Protocol Full Title prospective observational trial:

Who fares best with mindfulness meditation – understanding the individual effects of mindfulness

Protocol Acronym/short title:

Who fares best with mindfulness meditation

Version and date of final protocol:

Version 4 – 06.12.2024

Sponsor:

Name: KU Leuven
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Principal Investigator:

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1. Study Synopsis

Title of clinical trial	Who fares best with mindfulness meditation – understanding the individual effects of mindfulness
Protocol Short Title/Acronym	Who fares best with mindfulness meditation
Sponsor name	KU Leuven
Principal Investigator	Prof. dr. Filip Raes
Medical condition or disease under investigation	No specific medical condition, but the study will investigate 3 typical settings for the delivery of mindfulness-based interventions (MBIs): (1) a mindfulness centre for the general public, (2) a mindfulness centre related to a hospital for participants with mild complaints, (3) and a mindfulness centre for participants with a history of depression and staff from the public sector.
Purpose of clinical trial	The general objective of the project is to investigate how individual differences influence the effects of mindfulness meditation to gain a fundamental understanding of the personalised effects of mindfulness.
Primary objective	The primary aim is to identify the mechanisms underlying the effects of mindfulness meditation on mental health.
Secondary objective (s)	The secondary aim is to uncover for whom mindfulness is beneficial and for whom it may be harmful.

Trial Design	Multi-site interventional study in different sub-populations
Endpoints	Symptoms of anxiety, and depression; quality of life; wellbeing; adverse effects resulting from the mindfulness intervention
Sample Size	N=120 participants in in total
Summary of eligibility criteria	• At least 18 years of age • Enrolled in a mindfulness-based intervention at one of the participating sites • Sufficient knowledge of the Dutch or English language • Internet access
Maximum duration of treatment of a Subject	8 weeks
Version and date of final protocol	Version 2 - 17.11.2022
Version and date of protocol amendments	Version 4 – 06.12.2024

2. Background and rationale

Mindfulness meditation is often considered the answer to a range of problems, be it stress at the workplace or a depressive disorder. However, prior research has shown that Mindfulness-Based Interventions (MBIs) are not equally effective for everyone in promoting mental health (Farias et al., 2020). The crucial question is: "What treatment, by whom, is most effective for this individual with that specific problem, and under which set of circumstances?" (Paul, 1967) Investigating **how individual differences impact the effects of mindfulness** is essential to gain an understanding of the personalised effects of MBIs and uncover for whom mindfulness is beneficial and for whom it may be harmful.

MBIs are widely used in clinical and wellbeing interventions (Crane et al., 2017). They teach participants to become aware of their thoughts, feelings, and sensations without judging them, and to replace automatic reactions with conscious responses such as accepting one's pain instead of worrying if it will ever end (Kabat-Zinn, 1994). Meta-analyses reported several beneficial effects of MBIs including reduced stress, anxiety, depression, and pain, and improved quality of life in clinical and healthy populations (Goyal et al., 2014; Khoury et al., 2013; Khoury et al., 2015). However, effects are not always beneficial. A recent meta-analysis shows that negative effects occur in controlled, curricula-based MBIs (Farias et al., 2020). For more generally available meditation practices, the risk of adverse events is even higher, with a prevalence of 33.2% in observational studies. These findings suggest that MBIs may not be efficacious for everyone, but may be harmful for some individuals, highlighting the need to study the personalised effects of mindfulness.

To uncover for whom mindfulness meditation is beneficial and for whom it may have adverse effects, it is crucial to **first understand through which mechanisms mindfulness exerts its effects**.

Currently, these mechanisms are unknown and there is no consensus on a theoretical model of how mindfulness affects change (Alsubaie et al., 2017). Lindsay and Creswell posit that awareness and acceptance are the mechanisms underlying mindfulness (Lindsay & Creswell, 2017). They define awareness as directing attention to one's present moment experiences, while acceptance encompasses both a non-judgmental (without judging them as good or bad) and non-reactive/decentered (without reacting to or identifying with them) attitude towards one's experiences. Two meta-analyses generally support this theory by showing that global changes in mindfulness, including awareness and acceptance, mediate the effects of MBIs on mental health (Alsubaie et al., 2017; Gu et al., 2015). A recent systematic review on mechanisms of action in MBIs specifically identified acceptance and awareness as promising mechanisms underlying MBIs (Stein & Witkiewitz, 2020). In addition, two longitudinal studies comparing an MBI to progressive muscle relaxation or waitlist control and one meta-analysis on MBIs for depression suggest non-reactivity/decentering to be a mechanism of mindfulness (Gao et al., 2018; van der Velden, A. M. et al., 2015; Zou et al., 2020). However, evidence for these mechanisms is preliminary and more robust research with adequate sample sizes and, especially, more diverse populations is needed (Stein & Witkiewitz, 2020). This

project aims to address this gap by uncovering the mechanisms underlying mindfulness meditation across different populations (**Objective 1**).

In a second step towards a fundamental understanding of the personalised effects of mindfulness meditation, it is crucial to examine for whom the mechanisms of mindfulness might work better and for whom they might not work at all. Recently, it has been suggested that the effect of mindfulness on mental health may not be universally positive but that it depends on individual characteristics.

Identifying candidate factors that **moderate the effects of mindfulness** will help to understand for whom mindfulness is beneficial.

Three promising candidate factors are trauma symptoms, repetitive negative thinking and a tendency to dissociate. For trauma symptoms and repetitive negative thinking, there is already tentative evidence suggesting that these two candidate factors influence the effects of mindfulness on mental health. Specifically, previous research suggests that mindfulness may less beneficial or even harmful for individuals with trauma symptoms compared to individuals without trauma symptoms (Valdez et al., 2016; Zhu et al., 2019). In contrast, prior studies indicate that mindfulness may be more beneficial for individuals with high repetitive negative thinking compared to those with low repetitive negative thinking (Prins et al., 2014). Finally, tendency to dissociate was identified as a promising candidate factor because of the shared neurobiological correlates of mindfulness and dissociation. Notably, it is hypothesised that the decentered state of mindfulness is accomplished by activating the specific functions of the inferior parietal lobule that are responsible for dissociation (Farb et al., 2007; Sierra, 2009). Thus, mindfulness practice may induce dissociative experiences in individuals with a tendency to dissociate, while conferring benefits for individuals without this tendency. Support comes from a recent meta-analysis placing psychotic or dissociative symptoms in the top 4 of the most common adverse effects related to meditation (Farias et al., 2020). However, evidence for the moderating effects of the candidate factors is mostly based on short mindfulness inductions rather than full interventions, on post-hoc analyses or on uncontrolled studies. Systematic assessment of the moderating effects of all three candidate mechanisms is lacking to date. The present study will address this gap by uncovering how trauma symptoms, tendency to dissociate, and repetitive negative thinking influence the effect of mindfulness meditation on mental health (**Objective 2**). The study will extend previous studies by prospectively studying the positive and negative effects of mindfulness in a real-world sample using a combination of quantitative and qualitative research methods.

3. Trial objectives and Design

3.1 Trial objectives

This project aims to investigate how individual differences influence the effects of mindfulness meditation to gain a first understanding of the personalised effects of mindfulness and uncover for whom mindfulness is beneficial and for whom it may be harmful. Notably, the aim is not to evaluate the general efficacy of mindfulness meditation on a group level but to investigate how mindfulness

mediation affects mental health and wellbeing of each individual based on their personal characteristics. In a first step towards a better understanding of the effects of mindfulness mediation on each individual, we aim to identify the mechanisms underlying the effects of mindfulness meditation on mental health and wellbeing (first objective). Based on prior research, we hypothesise that mindfulness meditation exerts its effects via internal awareness, decentering, and non-judgment, but we will also explore other mindfulness skills as potential mechanisms. Knowing the underlying mechanisms will help us understand why mindfulness meditation leads to improved mental health in some individuals while it may lead to harm in other individuals. In a second step, we aim to examine specific characteristics of individuals that may influence whether mindfulness meditation has beneficial or possibly harmful effects. Specifically, we aim to examine how three candidate factors, namely trauma symptoms, tendency to dissociate, and repetitive negative thinking, influence the effect of mindfulness meditation on mental health and wellbeing (second objective). Knowing how these individual characteristics influence the effect of mindfulness meditation will clarify for whom mindfulness works best and for whom it may lead to undesired effects.

For both objectives, mental health and wellbeing will be measured using self-report questionnaires (see primary endpoints) to determine the effects of the mindfulness intervention on participants' mental health and wellbeing. To achieve the first objective, we will measure change of different mindfulness skills (the hypothesised mechanisms) with self-report questionnaires across the mindfulness intervention in order to test whether the mindfulness intervention leads to change in mindfulness skills, which in turn leads to change in outcomes. To achieve the second objective, we will measure baseline levels of candidate factors with self-report questionnaires in order to test whether these candidate factors influence in what way the mindfulness intervention affects mental health and wellbeing. Candidate factors are trauma history and symptoms, tendency to dissociate, and repetitive negative thinking. Additionally, we will measure obsessive-compulsive disorder related beliefs as potential candidate factors, as these beliefs influenced the effects of mindfulness in our own clinical practice. Meditation practice-related variables such as frequency, intentions and previous experience will be measured in order to control for potential practice-related effects on mental health.

3.2 Primary endpoints

- Symptoms of anxiety and depression; quality of life; wellbeing; adverse effects resulting from the mindfulness intervention, all measured with self-report questionnaires.

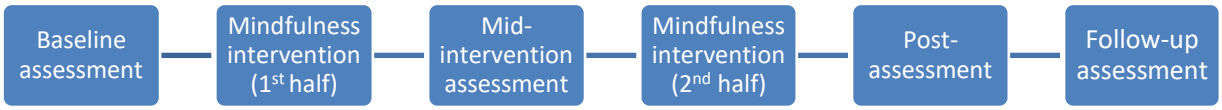
3.3 Secondary endpoints

- Subjective experience of the impact of mindfulness practice on participants' lives and what factors contributed to their experience of mindfulness practice, retrieved from semi-structured interviews.

3.4 Trial Design

This is a non-commercial interventional study in which the Faculty of Psychology & Educational Sciences (KU Leuven) is involved. The study uses a single-arm longitudinal design. Participants who enrolled for a Mindfulness-Based Intervention (MBI) at one of the participating study sites will complete self-report assessments before the start, during, after the mindfulness intervention and at follow-up. A subset of participants will be invited for a semi-structured interview after the end of the intervention. To control for baseline difference in the occurrence of meditation-related adverse events, participants will report on adverse events in relation to meditation practice in the past 4 weeks before the start of the intervention. Such single-arm longitudinal designs have already been used in previous health care research (Naliboff et al., 2020). This design allows us to detect variation in potential mechanisms, and individual differences in occurrence and nature of beneficial and adverse effects in a real-world sample of typical MBI participants. The inclusion of a randomized control group is not necessary nor feasible at this stage given that the main aim of this study is to get a first understanding of mechanisms and moderators of efficacy in routine care and is not designed to test the effectiveness of the MBI (Kazdin, 2007).

3.5 Study diagram



3.6 Trial Flowchart

	Enrolment	Baseline	Intervention	Mid-intervention assessment	Post-assessment	Follow-up assessment
ENROLMENT:						
Eligibility screen	x					
Informed consent	x					
INTERVENTION:						
Mindfulness-Based intervention			x			
ASSESSMENTS:						

Outcomes (mental health, wellbeing & quality of life)		x		x	x	x
Previous meditation-related adverse events		x		x	x	x
Mechanisms (mindfulness skills)		x		x	x	x
Moderators		x				
Mindfulness practice quality				x	x	x
Interview					x	

4. Selection and withdrawal of subjects

4.1 Inclusion criteria

The following inclusion criteria will be applied:

- The study is open to all adults >18 years of age
- Enrolled in a mindfulness-based intervention at one of the participating sites
- Written informed consent after having been informed on all aspects of the study

Participants will be recruited from three settings that are typical for the delivery of MBIs. The first setting is a mindfulness centre that offers MBIs for the general public. Participants are thus not selected based on any complaints they may have. The second setting is a stress clinic associated with a hospital that offers mindfulness courses for participants with mild complaints, such as stress or worry. The third setting is a mood disorders centre that offers mindfulness courses for participants with a history of depression and for staff of the public sector such as health care, social care, or police forces. The three settings will be analysed jointly in one statistical model. Using a variable indicating the setting where a participant was tested, this allows us to statistically detect the differences in effects across settings. If we analysed the samples separately we would not be able to detect statistical differences between the samples and could only compare the results without knowing whether they are statistically different..

4.2 Exclusion criteria

The following exclusion criteria will be applied:

- Insufficient knowledge of the Dutch or English language
- No internet access

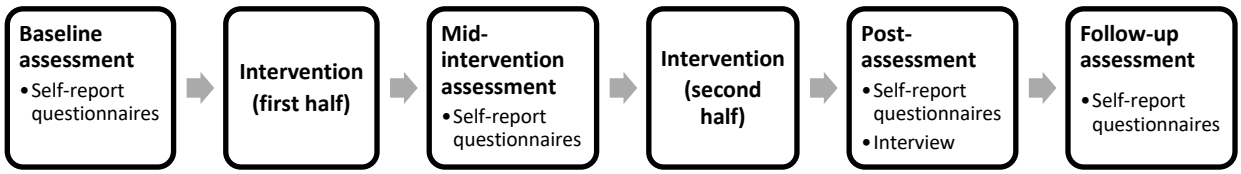
4.3 Expected duration of trial

The study will recruit participants from services that offer mindfulness-based interventions. The study will finish once the required sample size has been reached. We expect a study duration of 2.5 years.

5. Trial Procedures

5.1 Participant timeline

After the baseline assessment, participants receive (nearly) weekly sessions of a group mindfulness intervention spread over 8 weeks. Assessments take place after half of the sessions, at the end of the intervention and at 3-months follow-up.



5.2 Selection and recruitment of participants

Potential candidates will be recruited through services that offer mindfulness-based interventions. Everyone who wishes to enroll for a mindfulness-based intervention at one of the participating sites will be informed about this study by staff working at the respective services. Those who express an interest to participate in the study will be checked for inclusion and exclusion criteria by the research team at KU Leuven and informed about all aspects of the study before providing written consent to participate. Notably, staff at the respective services will not be included in the consent procedure nor in data collection for this study (for more detail, please refer to document “Recruitment procedure”).

5.3 Baseline assessment

Participants enrolled for a mindfulness-based intervention will complete a set of self-report questionnaires via Pavlovia Surveys (Open Science Tools, Nottingham, UK) just before the start of the mindfulness-based intervention. At baseline, outcomes (mental health, wellbeing & quality of life), moderators, and mechanisms will be assessed (for more details, see section data collection).

5.4 Mindfulness intervention

After the baseline assessment, participants will follow a mindfulness course consisting of group sessions of 2-3h duration that are organized (nearly) weekly and are spread over a period of eight

weeks. The specific timeline and organisation of the course may differ between the participating sites but all courses will involve a comparable amount of contact hours with the mindfulness trainer. Each session consists of guided experiential mindfulness exercises (e.g., body scan, breathing space, breath focus, walk meditation), sharing of experiences of these exercises, reflections in small groups, psychoeducation (e.g., stress, depression, self-care), and review of home practices.

The mindfulness courses are based on one of the two most well-known MBIs, Mindfulness-Based Cognitive Therapy (Segal et al., 2002) and Mindfulness-Based Stress Reduction (Kabat-Zinn, 1990), or a combination thereof. Key objectives are to increase awareness of one's experience in the present moment and to teach an open and accepting attitude towards one's experience. Specific implementation will depend on the study site, but all courses teach the same underlying principles of mindfulness, allowing to uncover mechanisms and moderators for MBIs more generally. Courses follow a standardised protocol with (nearly) weekly group sessions and daily homework tasks taught by experienced and certified mindfulness trainers. Courses may take place in person or online depending on the current COVID-19 related measures at the participating sites.

5.5 Outcome assessments

Participants will be assessed at mid-intervention (after half of the sessions), post-intervention (after the last session), and 3-months follow-up. Assessments include self-report questionnaires measuring outcomes (mental health, wellbeing & quality of life), adverse effects, and mechanisms (for more details, see section data collection). At post-intervention, a subset of participants will additionally be invited for a semi-structured interview. Selection of the subset of participants is iterative and will follow theoretical sampling. This means that in the first sampling step, participants with relevant expertise (those who have experienced at least one unpleasant experience related to their mindfulness practice) will be invited for interview. Data of this first set of participants will be analysed to uncover any gaps in the data. In the following steps, participants will be specifically invited based on their experiences (as gathered in the questionnaires) in order to fill the gaps in the data. During this interview, participants will be asked how they experienced their mindfulness practice, what impact these experiences had on them over the course of the MBI, and what factors contributed to their experience of mindfulness practice (for the preliminary set of questions, please refer to interview guide). For the interview part of the study, we will seek additional consent as not all participants will be invited for interview (please refer to recruitment document). Interviews will all be conducted online to ensure a standardized interview procedure across all participants.

5.6 End of study

The study ends about 5 months after baseline assessment with the follow-up measurements. As a reward for participation, participants will be reimbursed with a €5/£5 voucher of a local online shop (bol.com for the Belgian sample and Amazon for the UK sample). Additionally, we will donate €1/£1 to a local mental health charity for each participant who completed the study. For participants who participate in the interview part, we will make an additional donation of €1/£1 and these participants will also receive an additional voucher of €5/£5 of a local online shop (bol.com for the Belgian sample

and Amazon for the UK sample). When the study is finished, data analyses are completed, and first scientific reports are ready, participants that have indicated that they wanted to be informed about the study's results, will be informed via the email address they have provided on the ICF.

6. Data collection

Data will be collected using self-report questionnaires and semi-structured interviews. All questionnaires are attached. Participants will be asked to complete a subset of the questionnaires at each evaluation point (for an overview, see trial flowchart). Assessment of the self-report questionnaires will take ca. 30 minutes at baseline and ca. 20 minutes at all other assessment points.

- **Sociodemographic data:** age, gender, self-reported diagnoses of psychiatric disorders;
- **Symptoms of emotional distress (depression, anxiety):** measured by the Patient Health Questionnaire-4 (PHQ-4; Kroenke et al., 2009) – 4 items;
- **Quality of life:** measured by the Recovering Quality of Life (ReQoL-10) Questionnaire (Keetharuth et al., 2018) – 10 items;
- **Wellbeing:** measured by the Short Warwick–Edinburgh Mental Well-being Scale (SWEMWBS; Stewart-Brown et al., 2009) – 7 items;
- **Adverse effects specific to Mindfulness-Based Interventions** (assesses common meditation-related adverse events)**:** measured by the Meditation-Related Adverse Effects Scale, Mindfulness-Based Program version (MRAES-MBP; Britton et al., 2018) – 14 items;
- **Mindfulness skills:** measured by the Comprehensive Inventory of Mindfulness Experiences – Short Form (CHIME-SF; Cladder-Micus et al., 2019) – 24 items;
- **Tendency to dissociate:** measured by the Brief Dissociative Experiences Scale (DES-B; Bernstein & Putnam, 1986) – 8 items;
- **Repetitive negative thinking:** measured by the Perseverative Thinking Questionnaire (PTQ; Ehring et al., 2011) – 15 items;
- **Trauma history:** measured by a modified version of the Life Events Checklist for DSM-5 (LEC-5; Weathers et al., 2013) – 17 items;
- **Trauma symptoms:** measured by the International Trauma Questionnaire (ITQ; Cloitre et al., 2018) – 18 items;
- **Obsessive-compulsive disorder related beliefs:** measured by Obsessive Beliefs Questionnaire (OBQ-9; Gagné et al., 2018) – 9 items;
- **Quality of mindfulness practice**: measured by Practice Quality-Mindfulness (PQ-M; Del Re et al., 2013) - 6 items;
- Questions about **previous experience with meditation**, **frequency of home practice**, **intentions of meditation practice**, **training expectancy** and **session attendance**

7. Assessment of Safety

Risks

The risks associated with this study are minimal because participants are not allocated to treatment but sign up for the mindfulness course themselves. Therefore, participation in this study is completely independent of participation in the MBI and the support received from the mindfulness trainer. Only the participating site in Exeter, UK, specifically recruits vulnerable individuals with a previously diagnosed mental health problem. All participating sites in Belgium recruit healthy volunteers from the general public. We cannot rule out that these volunteers have previously been diagnosed with a mental disorder but volunteers are not specifically selected based on their diagnosis. The participating site in Exeter, UK, asks for information about mental and/or physical health and schedules an intake interview to determine whether the MBI would be safe for the participant.

For the questionnaires, the only potential harm we foresee is that participants may experience emotional distress when completing the questionnaires as these assess symptoms of anxiety and depression, trauma history, PTSD symptoms and meditation-related adverse events among others. Of note, the more distressing questionnaires about trauma history and PTSD symptoms are only administered at baseline. To minimize the risk with regard to these more distressing questionnaires particularly, participants are encouraged to contact the research team or their mindfulness trainer at any point during the study but especially after the baseline questionnaire. The mindfulness trainers are certified, have significant experience delivering mindfulness trainings to different participant groups and the necessary skills to manage any unintended distressing impacts in participants should this arise as a result of the questionnaires. The research team includes two clinical psychologists who have the required skills to support participants after distressing events if necessary. If participants wish to share their experiences anonymously, they can contact one of the mental health services from the list they receive at each assessment point. If the participant does not reach out but the research team notices a risk for the participant based on their responses to the questionnaires, the research team will contact the mindfulness trainer to enable them to protect and support the participant in any necessary way. Thus, participants' responses to the questionnaires are monitored regularly and the research team will respond quickly and appropriately to emerging risk if needed.

For qualitative interviews, the only potential harm we foresee is psychological distress associated with recounting experiences that may have been stressful or caused personal anguish, for example adverse events during mindfulness practice. Of note, participants are also questioned about their positive experiences with the mindfulness practice so there is not a single focus on distressing experience but this is set in context with the overall experience of the mindfulness course. We will make every effort to enable participants to feel at ease throughout the process; ensure participants are fully aware of their right to withdraw at any time without giving a reason and that any data will be fully anonymised. During the interviews, if the interviewer believes a participant is in distress, recording will be ceased, and support offered. In this event, the risk protocol will be followed to

provide appropriate signposting and support to the participant. Some people may find it helpful to recount their experiences in a qualitative interview setting, for both positive and negative experiences, and this interview may therefore be experienced as a benefit by some participants. Otherwise, there is no direct benefit to participants.

Burden

This study has been designed to impose a minimal burden on participating mindfulness centres and participants in this study. The research team takes care of all organisational tasks themselves, staff from the mindfulness centres will only be asked to inform their mindfulness course attenders about this study. With regards to participants in this study, efforts have been made to reduce time effort. Each survey will take no more than 20 minutes to complete (except for the baseline survey, which will take no more than 30 minutes to complete), which we consider a relatively small burden.

A slightly larger burden will fall on those agreeing to take part in qualitative interviews. We have reduced this burden by conducting these remotely and scheduling based on participant availability. We will aim for interviews to be a maximum of 45 minutes and continue beyond this only if a participant wishes to. For interviews taking place in person, we will follow all COVID-19 regulations.

7.1 Procedures for recording and reporting adverse events (AE)

Adverse events will be actively assessed at mid-intervention, post-intervention and follow-up assessment points using self-report questionnaires specifically designed for MBIs. If an emergent safety issue becomes apparent in the participant's responses to the questionnaires or during the interview, the risk protocol (attached) will be followed. In case participants report an emergent safety issue or a mindfulness trainer becomes aware of such issue in-between assessment points, this will be discussed immediately with one of the supervisors at the participating site. An adverse event form (attached) is available for documentation of any emerging safety issue, which will be provided to the Principal Investigator as soon as possible after awareness. The specific procedure (and form used) was used in the approved You.Mind! study (s63485) and has been checked with and developed in close collaboration with CTC (Johanna Geerinck).

7.2 Treatment stopping rules

Participants can stop the MBI and withdraw from the study at any time for any reason and without any consequences.

8. Statistics

8.1 Sample size

The study will employ a single-group longitudinal design with three subsamples, which will be recruited from 3 different settings typical for MBI delivery mentioned above. Because of the differences in

settings, potential participants at each of the centres will differ from each other on relevant measures. Participants recruited at the Mood Disorders Centre will have a history of depression or will have been exposed to large stressors as part of their work (e.g., police forces, doctors at the hospital) and will therefore most likely report higher symptoms of depression and anxiety and lower wellbeing than participants recruited in the other centres. Participants recruited at the stress clinic associated with ZNA Antwerp are healthy volunteers but generally experience mild complaints, such as stress or worry, that they aim to address with the mindfulness course. Thus, their symptom levels of depression and anxiety are expected to be naturally lower than the symptom levels of participants recruited at the Mood Disorders Centre. The opposite holds for their wellbeing levels. Finally, participants recruited from the mindfulness centre for the general public are healthy volunteers who have an interest in mindfulness or want to further boost their wellbeing with the mindfulness course. To take these baseline differences into account in the statistical model, a variable will be included to indicate the setting where the participant was tested. This approach allows us to analyse participants from all settings in one statistical model and statistically detect the differences in effects across settings. If we analysed the samples separately, we would not be able to detect statistical differences between the samples and could only compare the results without knowing whether they are statistically different. Moreover, due to the recruitment difficulties we experienced so far, treating the three settings as distinct samples would not be feasible and would mean that we cannot recruit sufficient participants to complete the study. Nevertheless, it is important that all 3 settings are included in this study as they reflect different settings very typical for MBI delivery. Only recruiting from one of the centres would largely limit the generalisability and value of our findings.

In total, 110 participants are needed to detect a medium-sized effect with a power of .80 with α=.05 for all quantitative analyses. We assumed a medium effect size (Cohen's f=0.39) on the basis of prior studies on (a) the effect of the MBI on mindfulness subprocesses (a-path; Gu et al., 2018; Gu et al., 2015; Zou et al., 2020), (b) the effect of mindfulness subprocesses on mental health (b-path; Gu et al., 2018; Gu et al., 2015; Zou et al., 2020), and (c) the moderation effects (Prins et al., 2014; Zhu et al., 2019). The sample size calculation is based on prior simulation studies for the mediation effect (Pan et al., 2018) and a Monte Carlo simulation of 1,000 datasets performed with a power tool designed to estimate power of moderation effects in multilevel models (Mathieu et al., 2012). Even with the highest within-subject correlation (ICC = 0.9), which has been shown to increase the required sample size, the sample size necessary to detect a mediation effect with a power of .80, α=.05 and 4 measurement points assuming a medium effect size for the a-path and b-path is 64 participants according to the simulation study by Pan et al. (2018). For the moderation analysis, we performed our own simulation study using the power tool by Mathieu et al. and following recommendations of the authors and results in the literature to set parameter values for the simulation. The stimulation suggests that a sample size of 110 participants would allow to detect moderation effects with a power of .808 and α=.05. To enable reproduction of the simulation study, we will attach the R code to this submission. To additionally account for attrition, we will oversample by 10% (i.e., 120 in total). For the qualitative analyses, a sample of 30 participants is sufficient based on recommendations in the literature (Thomson, 2010). Due to a halt in recruitment at one site and challenges at the second, all

interview participants will now be recruited from the third site. This limitation on participant availability means we aim to recruit between 15 and 25 individuals for the interviews.

8.2 Analysis

Quantitative data

Hypotheses will be examined with intention-to-treat analyses jointly for all subsamples, i.e. each of the three settings. Analyses are based on general linear modeling and multilevel mixed effects modeling. To test the intervention effect on outcomes (mental health, wellbeing, quality of life, and frequency of adverse effects) and potential mediators (mindfulness skills) over time, piecewise multilevel models with two levels will be used, with time points (Level 1) nested in persons (Level 2). In the models, change is described as separate slopes for each dummy coded time variable (mid-MBI, post-MBI, follow-up). To examine mediation effects, a time-lagged mediation model as outlined by Bauer (2006) will be estimated, in which within-person change in each mindfulness subprocess over time (baseline to mid-MBI; mid-MBI to post-MBI) predicts subsequent change in outcomes (mid-MBI to post-MBI; post-MBI to follow-up). Thus, to test for potential mechanisms (objective 1), one separate model will be estimated for each of the outcomes (depression & anxiety symptoms (measures by one combined score), quality of life, wellbeing, and frequency of adverse effects). In each model, there are four predictors: the three hypothesised mediators (internal awareness, decentering, and non-judgment) and time. Indirect effects of mindfulness skills will be tested using bootstrap confidence intervals (Bauer et al., 2006). To test moderation effects, multilevel models as described above will be estimated, in which the dummy coded time variables (as Level 1 variables), a moderator (as Level 2 variable), and their cross-level interactions predict outcomes. Significant moderators will afterwards be combined into one model to examine unique effects. Thus, to test for moderation effects (objective 2), one separate model will be estimated for each of the outcomes (depression & anxiety symptoms (measures by one combined score), quality of life, wellbeing, and frequency of adverse effects). In a first step, we will estimate separate models for each of the three moderators (trauma symptoms, repetitive negative thinking, and tendency to dissociate) with three predictors: time, the moderator, and the interaction between time and the moderator. In the second and final step, all significant moderators from the first step will be combined into one model with up to seven predictors: time, the three moderators and the interaction between time and each of the moderators. To explore whether the effect of a mindfulness skill on the outcomes is moderated by a specific candidate factor (moderated mediation), the mediation model will be re-estimated with moderators as predictors of the mediation effect as outlined by Bauer (2006). Moderation of the indirect effect will be tested using bootstrap confidence intervals.

A corrected significance level will be calculated for multiple comparisons according to the method described by Benjamini and Hochberg (1995). This method is preferable for our study design as it does not aim to avoid a single Type I error at the cost of losing statistical power. Multilevel models used in this study can handle missing data, which means all observed data points can be included in analysis

(including participants that miss certain data points). Especially in cases where mainly outcome data are missing, multilevel models will give valid results (Carpenter & Smuk, 2021). Quantitative analyses will be performed using R.

Qualitative data

Interviews will be audio-taped and transcribed. For analysis, a grounded theory approach will be followed as this is most suitable for the following reasons: Grounded theory aims to generate a data-based theoretical model and engages in constant comparisons between participants, allowing to identify both mechanisms of change and moderating factors that influence the experience of mindfulness practice across participants and subsamples (Charmaz, 2006; Frank et al., 2019). To simplify comparison between subsamples, the Framework Method using a 7- stage analysis process (Gale et al., 2013) will be applied in combination with the 3-step coding process of grounded theory (Charmaz, 2006). After transcription and familiarisation with the data, open coding will be used to develop categories and hypotheses. During focused coding, the most significant initial codes will be compared to develop a working analytical framework, which will be applied to subsequent interviews. During charting, data will be summarised by category and entered into a matrix. Finally, applying theoretical coding, relationships between categories will be integrated into a theory. Qualitative analyses will be performed with Nvivo.

9. Quality assurance

The Study must be performed in accordance with the protocol, current International Conference on Harmonisation (ICH) and ICH Good Clinical Practice (GCP) guidelines, and applicable regulatory and country-specific requirements. ICH guidelines are an international ethical and scientific quality standard for designing, conducting, recording, and reporting studies that involve the participation of human participants. Compliance with this standard provides public assurance that the rights, safety, and wellbeing of Study participants are protected, consistent with the principles that originated in the most recent version of the Declaration of Helsinki, and that the Study data are credible, reliable and reproducible.

10. Direct access to source data and documents

Restricted data will only be accessible by the involved researchers. Restricted data include personal information (e.g., names, ethnicity, diagnosis). Confidential (pseudonymized) data will be shared with regulatory authorities and ethical committees for trial-related monitoring and inspections. The key that links names of participants to research data will be deleted after the study.

11. Ethics and regulatory approvals

The trial will be conducted in compliance with the principles of the Declaration of Helsinki (2013), the principles of Good Clinical Practice (GCP) and in accordance with all applicable regulatory

requirements. This protocol and related documents will be submitted for review to the Ethische Commissie Onderzoek UZ/KU Leuven, Herestraat 49, 3000 Leuven, Belgium. Any subsequent protocol amendments, yearly progress reports and a copy of the Final Study Report will be submitted to EC UZ/KU Leuven and all local Ethics Committees, if applicable.

The Study can and will be conducted only on the basis of prior informed consent by the Subjects, or their legal representatives, to participate in the Study. The Participating Sites shall obtain a signed informed consent form (ICF) for all patients prior to their enrollment and participation in the Study in compliance with all applicable laws, regulations and the approval of the (local) Ethics Committee, if required. The Participating Sites shall retain such ICFs in accordance with the requirements of all applicable regulatory agencies and laws.

The Investigators and the Participating Sites shall treat all information and data relating to the Study as confidential and shall not disclose such information to any third parties or use such information for any purpose other than the performance of the Study. The collection, processing and disclosure of personal data, such as patient health and medical information, is subject to compliance with applicable personal data protection and the processing of personal data (Regulation (EU) 2016/679 also referred as the General Data Protection Regulation ("GDPR") and the Belgian Law of July 30 2018 on the protection of natural persons with regard to the processing of personal data).

12. Data Handling

This data management plan was developed using the online Data Management storage of the KU Leuven and the PPW Data Classification and Storage Guidelines.

Data collection, handling, processing, and transfer for the purpose of this Study will be performed in compliance with applicable regulations, guidelines for clinical studies and internal procedures. It remains the responsibility of the Investigator to check that all data relating to the Study, as specified in the Study protocol, are entered into the participant record in accordance with the instructions provided and that the forms are filled out accurately, completely and in a timely manner.

Each participant's record shall under no circumstances capture any identifying information such as but not limited to the participant or their relative(s) name, home address, contact details, full date of birth, medical record number (e.g., UZ Leuven EAD number), social security number etc. Therefore, as soon as informed consent forms have been signed, participants will receive a unique, anonymized participant ID. As this study includes multiple waves of data collection, a datafile that links the participants'-ID to the participants name will be stored throughout the study in a separate restricted online environment on KU Leuven's network storage. This datafile is the only link between participants'-ID and participants' name. When the study is finished the datafile connecting participants'-ID and participants' name will be deleted. After this file has been destroyed, participants'-ID will not be linked to the 'ordinary' personal data that is being collected in the study, and none of the identifying personal data will be included in any of the datasets.

All questionnaires will be hosted on a KU Leuven approved survey system (Pavlovia Surveys, Open Science Tools, Nottingham, UK) which is compliant with GDPR requirements. Interviews will be recorded, and the audio record will be stored in a restricted online environment alongside other strictly confidential information (see below). In case interviews are conducted online (to reduce participant burden), the audio of the interviews will be recorded through Microsoft Teams of KU Leuven, a secured platform offered by the university. Audio files will be given a numerical identifier and stored within a qualitative subfolder alongside other strictly confidential data (see below). Only the qualitative research team and the PI will have access to this. The interview recordings will be transcribed by a member of the research team. Following transcription of the interviews, the research team at KU Leuven will pseudonymise the transcript to remove any personally identifying elements and replace them with the participant ID before analysis takes place. The pseudonymised transcripts will be translated to English using deepl with a Pro license, which is compliant with GDPR regulations. Additional checks will be done to ensure participant identifiers have been fully pseudonymised prior to any form of data publication or submission of reports. Access to the data will be restricted to those directly involved in the analysis. Audio records of interviews will be deleted after transcription is completed.

Types of data that will be collected:

- Strictly confidential information: This includes all sensitive information. In this study we will collect the following: datafile linking participants' name to participant ID, contact information, signed informed consent forms, interview records (all collected electronically). Those data will be considered as restricted throughout the entire project. This means that this restricted information will be stored at a separate restricted area of KU Leuven's encrypted and secure network storage, each in separate folders. Only the research team members that are in contact with participants and the PI will have access to the datafile linking participants' name and participant ID, consent forms and contact information in order to be able to reach participants for each wave of data collection. Raw interview records will only be accessible to research team members who transcribe the data or who are directly involved in the anonymisation of the data as well as the PI.

- Confidential data collected: This contains moderately sensitive information. In this study we collect the following: age, demographic data, all other data coming from questionnaires and interview transcripts. This data will be stored on KU Leuven's encrypted and secure network storage. To allow for secure storage, management and sharing of files, involved researchers will have role-based access to the data using Multifactor authentication.

All data will be stored on KU Leuven's secure network storage (i.e., Onedrive for Business). This means that data are stored on a secure and encrypted network provided by the KU Leuven and data transfer will always take place in encrypted format via secured channels only. KU Leuven's network storage is compliant with GDPR regulations. It allows granular, role-specific access rights and provides access statistics for who has accessed data. Multifactor authentication via the KU Leuven

Authenticator App will be required for all authorized researchers to access the data. Authorizations for data access to both kinds of data will be checked regularly to ensure that they are still up to date. KU Leuven's network storage allows version control such that it saves all previous versions (possible to go back to original version), who has made changes and when. Finally, it is recommended for use with strictly confidential and confidential data by KU Leuven. All drives used for data storage are managed by ICTS personnel, bound by the KUL ICT code of conduct, and have automatic back-up procedures and disaster recovery in place.

In publication, results will only be reported at the group level. For interview data, no information that could personally identify a participant will be presented. Any reports resulting from this study will be screened for potential disclosure of personally identifiable information prior to submission (e.g. small cell counts).

13. Data Management

Pseudonymized data will be transferred encrypted via a secured method of transfer considering all applicable security arrangements and regulations (such as the European General Data Protection Regulation). The full pseudonymized dataset can also be shared with regulatory authorities, ethical committees, and colleague researchers upon request. The receiving party will be bound by contractual agreement to keep the transferred data confidential at all times, to only process the data for the purpose of the Study or for improving scientific knowledge about mindfulness and is not permitted to link the data with other data which might render the information more identifiable. To this end, appropriate Data Transfer Agreements (DTAs) will be established. Of course, information about data sharing will be part of the consent form. Participants' personal information (e.g., contact information, names, etc.) or audio files will never be shared.

In line with the KU Leuven RDM policy, all research data except for identifiable information (i.e., participants' names, contact details, etc.), the datafile linking participants'-ID to participants' name and the audio recordings of the interviews will be stored for at least 10 years on secure KU Leuven central servers. As a back-up, research data will be stored on a secure password-protected and encrypted Network Attached Storage (NAS) device provided by the research unit of the PI. The NAS is kept in locked office storage and is only connected to the KU Leuven network sporadically for updates.

14. Translational research

No biological material will be collected for this study.

15. Publication Policy

It is anticipated that the results of the overall Study shall be published in a multi-centre publication, involving the data of all clinical sites participating in the Study.

Participating Site is not allowed to publish any data or results from the Study prior to the multicentre publication, provided however that Participating Site is allowed to publish the results generated at the Participating Site if the multicentre publication has not occurred after 12 months from Study database lock.
Any publication by Participating Site will be submitted to the Sponsor for review at least thirty (30) days prior to submission or disclosure. Sponsor shall have the right to delay the projected publication for a period of up to three (3) months from the date of first submission to the Sponsor in order to enable the Sponsor to take steps to protect its intellectual property rights and know-how.

Publications will be coordinated by the Investigator of Sponsor. Authorship to publications will be determined in accordance with the requirements published by the International Committee of Medical Journal Editors and in accordance with the requirements of the respective medical journal.

16. Insurance/Indemnity

In accordance with the Belgian Law relating to experiments on human persons dated May 7, 2004, Sponsor shall assume, even without fault, the responsibility of any damages incurred by a Study Patient and linked directly or indirectly to the participation to the study and shall provide compensation therefore through its insurance.

17. Financial Aspects

FWO PhD Fellowship. Dossiernummer : 11I1622N.

References

Alsubaie, M., Abbott, R., Dunn, B., Dickens, C., Keil, T. F., Henley, W., & Kuyken, W [Willem] (2017). Mechanisms of action in mindfulness-based cognitive therapy (MBCT) and mindfulness-based stress reduction (MBSR) in people with physical and/or psychological conditions: A systematic review. *Clinical Psychology Review*, *55*, 74–91. https://doi.org/10.1016/j.cpr.2017.04.008

Bauer, D. J., Preacher, K. J., & Gil, K. M. (2006). Conceptualizing and testing random indirect effects and moderated mediation in multilevel models: New procedures and recommendations. *Psychological Methods*, *11*(2), 142–163. https://doi.org/10.1037/1082-989X.11.2.142

Benjamini, Y., & Hochberg, Y. (1995). Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. *Journal of the Royal Statistical Society: Series B (Methodological)*, *57*(1), 289–300. https://doi.org/10.1111/j.2517-6161.1995.tb02031.x

Bernstein, E. M., & Putnam, F. W. (1986). Development, reliability, and validity of a dissociation scale. *The Journal of Nervous and Mental Disease*, *174*(12), 727–735. https://doi.org/10.1097/00005053-198612000-00004

Britton, W. B., Lindahl, J. R., & Cooper, D. J. (2018). *Meditation-Related Adverse Effects Scale, Mindfulness-Based Program version (MRAES-MBP).* Brown University.

Carpenter, J. R., & Smuk, M. (2021). Missing data: A statistical framework for practice. *Biometrical Journal*, *63*(5), 915–947. https://doi.org/10.1002/bimj.202000196

Charmaz, K. (2006). *Constructing grounded theory: A practical guide through qualitative analysis*. Sage.

Cladder-Micus, M. B., Verweij, H., van Ravesteijn, H., van der Gucht, K., Raes, F., & Speckens, A. E. M. (2019). Validation of the Dutch Comprehensive Inventory of Mindfulness Experiences (CHIME) and Development of a Short Form (CHIME-SF). *Mindfulness*, *10*(9), 1893–1904. https://doi.org/10.1007/s12671-019-01125-7

Cloitre, M., Shevlin, M., Brewin, C. R., Bisson, J. I., Roberts, N. P., Maercker, A., Karatzias, T., & Hyland, P. (2018). The International Trauma Questionnaire: development of a self-report measure of ICD-11 PTSD and complex PTSD. *Acta Psychiatrica Scandinavica*, *138*(6), 536–546. https://doi.org/10.1111/acps.12956

Crane, R. S., Brewer, J., Feldman, C., Kabat-Zinn, J., Santorelli, S., Williams, J. M. G [J. M. G.], & Kuyken, W [W.] (2017). What defines mindfulness-based programs? The warp and the weft. *Psychological Medicine*, *47*(6), 990–999. https://doi.org/10.1017/S0033291716003317

Del Re, A. C., Flückiger, C., Goldberg, S. B., & Hoyt, W. T. (2013). Monitoring mindfulness practice quality: An important consideration in mindfulness practice. *Psychotherapy Research*, *23*(1), 54–66. https://doi.org/10.1080/10503307.2012.729275

Ehring, T., Zetsche, U., Weidacker, K., Wahl, K., Schönfeld, S., & Ehlers, A. (2011). The Perseverative Thinking Questionnaire (PTQ): Validation of a content-independent measure of repetitive negative thinking. *Journal of Behavior Therapy and Experimental Psychiatry*, *42*(2), 225–232. https://doi.org/10.1016/j.jbtep.2010.12.003

Farb, N. A. S., Segal, Z. V., Mayberg, H., Bean, J., McKeon, D., Fatima, Z., & Anderson, A. K. (2007). Attending to the present: Mindfulness meditation reveals distinct neural modes of self-reference. *Social Cognitive and Affective Neuroscience*, *2*(4), 313–322. https://doi.org/10.1093/scan/nsm030

Farias, M., Maraldi, E., Wallenkampf, K. C., & Lucchetti, G. (2020). Adverse events in meditation practices and meditation-based therapies: A systematic review. *Acta Psychiatrica Scandinavica*, *142*(5), 374–393. https://doi.org/10.1111/acps.13225

Frank, P., Stanszus, L., Fischer, D., Kehnel, K., & Grossman, P. (2019). Cross-Fertilizing Qualitative Perspectives on Effects of a Mindfulness-Based Intervention: An Empirical Comparison of Four Methodical Approaches. *Mindfulness*, *10*(11), 2452–2467. https://doi.org/10.1007/s12671-019-01227-2

Gagné, J.-P., van Kirk, N., Hernandez-Vallant, A., Potluri, S., Krompinger, J. W., Cattie, J. E., Garner, L. E., Crosby, J. M., Brennan, B. P., & Elias, J. A. (2018). Validating an abbreviated version of the Obsessive Beliefs Questionnaire. *Journal of Clinical Psychology*, *74*(10), 1791–1807. https://doi.org/10.1002/jclp.22629

Gale, N. K., Heath, G., Cameron, E., Rashid, S., & Redwood, S. (2013). Using the framework method for the analysis of qualitative data in multi-disciplinary health research. *BMC Medical Research Methodology*, *13*, 117. https://doi.org/10.1186/1471-2288-13-117

Gao, L., Curtiss, J., Liu, X., & Hofmann, S. G. (2018). Differential Treatment Mechanisms in Mindfulness Meditation and Progressive Muscle Relaxation. *Mindfulness*, *9*(4), 1268–1279. https://doi.org/10.1007/s12671-017-0869-9

Goyal, M., Singh, S., Sibinga, E. M. S., Gould, N. F., Rowland-Seymour, A., Sharma, R., Berger, Z., Sleicher, D., Maron, D. D., Shihab, H. M., Ranasinghe, P. D., Linn, S., Saha, S., Bass, E. B., & Haythornthwaite, J. A. (2014). Meditation Programs for Psychological Stress and Well-being: A Systematic Review and Meta-analysis. *JAMA Internal Medicine*, *174*(3), 357–368. https://doi.org/10.1001/jamainternmed.2013.13018

Gu, J., Cavanagh, K., & Strauss, C. (2018). Investigating the Specific Effects of an Online Mindfulness-Based Self-Help Intervention on Stress and Underlying Mechanisms. *Mindfulness*, *9*(4), 1245–1257. https://doi.org/10.1007/s12671-017-0867-y

Gu, J., Strauss, C., Bond, R., & Cavanagh, K. (2015). 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. *Clinical Psychology Review*, *37*, 1–12. https://doi.org/10.1016/j.cpr.2015.01.006

Kabat-Zinn, J. (1990). *Full catastrophe living: How to cope with stress, pain and illness using mindfulness meditation*. Delacorte.

Kabat-Zinn, J. (1994). *Wherever you go there you are: Mindfulness meditation in everyday life*. Hyperion.

Kazdin, A. E. (2007). Mediators and mechanisms of change in psychotherapy research. *Annual Review of Clinical Psychology*, *3*, 1–27. https://doi.org/10.1146/annurev.clinpsy.3.022806.091432

Keetharuth, A. D., Brazier, J., Connell, J., Bjorner, J. B., Carlton, J., Taylor Buck, E., Ricketts, T., McKendrick, K., Browne, J., Croudace, T., & Barkham, M. (2018). Recovering Quality of Life (ReQoL): a new generic self-reported outcome measure for use with people experiencing mental health difficulties. *British Journal of Psychiatry*, *212*(1), 42–49. https://doi.org/10.1192/bjp.2017.10

Khoury, B., Lecomte, T., Fortin, G., Masse, M., Therien, P., Bouchard, V., Chapleau, M.-A., Paquin, K., & Hofmann, S. G. (2013). Mindfulness-based therapy: A comprehensive meta-analysis. *Clinical Psychology Review*, *33*(6), 763–771. https://doi.org/10.1016/j.cpr.2013.05.005

Khoury, B., Sharma, M., Rush, S. E., & Fournier, C. (2015). Mindfulness-based stress reduction for healthy individuals: A meta-analysis. *Journal of Psychosomatic Research*, *78*(6), 519–528. https://doi.org/10.1016/j.jpsychores.2015.03.009

Kroenke, K., Spitzer, R. L., Williams, J. B., & Löwe, B. (2009). An Ultra-Brief Screening Scale for Anxiety and Depression: The PHQ–4. *Psychosomatics*, *50*(6), 613–621. https://doi.org/10.1016/S0033-3182(09)70864-3

Lindsay, E. K., & Creswell, J. D. (2017). Mechanisms of mindfulness training: Monitor and Acceptance Theory (MAT). *Clinical Psychology Review*, *51*, 48–59. https://doi.org/10.1016/j.cpr.2016.10.011

Mathieu, J. E., Aguinis, H., Culpepper, S. A., & Chen, G. (2012). Understanding and estimating the power to detect cross-level interaction effects in multilevel modeling. *The Journal of Applied Psychology*, *97*(5), 951–966. https://doi.org/10.1037/a0028380

Naliboff, B. D., Smith, S. R., Serpa, J. G., Laird, K. T., Stains, J., Connolly, L. S., Labus, J. S., & Tillisch, K. (2020). Mindfulness-based stress reduction improves irritable bowel syndrome (IBS) symptoms via specific aspects of mindfulness. *Neurogastroenterology & Motility*, *32*(9), e13828. https://doi.org/10.1111/nmo.13828

Pan, H., Liu, S., Miao, D., & Yuan, Y. (2018). Sample size determination for mediation analysis of longitudinal data. *BMC Medical Research Methodology*, *18*(1), 32. https://doi.org/10.1186/s12874-018-0473-2

Paul, G. L. (1967). Strategy of outcome research in psychotherapy. *Journal of Consulting Psychology*, *31*(2), 109–118. https://doi.org/10.1037/h0024436

Prins, B., Decuypere, A., & van Damme, S. (2014). Effects of mindfulness and distraction on pain depend on individual differences in pain catastrophizing: an experimental study. *European Journal of Pain*, *18*(9), 1307–1315. https://biblio.ugent.be/publication/4345522/file/4345553.pdf

Segal, Z. V., Williams, J. M. G [J. Mark G.], & Teasdale, J. D. (2002). *Mindfulness-based cognitive therapy for depression: A new approach to preventing relapse*. *Mindfulness-based cognitive therapy for depression: A new approach to preventing relapse*. Guilford.

Sierra, M. (2009). *Depersonalization: A new look at a neglected syndrome*. Cambridge University Press.

Stein, E., & Witkiewitz, K. (2020). Dismantling Mindfulness-Based Programs: a Systematic Review to Identify Active Components of Treatment. *Mindfulness*, *11*(11), 2470–2485. https://doi.org/10.1007/s12671-020-01444-0

Stewart-Brown, S., Tennant, A., Tennant, R., Platt, S., Parkinson, J., & Weich, S. (2009). Internal construct validity of the Warwick-Edinburgh Mental Well-being Scale (WEMWBS): A Rasch analysis using data from the Scottish Health Education Population Survey. *Health and Quality of Life Outcomes*, *7*(1), 1–8. https://doi.org/10.1186/1477-7525-7-15

Thomson, S. B. (2010). Sample size and grounded theory. *Journal of Administration and Governance*, *5*(1), 45–52.

Valdez, C. E., Sherrill, A. M., & Lilly, M. (2016). Present Moment Contact and Nonjudgment: Pilot Data on Dismantling Mindful Awareness in Trauma-Related Symptomatology. *Journal of Psychopathology and Behavioral Assessment*, *38*(4), 572–581. https://doi.org/10.1007/s10862-016-9548-8

van der Velden, A. M., Kuyken, W [Willem], Wattar, U., Crane, C., Pallesen, K. J., Dahlgaard, J., Fjorback, L. O., & Piet, J. (2015). A systematic review of mechanisms of change in mindfulness-based cognitive therapy in the treatment of recurrent major depressive disorder. *Clinical Psychology Review*, *37*, 26–39. https://doi.org/10.1016/j.cpr.2015.02.001

Weathers, F. W., Blake, D. D., Schnurr, P. P., Kaloupek, D. G., Marx, B. P., & Keane, T. M. (2013). *The Life Events Checklist for DSM-5 (LEC-5)*. https://www.ptsd.va.gov/professional/assessment/te-measures/life_events_checklist.asp

Zhu, J., Wekerle, C., Lanius, R., & Frewen, P. (2019). Trauma- and Stressor-Related History and Symptoms Predict Distress Experienced during a Brief Mindfulness Meditation Sitting: Moving toward Trauma-Informed Care in Mindfulness-Based Therapy. *Mindfulness*, *10*(10), 1985–1996. https://doi.org/10.1007/s12671-019-01173-z

Zou, Y., Li, P., Hofmann, S. G., & Liu, X. (2020). The Mediating Role of Non-reactivity to Mindfulness Training and Cognitive Flexibility: A Randomized Controlled Trial. *Frontiers in Psychology*, *11*, 1053. https://doi.org/10.3389/fpsyg.2020.01053

ANNEX: PROTOCOL FOR REPORTING RISK

Whenever any significant risk is identified the following steps should be completed:

- Seek support from a clinical psychologist within the research team (for clinically unqualified staff members).
- Provide participants with the list of mental health services that participants can contact for (immediate) help in their region (see document “Useful contact details”).
- Notify the person’s mindfulness trainer, as soon as this is reasonably possible, such that they can manage the emerging risk if necessary.
- Complete safety form as per study protocol.

When conducting online interviews in which risk may be disclosed, the interviewer should establish the telephone number and location of the participant at the start of the call and clarify the boundaries of confidentiality as per study protocol. If immediate risk is disclosed, the interviewer should not hang up if at all possible. In case contact is lost, the participant should be informed that the interviewer / supervisor will call them back straight away but that if they are unable to make contact the participant’s mindfulness trainer will be informed.