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Internet-Delivered Interpretation Training Reduces Worry and Anxiety in Generalized Anxiety Disorder: A Randomized Controlled Experiment

Colette R. Hirsch[1,2], Charlotte Krahé[1], Jessica Whyte[1], Hannah Krzyzanowski[1], Frances Meeten[1], Sam Norton[1] and Andrew Mathews[1,3]

[1]Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom

[2]South London and Maudsley NHS Foundation Trust, London, United Kingdom

[3]Department of Psychology, University of California, Davis, California, USA

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Abstract

Objective

Generalized anxiety disorder (GAD) is a debilitating condition, characterized by negative interpretations about ambiguous situations. This study tested whether entirely internet-delivered interpretation training (cognitive bias modification; CBM) vs. control promotes positive interpretations and reduces worry and anxiety in individuals with GAD, with or without depression.

Method

A two-arm (CBM; control) parallel-group randomized controlled experiment. Assessments were pre-intervention (T0), post-intervention (T1), one-month (T2) post-intervention, and three-months (T3) post-intervention.

Participants with GAD (with or without comorbid depression) were randomly allocated to either CBM (*n*=115) or control (*n*=115). Participants, but not researchers, were blind to allocated condition.

Participants completed up to ten online CBM or control sessions across one month. Interpretation bias (co-primary outcomes: scrambled sentence test, SST; recognition test, RT) and number of negative thought intrusions during a breathing focus task were measured at T0 and T1. Self-reported levels of worry (PSWQ-trait; PSWQ-weekly), anxiety (GAD7), depression (PHQ-9), rumination (RRS), and repetitive negative thinking (RNT; RTQ-trait) were assessed at T0-T3.

Results

The per-protocol analyses included *N*=186 participants (CBM *n*=94; control *n*=92). As predicted, we found moderate-to-large training effects on the primary outcome of interpretation bias at T1. Secondary outcomes of negative thought intrusions at T1 and self-reported symptoms at T2 were all significantly lower in the CBM vs. control condition. All but one effect (trait RNT) was sustained at T3.

Conclusions

In this randomized controlled study, we found that fully online interpretation training ameliorated core features of GAD in individuals with or without comorbid depression up to three months post-training.

Keywords: generalized anxiety disorder (GAD); cognitive bias modification (CBM) interpretation training; interpretation bias; worry; depression.

What is the public health significance of this article?

Generalized anxiety disorder is a common debilitating problem with uncontrollable worry at its core. It often co-occurs with clinical depression. The tendency to draw negative conclusions from unclear/ambiguous information (interpretation bias) maintains worry, anxiety and depression. This web-based study of people with generalized anxiety disorder (GAD; with or without depression) used computerized practice in generating positive interpretations and compared this training to another (control) condition which did not alter interpretations. Positive interpretation training reduced worry, anxiety and depression up to three months after training finished. The effects were due to changes in interpretation bias.

Given the online nature of the interpretation training, this indicates for the first time that interpretation training can be effective when delivered remotely to people suffering from GAD with or without depression, opening up the possibility that this approach could be used to help people recover from anxiety and depression without attending a clinic.

Internet-Delivered Interpretation Training Reduces Worry and Anxiety in Individuals with Generalized Anxiety Disorder: A Randomized Controlled Experiment

Generalized Anxiety Disorder (GAD) is characterized by repetitive negative thinking (RNT) in the form of uncontrollable worry about possible future danger (American Psychiatric Association, 2013). In a cognitive model of pathological worry, Hirsch and Mathews (2012) proposed that worry arises in GAD due to a combination of factors, such as an automatic cognitive bias in which emotionally ambiguous events are interpreted as threatening. Supporting this hypothesis, Krahé et al. (2019) demonstrated that worry is associated with a more negative interpretation bias, and evidence of a causal role for interpretation bias in the maintenance of worry and anxiety has been found in experiments using Cognitive Bias Modification (CBM). CBM for interpretation, pioneered by Grey and Mathews (2000) and Mathews and Mackintosh (2000), adapts paradigms designed to assess interpretation bias to train a certain – usually benign – interpretive style. CBM for interpretation typically involves participants reading or listening to short ambiguous scenarios across multiple trials. Ambiguity is resolved in a consistently positive or negative manner. CBM conditions can be compared to control conditions not designed to modify interpretations (but typically involving listening to or reading similar scenarios), to elucidate the causal role of interpretation bias in maintaining worry and anxiety (see Hirsch et al., 2016, and Gober et al., 2021, for reviews).

In the form of CBM used here, participants repeatedly practice a task that involves listening to ambiguous scenarios that eventually guides participants to a benign (non-threatening) interpretation (see Hirsch et al., 2020, and the present Method section for details). In several lab-based experimental studies, researchers have found that such

repeated practice leads to more benign interpretations being made on near-transfer tasks (i.e., tests of interpretation bias), accompanied by far-transfer effects involving reductions in worry and anxiety (Hayes et al. 2010; Hirsch et al. 2018; although see e.g., Salemink et al., 2014, MacDonald et al., 2020, Wilver & Cougle 2019, who reported similar improvements in both CBM and control conditions).

Because CBM is usually administered in relatively standard form on a computer, it has the potential advantage of reaching clients who are unable or unwilling to see a therapist or attend a clinic – an issue magnified by the ongoing Covid-19 pandemic. Consequently, several recent studies have explored forms of cognitive bias modification that can be delivered via the internet (e.g., Carlbring et al., 2012; Kuckertz et al., 2014; McDermott & Dozois, 2019; Salemink et al., 2014). Some of these studies have yielded promising results, while others have been more disappointing, with outcomes no better than control conditions (e.g., Salemink et al., 2014).

Several suggestions have been made as to why some internet-based studies of CBM have not replicated earlier laboratory-based results. These include the effects of a home-based context for training which could limit compliance or emotional engagement (see e.g., Carlbring et al., 2012; De Voogd et al., 2017). Other factors limiting interpretation bias change may include the extent to which participants self-identify with the ambiguous scenarios (Standage et al., 2014), self-generate positive alternatives (Hoppitt et al., 2010), or are able to imagine positive outcomes (Holmes et al, 2006).

The present study builds on Hirsch et al. (2018), which investigated the effects of interpretation training on worry in GAD and rumination in depression. Multiple sessions of practice interpreting emotionally ambiguous scenarios in a relatively positive manner

(compared to a control condition in which ambiguity was not resolved) led to reductions in both worry and rumination, as well as anxious and depressed mood. A second study (Hirsch et al., 2020) tested an enhanced method of CBM designed to increase emotional engagement with the scenarios. Previous research has shown that individuals with GAD engage in less mental imagery than non-anxious control participants, especially during worry (Hirsch et al., 2012). Furthermore, verbal thinking in the context of worry is associated with greater attention to threat (Williams et al., 2014) and increased negative thought intrusions (Hirsch et al., 2015). The enhanced version of training involved participants vividly imagining themselves experiencing positive outcomes for several seconds after each scenario had been presented, building on earlier findings that imagery can increase emotional effects relative to thinking about the same events verbally (Holmes et al., 2006). Furthermore, participants generated their own positive outcomes (Hoppitt et al., 2010) in half of the training trials. By promoting a more imagery-based mentation style, and by asking participants to produce idiosyncratic positive resolutions for the ambiguous scenarios, this form of CBM aimed to counteract the predominantly negative and verbal mentation style typical of worry, and increase participants' engagement with positive interpretations that could aid generalization to their day-to-day lives. While both the enhanced and original forms of training used by Hirsch et al (2020) were superior to the control condition, the enhanced interpretation training (for brevity referred to later only as CBM) fostered a greater positive interpretation bias at the end of the set of training sessions, and augmented training effects on rumination and worry one month after training had been completed.

The studies by Hirsch et al. (2018; 2020) involved most of the training being carried out at home via a web platform that administered the training and control conditions. However, the initial training session, as well as baseline and post-multisession assessments, were carried out in the laboratory. The present study was designed primarily to investigate whether the effects shown for interpretation training in individuals suffering from GAD (Hirsch et al 2018), or those experiencing high levels of RNT (Hirsch et al. 2020) could be maintained in the absence of any face-to-face contact prior to, or during, the training and follow-up periods. If so, this would have important implications for the implementation of CBM, either alone or as an adjunct to other treatments, in populations not able to regularly attend clinics. Furthermore, given the high comorbidity between GAD and depression (Sartorius et al., 1996), and the possibility that such comorbidity might reduce the effectiveness of training, the current study also examined the effectiveness of our enhanced training method, delivered entirely via the internet, to volunteers diagnosed with GAD either with or without comorbid depression. While far-transfer effects were consistently shown one month after training in Hirsch et al. (2018; 2020), to test the durability of changes in symptoms we assessed whether effects on anxiety, worry, RNT and depression were sustained three months post-training.

Building on Hirsch et al.'s (2020) CBM condition, in the present study we tried to maximize participants' engagement with CBM training as described earlier. Specifically, participants were encouraged to identify with the person described in the ambiguous scenarios (Standage et al., 2014), to generate some of the positive resolutions for themselves (Hoppitt et al., 2010), and to vividly imagine the positive outcomes for several seconds from a field-perspective point of view (Holmes et al., 2006). Furthermore, after a

few sessions of CBM, we specifically asked that when participants noticed themselves worrying in day-to-day life, they should try to identify potential positive outcomes for these situations.

Our key aims were thus as follows:

1) To investigate whether the superiority shown for interpretation training at one month follow up in previous studies would be maintained in the absence of any face-to-face contact prior to, or during, the training and follow-up periods.

2) To examine whether our new CBM method would have equivalent effects on individuals with GAD who either did or did not have comorbid depression.

3) To assess whether any training effects on symptoms at one-month follow-up would be maintained at a three-month follow-up.

Our hypotheses were that:

1) CBM would result in more positive interpretations of ambiguous information compared to the control condition immediately post-intervention, regardless of comorbidity or gender.

2) CBM would lead to fewer self-reported negative intrusions during a breathing focus task immediately post-intervention, and lower levels of worry and anxiety (as well as related secondary symptoms of rumination, trait RNT, and depression) at one-month and three-months post-intervention, compared to the control condition.

3) Changes in worry, RNT and anxiety at one-month and three-months post-intervention would be mediated by post-intervention level of interpretation bias.

Methods

Experimental Design

This study was a two-arm (CBM; control), parallel-group randomized controlled experiment, with assessments at four time-points: pre-intervention (T0); post-intervention (T1); one-month (T2) post-intervention; and three-months (T3) post-intervention. Community volunteers with GAD, were randomly allocated (1:1) to one of two conditions: CBM or a control condition (henceforth CONTROL).

Study Registration

The study was pre-registered with the Open Science Framework (DOI: 10.17605/OSF.IO/KHUAB). It should be noted that in keeping with Grafton et al. (2017), we take an experimental approach to intervention development and as such view the study as an experiment; therefore, we pre-registered the primary analysis for the study as per-protocol (though we also present the intention-to-treat analysis).

Participants

Participants (n=230) with either GAD (*n*=138) or co-morbid GAD and depression (*n*=92) were recruited via advertisements on social media, websites, newspapers and via emails from King's College London and MQ: Transforming Mental Health. Participants completed an online screening questionnaire to assess initial eligibility, followed by a screening phone call to determine GAD diagnosis and suitability for the study (see CONSORT diagram Figure 1). During this call, diagnosis of GAD or co-morbid GAD and depression was established using GAD and Major Depressive Episode parts of the Structured Clinical Interview for DSM-5 Axis I disorders (SCID; First et al., 2015). An independent rater coded

10% of SCID assessments to check diagnosis; interrater agreement was excellent (intraclass correlation coefficient = .89, 95% confidence interval [.75, .95]). Table 1 displays demographic characteristics of the per-protocol sample[1].

Inclusion criteria were meeting diagnostic criteria for GAD, fluency in English, normal or corrected-to-normal vision and hearing, being aged 18 to 65 years old, experience of clinical levels of worry (i.e., total score of ≥62 on Penn State Worry Questionnaire; PSWQ; Meyer et al., 1990), and clinical levels of anxiety (i.e., total score ≥ 10 on the GAD-7; Spitzer et al., 2006). Individuals taking psychotropic medication had to be stabilized on medication for at least three-months without remission. Exclusion criteria were residing outside the UK, no registration with a UK GP, severe depression (≥ 23 PHQ-9 score; Kroenke & Spitzer, 2002), past or current risk to self (self-harm in past 12 months / suicide attempt in last two years / PHQ-9 suicidal ideation item 9 scored >1; Williams, Blackwell, Mackenzie, et al., 2013), co-morbid psychosis, bipolar disorder, borderline personality disorder or substance abuse, as well as current (or within the past six months) psychological treatment.

Sample Size

The target sample size was 230, based on 172 participants (86 per condition) providing 90% power to detect an effect size of *d*=0.5 (alpha=.05), adjusting for a correlation of .4 between baseline and one-month assessments and inflating by 25% to account for potential attrition. Of 230 participants randomized, 186 (94 CBM; 92 CONTROL) comprised the per-protocol sample; that is, completed T0-T2 and ≥ eight of ten assignments. *N*=208

[1] See Table 2 for demographic information for the Intention-to-Treat sample.

(103 CBM; 105 CONTROL) comprised the modified[2] intention-to-treat (ITT) sample, that is, completed Assessment 1 (T0) and at least one post-training assessment. The CONSORT diagram (Figure 1) displays attrition rates and reasons for exclusion[3].

Interventions

Experimental Conditions

Participants completed ten training/control sessions (within one month) using a purpose-built online platform. All online sessions began with either an RNT induction (CBM) or a neutral task (CONTROL). Then, CBM participants listened to descriptions of ambiguous scenarios and imagined themselves in each described situation, whereas CONTROL participants listened to scenarios that remained ambiguous and were not asked to resolve the ambiguity or generate images of the outcome. Participants in both conditions answered a comprehension question after each scenario (as in Hirsch et al., 2020).

Pre-Session 1 Tasks: Imagery Training vs. Filler Questionnaires

Mental Imagery Training. Prior to the first online session, participants in the CBM condition completed an exercise designed to facilitate vivid and positive mental imagery during the online sessions. Adapted from Holmes and Mathews (2005), participants first practiced imagining five neutral non-ambiguous scenarios and then five positively resolved ambiguous scenarios, rating vividness and positivity for each scenario, followed by tailored

[2] Due to missing data, since some people were randomised but never provided post-randomization data, we could not undertake analysis that strictly adhered to the intention to treat principle. Without complete data it is impossible to undertake a strict ITT analysis (White et al., 2012) and so a modified version was used.
[3] See Figure 2 for the Modified Intention-to-Treat CONSORT diagram.

feedback from the platform to encourage generation of vivid positive images (see Hirsch et al., 2020, for further details).

Filler Questionnaires. To match the time taken on the mental imagery practice for the training condition, participants in the control condition completed questionnaires (for details see Hirsch et al., 2020).

Expectancy and acceptability ratings.

These questions were created to measure study expectancy and acceptability (based on Williams, Blackwell, Holmes, et al., 2013). At the end of T0, participants completed the following items: “At this point, how logical does the program offered to you seem?” and “How useful do you think this program will be in reducing your level or worry / rumination?”. At T1, they completed the items “After having completed the program, how logical was the program offered to you?”, “How useful was this program in reducing your level of worry / rumination?” and “With what degree of confidence would you recommend this program to a friend with the same level of worry / rumination as you have?” Participants responded on a 5-point scale from 0 (not at all logical/useful/confident) to 4 (very logical/useful/confident). Results are presented in Supplementary Materials.

Main Online Scenario-Based Sessions

Participants completed an assignment on average every 3 days within the one-month intervention period (range 1-7 days between assignments).

RNT Induction or Neutral Filler Task. The RNT induction used was identical to that used by Hirsch et al. (2018) and was adapted from Hertel et al. (2014). Participants selected

a current worry and wrote down their usual negative thoughts about the topic for three minutes and then worried silently about it for two minutes.

CONTROL participants completed a time-matched neutral filler task (see Hirsch et al., 2018) instead of the RNT induction, involving reading neutral stories and making grammatical correctness judgments before answering comprehension questions.

CBM. The CBM condition (see Additional Supplemental Materials for more details) required participants to listen to new scenarios in each session describing situations relating to common worry-related themes (e.g., social situations, work performance, health and the future) which were developed on the basis of interviews with people with lived experience of GAD (Hirsch, et al., 2018).[4] Participants were asked to generate vivid field-perspective mental images for 7 seconds of either the provided positive resolution to the ambiguous scenario (50% of trials) or they self-generated a to-be-imagined positive outcome for the ambiguous scenario (50% of trials), with 40 scenarios presented each session. Participants rated how positive the image was on half the trials, and how vivid the imagery was on the other half of trials using a 0 '*not at all'* to 100 '*extremely'* visual analogue scale, with tailored feedback to encourage generation of vivid positive images. Participants also answered Yes/No 'comprehension' question relating to the ambiguity of the scenario with accuracy feedback to reinforce the positive interpretations (see Supplementary Materials Table S1 for example scenarios and comprehension questions).[5]

[4] These scenarios also included materials developed or adapted from prior research (Blackwell et al., 2015; Grol et al., 2018; Hayes et al., 2010; Hertel et al., 2014; Hirsch et al., 2018; Hirsch et al., 2009; Holmes et al., 2006; Mathews & Mackintosh, 2000).

[5] For the CBM condition comprehension questions, answers in keeping with a negative interpretation were scored as zero and a positive one as 1. Average performance across sessions was *M* = .91 (SD = .08) in the per-protocol sample and *M* = .91 (SD = .09) in the ITT sample, demonstrating that participants generated positive interpretations, as instructed.

CONTROL. Participants heard 50 new ambiguous scenarios in each session (the increased number was selected to match time spent on the CBM assignments) taken from Hirsch et al. (2020). Unlike the active condition, the ambiguity remained unresolved and participants were not asked to resolve scenarios or generate any mental images. Scenarios were either followed by a Yes/No 'comprehension' question (as above) relating to participants' interpretation of the scenario but without feedback (50% of trials), or participants were asked questions relating to a factual element of the scenario (50% of trials), which were followed by accuracy feedback.[6]

Outcomes

Tasks assessing interpretation bias as well as a behavioral breathing focus task (assessing negative thought intrusions) and questionnaires assessing mood (anxiety and depression) and RNT (worry, rumination, trait RNT) were administered via the online platform at T0 and T1. Only questionnaires were re-administered online at T2 and T3.

Primary Outcome Measures: Interpretation Bias Measures

Scrambled Sentences Test (SST). The Scrambled Sentences Test (SST) is commonly used in the field as a measure of interpretation bias (Everaert et al., 2013, 2014; Hirsch et al., 2018; 2020). Originally developed by Wenzlaff & Bates, 1998, 2000), the task presents participants with six words in a jumbled order (e.g., '*achieve goals will I my won't*') and they are instructed to use five of the six presented words to create a grammatically correct sentence

[6] For the control condition, responses in keeping with negative and positive interpretations were scored as zero and 1, respectively. Average performance on the ambiguity comprehension questions across control condition sessions was *M* =.42 (*SD* = .18) in both per-protocol and ITT samples, indicating that participants were fairly even-handed in making negative and positive interpretations (as expected). For the fact-based accuracy questions, incorrect and correct answers were scored as zero and 1, respectively. Average performance was *M* = .84 (*SD* = .11) in the per-protocol sample and *M* = .83 (*SD* = .11) in the ITT sample, indicating that participants generally performed well in answering the factual questions.

whilst holding a string of six digits in mind. The trials are such that four of the words can be used to form an ambiguous sentence that is resolved in either a positive or negative manner depending on the selection of the fifth word (e.g., 'I will achieve my goals' or 'I won't achieve my goals'). This task therefore involves resolution of ambiguity due to the selection of one or the other meaning. A greater tendency to interpret ambiguous information in a negative manner is indexed by more sentences being completed in keeping with a negative interpretation. Participants completed 20 items (10 depression SST and 10 worry SST items; as in Hirsch et al., 2018, 2020). The worry SST shows excellent construct validity and reliability (Krahé, Meeten & Hirsch, in prep). Inclusion of this task enables an assessment of generalization of training to an interpretation task that is very different in format to the training itself.

Recognition Test (RT). Participants read ten ambiguous worry-related scenarios and later rated the similarity between each scenario and four presented statements (Mathews & Mackintosh, 2000; see Hirsch et al., 2018; 2020, for details and example items). Two statements resolved ambiguity in the scenario in either a positive or negative way (targets); the other two statements were positive or negative foils that were not related to possible interpretations. A recognition test (RT) index was computed by subtracting mean similarity ratings for negative targets from mean ratings for positive targets; higher scores denoted a more positive interpretation bias. Two fixed-order lists of ten items were generated and list order counterbalanced across participants at T0 and T1.

Secondary Outcome Measures

Breathing Focus Task. This task was adapted from an established behavioral measure of worry developed by Borkovec, Robinson, Pruzinsky, and DePree (1983) and refined by

Ruscio and Borkovec (2004). The task measures the frequency of negative thought intrusions (i.e., negatively valenced thoughts that come to mind unbidden) sampled during a breathing focus task. Worry involves streams of negative verbal thoughts triggered by an initial negative intrusive thought about possible threat or danger (Hirsch & Mathews, 2012). The occurrence of negative thought intrusions during breathing focus has previously served as a lab-based proxy of worry (Hayes et al., 2010; Hirsch et al., 2009). In the present study, participants were instructed to focus on their breathing for five minutes and indicate at randomly cued intervals whether they were focusing on their breathing, or experiencing a thought intrusion (Eagleson et al., 2016). Thoughts were sampled randomly every 20 to 30 seconds and participants categorized the thought content as 'breathing' 'negative', 'positive', or 'neutral' by selecting the relevant word on screen.

Standardized Self-Report Questionnaires. Trait worry was assessed using the PSWQ (computed in the ITT sample; Cronbach's α = .71 at baseline). Additionally, the Penn State Worry Questionnaire-Past Week (PSWQ weekly; Stöber & Bittencourt, 1998) assessed levels of worry over the past week (Cronbach's α = .81). Trait rumination was measured using the Ruminative Response Scale (RRS; Nolen-Hoeksema & Morrow, 1991; Cronbach's α = .90) and trait RNT was measured using the Repetitive Thinking Questionnaire (RTQ-T; McEvoy et al., 2014; Cronbach's α = .83). Depressive symptoms were assessed with PHQ-9 (Cronbach's α =.74) and anxiety symptoms using the GAD-7 (Cronbach's α = .73).

Randomization and Blinding

Participants were randomized to CBM or CONTROL conditions using a random allocation sequence generated by a researcher who was not part of the study using Microsoft Excel. Each cell of the randomly allocated list was concealed in Microsoft Excel

and individual cells were revealed by the experimenter only at the time of randomization. Experimenters enrolled participants and assigned them to conditions based on the allocation sequence. Participants, but not experimenters, were blind to the allocated condition until after the final follow-up assessment (a single-blind design).

Procedure

Upon enrolment into the study, participants were provided with secure access to the online platform where they could view the dashboard and access all the assessments and sessions, as well as seeing how many sessions they had completed to date. They were asked to complete the baseline assessment and first training session within 24 hours (i.e., CBM or CONTROL) and they then had up to a month to complete nine further sessions. At T0, participants completed SST, RT and breathing focus tasks and questionnaires (PSWQ trait, PSWQ weekly, RRS, PHQ-9, GAD-7, RTQ-T)[7]. Participants were given a rationale for completing the online sessions (same for both conditions; see Additional Supplementary Materials for wording) and completed acceptability and expectancy ratings (as in Hirsch et al., 2018; 2020). The same day, participants completed imagery training (CBM) or filler questionnaires (CONTROL) and their first training session (CBM or CONTROL). Participants then completed the remaining nine sessions (each lasting 30-35 minutes) across the next month. Researchers remotely monitored participant progress using the online platform and made brief contact with participants through their chosen communication method to facilitate engagement and trouble-shoot issues (see Additional Supplementary Materials for

[7]Participants also completed the Spontaneous Use of Imagery Scale (SUIS; Reisberg et al., 2003) at T0 and assimilation and imagination ratings based on Standage et al. (2014) at T1, not reported here (see Supplementary Materials Table 2 for an overview of which measures were completed at each time point, and Supplementary Materials for more information on assimilation and imagination ratings).

more information). Additionally, participants received automated emails and texts encouraging them to apply the techniques they were learning to day-to-day life (CBM condition) or to continue with their progress (CONTROL; see Additional Supplementary Materials for more details). Between 24-hours and one-week after completion of the final training session, participants completed the T1 assessment (questionnaires, interpretation bias measures, breathing focus task, acceptability ratings, and for the CBM condition, assimilation and positive outcome identification ratings).[8] Questionnaires were completed again at T2 and T3. Participants received £130 ($166) for completing the study. The study was approved by the first author's university ethics committee.

Statistical Methods

The main efficacy analyses, including key sensitivity analyses, were conducted by the study statistician (SN) blind to group allocation, following a pre-specified analysis plan. This plan was finalized and approved by the study team before completion of data collection and was published on the OSF (DOI: 10.17605/OSF.IO/KHUAB).

The main analyses, reported in the Results, were conducted on the 'per-protocol' sample (*N*=186) since the primary concern of this experimental study was to assess potential efficacy of an 'optimal dose' of CBM (set at ≥8/10 sessions; see Hirsch et al., 2018; 2020) in reducing anxiety and worry. In addition to completing at least eight sessions[9], participants in the per-protocol sample had completed all assessment points and had not started treatment or changed medication at any time point between T0 and T3. We repeated analyses using a

[8]See Supplementary Materials for details regarding these ratings. Additionally, T1-T3 contained an "adverse events form" (see Hirsch et al., 2018) and no adverse events or side-effects were reported.
[9] See Supplementary Materials Table S3 for number of participants completing up to a given number of assignments in per-protocol (n=186) and intention to treat samples (n=208).

modified 'intention-to-treat' (ITT; *N*=208) sample (see also White et al., 2012) including participants who had completed T0 and at least one post-training assessment (T1-T3). A 5% significance level was set for all analyses.

Training Efficacy Analyses

The training effect of CBM for interpretation bias (SST and RT) at T1 was estimated using linear regression. Training condition was entered as a dummy-coded variable and the baseline level of the outcome was included as a covariate. Co-morbid depression and gender were included as dummy-coded covariates. Robust standard errors were estimated to protect against violation of distributional assumptions. Participants who completed fewer than half the sentences on the SST were excluded from each analysis on a case-by-case basis.

For questionnaire outcomes assessed at T1-T3, CBM training effects were estimated using linear mixed-effects models. This method allowed for the inclusion of individuals with data available for at least one post-training assessment, under the assumption that where assessments were missing, the data were missing at random. The baseline level of the outcome (T0), training condition, time (dummy coded), and condition by time interaction terms were included as covariates to allow estimates of the effect of condition at each time point to be calculated. Again, co-morbid depression and gender were included as dummy-coded covariates. Robust standard errors were estimated to protect against violations of distributional assumptions.

Mediation Analyses

To confirm that the mechanism of action was as expected, we examined whether training-related changes in interpretation bias (assessed using SST and RT) mediated the

effect of training on worry (PSWQ trait and PSWQ weekly), RNT (RTQ-T) and anxiety (GAD-7). A latent variable modelling approach was used to estimate the indirect effect of CBM on each outcome at T2 and T3, via the putative mediator (interpretation bias) measured post-intervention (and controlling for baselines scores). Specifically, the indirect effect was estimated using the product of coefficients approach (MacKinnon, 2012). The indirect effect was expressed as standardized units and as the proportion of the total training effect.

Subgroup Analysis

The study was not specifically powered to investigate interaction effects. However, exploratory analyses were undertaken to examine whether training effects on measures of interpretation bias varied by gender. Furthermore, analyses were conducted to determine whether effects on measures of interpretation bias, worry (trait and weekly), anxiety and depression differed between those with or without comorbid depression. Although exploratory, this was part of the pre-registered analysis plan. Results are presented in Supplementary Materials Figures S1 and S2.

Results

Below, we report findings from the per-protocol analyses as the primary analysis of the study. Interpretation of the analyses using the intention to treat (ITT) sample (also presented below) in all cases mirrored those in the per-protocol sample, indicating that potential selection biases with regards to the per-protocol sample did not influence the substantive conclusions drawn from the results.

Efficacy of CBM in Promoting Positive Interpretations

As predicted (Hypothesis 1), CBM was associated with more positive interpretations at T1 compared to the control condition (see Table 3). Effects were moderate-to-large for both measures of interpretation bias. On the SST, participants in the CBM condition unscrambled more sentences in a positive manner than did participants in the control condition ($p < .001$; Hedge's $g = 0.67$): Mean (SD) SST index = .60 (.21) in the CBM condition and .49 (.23) in CONTROL (see Table 3). On the RT, again participants in the CBM condition made more positive interpretations than did the control condition ($p < .001$; Hedge's $g = 1.32$): Mean (SD) RT index = 1.18 (0.75) in CBM and 0.10 (1.02) in CONTROL. Subgroup analyses indicated that these effects were unlikely to vary by gender or by presence of co-morbid depression (see Figures S2 & S3). Data were missing for 9 and 1 participants in the per-protocol sample for the SST and RT, respectively. Pattern mixture models, including all randomized participants providing baseline data (n=221), demonstrated that under no feasible scenario would non-random missing data across either group reduce the group difference to non-significant (see Figure S3). Furthermore, the intention-to-treat sample, which included an additional 22 participants excluded from the per-protocol sample, indicated a very similar pattern of results (see Table 4).

Efficacy of CBM in Reducing Negative Thought Intrusions, Worry and Anxiety

Self-Reported Negative Thought Intrusions. At T1, participants in the CBM condition reported significantly fewer negative thought intrusions during the breathing focus task, compared to the control condition (Hedge's g = -0.80), supporting Hypothesis 2: Mean (SD) = 0.93 (1.25) in CBM and 2.50 (2.25) in CONTROL; see also Table 5. The same results were found in the ITT sample (Hedge's g = -0.83; see Table 6).

Worry and Anxiety. Participants in the CBM condition experienced significantly lower levels of worry (measured by PSWQ trait and PSWQ weekly) and anxiety (GAD-7) at T1 and T2, and effects were sustained at T3, providing support for Hypothesis 2 (see Table 5; see Table 6 for corresponding findings in the ITT sample). Effect sizes were moderate-to-large for worry (Hedge's g at three-months follow-up = -0.69 for PSWQ trait, *g* = -0.74 for PSWQ weekly) and smaller for anxiety (*g* = -0.47 for GAD-7). The number of participants who exhibited reliable improvement in anxiety by T3, a decrease of 4 points or more on GAD-7 (see Jacobson & Truax, 1991; Toussaint et al, 2020), was greater in the CBM than CONTROL condition, as shown in Table S4 in supplementary materials. The number of participants experiencing reliable deterioration by T3 was less than 5% for both conditions.

Efficacy of CBM in reducing secondary symptom measures of rumination, trait RNT and depression

Supporting Hypothesis 2, participants in the CBM (vs. CONTROL) condition experienced significantly lower levels of rumination (RRS), general RNT (RTQ-T) and depression symptoms (PHQ-9) at T1 and T2. These effects were also found at T3, except for the RTQ-T, for which the group difference was not significant at T3 (see Table 5; Table 6 shows corresponding findings in the ITT sample). Effect sizes were small to moderate (Hedge's *g* at three-month follow-up = -0.34 for RRS, -0.33 for the RTQ-T, and -0.43 for PHQ-9).

Together, these results support Hypothesis 2. CBM was successful in reducing levels of negative intrusions immediately post-intervention, and in effecting continued reductions in levels of worry, anxiety, and secondary symptom measures of depression, rumination and trait RNT one month following the end of the online program. Importantly, these beneficial effects of CBM were still evident at three-month follow-up.

Mediation Analyses

Interpretation bias as measured by both the SST and RT mediated effects of CBM on PSWQ trait, PSWQ weekly, RTQ-T and GAD-7 at T1–T3, with the proportion of the effect mediated ranging from 7% to 100% (see Table 7). Given that T1 measures of interpretation bias (SST and RT) were strongly correlated (r = .47), and all outcomes were also correlated (see Supplementary Materials Table S5 for table of correlations), the separate mediation analyses do not represent independent mediated effects, but together provide support for the hypothesized mechanism of interpretation bias mediating effects on psychological outcomes (i.e., worry, repetitive thinking and anxiety; Hypothesis 3).

Discussion

This is the first study of GAD to assess whether interpretation bias can be effectively modified using a fully internet-delivered program, with no face-to-face contact, and whether this leads to sustained reductions in worry and anxiety. Our hypotheses regarding the efficacy of CBM were fully supported: interpretation training, enhanced with engagement in prolonged mental imagery and self-generation of positive outcomes, promoted a more positive interpretation bias. Importantly, interpretation training was also associated with reductions in negative intrusions on the breathing focus task immediately post-training, and reduced levels of worry in the past week, as well as levels of trait worry, RNT and anxiety at one-month follow-up. Notably, all differences remained significant at three-month follow-up, with the single exception of the trait RNT questionnaire. Indeed, on the basis of clinically significant change scores in anxiety based on the GAD-7 (Toussaint et al., 2020), by 3 months follow-up 78.43% of participants in the CBM condition showed improvement, compared to 57.69% of the control condition. There was also no indication of iatrogenic effects of CBM

relative to the control condition. Moreover, the training effects generalized to greater reductions in rumination and depression in the CBM condition compared to the control condition, suggesting that this form of interpretation training could also be beneficial for those with depressive disorders alone.

A review of meta-analyses has called for improved CBM methods to target key cognitive processes in psychopathology in order to facilitate sustained symptom reduction (Jones & Sharpe, 2017). The current experiment achieved this aim. It replicated and extended findings of Hirsch et al. (2018) and Hirsch et al. (2020) by utilizing an enhanced form of training completed fully online. Our results show that the CBM intervention was highly effective in promoting a more positive interpretation bias, compared to a control condition, in those suffering from GAD. To our knowledge, this is the first study of interpretation training in GAD to demonstrate such promising findings from a fully web-based interpretation training program. It is particularly encouraging that comorbid depression did not mitigate these effects. Indeed, despite all participants being trained using worry-related materials (rather than tailoring materials to participants' dominant form of RNT as in Hirsch et al., 2020), the intervention also led to sustained reductions in levels of rumination and depression symptoms. Taken together, this supports the view that worry and rumination are two forms of a more general repetitive negative thinking process (Ehring & Watkins, 2008). Furthermore, mediation analyses confirmed the key role of interpretation bias as the mechanism of action in reducing anxiety, worry and RNT. Hence, our findings support the causal role of interpretation bias in maintaining worry and anxiety in those with GAD (see Hirsch & Mathews, 2012), as well as supporting transdiagnostic approaches to

intervention where the underlying mechanisms are assumed to be common across disorders.

We conceived of this study primarily as an experiment to test whether an online intervention with assessments and training administered solely via the internet could reduce worry and anxiety in GAD. Given this aim, we consider the per-protocol analyses as the primary test of hypotheses, while also noting that the intention-to-treat analyses provided essentially the same results. No adverse events associated with the intervention (or control condition) were reported. Furthermore, 94% of participants completed at least the baseline assessment and one training/control session, and 82% of participants in the training condition and 80% in the control condition completed at least 8/10 sessions. Good engagement and acceptability were demonstrated by high accuracy on comprehension questions embedded in the online sessions and by acceptability ratings (see Supplementary Materials). Together, these features indicate the potential clinical scalability of the intervention, which can be completed at times and locations most convenient for clients. This may prove particularly helpful for those who are unable or unwilling to attend clinical facilities, and more generally during the ongoing Covid-19 pandemic, which has seen a move to remote therapy (Moreno et al., 2020) as well as a rise in mental health app usage (ORCHA, 2021). Critically, Holmes et al. (2020) noted that developing digital psychological interventions based on knowledge of the underlying mechanisms driving poor mental health is a key research priority during the Covid-19 pandemic. Our CBM intervention is an example of a mechanism-focused online intervention, with good efficacy over 3-month follow up, that can easily be accessed in people's homes.

Whilst future clinical trials are needed to confirm its efficacy as a standalone intervention, the effect size for anxiety (post CBM) in the current study was 0.60 (T1; intention-to-treat sample for comparability). Whilst this is lower than the end-of-treatment effect reported in a recent meta-analysis of online interventions for GAD (0.79; Eilert et al., 2021), it is nonetheless encouraging given that most of the studies included in the meta-analysis compared treatment to a waitlist control. By comparison, we used a control condition that matched CBM for time online and listening to scenarios. We therefore propose that CBM may have utility as a low-intensity intervention in its own right, and could be offered by mental-health services or non-mental health specialists and support organizations. It could also form an adjunct to high-intensity treatments such as cognitive behavior therapy (CBT), or be combined with specific elements of CBT, such as behavioral experiments, in keeping with Amir et al.'s (2015) hybrid approach which combined CBM and exposure.

There are a number of strengths to the present research. This randomized controlled experiment included a large sample of individuals meeting full diagnostic criteria for GAD, recruited from across the UK (with or without co-morbid depression) and demonstrated that a low-intensity online intervention provided beneficial effects on key symptoms of GAD. In contrast to many control conditions in psychological research (typically waitlist or treatment-as-usual, with associated differences in expectancy, drop-out and difficulty testing mechanisms of action due to confounding variables of time, engagement etc; see Guidi et al., 2018, for discussion), the control condition was well-matched regarding online exposure to the training material. It differed only in terms of lacking any guidance as to how the scenarios were to be interpreted. Indeed. interpretation bias was not altered in the

control condition, revealing a clear role for interpretation bias change in mediating effects on worry and anxiety.

Limitations of the research include that participants in this study were volunteers who were paid after completion of assessments, which might have influenced motivation for engaging in the research. However, payments were given irrespective of how many assignments were completed and yet completion rates of both assessments and assignments were high, suggesting that participants were generally motivated to engage in paid and non-paid aspects of the study. Participants were recruited from across the UK via advertisements and social media, rather than via clinical services, and those with very severe depression or high suicidal risk were excluded. Large-scale effectiveness RCTs are needed to evaluate the usefulness of enhanced interpretation training as a stand-alone, low-intensity clinical intervention, with a treatment as usual or another online intervention comparison condition. Research could also investigate its utility as an adjunct to established treatments such as CBT in those seeking treatment for GAD from clinical services. Furthermore, while we view anxiety and worry problems as being on a continuum, and thus measures used here seem appropriate, we did not re-assess GAD diagnosis immediately after the intervention or at follow-up. Diagnosis for GAD covers a 6-month duration (American Psychiatric Association, 2013), so future research assessing diagnostic status beyond three-month follow up is needed to determine whether the intervention can help individuals with GAD to no longer meet diagnostic criteria for this disabling clinical problem.

In summary, in addition to confirming our hypothesis that interpretation bias can be modified remotely and is a causal factor in maintaining worry (and negative mood), the present results have implications for the potential use of enhanced CBM as a low-intensity or

adjunct intervention to target anxiety that can be accessed by individuals at a time convenient to them, thus potentially reducing the burden on mental health services.

Authorship Statement

CH, CK and AM designed the study. JW and HK ran the study and collected the data. FM served as second coder for the clinical interviews. SN analyzed the data. CH, CK, SN and AM interpreted the results and drafted the paper, with help from HK. All authors read and approved the final version of the manuscript.

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Correspondence concerning this article should be addressed to Dr Colette R. Hirsch, Department of Psychology, Institute of Psychiatry, Psychology and Neuroscience, King's College London, De Crespigny Park, London SE5 8AF, UK. Email: colette.hirsch@kcl.ac.uk; Phone: +44 207 848 0697

Dr Charlotte Krahé is now at Department of Psychological Sciences, University of Liverpool, Whelan Building, Brownlow Hill, Liverpool L69 3GB. Jessica Whyte is now at Institute

of Health and Wellbeing, College of Medical, Veterinary and Life Sciences, University of Glasgow, 2nd floor, Administration Building, Gartnavel Royal Hospital, 1055 Great Western Road, Glasgow G12 0XH. Dr Frances Meeten is now at School of Psychology, University of Sussex, Falmer, BN1 9QH.

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Table 1

Demographic and clinical characteristics of per-protocol sample at T0 (N=186)

Baseline Characteristic		Control (N=92	CBM (N=94)
		n %	n %
Age - mean (SD)		36 (11.51)	33.54 (10.94)
Gender (F/M ratio)		83/9	84/10
Co-morbid GAD + DEP		35 (38.0)	36 (38.3)
Nationality	British	73 (79.3)	80 (85.1)
	Other European	10 (10.9)	6 (6.4)
	World	9 (9.8)	8 (8.5)
Highest level of education	Secondary	25 (27.2)	30 (31.9)
	Bachelor	33 (35.9)	30 (31.9)
	Master	16 (17.4)	18 (19.1)
	Doctoral	4 (4.3)	1 (1.1)
	Other	14 (15.2)	15 (16.0)
Marital status	Single, never married	41 (44.6)	50 (53.2)
	Married /domestic partnership	44 (47.8)	35 (37.2)
	Separated, divorced, widowed	7 (7.6)	9 (9.6)

Note. GAD – Generalized anxiety disorder; DEP – Depression; CBM – Cognitive bias modification of interpretation.

Table 2

Demographic and clinical characteristics of Intention-to-Treat sample at T0 (n=208)

Variable		Control (N=105)	CBM (N=103)
Age - mean (SD)		35.70 (11.47)	33.37 (10.85)
Gender (F/M ratio)		94/11	93/10
Co-morbid GAD + DEP (%)		41 (39.0)	40 (38.8)
Nationality - N (%)	British	84 (80.0)	88 (85.4)
	Other European	11 (10.5)	7 (6.8)
	World	10 (9.5)	8 (7.8)
Highest level of education - N (%)	Secondary	33 (31.4)	36 (35.0)
	Bachelor	36 (34.3)	31 (30.1)
	Master	17 (16.2)	18 (17.5)
	Doctoral	4 (3.8)	2 (1.9)
	Other	15 (14.3)	16 (15.5)
Marital status - N (%)	Single, never married	50 (47.6)	56 (54.4)
	Married /domestic partnership	47 (44.8)	37 (35.9)
	Separated, divorced, widowed	8 (7.6)	10 (9.7)

Note. GAD – Generalized anxiety disorder; DEP – Depression; CBM – Cognitive bias modification of interpretation.

Table 3

Descriptive statistics and regression results for the two interpretation bias measures in the per-protocol sample

		Control			CBM			Adjusted mean difference						
Variable	Time	N	Mean	SD	N	Mean	SD	Difference	SE	z	*p* value	95%ll	95%ul	Hedge's *g*
SST	T0	90	0.44	0.21	93	0.39	0.19							
	T1	87	0.49	0.23	90	0.60	0.21	0.13	0.03	4.66	<.001	0.08	0.19	0.67
RT	T0	92	-0.05	0.81	94	-0.03	0.80							
	T1	92	0.10	1.02	93	1.18	0.75	1.07	0.13	8.48	<.001	0.82	1.31	1.33

Note. T0 = pre-intervention, T1= post-intervention; SST = Scrambled Sentences Test; RT = Recognition Test; ll = 95% confidence interval lower limit; ul = 95% confidence interval upper limit.

Table 4

Descriptive statistics and regression results for the two interpretation bias measures in the intention-to-treat sample

		Control			CBM			Adjusted mean difference						
Variable	**time**	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**	**Difference**	**SE**	**z**	***p*-value**	**95%ll**	**95%ul**	**Hedge's *g***
SST	T0	104	0.44	0.22	102	0.40	0.20							
	T1	101	0.47	0.24	100	0.58	0.23	0.13	0.03	4.78	<.001	0.08	0.19	0.63
RT	T0	105	0.00	0.80	103	-0.04	0.80							
	T1	103	0.11	1.00	101	1.20	0.76	1.10	0.12	9.10	<.001	0.86	1.33	1.36

Note. T0 = pre-intervention; T1=post-intervention SST = Scrambled Sentences Test; RT = Recognition Test; 95%ll = 95% confidence interval lower limit; 95%ul = 95% confidence interval upper limit.

Table 5

Descriptive statistics and model results for measures of repetitive negative thinking, anxiety, and depression in the per-protocol sample

		Control			CBM-I			Adjusted mean difference					
Variable	**Time**	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**	**Difference**	**SE**	**z**	***p*-value**	**95%ll**	**95%ul**	**Hedges's *g***
BFT	T0	90	3.17	2.25	88	2.72	2.5							
	T1	90	2.5	2.25	88	0.93	1.25	-1.46	0.27	-5.47	0.001	-1.98	-0.94	-0.8
PSWQ trait	T0	92	71.51	6.26	94	71.98	5.19							
	T1	92	69.52	7.06	94	67.13	7.7	-2.63	1.02	-2.58	0.01	-4.62	-0.63	-0.46
	T2	92	67.49	7.93	94	61.97	9.46	-5.76	1.21	-4.74	<.001	-8.13	-3.38	-1
	T3	91	64.12	10.05	93	60.51	9.74	-3.95	1.36	-2.9	0.004	-6.61	-1.28	-0.69
PSWQ weekly	T0	92	77.47	8.26	94	77.13	8.56							
	T1	92	70.32	12.74	94	64.55	11.83	-5.54	1.62	-3.42	0.001	-8.72	-2.37	-0.66
	T2	92	66.51	13.88	94	58.76	14.59	-7.54	1.94	-3.89	<.001	-11.34	-3.74	-0.9
	T3	91	63.49	15.19	93	57.14	15.54	-6.25	2.1	-2.97	0.003	-10.37	-2.13	-0.74
RTQ-T	T0	92	43.3	5.63	94	43.47	5.33							
	T1	92	40.23	7.41	94	37.65	7.21	-2.69	0.89	-3.03	0.002	-4.43	-0.95	-0.49
	T2	92	37.88	8.07	94	35.19	7.86	-2.8	1.04	-2.7	0.007	-4.83	-0.77	-0.51
	T3	91	35.99	9.35	93	34.38	7.99	-1.78	1.19	-1.5	0.134	-4.11	0.55	-0.33
RRS	T0	92	61.86	11.94	94	62.66	11.12							
	T1	92	58.2	13.51	94	55.43	12.26	-3.36	1.22	-2.77	0.006	-5.75	-0.98	-0.29
	T2	92	54.13	14.11	94	50.11	12.93	-4.62	1.6	-2.88	0.004	-7.76	-1.48	-0.4
	T3	91	52.45	15.33	93	49.04	12.72	-3.96	1.71	-2.31	0.021	-7.32	-0.6	-0.34
GAD7	T0	92	15.62	3.15	94	15.51	3.47							

	T1	92	13	4.6	94	11.13	4.58	-1.81	0.56	-3.23	0.001	-2.9	-0.71	-0.55
	T2	92	11.02	4.86	94	8.69	4.84	-2.26	0.64	-3.54	<.001	-3.52	-1.01	-0.68
	T3	91	10.13	5.07	93	8.49	4.73	-1.56	0.7	-2.23	0.026	-2.93	-0.19	-0.47
	T0	92	14.68	5.1	94	14.63	4.23							
PHQ9	T1	92	11.98	5.26	94	10.13	4.81	-1.82	0.57	-3.18	0.001	-2.94	-0.7	-0.39
	T2	92	10.15	5.55	94	8.71	5.07	-1.41	0.67	-2.11	0.035	-2.72	-0.1	-0.3
	T3	91	9.89	5.64	93	7.87	4.99	-2	0.73	-2.75	0.006	-3.43	-0.57	-0.43

Note. T0 = pre-intervention, T1= post-intervention, T2 = 1-month post-completion of intervention, T3 = 3-months post completion of intervention. BFT = Breathing Focus Task; PSWQ trait = Penn State Worry Questionnaire; PSWQ weekly = Penn State Worry Questionnaire- past week; RTQ-T = Repetitive Thinking Questionnaire- trait; RRS = Ruminative Response Scale; GAD-7 = Generalized Anxiety Disorder scale (measure of anxiety); PHQ-9 = Patient Health Questionnaire (measure of depression); T0 = Baseline; T1 = etc.; ll = 95% confidence interval lower limit; ul = 95% confidence interval upper limit.

Table 6

Descriptive statistics and model results for measures of repetitive negative thinking, anxiety, and depression in the intention-to-treat sample

		Control			CBM			Adjusted mean difference						
Variable	**time**	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**	**Difference**	**SE**	**z**	***p*-value**	**95%ll**	**95%ul**	**Hedge's *g***
BFT	T0	102	3.16	2.31	102	2.72	2.41							
	T1	102	2.57	2.38	102	0.89	1.22	-1.56	0.25	-6.20	.001	-2.05	-1.06	-0.83
PSWQ trait	T0	105	71.18	6.86	103	71.85	5.24							
	T1	104	69.32	7.13	102	67.10	7.55	-2.46	0.93	-2.65	.008	-4.28	-0.64	-0.40
	T2	104	67.35	8.12	102	62.26	9.78	-5.42	1.17	-4.64	.000	-7.71	-3.13	-0.89
	T3	103	63.95	9.86	102	60.24	10.29	-4.28	1.31	-3.26	.001	-6.85	-1.71	-0.70
PSWQ weekly	T0	105	76.93	9.21	103	76.89	8.80							
	T1	104	70.20	12.79	102	64.56	12.05	-5.34	1.51	-3.54	.000	-8.30	-2.39	-0.59
	T2	104	66.44	14.13	102	59.32	15.19	-7.04	1.87	-3.77	.000	-10.70	-3.38	-0.78
	T3	103	63.69	15.17	102	57.75	16.12	-6.14	2.02	-3.03	.002	-10.11	-2.17	-0.68
RTQ-T	T0	105	43.35	5.53	103	43.41	5.26							
	T1	104	40.21	7.41	102	37.94	7.20	-2.15	0.83	-2.59	.010	-3.78	-0.52	-0.40
	T2	104	37.80	8.38	102	35.31	7.96	-2.45	0.99	-2.48	.013	-4.39	-0.52	-0.46
	T3	103	36.20	8.95	102	34.45	8.47	-1.86	1..11	-1.68	.093	-4.04	0.31	-0.35
RRS	T0	105	61.84	11.74	103	63.16	11.16							
	T1	104	58.38	13.24	102	56.07	12.34	-2.97	1.14	-2.61	.009	-5.21	-0.74	-0.26
	T2	104	54.31	14.01	102	50.70	13.20	-4.42	1.50	-2.95	.003	-7.36	-1.48	-0.39
	T3	103	53.10	14.89	102	49.19	13.17	-4.70	1.62	-2.90	.004	-7.87	-1.53	-0.41

GAD-7	T0	105	15.48	3.29	103	15.63	3.58						
	T1	104	13.11	4.72	102	11.08	4.84	-2.07	0.56	-3.69	.000	-3.16	-0.97	-0.60
	T2	104	11.29	4.98	102	8.89	5.02	-2.40	0.63	-3.83	.000	-3.63	-1.17	-0.70
	T3	103	10.43	5.01	102	8.70	4.92	-1.87	0.67	-2.78	.005	-3.18	-0.55	-0.54
PHQ-9	T0	105	14.73	5.08	103	14.83	4.46						
	T1	104	12.30	5.39	102	10.19	5.08	-2.13	0.57	-3.71	.000	-3.25	-1.01	-0.45
	T2	104	10.73	5.83	102	9.03	5.57	-1.66	0.67	-2.47	.014	-2.99	-0.34	-0.35
	T3	103	10.12	5.57	102	8.12	5.36	-2.11	0.70	-3.02	.002	-3.47	-0.74	-0.44

Note. This study employed a 4-assessment intervention T0 = pre-intervention, T1 = post completion of intervention, T2 = 1-month post completion of intervention, T3 = 3 -months post completion of intervention. BFT = Breathing focus task; PSWQ trait = Penn State Worry Questionnaire; PSWQ week = Penn State Worry Questionnaire- past week; RTQ-T = Repetitive Thinking Questionnaire- trait; RRS = Ruminative Response Scale; GAD-7 = Generalized Anxiety Disorder scale (measure of anxiety); PHQ-9 = Patient Health Questionnaire (measure of depression). 95%ll = 95% confidence interval lower limit; 95%ul = 95% confidence interval upper limit.

Table 7

Mediation effects of the Recognition Test (RT) and Scrambled Sentences Test (SST) at Time 2 on worry (PSWQ trait), worry in the past week (PSWQ weekly), repetitive negative thinking (RTQ-T), and anxiety (GAD-7) at timepoints 1, 2 and 3 in the per-protocol sample

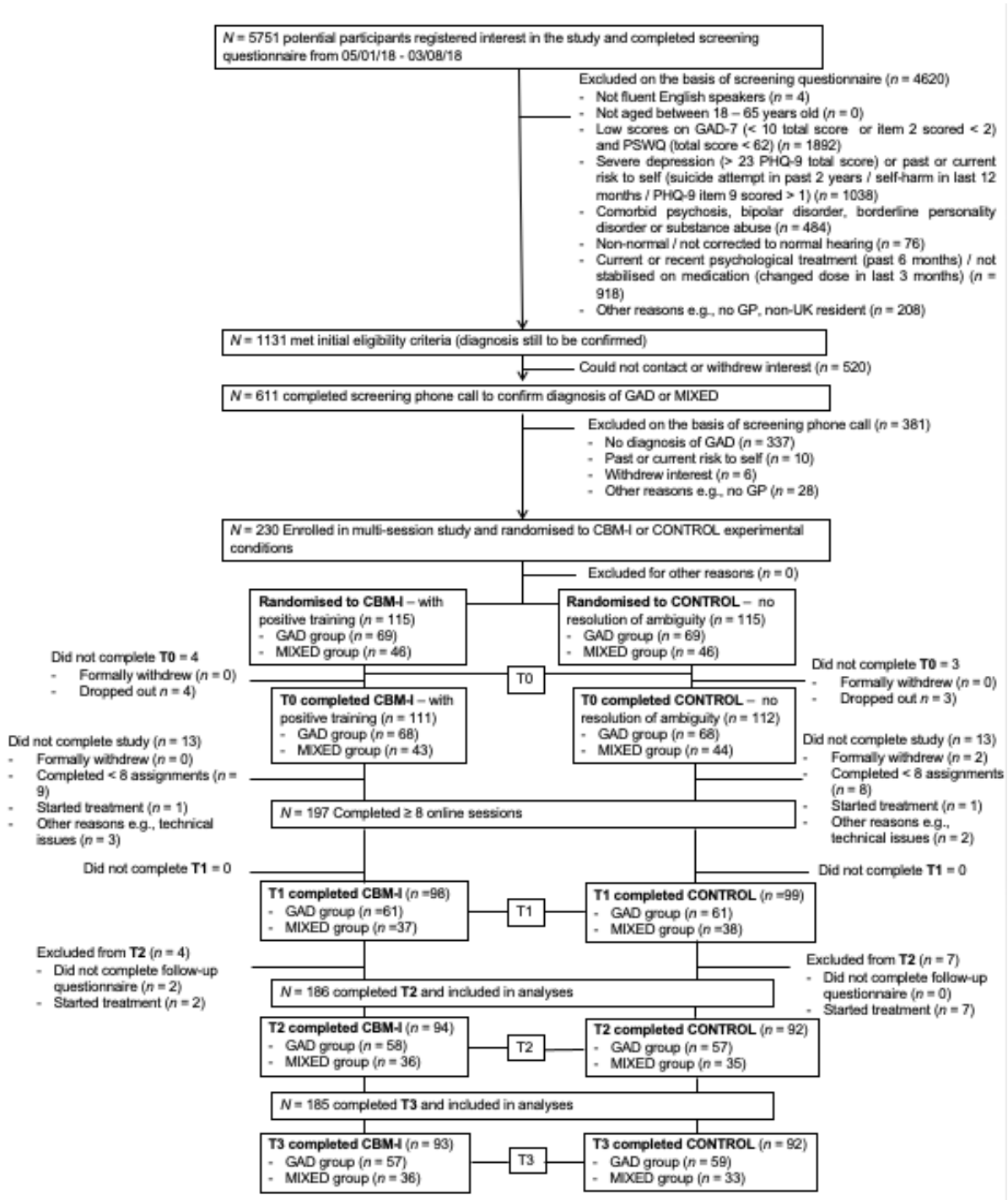
Outcome	Mediator	Time	Total effect					Indirect effect					Proportion Mediated
			Unstand	SE	z	*p-value*	Stand	Unstand	SE	z	*p-value*	Stand	
PSWQ trait	RT	T1	-2.44	1.02	-2.40	.016	-0.17	-1.36	0.62	-2.19	.029	-0.09	0.56
		T2	-5.70	1.22	-4.68	.000	-0.31	-2.45	0.76	-3.20	.001	-0.13	0.43
		T3	-3.88	1.36	-2.85	.004	-0.19	-2.07	0.83	-2.51	.012	-0.10	0.53
	SST	T1	-2.43	1.04	-2.33	.020	-0.17	-1.12	0.42	-2.69	.007	-0.08	0.46
		T2	-5.69	1.25	-4.54	.000	-0.31	-1.07	0.44	-2.42	.015	-0.06	0.19
		T3	-3.74	1.38	-2.71	.007	-0.19	-0.72	0.41	-1.77	.077	-0.04	0.19
PSWQ weekly	RT	T1	-5.53	1.62	-3.42	.001	-0.22	-3.29	1.02	-3.23	.001	-0.13	0.59
		T2	-7.36	1.94	-3.93	.000	-0.26	-2.98	1.20	-2.49	.013	-0.10	0.40
		T3	-6.30	2.10	-3.00	.003	-0.20	-3.07	1.28	-2.41	.016	-0.10	0.49
	SST	T1	-5.48	1.67	-3.28	.001	-0.22	-2.45	0.83	-2.97	.003	-0.10	0.45
		T2	-7.34	1.98	-3.72	.000	-0.25	-1.65	0.69	-2.39	.017	-0.06	0.22
		T3	-5.69	2.12	-2.68	.007	-0.18	-1.51	0.69	-2.18	.030	-0.05	0.27
RTQ-T	RT	T1	-2.70	0.89	-3.04	.002	-0.18	-0.76	0.55	-1.40	.161	-0.05	0.28
		T2	-2.81	1.03	-2.71	.007	-0.18	-1.67	0.65	-2.57	.010	-0.11	0.59
		T3	-1.76	1.18	-1.49	.137	-0.10	-2.02	0.74	-2.73	.006	-0.12	1.00
	SST	T1	-2.53	0.92	-2.74	.006	-0.17	-0.78	0.33	-2.39	.017	-0.05	0.31
		T2	-2.75	1.08	-2.55	.011	-0.17	-1.01	0.40	-2.51	.012	-0.06	0.37
		T3	-1.34	1.21	-1.11	.268	-0.08	-0.09	0.40	-2.17	.030	-0.51	0.07
GAD-7	RT	T1	-1.75	0.55	-3.19	.001	-0.19	-0.97	0.34	-2.82	.005	-0.11	0.55
		T2	-2.28	0.64	-3.57	.000	-0.23	-0.85	0.39	-2.16	.031	-0.09	0.37
		T3	-1.60	0.69	-2.31	.021	-0.16	-0.92	0.42	-2.17	.030	-0.09	0.58
	SST	T1	-1.77	0.56	-3.15	.002	-0.20	-0.62	0.23	-2.67	.008	-0.07	0.35
		T2	-2.29	0.66	-3.46	.001	-0.24	-0.58	0.24	-2.40	.016	-0.06	0.25

	T3	-1.59	0.70	-2.29	.022	-0.17	-0.47	0.23	-2.07	.039	-0.05	0.30

Note. T0 = pre-intervention, T1= post-intervention, T2 = 1-month post-completion of intervention, T3 = 3-months post completion of intervention. SST = Scrambled Sentences Test; RT = Recognition Test; PSWQ trait = Penn State Worry Questionnaire; PSWQ weekly = Penn State Worry Questionnaire- past week; RTQ-T = Repetitive Thinking Questionnaire- trait; GAD-7 = Generalized Anxiety Disorder scale (measure of anxiety). Unstand: unstandardised, stand: standardized

Figure 1

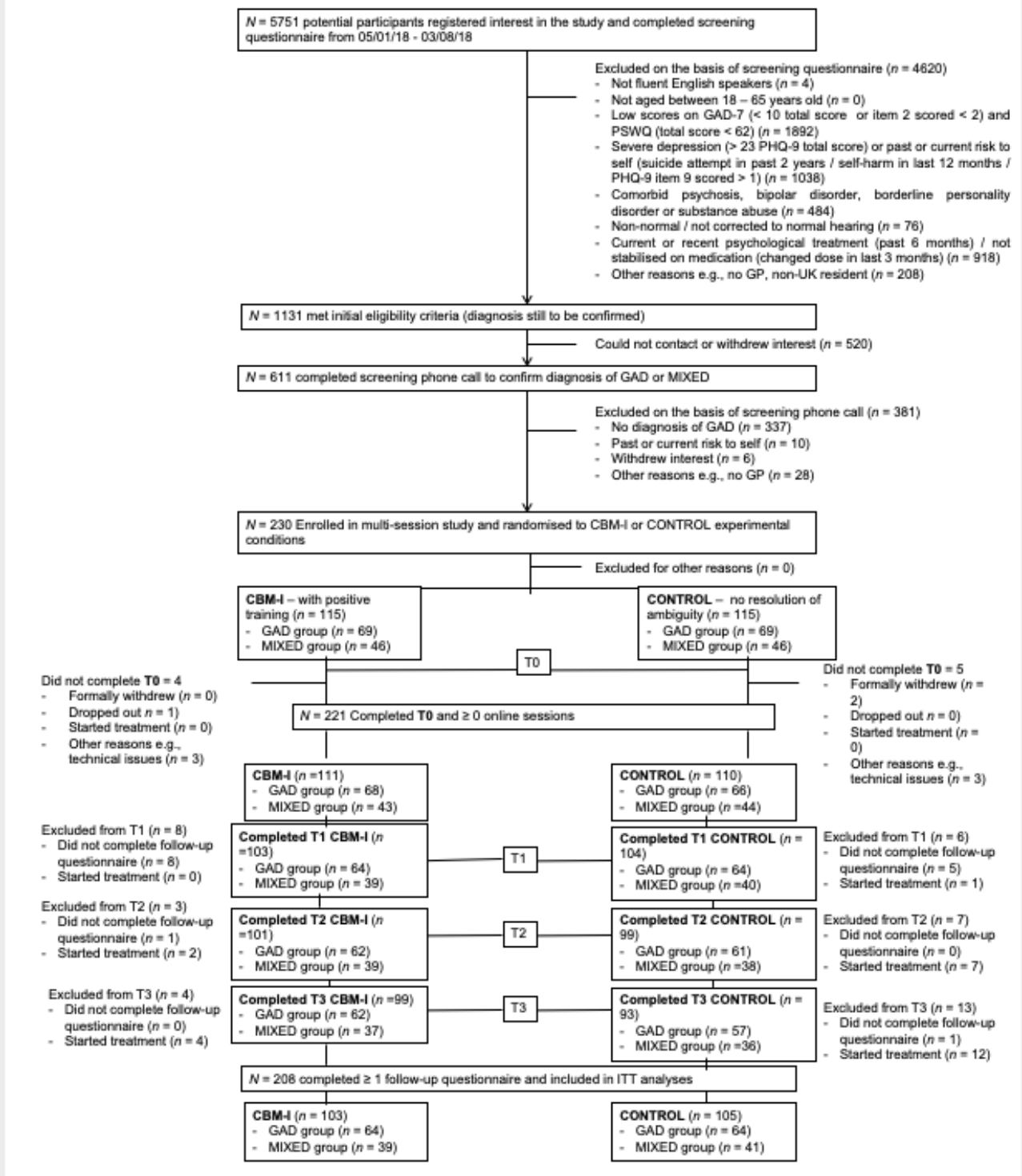
CONSORT diagram for those included in per-protocol analysis



Note. CBM = cognitive bias modification; GAD = Generalized Anxiety Disorder; MIXED = Co-morbid GAD and Depression.

Figure 2

CONSORT diagram to show flow of modified Intention to Treat (ITT) analysis subgroup



Note. CBM = cognitive bias modification; GAD = Generalized Anxiety Disorder; MIXED = Co-morbid GAD and Depression