-effectiveness and ensuring intervention harm minimisation⁴¹.

We plan to conduct a systematic review and individual participant data meta-analysis to answer the following main research question: Do selected participant-level characteristics moderate the effect of mindfulness-based programmes (MBPs) on psychological distress among adults in non-clinical settings, and if so, how do they do it? Our main aim is to see whether and how baseline psychological distress, gender, age, education, and dispositional mindfulness moderate the effect of MBPs on psychological distress compared with no intervention. Moderators for this IPD meta-analysis have been selected based on existing theories and empirical evidence, and on availability as they are commonly reported among trials and are comparable across international samples. Exploring these potential moderators with IPD will address current limitations and support our understanding of individual differences in response to MBPs ⁴².

METHODS AND ANALYSIS

This protocol follows PRISMA-P guidelines ⁴³.

Study search and selection

The search will update that of our previous review ¹¹. Thirteen databases will be included: Allied and Complementary Medicine (AMED), Applied Social Sciences Index and Abstracts (ASSIA), the Cochrane Central Register of Controlled Trials (CENTRAL), the Cumulative Index to Nursing and Allied Health Literature (CINAHL), Education Resources Information Center (ERIC), Electronic Theses Online Service (ETHOS), Excerpta Medica Database (EMBASE), Medical Literature Analysis and Retrieval System Online (MEDLINE), ProQuest, PsycINFO, Scopus, Web of Science and World Health Organization International Clinical Trials Registry Platform. Predefined search strategies using keywords and controlled vocabulary will be adapted and applied to each database. Where possible the search terms mindful and meditation will be combined with a pre-tested, sensitive filter for randomised controlled trials designed by the Scottish Intercollegiate Guidelines Network (2018), otherwise they will be combined with “randomize”, “RCT”, “random allocation” and “random assignment”. Search terms will be modified to include truncation, proximity indicators and wild cards. Additionally, when applicable, subject headings will be exploded. The database search strategy for EMBASE is available in Appendix 1 of the online supplementary materials as an example; all the strategies are also available in the publication of our previous review ¹¹. In addition to the electronic search, we will inspect the reference lists of identified RCTs and reviews. No language limitations will be included. Non-public sources of studies will not be used in the searches ⁴⁴, but authors will be contacted to provide information as outlined herein.

The review inclusion criteria are presented in Table 1. These are similar but narrower in scope than our previous review in order to produce a more focused and better-quality analysis, and because it is infeasible for us to collect IPD from the 136 RCTs included in that review. Online MBPs were excluded because we believe they are different enough from in-person MBPs (e.g. typically not group-based, and fully or semi-automated) to merit their own separate analysis ⁴⁵.

Trials included in our previous review and studies found through the search update will be assessed for inclusion in this IPD meta-analysis. Two researchers will independently review the titles and abstracts of all records retrieved by the search. If both reviewers agree that a record does not meet eligibility criteria, it will be excluded. The full text of all remaining records will be obtained, and the same eligibility criteria will be applied to them by the two reviewers for a final selection.

Disagreements will be decided via consensus between two senior team members (TD and PBJ) blind to trial results.

Data collection and processing

Two reviewers will independently extract study-level characteristics of newly-identified studies into extraction forms similar to those used in our previous review (Appendix 2 of the Online Supplementary Material). Participant-level data characteristics will be checked using new forms, shown in Appendix 3 of the Online Supplementary Material. Authors of eligible studies will be invited to collaborate. Publication co-authorship, help with data preparation and transfer, and secure and confidential data management will be offered. If necessary, authors other than the correspondent author will be contacted. IPD will be considered unavailable where no authors have responded to multiple contact attempts, where authors indicate that they no longer have access to the data, or where authors decline to participate. If authors are unable to share the data but wish to participate, we will explore alternatives (e.g. we send them analysis code for them to run on their data).

Anonymised trial IPD relevant to the analyses proposed herein will be requested from authors who accept our invitation. We will request IPD for all randomised participants, independently of whether trial publications used all of the data or only a fraction. We will prefer datasets without imputed missing data.

IPD from each trial will be checked for missing participants (e.g. compare IPD samples against trial CONSORT diagrams to ensure that IPD from all randomised participants is included if available), and for invalid, out of range or inconsistent items (e.g. unusually old or young participants), before being converted to standard format. Inconsistencies will be discussed with trial authors.

Risk of bias assessment

Two reviewers will independently assess newly-found trials' risk of bias using the revised Cochrane risk-of-bias tool (RoB2) for randomised trials applied to the outcomes included in this review^{46 47}. This tool stringently measures potential bias across five sources: (1) randomisation, (2) deviations from intended interventions, (3) missing outcome data, (4) measurement of the outcome, and (5) selection of the reported result.

Our previous review has found that many trials have high risk of bias from several sources, reducing confidence in the cumulative evidence. To understand how results were affected, we performed a sensitivity analysis removing trials deemed to be at high risk of bias from three or more sources, which divided the sample into roughly equal parts. Accordingly, to maximize confidence in the IPD meta-analysis results and to maintain consistency with our previous review, we plan to only include trials with a maximum of two high risk-of-bias domains, as assessed before obtaining IPD. We will resolve discrepancies through discussion, involving a third reviewer where necessary.

Once studies have been selected and IPD obtained, risk of bias for individual studies will be updated according to the IPD available (e.g. risk lowered if IPD includes participants missing in published trial reports). We will check allocation for any unusual patterns. When key aspects are unclear, we will seek information from study authors. In order to assess the confidence in the cumulative evidence, we will use the GRADE approach (Guyatt et al. 2008).

Effect measures

The main outcome will be self-reported psychological distress measured between one and six months after programme completion using psychometrically valid questionnaires scored on a continuous scale (e.g. Perceived Stress Scale, General Health Questionnaire, Depression, Anxiety and

Stress Scale). Questionnaires asking about fleeting states (e.g. "How do you feel now?") will be excluded.

Post-intervention psychological distress measures (i.e. those taken less than one month after programme completion) will be grouped and considered as a secondary outcome: they do not inform stable changes, therefore are less useful for understanding the real-life impact of MBPs. Psychological distress follow-up measured beyond 6 months will be grouped and also considered as a secondary outcome. If a study measured the outcome more than once within the time point range of interest, the longest follow-up will be used.

We expect that trials will use different questionnaires to measure psychological distress, therefore we will use the standardised mean difference adjusted for small sample bias (SMD, also known as Hedges' *g*) as a measure of treatment effect. We will calculate the SMD using the ANCOVA estimate (final score adjusted for baseline score) ⁴⁸.

If a trial reports more than one psychological distress measure within the same time point range, we will prefer the one assigned as primary outcome by the trialists; if this is not stated or none are primary outcomes, the one with best psychometric properties; if they have similar properties, the one that is used most frequently in the other studies. Full scales and untransformed data will be preferred. We shall request individual scale items and recalculate scales where possible.

Data synthesis

Although this project focuses on the effect moderator analyses, overall effects will be calculated and will be compared with those found in our previous review. Data synthesis will be quantitative, using pairwise random-effects meta-analyses within comparator categories. Two-stage IPD meta-analyses will be performed to allow synthesis of SMDs. They will be univariate for the time-point ranges for which data from all the trials are available, otherwise they will be multivariate and include all available time-point ranges ⁴⁹.

The main analysis will compare MBPs with a combination of all the passive control groups. If the included trials also compared MBPs with other interventions, these will be grouped under the comparator 'active control', and moderation effects will be explored for this comparison in secondary analyses. In the event of finding multi-armed trials with multiple control groups that fit one category, these control groups will be combined. Two-arm trials that compare two eligible MBPs with each other will not be included. In multi-arm trials that do this, the two MBP arms will be combined for meta-analysis.

Estimation of heterogeneity will be performed using restricted maximum likelihood. To quantify the heterogeneity in the intervention effect, approximate prediction intervals will be calculated ⁵⁰. Intention-to-treat analyses of individual trials will be conducted for verification, to compare against published analyses and to discuss reasons for potential differences.

Multiple imputation strategies will be applied to missing data ⁵¹. A sensitivity analysis will compare results of imputed datasets with observed datasets. We will assess departures of the data missing at random assumption in sensitivity analyses at the individual study level, modelling missing data as 10% and 20% worse psychological stress scores than observed data. Trials for which IPD is not made available will be included in a sensitivity analysis incorporating the available aggregate data, and results will be compared with IPD-data-only results ¹⁶.

The main moderator analyses will look at the effect of the moderators of interest one by one; if multiple interaction effects are found we will explore multivariable options to adjust for confounding

as a secondary analysis. For each of the main moderator analyses, a treatment by participant covariate interaction term will be incorporated in the main effect trial regression models (first-stage of two-stage meta-analysis), and the estimated interactions will be combined in a random effects meta-analysis (a common effect is highly implausible). This method, known as the “deft” approach, will account for clustering of participants and separate out within-study and across-study information, avoiding ecological bias^{52 53}.

We will estimate subgroup-specific intervention effects by repeating the analysis procedure with the interaction parameters fixed at their “deft” estimates. Trials and/or individuals with missing values on an effect moderator will be excluded from the estimation of that interaction. If we find interaction effects after confounding adjustment, we will present a predictive model. We will test whether there is evidence of non-linear effects; if we find such evidence we will explore nonlinear models^{52 54}.

Continuous variables will not be categorised for analysis. We expect that trials will use different questionnaires to measure baseline psychological distress and dispositional mindfulness; we will standardise them using z-scores. Education level data are usually collected in the form of categories with a natural ordering; if that is the case then a linear trend across categories will be assumed⁵³. Where trials have used different categories for collecting education level data, we shall strive to retain an ordered-categorical approach where levels have been collapsed by, for instance, PhD=1, BA=2, PhD/BA=1.5. Genders other than man/woman will be combined into an “other” category.

ETHICS AND DISSEMINATION

No local ethics approval was deemed necessary for this project following consultation with the research governance team. Trial authors will be requested to anonymise data sets prior to sharing them, and asked to confirm they have obtained ethical approval for sharing trial data anonymously. Data management and analysis will take place at the Department of Psychiatry, University of Cambridge. Data as obtained from individual trial authors will be stored at the highly secure Clinical School Secure Data Hosting Service and checked for any residual identifiable data before making copies to be used in normal workstations.

Findings will be disseminated within the academic community through publication in high-impact journals, conference presentations and networking. Professional stakeholders will be reached through activities focused on discussing the applicability of the findings. Media channels, social media (@MSSatUoC), and a variety of presentation formats will be used to engage with the wider public.

PATIENT AND PUBLIC INVOLVEMENT

A public stakeholder group has been put together to provide input throughout the life of this project. They bring experiential expertise on mindfulness’ effects and how they interact with contextual or personal factors, and on mental health promotion in daily life. They are equipped to conceptually understand the study so that they can co-produce it. Stakeholders shaped the research questions and prioritised outcomes and moderation analyses. They will be invited to contribute to the day-to-day research process as research partners, for example by selecting studies and extracting data. They will be involved in interpreting the results, creating an impact plan, and disseminating the findings. We are also involving a group of professional stakeholders.

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AUTHORS' CONTRIBUTIONS

JG applied for research funding and is the guarantor. JG, PBJ, TD and IRW planned the study. JG and CF wrote the manuscript that was revised through discussion with all the authors. All authors read and approved the final manuscript.

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COMPETING INTERESTS STATEMENT

The authors have no conflicts of interest to declare.

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TABLES

TABLE 1. REVIEW INCLUSION CRITERIA

Study aspect	Inclusion criterion
<i>Design</i>	Parallel-arm randomised controlled trials (RCTs) including cluster RCTs
<i>Intervention</i>	Group-based first generation MBPs as defined by Crane et al ¹⁰ , with a minimum intensity of four one-hour in-person teacher-led sessions or equivalent*.
<i>Comparison</i>	Passive control groups such as no intervention, waitlists, or treatment-as-usual if the MBP arm also had access to it.
<i>Population</i>	Adult (18+ year old) participants living in the community, as long as the trial had not selected them for having any particular clinical condition. MBPs targeting specific community groups were included. Trials with slightly younger participants (e.g. those in university settings where some students will turn 18 during the first academic year) will be included.
<i>Outcomes</i>	Self-reported psychological distress measured between one and six months after MBP completion.
<i>Moderators</i>	At least one of the following has been measured: baseline psychological distress, gender, age, education, and dispositional mindfulness.
<i>Quality</i>	A maximum of two high risk-of-bias sources as assessed using the RoB2 tool ⁴⁷ before obtaining IPD.

* Four MBP sessions were used as the “minimum dose” for participants in previous studies ⁵⁵, and one-hour sessions are common in non-clinical settings ⁵⁶