Remote Cognitive Behavioral Therapy for Panic Disorder: A Meta-Analysis

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Abstract

Cognitive behavioral therapy (CBT) is an established treatment for panic disorder (PD). Remote CBT (RCBT) is becoming increasingly popular and has the potential to enhance access to this treatment. The aim of this study was to examine the efficacy of RCBT for PD using a meta-analytic approach. An electronic database search was used to identify relevant articles and the references of previously completed reviews. Twenty-one studies (*n* = 1,604; mean age range: 31.9 – 43.9; mean female representation = 71%) were included in the meta-analysis. 14/21 (67%; n = 817 of the included studies were randomised controlled trials and 7/21 (33%; n = 787) were open trials or non-randomised controlled trials. Pooled within-group effect sizes across all remote treatments for PD symptoms were large from pre-treatment to post-treatment (Hedges' *g* = 1.18; 95% CI: 0.99 – 1.36) and pre-treatment to follow-up (Hedges' *g* = 1.51; 95% CI: 1.22 – 1.79). Pooled between-group findings indicate that remote CBT treatments are more effective than passive control (Hedges' *g* = 1.17; 95% CI: 0.85 - 1.50), but are similar to other active treatments on measures of PD symptoms (e.g., face-to-face CBT) (Hedges' *g* = 0.02; 95% CI: -0.43 – 0.48). Internet-delivered CBT (Hedges' *g* = 1.10, 95% CI: 0.91–1.30), videoconferencing-delivered CBT (Hedges' *g* = 1.40, 95% CI: 0.85– 1.95) and bibliotherapy-delivered CBT (Hedges' *g* = 1.51, 95% CI: 0.95 – 2.06) each produce large effect sizes on measures of PD symptoms. The results have important implications for the dissemination of entirely remote stepped-care treatments for PD.

Keywords: panic disorder, remote treatment, cognitive behavioral therapy, meta-analysis

1. Introduction

Panic disorder (PD) is characterized by recurrent, unexpected panic attacks, followed by at least one month of persistent concern about the recurrence of symptoms and/or maladaptive changes in behaviour (American Psychiatric Association, 2013). While almost a quarter of people are likely to experience a panic attack in their lifetime (Kessler et al., 2006), it is reported that PD has a 12-month prevalence rate of approximately 2% and a lifetime morbid risk of 7%, with an average age-of-onset in the early 20s (Kessler et al., 2012). Common comorbid conditions include other anxiety disorders, mood disorders, impulse control disorders, and substance use disorders (Goodwin et al., 2005; Kessler et al., 2005). Individuals with PD experience substantial impairment in quality of life and functional disability (Alonso et al., 2004; Barrera & Norton, 2009).

1.1. Cognitive Behavioral Therapy for Panic Disorder

Cognitive behavioral therapy (CBT) is recommended as the first line of treatment for PD (National Institute for Health and Care Excellence [NICE], 2011). CBT is generally delivered face-to-face and commonly delivered interventions include psychoeducation (providing the patient with information about the condition), cognitive restructuring (identification and challenging of maladaptive cognitions), breathing retraining (training in exercises to slow diaphragmatic breathing), interoceptive exposure (exposure to feared bodily sensations), and in-vivo exposure (graded exposure to avoided situations) (Pompoli et al., 2018). CBT is often delivered in weekly sessions (e.g., Öst et al., 2004; Vos et al., 2012), although more intensive treatments, where treatment is delivered three or more times per week, have also been demonstrated to be efficacious (Bitran et al., 2008; Deacon & Abramowitz, 2006; Wootton & MacGregor, 2016).

A recent meta-analysis comparing each of the key CBT components in treating PD found that interoceptive exposure was an important predictor of symptom improvement, and

breathing retraining was one of the least effective treatment components (Pompoli et al., 2018). Some argue that breathing retraining may potentially be used as a safety behaviour for some patients (Craske et al., 1997). Safety behaviors are overt or covert behaviors that are used to reduce anxiety in an anxiety provoking situation, and are generally seen as counter-productive in CBT as they prevent patients from learning disconfirming evidence that are counter to their maladaptive and catastrophic beliefs (Lovibond et al., 2009; Piccirillo et al., 2016). While there is evidence that clinicians practicing in the community use breathing retraining more frequently than other interventions, such as interoceptive exposure, when treating patients with panic disorder (Wolf & Goldfried, 2014), some clinicians and researchers have omitted this intervention entirely from their PD treatment protocols (e.g., Deacon & Abramowitz, 2006; Hedman et al., 2013; Wims et al., 2010; Wootton & MacGregor, 2016). Thus further research regarding the utility of breathing retraining is needed in order to inform the best-practice delivery of CBT for PD.

Despite the demonstrated efficacy of CBT for PD (Cuijpers et al., 2016; Pompoli et al., 2018; Sánchez-Meca et al., 2010), as well as the effectiveness of this treatment in real-world settings (Stewart & Chambless, 2009; Stuart et al., 2000; Wootton, Bragdon, et al., 2015), there are many barriers to accessing treatment. These include direct and indirect barriers such as not knowing where to access treatment, affordability of treatment, and long wait times to access treatment (Craske et al., 2005). The COVID-19 pandemic has also been a recent barrier to accessing evidence-based care, as many jurisdictions are locked down and patients are unable to access a face-to-face therapist. This points towards a need for more accessible evidence-based treatments for PD. Remote treatments, which do not require the therapist and patient to be in the same location, address these barriers and may assist in the uptake of CBT for PD.

1.2. Remote Treatment

Remote treatments can take many forms, but can generally be divided into high-intensity and low intensity treatments (Wootton, 2016), which differ substantially. High intensity remote treatments are analogous to face-to-face treatments and involve the clinician and patient communicating synchronously. Commonly delivered high intensity interventions include internet-videoconferencing delivered CBT (VCBT) or telephone delivered CBT (TCBT) (e.g., Matsumoto et al., 2018; Vogel et al., 2014), and many clinicians rapidly switched to using such approaches during the COVID-19 pandemic. Low intensity remote treatment approaches involve the patient engaging with pre-prepared material without synchronous communication. Commonly delivered low intensity interventions include bibliotherapy delivered CBT (BCBT) (e.g., Lidren et al., 1994; Wootton et al., 2018), internet delivered CBT (ICBT) (e.g., Bergström et al., 2010; Wims et al., 2010), or mobile application delivered CBT (e.g., Ebenfeld et al., 2020).

The efficacy of various remotely delivered CBT approaches for anxiety and related disorders has been documented across numerous meta-analyses (Andrews et al., 2018; Carlbring et al., 2018; Marrs, 1995; Sijbrandij et al., 2016). However, few meta-analyses consider the full spectrum of remote treatment approaches, which is important given the vast differences in treatment approaches, and significantly different costs associated with each approach. One meta-analysis that has investigated the efficacy of both low intensity and high intensity remote treatment approaches for obsessive-compulsive disorder (OCD) found large effect sizes from pre-treatment to post-treatment for both low intensity (g = 1.36) and high intensity (g = 1.64) interventions, with no statistical difference between them (Wootton, 2016). However, the study further found that some forms of remote treatment (VCBT, TCBT, ICBT) resulted in larger effect sizes than other forms of remote treatment (BCBT and

computerised CBT) (Wootton, 2016), which has important implications for understanding how to best disseminate RCBT.

1.3. Remote Treatment for Panic Disorder

There is growing support for the efficacy of remote CBT in the treatment of PD. For example, a meta-analysis of 8 studies comparing guided ICBT to waitlist control conditions for PD reported large between-group pooled effects (d = 1.52) (Olthuis et al., 2016). Similarly, Stech et al. (2020) found large pooled between-group effect size for ICBT treatments for PD symptoms relative to waitlist/informational control conditions (g = 1.22) and large within-group effects from pre-treatment to post-treatment (g = 1.16). Additionally, meta-analyses by Olthuis et al. (2016), Carlbring et al. (2018), and Stech et al. (2020) also demonstrate that ICBT for PD has similar efficacy compared to standard face-to-face CBT.

While these studies provide important contributions to the literature on remote CBT interventions for PD, there are a number of notable limitations. Firstly, all of these meta-analyses focus on the efficacy of ICBT for PD only, and neglect to examine other forms of remote treatment. It is important to compare the efficacy across remote treatment approaches to inform decision making around mental health treatment policy for PD. Secondly, Olthuis et al. (2016) and Stech et al. (2020) included studies where participants were not diagnosed with PD using a structured diagnostic interview and/or included patients with sub-clinical PD symptoms, thus it is unclear how these findings relate to individuals with diagnosed PD. Therefore, the aim of the current study is to address these limitations of the existing literature by examining the efficacy of the full spectrum of remote CBT approaches in patients diagnosed with PD using a meta-analytic approach.

2. Method

2.1. Search Procedure

After the protocol of the review was registered with PROSPERO (REMOVED FOR PEER REVIEW), relevant articles were identified through electronic databases (PsycINFO, Medline and Scopus) up until 23rd February 2020. The search terms used in the electronic databases included 'panic disorder' AND 'CBT' OR 'cognitive behav* therap*' OR 'cognitive therap*' OR 'behav* therap*' OR 'treatment*' AND 'remote' OR 'self-help' OR 'internet' OR 'bibliotherap*' OR 'video conferenc*' OR 'tele health' OR 'telehealth' OR 'telephone'.

The title and abstract of all studies were screened in full by the first author (REMOVED FOR PEER REVIEW). The same author then reviewed all relevant full text articles against the inclusion criteria. At least 10% of articles at the abstract and full text review stage were reviewed by the second author (REMOVED FOR PEER REVIEW). Data from the included studies were independently extracted by both authors and compared for accuracy. Any discrepancies were discussed and resolved between the two authors. Reference lists of all included studies were examined, as were the reference lists of previously completed meta-analyses on the topic (e.g., Carlbring et al., 2018; Olthuis et al., 2016; Stech et al., 2020). Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009) were followed and the study flow can be seen in Figure 1.

2.2. Study Selection

To be included in the meta-analysis, studies were required to meet the following criteria: 1) the study must include a clinical sample of more than five people; 2) participants must be aged at least 18 years; 3) participants must have a diagnosis of panic disorder assigned by a structured diagnostic interview; 4) the treatment must primarily target

symptoms of panic disorder (i.e., not a transdiagnostic treatment); 5) at least one study arm must evaluate a remote CBT intervention as a monotherapy; 6) the remote treatment must involve less than 120 minutes of face-to-face contact across the course of treatment (a limit that has been used in similar meta-analyses; Wootton, 2016); 7) the study must be in English, published in a peer-reviewed journal, and adequately describe the treatment methodology; 8) must consist of original data (i.e., not duplicate data); 9) must provide sufficient data to calculate effect sizes; and 10) must use a well validated measure of panic disorder symptoms. Treatments were categories as low intensity or high intensity based on criteria used in previous similar meta-analysis where ICBT or BCBT were considered low intensity interventions and VCBT or TCBT were considered high intensity interventions (Wootton, 2016). Both controlled and uncontrolled trials were included in this meta-analysis, as were efficacy and effectiveness studies. The most conservative outcomes from each study were used where possible (i.e., intention to treat (ITT) analysis) and completer data was used when ITT was unavailable.

2.3. Data Analysis

Version 3.0 of Comprehensive Meta-Analysis (Borenstein et al., 2013) was used to analyse the effect size data. Effect sizes were calculated from the identified primary outcome measure. If the primary outcome was not specified the Panic Disorder Severity Scale (PDSS; Shear et al., 1997) was used if available, followed by the next most common measure of PD severity [i.e. Panic Disorder Severity Scale-Self-Report (PDSS-SR; Houck et al., 2002), Panic and Agoraphobia Scale (P&A; Bandelow, 1995), Body Sensations Questionnaire (BSQ; Chambless et al., 1984), or the Panic Attack Symptoms Questionnaire (PASQ; Clum et al., 1990)]. Random effects models were used to analyse both within-group and between-group outcomes. The strength of treatment effects were calculated with Hedges' g and effect sizes of 0.2, 0.5 and 0.8 were interpreted as small, medium and large respectively. For within-

group comparisons a positive *g* value indicates improvement in PD symptoms. For between-group comparisons a positive *g* value indicates that the remote treatment performed better than the control treatment. A number of planned moderator analyses were conducted including 1) type of treatment (ICBT, VCBT, BCBT); 2) intensity of treatment (low intensity vs. high intensity remote treatment); 3) level of therapist guidance (self-guided vs. clinician-guided); 4) trial type (efficacy vs effectiveness studies); and 5) inclusion of breathing retraining in the treatment protocol (inclusion vs exclusion). Moderators were only conducted where sample size allowed for it (i.e., when there were at least 3 studies included in the analysis). Efficacy studies were classified as those that provided treatment as part of a clinical trial and effectiveness studies were those studies that provided treatment as part of routine care.

The I^2 statistic was used to evaluate the heterogeneity of effect sizes. Heterogeneity is considered low if found to be 25%, moderate at 50% and high at 75% (Higgins et al., 2003). The 'one-study removed' method was used as a sensitivity analysis to assess how the combination of studies impacted individual studies. This was analysed by the overall effect size after the removal of each study. Duval and Tweedie's Trim and Fill method was used to assess publication bias and to calculate an adjusted effect size (Duval & Tweedie, 2000). This was done by removing the most extreme small positive studies from the analysis and replacing them with a mirror image, resulting in the best estimate of the unbiased effect size (Borenstein et al., 2009).

The quality of studies was examined using the psychotherapy outcome study methodology rating form Öst (2008), which was independently assessed by both authors. Inter-rater reliability was analysed using IBM SPSS Statistics (Version 26) predictive analysis software. Intraclass correlation coefficient (ICC) estimates were calculated based on mean-rating (k = 2), absolute agreement, 2-way mixed effects model. The first author's

scores were used as the final study quality scores (outlined in Table 1) as inter-rater reliability was good (ICC = .82; 95% CI = 0.10-0.95).

3. Results

The search yielded a total of 446 articles. The title and abstract were reviewed initially and 357 articles were excluded, resulting in 89 articles which were reviewed in full against the inclusion and exclusion criteria using a comprehensive coding sheet. A further 68 articles were excluded, resulting in 21 studies included in the current meta-analysis. The study flow chart is outlined in Figure 1. Data from the final 21 studies were independently extracted by both authors and compared for accuracy. Any discrepancies were discussed and resolved between the two authors before analyses were conducted.

3.1. Study Characteristics.

Across the 21 studies, 25 remote treatment conditions were examined and 1,604 individuals (n = 1286 in the treatment conditions and n = 318 in the control conditions) were included in the analysis (mean age range: 31.9 – 43.9; female representation range: 59%-100%; mean percentage of female representation = 71%). Control conditions included both active (i.e., therapist-delivered CBT and applied relaxation CBT) and passive (i.e., waitlist and information) control groups. A summary of the study characteristics can be found in Table 1. The majority of the studies were RCTs (14/21; 66.7%), one was a controlled trial (not randomized) (1/21; 4.8%) and the remaining six (6/21; 28.6%) were uncontrolled studies. The studies were conducted in Australia (9/21; 42.9%), Europe (8/21; 38.1%), North America (3/21; 14.3%), and Japan (1/21; 4.8%). In terms of remote treatment approaches, 19/25 (76%) investigated an ICBT treatment, 3/25 (12%) investigated a BCBT treatment, and 3/25 (12%) investigated a VCBT treatment. Finally, 18/21 (85.7%) were efficacy studies and 3/21 (14.3%) were effectiveness studies. Study quality ranged from 15 (lowest quality study) to 34 (highest quality study) from a possible rating of 0 to 44.

3.2. Within-Group Analyses

The within-group effect sizes are outlined in Table 2 for each of the included studies. The pooled within-group mean effect size was large across all remote treatments from pre-treatment to post-treatment (k = 25; g = 1.18; 95% CI: 0.99–1.36). A high level of heterogeneity across studies was indicated (I^2 = 88.54). The Trim and Fill method indicated evidence of publication bias with ten studies trimmed (adjusted g = 0.82; 95% CI: 0.63–1.01). Effect sizes remained unchanged after the one study removed method was used.

The pooled within-group effect size was also large for remote treatments from pre-treatment to follow-up (k = 17; g = 1.51; 95% CI: 1.22–1.79). A high level of heterogeneity across studies was indicated (I^2 = 94.00). The Trim and Fill method indicated evidence of publication bias with eight studies trimmed (adjusted g = 0.92; 95% CI: 0.64–1.21). Effect sizes remained unchanged using the one study removed method.

3.2.1. Moderator Analyses

3.2.1.1. Remote Treatment Type. Type of remote treatment did not moderate treatment outcome from pre-treatment to post-treatment (Q_2 = 2.54, p > .05). Within-group pooled effect sizes were large for each type of remote treatment from pre-treatment to post-treatment (ICBT: k = 19, g = 1.10, 95% CI: 0.91–1.30, I^2 = 89.33; VCBT: k = 3, g = 1.40, 95% CI: 0.85– 1.95, I^2 = 82.22; and BCBT: k = 3, g = 1.51, 95% CI: 0.95 – 2.06, I^2 =0.00). Pre-treatment to follow up moderator analyses for treatment type were unable to be conducted due to sample size.

3.2.1.2. Treatment Intensity. Treatment intensity did not moderate treatment outcome from pre-treatment to post-treatment (Q_1 = 0.67, p > .05). Large pooled within-group effect sizes were found for high intensity conditions (i.e., VCBT) (k = 3; g = 1.40; 95% CI: 0.84 – 1.96; I^2 = 82.22) and for low intensity conditions (i.e., ICBT and BCBT) (k = 22; g

= 1.15; 95% CI: 0.96 - 1.34; I^2 = 88.50). Pre-treatment to follow up moderator analyses for treatment intensity were unable to be conducted due to sample size.

3.2.1.3. Breathing Retraining. The inclusion of breathing retraining did not moderate treatment from pre-treatment to post-treatment (Q_1 = 0.03, p > 0.05), with large pooled within-group effect sizes found for studies that did include breathing retraining (k = 20; g = 1.20; 95% CI: 0.97-1.44; I^2 = 89.61), as well as for those that did not (k = 5; g = 1.15; 95% CI: 0.69 - 1.62; I^2 = 82.40). The inclusion of breathing retraining also did not moderate treatment outcome from pre-treatment to follow-up (Q_1 = 0.11, p > .05). Large pooled within-group effect sizes were found for studies that did include breathing retraining (k = 14; g = 1.56; 95% CI: 1.17 - 1.95; I^2 = 94.23) as well as for those that did not (k = 3; g = 1.41; 95% CI: 0.59 – 2.22; I^2 = 94.87).

3.2.1.4. Trial Type. Trial type did not moderate treatment outcome from pre-treatment to post-treatment (Q_1 = 0.97, p > .05) or pre-treatment to follow up (Q_1 = 1.15, p > .05). Large pooled within-group effect sizes were found for effectiveness studies (k = 3; g = 0.95; 95% CI: 0.44 - 1.46; I^2 = 97.53) and for efficacy studies (k = 22; g = 1.22; 95% CI: 1.02 - 1.43; I^2 = 80.74) from pre-treatment to post-treatment. Large within group pooled effect sizes were also found from pre-treatment to follow up for effectiveness studies (k = 3; g = 1.18; 95% CI: 0.51 - 1.85; I^2 = 98.15) and efficacy studies (k = 14; g = 1.59; 95% CI: 1.26 - 1.92; I^2 = 89.14).

3.3. Between-Group Analyses

The between-group effect sizes are outlined in Table 3 for each of the included studies. The pooled between-group mean effect size was large across all remote treatments at post-treatment (k = 16; g = 0.82; 95% CI: 0.44 – 1.20). A high level of heterogeneity across studies was indicated (I^2 = 83.74). The Trim and Fill method indicated evidence of publication bias with three studies trimmed (adjusted g = 0.52; 95% CI: 0.10 – 0.94). Effect

sizes remained unchanged using the one study removed method. The pooled between-group effect size was small and non-significant across all remote treatments at follow up (k = 3; g = 0.41; 95% CI: -0.07 – 0.89). A low level of heterogeneity across studies was indicated (I^2 = 45.70). The Trim and Fill method indicated no publication bias and effect sizes remained unchanged using the one study removed method.

3.3.1. Moderators

3.3.1.1. Active control group vs. passive control group. A total of eight studies (11 comparisons) compared a remote treatment to a passive control group (i.e., waitlist control or informational control) in a randomized controlled design at post-treatment. Seven of the eleven comparisons (63.6%) were waitlist control and the remaining four conditions were informational control (36.3%). A total of five studies (5 comparisons) compared a remote CBT treatment to an active control treatment at post-treatment. Active controls were therapist-delivered CBT (four studies) and applied relaxation (one study). Type of control group moderated between-group effect sizes (Q_1 = 16.168, p < 0.001), with large pooled between-group effect sizes found for studies that used a passive control group (k = 11; g = 1.17; 95% CI: 0.85 - 1.50; I^2 = 74.26), and small effect sizes for those that used an active control group (k = 5; g = 0.02; 95% CI: -0.43 – 0.48; I^2 = 0.00).

4. Discussion

4.1. Efficacy of RCBT for PD

The aim of the current study was to 1) examine the efficacy of remote cognitive behavioural therapy (CBT) for panic disorder (PD) symptomatology and 2) examine potential moderators of outcome. Overall remote CBT (RCBT) for PD is effective with large within-group effect sizes seen from pre-treatment to post-treatment (g = 1.18; 95% CI: 0.99–1.36) and between-group differences were also large in size at post-treatment (g = 0.82; 95% CI: 0.44 – 1.20) on measures of PD symptoms. The results of the current study are consistent

with previously published meta-analyses that have examined specific types of remote treatment for panic disorder (e.g., Olthuis et al., 2016; Stech et al., 2020). For instance, most recently, Stech et al. (2020) found overall pooled within-group effects of (g = 1.16) at post-treatment for ICBT. The findings are also consistent with the wider literature demonstrating that remote CBT is effective across anxiety and related disorders (Wootton, 2016).

Large pooled within-group effect sizes were also observed at follow-up (g = 1.51; 95% CI: 1.22–1.79) on measure of PD symptoms. For the between-group comparisons treatment effects were small at follow-up (g = 0.41; 95% CI: -0.07 – 0.89), indicating that differences between treatments were no longer significant at follow-up. However, this analysis was based on only 3 comparisons and included both active (i.e,. face to face treatment) and passive control (i.e., waitlist control) groups, which introduces considerable heterogeneity to the studies. Unfortunately there were too few studies to examine the between-group effects of active and passive controls separately due to sample size. Overall, the findings are consistent with other studies demonstrating that RCBT produces durable outcomes for patients with anxiety and related disorders (Titov et al., 2014; Wootton, Dear, et al., 2015). However, it is also important for future studies to include long term follow-up assessments in order to inform our understanding of the durability of improvements from RCBT for PD.

4.2. Efficacy of Various RCBT Modalities

The primary moderator examined in the current study was remote treatment type. The results indicated that each type of remote treatment examined in the present study (internet-delivered CBT (ICBT), videoconference-delivered CBT (VCBT) and bibliotherapy-delivered CBT (BCBT)) resulted in similar effect sizes at post-treatment on measure of PD symptomatology (ICBT: k = 19, g = 1.10, 95% CI: 0.91–1.30; VCBT: k = 3, g = 1.40, 95% CI: 0.85– 1.95; and BCBT: k = 3, g = 1.51, 95% CI: 0.95 – 2.06), with no significant

differences in outcomes across treatment type. This finding is largely consistent with meta-analyses that have examined a similar research question (Wootton, 2016). For instance, Wootton (2016) found that ICBT, VCBT, BCBT and telephone delivered CBT resulted in large within-group effect sizes, while computerized CBT resulted in medium effect sizes. This finding highlights that each of the contemporary remote treatment approaches (ICBT, BCBT, and VCBT) can be reliably delivered to patients, however the type of approach may be best guided by treatment availability in the patient's jurisdiction, as well as patient preferences. Controlled trials directly comparing the acceptability, efficacy, and cost-effectiveness of different RCBT modalities are also needed using large representative samples in order to inform how to best deliver RCBT interventions for PD.

4.3. Efficacy of Low Intensity and High Intensity RCBT

Treatment intensity also did not moderate treatment outcome indicating that outcomes on measurs of PD symtoms are similar for low intensity treatments (g = 1.15; 95% CI: 0.96 - 1.34) and high intensity treatments (g = 1.40; 95% CI: 0.84 – 1.96). This finding is also consistent with similar meta-analyses examining high and low intensity RCBT treatments for a number of anxiety and related disorders (Wootton, 2016) and also highlights the potential for remote stepped care approaches to treatment for PD whereby patients with PD can commence treatment with low intensity RCBT approaches, which are more cost effective for treatment providers and patients, prior to stepping up to higher intensity RCBT services. Entirely remote stepped care approach to treatment are important for individuals who cannot access traditional high intensity services, such as face-to-face treatment, and as such further research in to the delivery of entirely remote stepped care treatments for individuals with PD are needed.

4.4. Usefulness of Breathing Retraining in RCBT Protocols

The inclusion of breathing retraining as part of the treatment protocol did not moderate treatment outcome from pre-treatment to post-treatment or pre-treatment to follow-up. This finding indicates that RCBT protocols that included breathing retraining performed as well as those that did not. This finding is consistent with the literature demonstrating that breathing retraining has little additional effects over other cognitive-behavioral interventions (such as interoceptive exposure, in-vivo exposure and cognitive restructuring) (Pompoli et al., 2018).

It has been argued that the use of breathing retraining, or other preparatory strategies prior to exposure, can be used as safety behaviors by patients (i.e., overt or covert behaviors that aim to reduce arousal in anxiety eliciting situations, preventing patients from learning evidence to disconfirm their maladaptive beliefs) and should thus be avoided (Lovibond et al., 2009; Piccirillo et al., 2016). Given that breathing retraining has the potential to be used as a safety behaviour and that there is evidence from this study, as well as others (Schmidt et al., 2000), that breathing retraining does not add any benefit over other CBT interventions it is possible that breathing retraining may be able to be successfully omitted from RCBT protocols moving forward in order to conserve time and resources. However future research may wish to assess this in randomized controlled trials.

4.5. Dissemination of RCBT to 'Real World' Clinical Settings

Finally, trial type did not moderate treatment outcome indicating that RCBT produces similar effects in 'real world' non-research settings as it does in tightly controlled clinical trials. While this finding is consistent with other studies examining this difference in individuals with panic disorder, who were treated transdiagnostically (Staples et al., 2019), it is contrary to other studies that have found that efficacy studies have larger effects than effectiveness studies for anxiety and related disorders (Stech et al., 2020). While further

research in this area is important, the results from the current study adds to the growing literature supporting the widescale dissemination of RCBT for PD in the community.

4.6. Limitations

The current study demonstrates that RCBT is an effective treatment for PD and highlights a number of ways that RCBT could be disseminated based on treatment preference or using a remote stepped care model. Despite these encouraging findings it is important to highlight a number of limitations to this meta-analysis. Firstly, the study included only published research and thus there is a higher chance that studies will null findings could have been omitted. Future research may wish to include such grey literature and contact researchers in the field to ascertain if they have any unpublished data that could be included in the meta-analysis. Secondly, it is important to highlight that many moderators could not be examined for the long term effect due to small sample sizes. Thus as the field progresses it is important for future studies to examine the long term benefits of each type of remote treatment in order to inform treatment planning and policy for individuals with PD. Thirdly, many of the studies contained samples that were overwhelmingly female, and others were of low quality. It is important for robust and high quality (i.e., adequately powered with representative samples of individuals with PD) randomized controlled trials are examined in the future in order to inform our understanding of the efficacy of RCBT for PD. Finally, high levels of heterogeneity and potential for publication bias across some analyses indicate that it is important for future research to examine other potential moderators of treatment outcome, and also to interpret some results with caution where publication bias was indicated.

4.7. Conclusions

This meta-analysis demonstrates that RCBT for PD is an efficacious treatment approach. Furthermore, this study is the first to demonstrate that different remote treatment approaches result in similar outcomes, such as low intensity and high intensity interventions.

This highlights that remote treatments may be able to be disseminated based on treatment preference, and also highlights the potential for an entirely remote stepped care approach to treatment for PD. The findings further suggest that RCBT protocols may be able to omit breathing retraining without deleterious effects on outcome, however further research is required. Finally, the results demonstrate preliminary evidence to suggest that when RCBT for PD is disseminated in real world settings, outcomes may be similar to those in seen in well controlled clinical trials. These findings have important implications for treatment planning for individuals with PD.

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Table 1

Characteristics of Included Studies

Study	Country	Study type	Treatment type	Treatment intensity	Outcome measure	N	Mean age (SD)	% female	Analysis	Longest follow-up (months)	Study quality
Allen et al. (2016)	Australia	RCT	ICBT #	Low	PDSS-SR	27	--	--	ITT	3	24
			WLC	--		36					
Bergström et al. (2010)*	Sweden	RCT	ICBT	Low	PDSS	50	33.8 (9.7)	64	ITT	6	25
			T-CBT	--		54	34.6 (9.2)	59			
Bouchard et al. (2000)	Canada	OT	VCBT #	High	P&A	8	--	63	ITT	--	25
Carlbring et al. (2003)	Sweden	RCT	ICBT #	Low	BSQ	11	37.9 (8.6)	68	ITT	--	23
			AR	--		11					
Carlbring et al. (2005)	Sweden	RCT	ICBT #	Low	BSQ	25	35.0 (7.7)	71	ITT	12	34
			T-CBT	--		24					
Carlbring et al. (2006)	Sweden	RCT	ICBT #	Low	BSQ	30	36.7 (10.0)	60	ITT	9	25
			WLC	--		30	–	–			
Ciuca et al. (2018)	Romania	RCT	VCBT #	High	PDSS-SR	36	35.2 (10.3)	68	ITT	6	31

			ICBT #	Low		37					
			WLC	--		38					
Fogliati et al. (2016)	Australia	RCT ^	ICBT #	Low	PDSS-SR	68	39.4 (11.1)	85	ITT	24	30
Gould et al. (1993)	USA	RCT	BCBT #	Low	PASQ	11	35.7 (10.2)	65	CA	--	23
			T-CBT #	--		9					
			WLC	--		11					
Gould and Clum (1995)	USA	RCT	BCBT #	Low	PASQ	12	36.2 (7.7)	84	CA	2	19
			WLC	--		13					
Hedman et al. (2013)*	Sweden	OT	ICBT	Low	PDSS-SR	570	37.3 (10.7)	61	ITT	6	24
Kiropoulos et al. (2008)	Australia	RCT	ICBT #	Low	PDSS	46	39.0 (11.1)	72	ITT	--	29
			T-CBT	--		40					
Klein et al. (2006)	Australia	RCT	ICBT #	Low	PDSS	19	--	80	ITT	3	29
			BCBT #	Low		18					
			IC	--		18					
Klein et al. (2009)	Australia	RCT	ICBT #	Low	PDSS	28	39.5 (10.7)	83	ITT	--	28
			ICBT #	Low		29					
Matsumoto et al. (2018)	Japan	OT	VCBT	High	PDSS	10	38.8 (9.8)	100	ITT	--	26

Nordgreen et al. (2010)	Norway	OT	ICBT #	Low	BSQ	27	40.5 (12.4)	70	ITT	6	19
Nordgreen et al. (2018)*	Norway	OT	ICBT#	Low	BSQ	124	35.9 (11.8)	65	ITT	6	17
Richards et al. (2006)	Australia	RCT	ICBT #	Low	PDSS	11	37.4 (8.6)	69	ITT	3	28
			ICBT #	Low		12	31.9 (9.3)				
			IC	--		9	41.2 (10.7)				
Shandley et al. (2008)	Australia	CT ^	ICBT #	Low	PDSS	38	43.5 (12.4)	77	ITT	6	23
Wims et al. (2008)	Australia	OT	ICBT	Low	PDSS	10	43.9 (7.78)	60	ITT	--	15
Wims et al. (2010)	Australia	RCT	ICBT	Low	PDSS	29	42.1 (12.3)	76	ITT	1	20
			WLC	--		25					

Note. * indicates that study was an effectiveness study. USA = United States of America; RCT = Randomized Controlled Trial; CT = Controlled Trial (non-randomized); OT = Open Trial; ^ indicates that the control group was not examined in this study because it violated the inclusion criteria; # indicates breathing retraining/controlled breathing was used as part of the intervention; ICBT = internet administered CBT; BCBT = bibliotherapy administered CBT; VCBT = videoconferencing administered CBT; WLC = Waitlist control; IC = Informational Control; T-CBT = Therapist delivered CBT; AR = Applied Relaxation; PDSS-SR = Panic Disorder Severity Scale (Self-Report); PDSS = Panic Disorder Severity Scale; P&A = Panic and Agoraphobia Scale; BSQ = Body Sensations Questionnaire; PASQ = Panic Attack Symptoms Questionnaire; ITT = Intention to Treat; CA = Completer Analysis.

Table 2

Within-group Effect Sizes from Pre-treatment to Post-treatment and Pre-treatment to Follow-up.

Study	Type of remote treatment	Treatment intensity	Pre-treatment to post-treatment		Weight of included study	Pre-treatment to follow-up		Weight of included study
			g	95% CI		*g*	95% CI	
Allen et al. (2016)	ICBT	Low	1.17	0.80 – 1.55	4.31	1.58	1.15 – 2.01	6.02
Bergström et al. (2010)	ICBT	Low	1.70	1.36 – 2.03	4.47	2.32	1.91 – 2.73	6.10
Bouchard et al. (2000)	VCBT	High	1.06	0.44 – 1.69	3.26	--	--	--
Carlbring et al. (2003)	ICBT	Low	0.72	0.24 – 1.20	3.85	--	--	--
Carlbring et al. (2005)	ICBT	Low	1.41	0.98 – 1.83	4.11	1.39	0.97 – 1.80	6.07
Carlbring et al. (2006)	ICBT	Low	1.85	1.40 – 2.30	3.98	1.58	1.17 – 1.99	6.10
Ciuca et al. (2018)	VCBT	High	2.06	1.62 – 2.50	4.40	2.23	1.76 – 2.70	5.88
	ICBT	Low	1.44	1.09 – 1.79	4.01	2.73	2.19 – 3.27	5.60
Fogliati et al. (2016)	ICBT	Low	0.78	0.57 – 0.99	4.92	1.16	0.93 – 1.40	6.65
Gould et al. (1993)	BCBT	Low	1.60	0.93 – 2.27	3.09	--	--	--

Gould and Clum (1995)	BCBT	Low	1.34	0.76 – 1.92	3.43	1.74	1.06 – 2.41	5.04
Hedman et al. (2013)	ICBT	Low	0.91	0.83 – 0.98	5.20	0.99	0.91 – 1.07	6.92
Kiropoulos et al. (2008)	ICBT	Low	0.89	0.62 – 1.16	4.71	--	--	--
Klein et al. (2006)	BCBT	Low	1.58	1.05 – 2.10	3.67	3.18	2.31 – 4.06	4.25
	ICBT	Low	2.48	1.78 – 3.17	2.99	1.50	1.00 – 1.99	5.77
Klein et al. (2009)	ICBT	Low	0.64	0.31 – 0.98	4.46	--	--	--
	ICBT	Low	0.65	0.34 – 0.96	4.57	--	--	--
Matsumoto et al. (2018)	VCBT	High	0.87	0.18 – 1.55	3.04	--	--	--
Nordgreen et al. (2010)	ICBT	Low	0.59	0.28 – 0.90	4.57	0.41	0.11 – 0.70	6.48
Nordgreen et al. (2018)*	ICBT	Low	0.32	0.18 – 0.46	5.09	0.36	0.22 – 0.50	6.85
Richards et al. (2006)	ICBT	Low	1.24	0.68 – 1.80	3.53	1.49	0.88 – 2.11	5.28
	ICBT	Low	2.82	1.82 – 3.83	2.03	2.47	1.57 – 3.38	4.13
Shandley et al. (2008)	ICBT	Low	0.92	0.63 – 1.21	4.64	0.90	0.61 – 1.18	6.51
Wims et al. (2008)	ICBT	Low	1.43	0.77 – 2.08	3.15	--	--	--
Wims et al. (2010)	ICBT	Low	0.89	0.57 – 1.22	4.50	0.96	0.63 – 1.30	6.36
Overall			**1.18**	**0.99-1.36**		**1.51**	**1.22-1.79**	

Note. ICBT = internet administered CBT; BCBT = bibliotherapy administered CBT; VCBT = videoconferencing administered CBT

Table 3

Between-group Effect Sizes Comparing Remote CBT treatment to Control at Post-treatment and Follow-up.

Study	Type of remote treatment	Treatment intensity	Type of control group	Post-treatment		Weight of included study	Follow-up		Weight of included study
				g	95% CI		*g*	95% CI	
Allen et al. (2016)	ICBT	Low	WLC (Passive)	0.98	0.46 – 1.50	6.81	--	--	--
Bergström et al. (2010)	ICBT	Low	T-CBT (Active)	0.00	-0.38 – 0.38	7.24	--	--	--
Carlbring et al. (2003)	ICBT	Low	AR (Active)	0.14	-0.66 – 0.95	5.79	--	--	--
Carlbring et al. (2005)	ICBT	Low	T-CBT (Active)	-0.05	-0.60 – 0.50	6.71	-0.02	-0.57 – 0.53	37.22
Carlbring et al. (2006)	ICBT	Low	WLC (Passive)	1.94	1.33 – 2.55	6.51	--	--	--
Ciuca et al. (2018)	ICBT	Low	WLC (Passive)	0.81	0.34 – 1.27	6.99	--	--	--
Ciuca et al. (2018)	VCBT	High	WLC (Passive)	1.22	0.73 – 1.72	6.91	--	--	--
Gould et al. (1993)	BCBT	Low	T-CBT (Active)	0.25	-0.60 – 1.10	5.63	--	--	--

Gould et al. (1993)	BCBT	Low	WLC (Passive)	0.34	-0.47 – 1.15	5.77	--	--	--
Gould and Clum (1995)	BCBT	Low	WLC (Passive)	0.08	-0.68 – 0.84	5.96	0.61	-0.16 – 1.37	25.06
Kiropoulos et al. (2008)	ICBT	Low	T-CBT (Active)	-0.12	-0.55 0.32	7.08	--	--	--
Klein et al. (2006)	BCBT	Low	IC (Passive)	1.58	0.84 – 2.31	6.05	--	--	--
Klein et al. (2006)	ICBT	Low	IC (Passive)	2.46	1.62 – 3.31	5.64	--	--	--
Richards et al. (2006)	ICBT	Low	IC (Passive)	2.19	1.11 – 3.28	4.79	--	--	--
Richards et al. (2006)	ICBT	Low	IC (Passive)	1.30	0.38 – 2.22	5.37	--	--	--
Wims et al. (2010)	ICBT	Low	WLC (Passive)	0.59	0.05 – 1.12	6.75	0.70	0.16 – 1.25	37.72
Overall				**0.82**	0.44 – 1.20		**0.41**	**-0.07-0.89**	

Note. ICBT = internet administered CBT; BCBT = bibliotherapy administered CBT; VCBT = videoconferencing administered CBT; WLC = Waitlist control; IC = Informational Control; T-CBT = Therapist delivered CBT; AR = Applied Relaxation;

Figure 1.
Flowchart