ASSESSING THE EFFICACY OF IMAGERY-ENHANCED COGNITIVE BEHAVIORAL GROUP THERAPY FOR SOCIAL ANXIETY DISORDER: A PILOT STUDY

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ABSTRACT

Cognitive behavior group therapy (CBGT) is effective for social anxiety disorder (SAD), but a substantial proportion of patients do not typically achieve normative functioning. Cognitive behavioral models of SAD emphasize negative self-imagery as an important maintaining factor, and evidence suggests that imagery is a powerful cognitive mode for facilitating affective change. This study will compare two group CBGT interventions, one that predominantly uses verbally-based strategies (VB-CBGT) and another that predominantly us imagery-enhanced strategies (IE-CBGT), in terms of (a) efficacy, (b) mechanisms of change, and (c) cost-effectiveness.

This study is a parallel group (two-arm) single-blind randomized controlled trial. A minimum of 96 patients with SAD will be recruited within a public outpatient community mental health clinic in Iran. The primary outcomes will be self-reported symptom severity, casernes (SAD present: yes/no) based on a structured diagnostic interview, and clinician-rated severity and life impact. Secondary outcomes and mechanism measures include blind observer-rated use of safety behaviors, physiological activity (heart rate variability and skin conductance level) during a standardized speech task, negative self-beliefs, imagery suppression, fear of negative and positive evaluation, repetitive negative thinking, anxiety, depression, self-consciousness, use of safety behaviors, and the EQ-5D-5L and TiC-P for the health economic analysis. Homework completion, group cohesion, and working alliance will also be monitored. The outcomes of this trial will inform clinicians as to whether integrating imagery-based strategies in cognitive behavior therapy for SAD is likely to improve outcomes. Common and distinct mechanisms of change might be identified, along with relative cost effectiveness of each intervention.

Keyword: *Behavioral group therapy, social, Anxiety Disorder, Efficacy, CBGT*

1. INTRODUCTION

Social anxiety disorder (SAD) is characterized by significant and persistent fear of social situations where embarrassment, rejection, or scrutiny is possible [1]. SAD is one of the most common anxiety disorders [2], with 12.1% of adults suffering from the condition in their lifetime [3]. The National Institute for Health and Care Excellence (NICE) recommend cognitive behavioral therapy (CBT) as the first line treatment [4], and a range of CBT-based protocols have been evaluated and deemed efficacious, whether delivered in groups or individually [5]. However, in group CBT the majority of patients fail to return to normative functioning, so further treatment innovations are required [6].

CBT for SAD typically targets maintaining factors described in Clark and Wells' [7,8] and Rapee and Heimberg's [9] models. Individuals with SAD develop excessively high standards for social performance, leading to negative predictions about the consequences of such interactions (e.g., “If I express my opinion, I'll be rejected”), and

unconditional negative beliefs about the self (e.g., "I'm unlikeable"). People with SAD also form a mental representation of the self and how others see them (i.e., from an observer perspective) [9,10]. Critically, this mental representation is not based on objective feedback, but is rather internally constructed based on a combination of long-term memory, internal cues, and observable feedback from others. The aim of CBT in SAD is to assist clients to modify these processes via verbal-linguistic techniques such as identifying negative thoughts, considering contrary evidence, and developing more realistic probability and cost estimates of the feared outcome. Avoidance and safety behaviors are relinquished via behavioral experiments so that negative thoughts can be directly tested and, ultimately, more realistic memories of social situations can be created. Attentional biases and excessive self-focused attention are corrected via training to refocus on the task at hand [11,12], and negatively biased self-images are modified via video feedback [12–14]. Some individual CBT protocols have included additional mental imagery-based techniques (e.g., imagery descripting [11]). However, it has recently been argued that using imagery-based strategies more comprehensively in therapy may more powerfully exploit the particularly strong relationship between imagery and emotion both for reducing negative emotion and bolstering positive emotion [15–18]. The aims of the present study are to compare IE-CBGT with verbally based cognitive behavioral group therapy (VB-CBGT) for SAD in terms of (a) efficacy, (b) mechanisms of therapeutic change across behavioral and physiological parameters, and (c) cost-effectiveness.

2. MATERIAL AND METHODS

2.1. Design

This study is a parallel group (two-arm) single-blind randomized controlled trial (RCT) comparing the efficacy, mechanisms of change, and cost-effectiveness of a novel group cognitive behavioral therapy (IE-CBGT), with VB-CBGT in patients with SAD. The unit of randomization will be the patient. Primary outcomes will be measured in both arms at baseline (intake assessment), 1-month, and 6-month follow-ups.In addition, the primary self-report symptom measure will be measured prior to treatment sessions 4, 8, and 12 of both 12-session treatments. Patients will complete a video-recorded speech task with concurrent physiological monitoring at baseline and 1-month and 6-month follow-ups.

The resulting videos will be blind rated for behavioral manifestations of anxiety. Other mechanism and/or symptom measures will be administered prior to every session (i.e., depression, anxiety, fear of negative and positive evaluation, probability and cost of a reference negative social outcome), or prior to the 1st, 4th, 8th and 12th sessions (i.e., negative self-portrayals, imagery suppression, imagery ability, self-consciousness, performance anxiety, safety behaviors, self-beliefs), in addition to the follow-up sessions. A measure of repetitive negative thinking will be administered at baseline and at the follow-ups only. For the health economic analyses, a measure of health-related quality of life will be administered at baseline and both follow-ups, and a measure of medical consumption and productivity losses associated with psychiatric illness will be administered at baseline and 6-month follow-up. A measure of homework completion will be administered prior to sessions 2, 5, 8, and 11, a measure of working alliance will be administered prior to sessions 3, 6, and 9, and a measure of group cohesion will be administered prior to sessions 4, 7, and 10. The trial will be conducted in a community mental health clinic that administers additional measures for service evaluation that will not be used as primary or secondary outcomes of this trial. Any subsequent studies exploring outcomes on these additional measures will explicitly state that they were not preregistered as primary or secondary trial outcomes.

2.2. Hypotheses

Our primary hypothesis is that IE-CBGT will be superior in reducing social anxiety symptoms as measured by the Social Interaction Anxiety Scale (SIAS) [20], the percentage of individuals with a SAD diagnosis as measured using the Structured Clinical Interview for DSM-5 (SCID-5) [1], and clinician-rated severity (8-point severity scale) at 1-month and 6-months post-treatment. Clinician-rated severity at 1-month follow-up will be based on current severity, not 6-month severity. Our secondary hypotheses are that patients receiving IE-CBGT will show more adaptive behavioral and physiological responding to a social stress task [21] at 1-month post-treatment. In addition, changes in negative self-beliefs [22], repetitive negative thinking [23], self-focused attention [24], and avoidance and safety behaviors [25,26] are expected to mediate symptom change for both treatments, but IE-CBGT is expected to result in larger decreases in these mediators. A reduction in imagery suppression [27] is expected to only mediate symptom changes for IE-CBGT. It is further hypothesized that IE-CBGT will be more cost-effective than VB-

CBGT in terms of i) cost per quality adjusted life years (QALYs) gained, and ii) cost per unit symptom improvement, as measured using the TiC-P [28] and EQ-5D-5L [29].

2.3. Eligibility criteria

All patients referred to the clinical service for SAD will initially be invited to participate. Patients who are over 18 years of age, who have had stable medications for ≥1 month, who are willing to be randomized, and who meet criteria for SAD on the SCID-5 [1], will be eligible to participate. Patients will be excluded if they meet diagnostic criteria for bipolar disorder, psychosis, or substance use disorder on the SCID-5, are currently receiving CBT elsewhere, or are deemed to be of high suicidal or self-harm risk (i.e., with plans and/or intent). All participants will remain under the care of their referring psychiatrist or general practitioner and may hence be offered psychotropic medication (e.g., antidepressants) if needed. There are no restrictions on the use of medications in the trial (except stable dosage/type for ≥1 month prior to trial enrolment) but any changes in the type of medication taken or dosage used will be recorded.

2.4. Recruitment

The primary recruitment port will be the Centre for Clinical Interventions (CCI) located in iran. The CCI is a specialist public mental health service that 1) treats adults suffering from complex anxiety, affective and eating disorders, 2) conducts clinically applied research, and 3) provides training and supervision for mental health practitioners in psychotherapy. As a clinical facility that regularly conducts clinically applied quality improvement and research studies, psychologists and psychiatrists, and has systems in place for undertaking basic research (e.g., using self-report questionnaires) with all patients undergoing treatment, as well as conducting more complex studies (e.g., RCTs). We plan to recruit a minimum of 96 patients, 48 in each treatment arm.

The psychologist conducting the initial evaluation via telephone will invite patients who are deemed suitable for the service to discuss the study with a treating clinical psychologist at their first in-person appointment. The treating clinical psychologist will provisionally assess the patient's eligibility for research based on clinical judgment of the above criteria and confirm diagnostic decisions using the SCID-5 [1]. If eligible (i.e., diagnostically on SCID-5) and interested in participating, the patient will proceed to meet with a trial assessor with Masters or PhD level psychology qualifications, who will obtain written informed consent. Patients meeting the inclusion criteria will be included in the study, and a baseline assessment will be conducted that includes self-report questionnaires and a social stress test alongside behavioral/ physiological monitoring [21]. The trial assessor will administer the SCID-5 [1] to 20% of the sample – randomly selected from a list derived from www.random.org to judge diagnostic concordance between raters. After the baseline assessment, patients will be randomly assigned to receive one of the two treatments.**2.5.**

2.5. Randomization and concealment

The randomization schedule will be arranged prior to recruitment within random block sizes of 24 or 26 with an equal allocation to IECBGT or VB-CBGT within each block. Random block sizes of 24 or 26 were chosen to ensure that if the maximum of 12 participants per groupis reached for any pair of groups (total N = 24) then the allocation of the final participants cannot be guessed and thus unmasked at any point prior to treatment commencing. All assessors and clinicians will be blind to block size and condition allocation prior to treatment, and clinicians will be provided with a client list immediately prior to the commencement of each group. Assessors will remain blind throughout the trial. The randomization will be concealed from the trial clinical psychologist and assessors by use of an off-site computer-based randomization procedure (www.random.org). The randomness is derived from true random number generation, which for many purposes is superior to pseudo-random number algorithms typically used in computer programs. The sequence will be generated by the study statistician (RTK). This sequence will be provided to the research coordinator (MPH) in concealed, sequentially numbered envelopes who will provide participants with details of their group in their randomized condition only after their pre-treatment assessment has been completed.

2.6. Interventions

Both protocols target the same maintaining factors (e.g., negative cognitions, avoidance, safety behaviors, self-focused attention, negative beliefs about how others perceive them, and core beliefs), but differ critically in the mode within which they are modified. In this trial, both treatments will consist of 12, 2-hour group therapy sessions (of between 6 and 12 individuals) scheduled on a weekly basis plus a one-month group follow-up session. Separate

follow-up assessment appointments will be made at 1-month and 6-months post-treatment. The verballybased protocol uses verbal-linguistic techniques with no explicit reference to mental imagery. This protocol is similar to one that has previously been detailed extensively [12], so will only briefly be overviewed here. Across sessions, patients are taught about the causes and maintenance of SAD, and are subsequently coached to identify and challenge unrealistic beliefs through consideration of alternative evidence. For example, individuals are given the opportunity to identify anxiety-provoking situations and attendant thought processes, to estimate the likelihood of feared outcomes, and are encouraged to develop alternative explanations for these. Verbal strategies (e.g., downward arrowing and evidence-gathering) are used in VB-CBGT to challenge and modify core beliefs. Video-feedback arguably challenges selfimages, but within the VB-CBGT protocol this technique is completed with reference to challenging how patients think they appear to others rather than self-images specifically.

The imagery-enhanced protocol has been extensively described elsewhere [14,19], and encourages patients to focus on multi-sensory negative social images as a key maintaining factor and imagery monitoring, rather than verbal thoughts and thought monitoring. Cognitive challenging involves identifying predictions about social threat within the imagery mode with the rationale of increasing specificity and vividness, and increasing affective engagement. Following an investigation of the probability and cost of key elements of this image, participants elicit a description of and then vividly evoke a more helpful image. Behavioral experiment predictions are guided by negative imagery rather than thoughts, and after new information is collected from an experiment patients are encouraged to envisage the situation again whilst incorporating the new, non-threatening information. Imagery exercises are included in all within-session behavioral experiments, such as prior to manipulating the use of safety behaviors (e.g., imagining engaging in a conversation with and then without safety behaviors prior to completing this task in vivo; imagining fully engaging attention on the task at hand prior to engaging in an attention focusing task during an in vivo conversation). Negative core beliefs are identified and challenged in IE-CBGT via past imagery receipting techniques and new, more positive core beliefs are developed via future-oriented imagery techniques. The rationale provided for video-feedback is explicitly to challenge self-imagery. Detailed descriptions of all elements of the treatment are provided in McEvoy et al. [30]. In both treatments, weekly homework will be allocated and compliance monitored [31]. Client-therapist alliance [32] and group cohesion [33] will be assessed at 3-weekly intervals throughout treatment.

2.7. Intervention fidelity

Treating clinicians will include existing certified CCI clinical psychologists plus one trial-specific (assessing) clinical psychologist. Treating clinical psychologists will be thoroughly trained by the project investigators (PMM, LMS) who have extensive experience with the protocols, involving (a) reading comprehensive manuals with detailed therapist instructions, scripts, and client handouts; and (b) co-facilitation of one group with an experienced facilitator (PMM, LMS) or another certified clinician, before being certified. All sessions will be recorded and two sessions from every group will be randomly selected and independently coded for protocol compliance. Treatment fidelity will be evaluated using the Cognitive Therapy Rating Scale (CTRS) [34], which will be rated annually by independent clinicians to detect any potential therapist drift. Treating clinicians will be trained in and alternately run both protocols to control for therapist-specific factors, and will receive weekly supervision to review client progress and address clinical issues arising from sessions. All sessions will be co-facilitated by a secondary clinician or clinical psychology trainee. Treating clinicians will require a masters and/or doctorate in clinical psychology.

3. OUTCOME

3.1. Primary outcomes

The primary outcomes include one self-reported symptom measure, diagnosis based on a structured diagnostic interview, and clinician rated severity. Self-reported social anxiety severity will be assessed using the SIAS [20], which is a measure of social interaction anxiety.

Blind assessors will administer the SCID-5 [1] to determine the presence or absence of DSM-5 defined SAD at 1-month and 6-months post treatment. Clinician-rated symptom severity will be assessed on an 8- point rating scale reflecting severity relative to other people with the disorder and life impact.

3.2. Secondary outcomes

Secondary outcomes will be measured at baseline, throughout the trial at various points, and at 1- and 6-month follow-ups as per Table 1.

Table 1

Administration schedule for outcome measures.

	Assessment point														
Measure	**Pre-Tx**	**Sess.1**	**Sess. 2**	**Sess. 3**	**Sess. 4**	**Sess. 5**	**Sess. 6**	**Sess. 7**	**Sess. 8**	**Sess. 9**	**Sess. 10**	**Sess. 11**	**Sess. 12**	**1 M F/U**	**6 M F/U**
BFNE-S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FPE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROMIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tracking Measure		+	+	+	+	+	+	+	+	+	+	+	+	+	+
SIAS*	+	+			+				+				+	+	+
SPS	+	+			+				+				+	+	+
CAQ	+				+				+				+	+	+
SAFE	+				+				+				+	+	+
SBSA	+				+				+				+	+	+
SCS	+				+				+				+	+	+
VVIQ	+				+				+				+	+	+
NSPS	+				+				+				+	+	+
EQ-5D-5L	+													+	+
SCID-5*	+													+	+
RTQ-10	+													+	+
TiC-P	+													+	+
HRS-II			+			+			+			+			
WAI					+		+			+					
GCS						+		+			+				
TSST (+Psychophysiology)	+													+	+

Note: Pre-Tx: Pre-treatment/baseline; Sess. 1 … Sess. 12: Sessions 1–12; 1 M F/U: 1-month follow-up; 6 M F/U: 6-month follow-up. Measures: BFNE-S: Brief Fear of Negative Evaluation– Short Form; CAQ: Cognitive Avoidance Questionnaire; EQ-5D-5L: Europol Five Dimension Health Questionnaire; FPE: Fear of Positive Evaluation Questionnaire; GCS: Gross Cohesion Scale; HRS-II: Homework Rating Scale; NSPS: Negative Self Portrayal Scale; PROMIS: Patient Reported Outcome Measurement System; RTQ-10: 10-item Repetitive Thinking Questionnaire; SAFE: Subtle Avoidance Frequency Examination; SBSA: Self-Beliefs Related to Social Anxiety Scale; SCID-5: Structured Clinical Interview for DSM-5; SCS: Self Compassion Scale; SIAS: Social Interaction Anxiety Scale; SPS: Social Phobia Scale; Tic-P: Questionnaire on Medical Consumption and Productivity Losses Associated with Psychiatric Illness; TSST: Trier Social Stress Test; VVIQ: Vividness of Visual Imagery Questionnaire; WAI: Working Alliance Inventory. Asterisks indicate primary outcomes (SIAS, SCID-5 diagnosis and severity).

Consistent with previous SAD trials patients will complete a video-recorded speech task, which is modeled on the Trier Social Stress Test (TSST) [21] at baseline and at the 1-month follow-up. Participants are asked to perform an impromptu speech about their suitability for a mock job opportunity to the experimenter and a video camera. Physiological activity (heart rate variability via electrocardiogram and skin conductance level) is recorded before, during, and after the speech. A range of symptom and cognitive self-report measures will be administered to test

hypotheses about mechanisms and moderators of change. The Social Phobia Scale (SPS) [20] is a measure of anxiety in situations involving observation by others, and thus more strongly assesses performance anxiety than other facets of SAD. It has high internal consistency (α= 0.94) and test-retest reliability (r= 0.93). The Negative Self Portrayal Scale (NSPS) [22] assesses concern about perceived negative self-attributes (e.g., lacking personality, stuttering) exposed for public scrutiny in social situations. It has excellent internal consistency (α = 0.96), and good test-retest reliability (r =0.75). The Cognitive Avoidance Questionnaire (CAQ) [24] will act as a key IECBGT-specific mediator measuring imagery suppression; tendency to actively transform distressing images into less distressing verbal thoughts. It has high internal reliability (α =0.87). The Vividness of Visual Imagery Questionnaire (VVIQ) [27] will be administered to measure self-reported imagery ability as a potential treatment moderator. The Brief Fear of Negative Evaluation – Straightforwardly Worded (BFNE-S) [35] is a self-report measure of fear or worry about being negatively evaluated. It has excellent internal reliability (α =0.96) and validity [36]. The Fear of Positive Evaluation Scale (FPE) [37] measures fear and distress related to positive evaluation from others, a core feature of social anxiety. It has high internal consistency (α= 0.80) and test-retest reliability (ICC= 0.70, $p < 0.001$). The Repetitive Thinking Questionnaire (RTQ-10) [23] is a transdiagnostic measure of repetitive negative thinking with high internal reliability (α > 0.90) and sensitivity to change. The Self Consciousness Scale (SCS) [24] will be administered; this scale consists of 7 public selfconsciousness items plus 6 items assessing tendency to take an external, observer's perspective during interactions. Internal consistency is excellent (α =0.93). The Self-Beliefs Related to Social Anxiety (SBSA) Scale [38] will be administered to assess enduring maladaptive beliefs related to social evaluative situations. The SBSA indexes three types of beliefs across three subscales (high standard, conditional, and unconditional).

The SBSA has good test-retest reliability – full scale (r =0.81), and subscales (all r = 0.78), whilst internal consistency is high – full scale (α= 0.94), and subscales (range α= 0.85–0.91) [39]. Emotional symptoms will be assessed by the PROMIS (Patient Reported Outcome Measurement System) anxiety and depression scales [40], which are 8-item measures of anxiety and depression. Self-reported safety behaviors and subtle avoidance will be measured using the 32-item Subtle Avoidance Frequency Examination (SAFE) [25], which has strong internal reliability (α= 0.91) and clear convergent and discriminant validity. The primary outcome measure of health-related quality of life will be the EQ-5D-5L [29], a standardized self-report measure providing a single value for health status. It comprises five dimensions (mobility, self-care, usual activities, pain or discomfort, anxiety or depression) with each dimension having five response levels, and has been shown to have good convergent validity with the World Health Organization 5-item Wellbeing questionnaire. Data on health services used by patients and costs arising as a result of productivity losses will be collected using an adapted version of the TiC-P Adults Questionnaire on Medical Consumption and Productivity Losses associated with Psychiatric Illness [28]. The Homework Rating Scale (HRSII) [31] consists of 12 questions regarding homework completion over the past week. This will be completed prior to every third treatment session. A brief, in-house developed, 'tracking measure' indexing clients' perceived probability and cost of social fears during a hypothetical performance situation will be administered at each treatment session and at follow-up. Working alliance will be assessed using the 12-item Working Alliance Inventory (WAI) [32]. This measure is a reduced revision of an original 36-item measure of therapist-client alliance and has demonstrated good psychometric characteristics. The 9-item Gross Cohesion Scale (GCS) [33] is a brief measure designed to assess the degree of perceived cohesiveness and bond among members of a group. The GCS has shown adequate reliability and validity, and has been used as measure of group cohesiveness in CBT trials for anxiety. Treatment fidelity will be evaluated using the Cognitive Therapy Rating Scale for Social Phobia (CTRS) [34], which will be adapted to assess the two protocols and rated by independent clinicians.

3.3. Adverse events

Risk assessments will be conducted on each patient during the initial clinical and trial assessment. Patients assessed as high risk will be referred to the appropriate services according to risk management protocols at CCI. Patients who disclose an increase in their risk during treatment will be managed as per CCI's risk management protocol and this will be documented and reported as an adverse event. Patients whose risk becomes high during the trial will be excluded from the study and this will be reported to the relevant ethics committees at WA Health and Curtin University within one month. Serious adverse events, such as suicide attempts, will be managed according to CCI's risk management protocols and the WA Health and Curtin ethics committees will be informed immediately (within 24 h of the lead investigator being notified). Clinicians will all be informed that the project chief investigator (PMM) must be informed of all adverse events. PMM will provide weekly clinical supervision so that any adverse events can be closely monitored. All project staff will be inducted and made aware of risk management protocols prior to commencing employment at CCI.

3.4. Monitoring of additional treatments

Our inclusion criteria state that patients who have been prescribed medications are required to have had a stable dose (including antidepressant medication) for ≥1 month prior to starting group therapy. Participants will be asked at follow-up what, if any, medications or alternative treatments they have used during or after treatment so that this can be considered as a potential confound. Specifically, patients will be asked "Have you engaged in any treatment (medications, psychological, alternative, or any others) for your social anxiety disorder (or other psychological disorder) since you completed treatment at CCI? If so, what and how often?" The Tic-P [28] will comprehensively assess use of health services at 6-month follow-up.

4. STATISTICAL CONSIDERATIONS

4.1. Data analysis

4.1.1. Analyzing continuous treatment outcomes

Non-linear change across the duration of the study is expected. In these circumstances, the most powerful approach to data analysis (regardless of the significance of the Time x Group interaction) is to teatime as an ordered categorical (i.e., ordinal) variable and focus on between- group comparisons at each post-treatment assessment (e.g., post treatment, 1-month follow-up, 6-month follow-up) after controlling for between-group differences at baseline. The 1-month follow-up is nominated as the primary endpoint, because historical data suggest that differences between treatments will be optimal at that point [14]. If the outcome measure does not have a normal distribution, but is nevertheless distributed according to a well-understood function (e.g., gamma, inverse Gaussian), then between-group comparisons will be tested via a Generalized Linear Mixed Model (GLMM) that specifies this function. Two types of GLMM will be tested. The potential clustering of outcome data within treatment groups will be acknowledged in one model but not the other. The better fitting model will be selected. The method of analysis will depend on whether the slope of the treatment trajectories is non-linear (in which case time would once again be treated as an ordered categorical variable and analyzed as before) or linear (indicating a piecewise growth curve analysis [41]). Standardized rates of reliable and clinically significant change will be calculated and compared at 1- and 6-month follow-up (e.g., [42]). For each outcome variable, a GLMM will be developed in which working alliance, group cohesion, homework compliance, and group size are tested as potential predictors of the outcome. Significant predictors will then be included as covariates in the analysis of that outcome.

4.1.2. Analyzing the binary diagnostic outcome

A GLMM will be tested to determine whether the imagery-enhanced group contributes to a better diagnostic outcome for SAD than the verbally-based group. The GLMM will include one nominal random effect (participant), one nominal fixed effect (group: imagery-enhanced, verbally-based), one ordinal fixed effect (time: 1-month follow-up, 6- month follow-up), and the Group× Time interaction. The GLMM will use a binomial probability distribution for the outcome (SAD: yes, no) and link it to the fixed effects with a logit function. Once again, two types of GLMM will be tested. The potential clustering of outcome data within treatment groups will be acknowledged in one model but not the other. The better fitting model will be selected. Simple main effects tests will be used to test for between group differences in casernes at 1- and 6-month follow ups.

4.1.3. Testing moderated mediation

Structural Equation Modeling (SEM), with single indicator latent variables to control for measurement error, will be used to determine i) whether the relationship between time (Session 4, Session 8, post treatment, 1-month follow-up, 6-month follow-up) and SIAS is mediated by changes in negative self-beliefs, repetitive negative thinking, self-focused attention, and avoidance and safety behaviors, and ii) whether group (IE-CBGT, VB-CBGT) moderates the strength of the time mediator pathway and the mediator-symptomatology pathway. The approach to the moderated mediation analysis follows that of Hofmann et al. [43]. The error inherent in the psychometric measures will be included in the estimation of the SEMs. Clustering of outcome data within treatment groups will be accommodated by using a sandwich estimator for the standard error of each path coefficient [44]. Standard errors will then be adjusted with a bootstrapping procedure in order to minimize the impact of any non-normality in the data.

4.1.4. Balancing Type I and Type II error rates

Conducting multiple statistical tests on the secondary outcomes will inflate the familywise error rate (FWER; the probability of at least one false positive). Inflation of the familywise error rate is normally controlled by applying a Bonferroni adjustment to the per-test alpha-level.

This involves partitioning the familywise alpha of 0.05 equally across the secondary outcomes. Because tentative hypotheses were formulated for each of the secondary outcomes, however, the FWER can be partitioned across the hypotheses according to the relative importance attributed to each (cf. the Holm's procedure, cited in [45]). If there are three hypotheses, for instance, and it is considered to be three times more important to test Hypotheses 1 than the other 2, then the familywise alpha can be divided in a way that reflects this weighting. This would involve setting the per-test alpha at 0.03 for H1, and 0.01 for both H2 and H3. Analyses of the primary outcomes (SIAS, SAD diagnosis, and severity) are driven by hypotheses derived from strong empirical and theoretical bases, and will therefore be evaluated at the conventional per-test alpha level of 0.05.

4.2. Sample size estimation

We are planning for a minimum of 12 groups with an average of 8/ group (N = 96) to ensure feasibility to detect a small to medium effect size, as indicated by our pilot work [14]. However, we will continue to recruit for the duration of the funding period (from July 2016 until December 2019) to derive a larger sample size so that smaller effect sizes can be detected. Larger numbers will enable greater precision in effect size estimates and will also allow for multiple comparisons and additional analyses of multiple moderators/mediators. Assuming negligible variance is accounted for by dependencies on the outcome measures within the 12 treatment groups, 98 participants (49 in each group) are required for an 80% chance of detecting a 'moderate' (d = 0.51) difference between the two group means for a one-tailed test at an alpha-level of 0.05. There are many procedures for estimating an adequate sample size for the binary logistic regression - each procedure based on its own prescriptive set of assumptions. We estimated the sample size required for capturing a 'moderate' association between group (imagery-enhanced, verbally-based) and recovery (yes, no) at each post-treatment assessment. Assuming once again that negligible variance is accounted for by intra-group dependencies on the diagnostic measure, 96 participants (48 in each group) will provide sufficient power for an 80% chance of detecting a 'moderate' (w = 0.29) association between group and recovery. Each of the four moderated mediator models (one for each of the four mediators) includes 15 free parameters (i.e., parameters that must be estimated from the data). In order to reliably test an SEM, Kline [46] has recommended that we have at least five participants for each free parameter in the model. Our planned sample size of 96 exceeds the minimum sample size (N = 75) required for testing our model, hence contributing to the appropriateness of implementing SEM.

4.3. Handling missing data

Missing outcomes can potentially bias the results of clinical trials. We will limit the frequency of missing data by attempting to collect follow up measures from all participants, including those who do not complete treatment. Participants will receive a series of phone, text, and email contacts to schedule, and reschedule (where necessary), assessment appointments. If participants refuse to return to the clinic to complete a full assessment, permission will be sought to collect diagnostic interview data via telephone as a minimum. Contact will be made within three days of each assessment via a phone call and one text message reminder. All missed treatment sessions will be followed up by the treating clinician by phone call and/or text message, plus an email with the weekly questionnaires to be completed and returned at the next session. Individual sessions will be allowed if clients are in crisis or specifically request this, which will be noted for consideration in subsequent analyses. Analyses will utilize techniques (such as GLMM and multiple imputation) that make full use of all observed data and help correct for potential biases caused by missing observations. We will conduct sensitivity analyses to evaluate the potential impact of missing data on the robustness of our findings, as recommended by the National Research Council Panel on Handling Missing Data in Clinical Trials [47].

4.3.1. Data management

Data will be stored securely in password protected and de-identified databases at CCI and Curtin University. A separate password protected database will be stored in the same location containing participant's names and ID numbers only. All paper-based questionnaires will be securely stored on site at the clinic in a locked medical records room. Twenty percent of all data will be independently checked for accuracy. Once the study has been completed, the electronic data will be stored in the University's data repository.

4.3.2. Statistical software

The software used to implement the analyses described above will be chosen at the time of the analysis; possible packages are SPSS [48], Mplus [49], SmartPLS [50], Stata [51], and R [52].

4.3.3. Cost-effectiveness analysis

The primary economic evaluation will be a cost-effectiveness analysis comparing differences in costs and quality adjusted life years (QALYs) between the two groups over the duration of the trial and at 1- and 6-month follow-ups. Differences in costs (use of services and productivity losses) and health effects will be estimated as the difference between values at post-treatment time points (i.e., 1- and 6-month follow-ups for the ED-5D-5L, 6-month follow-up for the TiC-P) and pretreatment values and then summarized by each treatment arm. Unadjusted differences in costs and health outcomes will be tested using paired t-tests for each group. Simple regression analysis will be conducted to guide the extent to which more complex analysis can be undertaken to take account of the distributional characteristics of the data, repeated measures, and any differences in baseline characteristics despite random allocation.

5. ETHICAL CONSIDERATIONS

The trial will be conducted in accordance with the National Statement on Ethical Conduct in Human Research (2007) [53]. All patients will be informed about the research project prior to their first appointment. The purpose of the research will not be concealed from patients, although no information about the study's superiority hypotheses will be provided, and each patient will be given the opportunity to provide written informed consent prior to participating. No significant adverse side effects are expected for either VB-CBGT or IECBGT. Participants will not be paid for taking part in the research, but all therapeutic interventions will be provided without charge. Participants will be assigned a unique ID upon consenting to the study, which will be applied to all data sources throughout the trial for all study documentation (e.g., clinical measures) and recordings (e.g., physiological/ video-recordings). This unique ID will be linked to a password protected main database containing patient names, contact details and demographics, which will only be accessible to the lead investigator (PMM) on the project and study coordinator (MPH).

6. DISCUSSION

SAD is common and often disabling, and a significant proportion of sufferers do not achieve normative functioning with current treatments. Treatment innovations are clearly required that build on recent knowledge from psychological science on the impact of mental imagery on emotion [56]. This paper described the protocol for an RCT comparing two group interventions for SAD, imagery-enhanced group CBT and verbally-based group CBT. Imagery features prominently in contemporary theories of SAD [8,9,57], and evidence suggests that imagery enjoys particularly strong associations with emotion relative to verbal linguistic cognitive activity [18,58]. Preliminary evidence suggests that imagery-enhanced cognitive behavioral group therapy is particularly efficacious in reducing social anxiety symptoms [14], suggesting that use of this mode in clinical settings is likely to provide benefit to patients and treatment providers. The novel treatment approach to be tested in this study may eventually provide an alternative to patients who would otherwise not achieve full remission with ‘gold standard’ cognitive behavioral interventions [14]. In addition to measuring clinical outcomes, this study will investigate a range of potential mediators of symptom change as well as the cost-effectiveness of the imagery-enhanced treatment. If IE-CBGT improves outcomes for SAD beyond verbal-linguistic approaches, and is more cost-effective, this may have important implications for the treatment of other emotional disorders. Based on trials demonstrating large effect sizes for individual CBT (e.g., [11,13]), and superior outcomes from individual compared to group CBT [59,60], current NICE guidelines recommend individual CBT as a first line treatment for SAD [4]. While recent meta-analyses have failed to find significant differences between the efficacy of individual and group CBT [61,62] there is evidence that despite being substantially more expensive individual CBT is more cost-effective, which the authors attributed to larger effect sizes from individual CBT [63]. Our open trial of IE-CBGT demonstrated effect sizes that were substantially larger than those found in other group treatments and comparable to individual treatment effects but with less therapist time per patient [14]. It is also noteworthy that these effect sizes were achieved with larger groups sizes compared to previous group CBT trials, thereby further increasing cost-effectiveness. It is possible, however, that imagery- enhanced CBT would still be more effective and cost-effective if delivered individually. If the results of the current trial are positive, it will be important to directly compare individual versus group imagery

enhanced CBT in terms of effectiveness and cost-effectiveness. If IECBGT were found to be similarly effective and more cost-effective compared to individual imagery-enhanced CBT, this would have significant potential for increasing access to effective treatment and cost savings from a health service perspective.

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