A randomised controlled trial investigating an intervention to boost decentering in response to distressing mental experiences during adolescence: the Decentering in Adolescence Study (DECADES)

Statistical Analysis Plan

Version 2

20th April 2023

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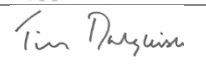
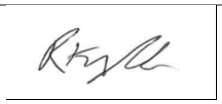
Tim Dalgleish	Principle Investigator		27-07-2023
Rachel Knight	PhD Student		27-07-2023

SAP REVISION HISTORY

Document Name	Version No.	Effective Date
DECADES Statistical Analysis Plan	1	03-05-2023
DECADES Statistical Analysis Plan	2	27-07-2023

Contents

1.0 Administrative Information

Sponsor:

Sponsor Reference:

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Chief Investigator: Tim Dalgleish

Trial Statistician: Peter Watson

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Latest Protocol:

The purpose of the document is to specify the data analyses, prior to commencement, for the DECADES clinical trial.

2.0 Abbreviations

ADI	*Adolescent Decentering Inventory*
CAMM	*Child and Adolescent Mindfulness Measure*
CAS	*Coronavirus Anxiety Scale*
CES-D	*Centre for Epidemiological Studies – Depression Scale*
CERQ	*Cognitive Emotion Regulation Questionnaire*
DERS	*Difficulties in Emotion Regulation Scale*
ESM	*Experience Sampling Methods*
ESRC	*Economic & Social Research Council*
ESST	*Emotional Stop Signal Task*
EQ	*Experiences Questionnaire*
OBT	*Own Body Task*
RCADS	*Revised Child Anxiety and Depression Scale*
RT	*Reaction Time*
SD	*Standard Deviation*
SDQ	*Strengths and Difficulties Questionnaire*
STAXI	*State-Trait Anger Expression Inventory-2*
WEMWBS	*Warwick-Edinburg Mental Wellbeing Scale*

3.0 Introduction

The purpose of this Statistical Analysis Plan (SAP) is to provide a framework that addresses the protocol objectives in a statistically rigorous fashion, with minimized bias or analytical deficiencies. Specifically, this plan has the following purpose to prospectively (a priori) outline the types of data analyses and presentations that will address the study objectives in the protocol, and to explain how the data will be handled and analyzed, adhering to commonly accepted standards and practices of statistical analysis.

3.1 Background and Rationale

Adolescence is a key period for development of common mental health difficulties such as anxiety or depression [1]. As such, this developmental stage presents a key opportunity to intervene in early mental health difficulties and to bolster good mental wellbeing. One strategy for intervention is through targeting of therapeutic skills that may assist young people in managing distressing internal events, for example unpleasant thoughts, feelings or memories, which otherwise lead to short-term distress and long-term risk of mental health difficulties such as anxiety and low mood. Psychological decentering may be one such skill.

Psychological decentering, or decentering, is a ubiquitous therapeutic skill defined as an adaptive way of observing the self, in which one can attend to not only the content of distressing internal experiences, but also the idea that these internal experiences are imperfect models of the real-world rather than precise reflections [2]. Decentering therefore relates to how individuals interact with uncomfortable mental experiences, by creating an objective self-perspective in which one can notice these experiences as inexact models of the real-world, rather than the "absolute truth". For example, in response to a disappointing exam result, one might think "I am noticing I am having a thought that I'm stupid" rather than immediately believing the thought "I am stupid". By doing this, decentering reduces the impact of these distressing experiences on emotion, mood, behavior and self-concept [3]. Indeed, therapeutic exercises that elicit an objective self-perspective in acute moments of distress have been found to attenuate emotional reactivity towards unpleasant internal events. In addition, current literature indicates that higher self-reported decentering is associated with fewer symptoms of anxiety and depression in adolescence, and improved wellbeing (Knight et al, in prep).

Research suggests that decentering is a malleable skill which can be developed through specific practice, typically during psychological therapy [4]. Medium-to-large changes in self-reported decentering are observed in adults experiencing anxiety and depression following a range of interventions, including cognitive behavioural therapy, acceptance-based approaches, and mindfulness training [2]. There is initial evidence to suggest that therapy-related changes in decentering precede reductions in symptoms, thus may be a common pathway through which psychological interventions impact anxiety and depression [5], [6]. Recent studies have aimed to investigate whether decentering can be specifically trained with the aim of reducing mental health symptoms. This has been achieved with adults, with participants trained in self-distancing techniques reporting a significant increase in self-reported decentering compared with an active control group [7]. The self-distancing group also rated negative memories as less distressing upon completion of the intervention. At present, there have been no studies to the authors' knowledge that have investigated whether decentering could be specifically trained in an adolescent population, and whether this would impact their mental health.

The Current RCT

This is an RCT of a novel intervention for adolescents with significant symptoms of low mood. It aimed to evaluate an intervention training decentering as a cognitive skill, developed by the researchers. This intervention incorporates a range of decentering techniques taken from a number of evidence-based psychological therapies. The universal nature of this technique across therapeutic interventions may point to decentering as an active ingredient in psychological therapy, thus training decentering may lead to increases in mental wellbeing.

3.2 Objectives

The *primary* objective of the trial is to evaluate the efficacy of a novel intervention targeting development of psychological decentering as a cognitive skill, delivered over audio tapes, for the treatment of symptoms of low mood in adolescents not currently receiving formal psychological input, compared with an active control condition.

4.0 Study Methods

4.1 Trial Design

The design is a randomised controlled feasibility trial (comparing effectiveness of psychological decentering training to an active control programme) with school aged adolescents. Participants were allocated to decentering or active control in a 1:1 ratio.

4.2 Randomisation

Following baseline assessment, participants will be stratified according to depression severity (using the CES-D). They will then be randomly assigned to either the decentering training programme or the active control condition. This will be managed by the trial statistician using a minimisation procedure.

4.3 Sample Size

The primary training outcome is self-rated decentering and this will be assessed using both a popular inventory of decentering (Experiences Questionnaire; EQ [8]). Power and sample calculations were therefore based on the effect of training condition on EQ scores. A power analysis calculated in G*Power indicated that a total sample size of 90 is powered at 80% to observe a significant effect of training condition (decentering vs active control) on post-intervention decentering, with a medium effect size of $f=0.3$ ($\alpha=0.05$) after adjusting for baseline EQ score. A medium effect size is plausible given that previous research reports a medium–large effect of extant psychological intervention on EQ scores. An attrition rate of around 20% is anticipated based on our previous research. Therefore, with 57 participants in each group, the current study is adequately powered to observe a medium to large effect of decentering training on our candidate training outcome measures and to determine the nature of this interaction. Regarding our secondary mental health outcomes (i.e., anxiety, depression and psychological well-being), a sample size of 57 per group is consistent with our previous research to evaluate the impact of novel psychological interventions. That is, such group sizes can provide a reasonable range of point estimates of the effect on mental health outcome measures that are sufficient to guide later research; for example, 57 participants per group is powered at 88% to observe a significant ($p<0.05$) main effect of group (decentering vs active control) on baseline adjusted mental health outcomes with an effect size $f=0.26$.

4.4 Framework

DECADES is a two-group, parallel, feasibility trial, using a frequentist approach to data analysis.

4.5 Interim analyses and stopping guidance

No efficacy interim analyses were planned. However, analysis of recruitment rates, withdrawal rates, etc. were conducted at intervals during the study. There were no formal stopping rules for the trial.

4.6 Timing of outcome assessments

Self-rated inventories of training and mental health outcomes will be assessed at three time points: within 1 week prior to the start of programme (baseline); within the third week of training (mid-intervention); and 1 week after the programme has finished (post intervention).

5.0 Statistical Principles

All hypothesis testing will be at the two-side 5% statistical significance level. Confidence intervals for parameter estimates will be at the corresponding 95% level. Analyses will be carried out by the trial statistician or delegated to an appropriately skilled statistician. Analysis will be blinded to group identity, (i.e. 'subgroup' blind).

5.1 Adherence and protocol deviations

All data will be collected irrespective of participant adherence. Should a patient withdraw consent or be lost at mid or post intervention time points, all data will be included in the study dataset up to the point of consent withdrawal or loss to mid or post intervention and will be included in the study database, unless explicitly refused by the participant.

5.2 Analysis population

The primary analysis will be of the 'Intention-to-Treat' population (ITT) defined as all subjects briefed for the intervention to which they were allocated irrespective of treatment actually received or adherence to intended treatment. No further populations have been defined for analysis.

6.0 Trial Population

6.1 Eligibility

6.1.1 Participant Inclusion Criteria

Trial participants must:

- be aged 16-19 at trial entry;
- score 16 or greater on the CES-D;
- have given consent to be contacted for further studies; and
- have access to a laptop/desktop computer and a personal smartphone.

6.1.2 Participant Exclusion Criteria

Exclusion criteria are:

- currently taking part in a regular (once or more per week) yoga and/or mindfulness class/workshop;
- have participated in prior formal meditation training or a mindfulness-based stress reduction course;
- currently experiencing chronic illness (e.g., epilepsy, chronic pain, cancer);
- lack fluency in English;
- have a recent (within past 6 months) diagnosis of, and are currently receiving medical/psychological treatment for, a mental health condition including (but not limited to) anxiety disorder, major depressive disorder or a traumatic stress disorder;
- have a diagnosis of a neurodevelopmental condition such as autism spectrum disorder or attention deficit/hyperactivity disorder; and
- have severe hearing difficulties.

6.2 Recruitment and participant flow

Patient recruitment and flow will be illustrated through a diagram as indicated in the Appendix, consistent with the CONSORT guidelines.

6.3 Withdrawal

Withdrawal from the study will be summarised and reasons documented. Non-adherence to treatment does not constitute study withdrawal.

6.4 Baseline participant characteristics

A comparison will be made of baseline characteristics between the study groups. This will be through the use of summary statistics alone with no inferential analyses.

The following patient variables will be reported at baseline:

(i) Demographic details, including age and sex.
(ii) CES-D score [9]
(iii) Experiences Questionnaire (EQ) score [8]
(iv) Revised Child Anxiety and Depression Scale (RCADS) [10]
(v) Warwick-Edinburg Mental Wellbeing Scale (WEMWBS) [11]
(vi) State-Trait Anger Expression Inventory-2 (STAXI-2) [12]
(vii) Strengths and Difficulties Questionnaire (SDQ) [13]
(viii) Cognitive Emotion Regulation Questionnaire (CERQ) [14]
(ix) Difficulties in Emotion Regulation Scale (DERS) [15]
(x) Child and Adolescent Mindfulness Measure (CAMM) [16]
(xi) Adolescent Decentering Inventory (ADI)
(xii) Coronavirus Anxiety Scale (CAS) [17]

7.0 Analysis

The primary null hypothesis is that there is no difference in EQ scores between decentering and active control groups at mid and post intervention time points. Statistical significance, (i.e the level to reject the null hypothesis) is set at the two-sided 5% level.

7.1 Outcome definitions

7.1.1 Primary Outcome

The primary outcome is the EQ score at mid and post intervention time points. The EQ, a validated self-report questionnaire, is the gold standard questionnaire used to measure decentering. The analysis will include an adjustment for baseline scores.

7.1.2 Secondary Outcomes

The following mental health related outcomes will be analysed at mid and post intervention, adjusted for baseline score:

- Depression using the CES-D
- Anxiety using the RCADS
- Broad Strengths and Difficulties using the SDQ
- Anger using the STAXI
- Wellbeing using the WEMWBS

7.1.3 Additional Questionnaire Data

A number of exploratory analyses will also be conducted on additional mid and post study questionnaires, adjusted for baseline score:

- Emotion Regulation, using the CERQ and the DERS
- Mindfulness, using the CAMM
- Covid-19 related anxiety, using the CAS

7.1.4 Additional Task Data

Two cognitive tasks were included at the three time points. For these tasks, a number of variables will be calculated from the raw data, detailed below:

- Self-Referential Processing Task (or Own Body Task (OBT)) [18]
    - Commission Error Index
    - Mean Reaction Time Index
- Affective Cognitive Control Task (or Emotional Stop Signal Task (ESST)) [19]
    - Sustained Attention & Inhibitory Control in Emotionally Neutral Circumstances
        - Mean Reaction Time on Go trials
        - Inter-Trial Variability
        - Mean Stop Signal Reaction Time
    - Sustained Attention & Inhibitory Control in Negative Emotionally Valenced Circumstances
        - Mean Reaction Time on Go trials
        - Inter-Trial Variability
        - Mean Stop Signal Reaction Time

For further information on how these variables were calculated, please see supplemental materials. These variables will be analysed at mid and post intervention, adjusted for baseline score.

7.1.5 Daily Mood Data

A brief end of day questionnaire included a measure of mood, assessing presence and duration of different mood states. Nine moods were investigated—happy, lively, content, satisfied, depressed, bored, anxious, irritable and tense. Exploratory analysis of how individuals' moods may relate to the two experimental conditions will be conducted.

7.1.6 Adherence Data

The end of day questionnaire also included a question to indicate engagement with the programme on a given day. This will be analysed to explore possible effects of group on adherence.

7.1.7 Experience Sampling Methods (ESM) Data

The initial study protocol indicated that a minimum of 33% completion of ESM questionnaires would be needed to analyse ESM data. As only 29% of participants met this minimum threshold, analysis of ESM data will not be included.

7.2 Analysis Methods

For primary and secondary outcomes, analysis of covariance will be calculated to estimate the effect of training condition on outcome measures after adjusting for baseline performance and grouping stratification variables. This model will be calculated for our primary end-point, that is, post-intervention (i.e., post intervention outcome adjusted for baseline score). This model will additionally be calculated for our mid-intervention time point (i.e., mid-intervention outcome adjusted for baseline score).

Additional questionnaires will be analysed in the same manner using analysis of covariance, estimating effect of training condition on measures after adjusting for baseline performance and grouping stratification variables. This model will be calculated for mid and post intervention time points.

Initial analyses will be performed to check task validity. For the OBT, this will include a 2x2 analysis of variance to confirm that participants had slower reaction times (RTs) and higher rates of error on difficult trials during the task. For the ESST, this will include validating that the task adjusted to produce ~50% successful stops when participants were presented with the stop signal. This will also include ascertaining whether participants were slower to respond on negatively valenced trials compared with neutral. Subsequently, analysis of covariance will be calculated to estimate the effect of training condition on task performance after adjusting for baseline performance and grouping stratification variables. This model will be calculated for mid-intervention and post-intervention time points.

7.3 Missing Data

All efforts to avoid missing data will be made i.e. researchers will check that measures are completed at each assessment point. For both the primary and secondary outcomes the extent and possible patterns of missing data will be checked. The relationship between baseline variables and missing primary outcome data will be examined.

If a subset of items of a measure (<20% within-measure missing data), a total score will be calculated using the mean score across the non-missing items. Otherwise, the score for that measure will be noted as missing. We will assume that data will be missing at random and address this using standard imputation approaches in SPSS for baseline data.

7.4 Sensitivity analyses

For this analysis, the primary efficacy analysis will be repeated including only those participants who completed questionnaires at all three time points.

7.5 Deviations from planned analysis

Should any additional statistical analyses be required during the final analysis, appropriate methods will be used, and any changes, including the rationale for use, will be documented in the clinical study report or manuscript.

7.5 Safety data

Safety data (adverse events reported from time of briefing to 1 week post-intervention) will be summarized by group. Any serious adverse events will be described in full including possible relationship to the intervention.

8.0 Description of Tables and Figures

All raw data will be presented to the original number of decimal places. The mean and standard deviation will be presented with to 2 decimal places or 3 significant figures depending upon the nature of the data. Percentages will be presented in to 1 decimal place. All categories of variables will be presented even if there is no data. Blank cells, were data are not expected, will be filled by '-' in reporting of results.

Precision of p-values will be 3 decimal places, i.e. p-values less than 0.001 will be presented as <0.001 and if equal to 1 then ≥ 0.999.

9.0 Software

Analysis will be performed using SPSS® Software version XX.

10.0 References

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11.0 Appendix

Illustration of Participant Flow

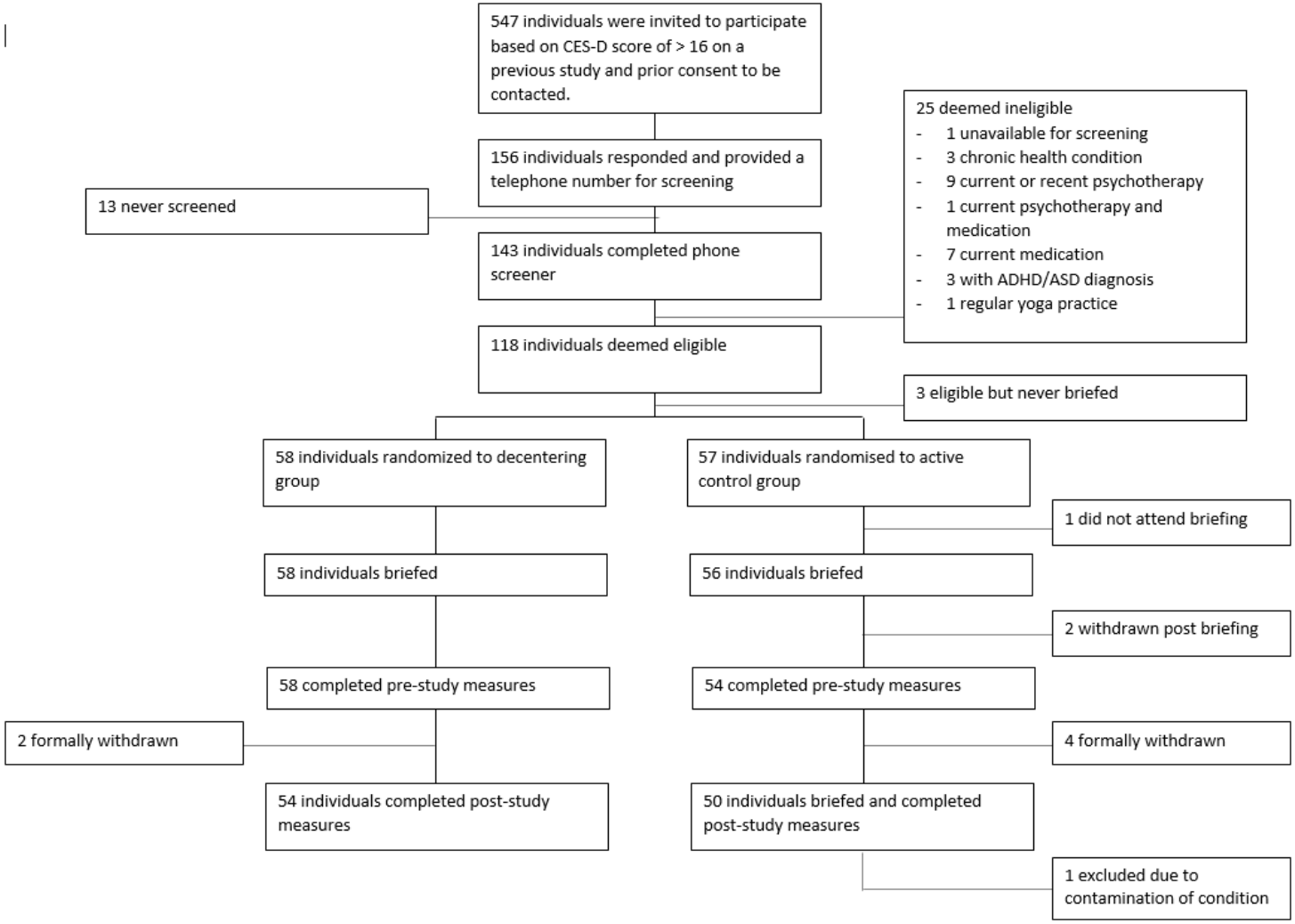

Table 1.0 *Exclusion criteria at screening/baseline*

Exclusion Criteria:	
Chronic Health Condition	3
Current or Recent Psychotherapy	10
Medication	7
ADHD/ASD Diagnosis	3
Regular Yoga Practice	1
Unavailable for Screening	1
Eligible but Did Not Attend Briefing	3
Total	28

Supplemental Information: *Further Information on Calculation of Task Analysis Variables*

OBT

Further information on the OBT is available here [2]. The OBT has two conditions with two possible iterations. For the own body condition, the participant must indicate whether the glove is on the left or right hand for an easy condition (facing away from the participant) and a hard condition (facing towards the participant). For the lateralization condition, the participant must indicate whether the glove is on the left or right side of the screen:

- Own Body Condition (Hard) – Front Facing
- Own Body Condition (Easy) – Back Facing
- Lateralisation Condition – Front Facing
- Lateralisation Condition – Back Facing

The calculated variables from this task are shown below:

Variable	
Commission Errors Index	(Front Facing Own Body % Errors – Front Facing Lateralisation % Errors) – (Back Facing Own Body % Errors - Back Facing Own Body % Errors)
Reaction Time Index	(Front Facing Own Body Mean RT – Front Facing Lateralisation Mean RT) – (Back Facing Own Body Mean RT - Back Facing Own Body Mean RT)

ESST

Further information on the ESST is available here [2]. During the ESST, participants respond to a go-signal (e.g. press left to a left arrow) unless it is followed by a stop-signal (an upwards arrow). In the ESST, go-signals are preceded by a neutral or negative image.

The calculated variables from this task are detailed below:

Sustained Attention & Inhibitory Control	
Reaction Time	Mean RT on Neutral Go Trials
Inter-Trial Variability	Mean RT on Neutral Go Trials/SD on Neutral Go Trials

Stop Signal Reaction Time	Mean Stop Signal Reaction Time on Neutral Trials
Sustained Attention & Inhibitory Control in Emotional Circumstances	
Reaction Time Difference on Emotional Trials	Mean RT on Negative Go Trials - Mean RT on Neutral Go Trials
Inter-Trial Variability Difference on Emotional Trials	(Mean RT on Negative Go Trials/SD on Negative Go Trials) - (Mean RT on Neutral Go Trials/SD on Neutral Go Trials)
Stop Signal Reaction Time Difference on Emotional Trials	Mean Stop Signal Reaction Time on Negative Trials - Mean Stop Signal Reaction Time on Neutral Trials