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# Disorder-specific versus transdiagnostic and clinician-guided versus self-guided internet-delivered treatment for panic disorder and comorbid disorders: A randomized controlled trial

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ABSTRACT

Transdiagnostic cognitive behaviour therapy (TD-CBT) aims to target the symptoms of multiple disorders whereas disorder-specific CBT (DS-CBT) targets the symptoms of principal disorders. This study compared the relative benefits of internet-delivered TD-CBT and DS-CBT when provided in clinician-guided (CG-CBT) and self-guided (SG-CBT) formats for people with a principal diagnosis of Panic Disorder (PD). Participants (n = 145) were randomly allocated to receive TD-CBT or DS-CBT and CG-CBT or SG-CBT. Large reductions in symptoms of PD (Cohen's $d \geq 0.71$; avg. reduction $\geq 36\%$) and moderate-to-large reductions in symptoms of comorbid depression (Cohen's $d \geq 0.71$; avg. reduction $\geq 33\%$), generalised anxiety disorder (Cohen's $d \geq 0.91$; avg. reduction $\geq 34\%$) and social anxiety disorder (Cohen's $d \geq 0.50$; avg. reduction $\geq 15\%$) were found over the 24-month follow-up period. Highlighting their efficacy and acceptability, no marked and consistent differences were observed between TD-CBT and DS-CBT or CG-CBT and DS-CBT.


## 1. Introduction

Panic Disorder (PD) is an anxiety disorder characterized by excessive fear of the occurrence and health implications of panic attacks (American Psychiatric Association, 2013). PD has a 12-month prevalence of 2.7% and a lifetime prevalence of 4.7% in the United States (Kessler, Chiu, Demler, & Walters, 2005) and an estimated 12-month prevalence of 1.8% and lifetime prevalence of 3.5% in Australia (McEvoy, Grove, & Slade, 2011). PD can cause significant functional impairment and is highly comorbid with other anxiety and depressive disorders (Allen et al., 2010). Cognitive behavioural therapy (CBT) is effective at treating PD (Butler, Chapman, Forman, & Beck, 2006; Stewart & Chambless, 2009; Sánchez-Meca, Rosa-Alcázar, Marín-Martínez, & Gómez-Conesa, 2010; Hoffman, Asnaani, Vonk, Sawyer, & Fang, 2012). Several studies have also demonstrated that internet-delivered CBT for PD produces superior outcomes to control conditions (Klein, Richards, & Austin, 2006), produces similar outcomes as CBT delivered in a face-to-face format (Bergstrom et al., 2010; Carlbring et al., 2005; Kiropoulos et al., 2008), and can be successfully delivered in routine psychiatric care (Hedman, Ljótsson, Kaldo et al., 2013; Hedman, Ljótsson, Rück et al., 2013).

At least two different CBT treatment approaches have been used to treat PD to date (Craske et al., 2007; McEvoy, Nathan, & Norton, 2009). The first is a disorder-specific CBT (DS-CBT) approach, which aims to specifically target panic symptoms and the cognitive and behaviour processes known to contribute to PD (e.g., Salkovskis, 2004; Otto & Deveney, 2005). The second is a transdiagnostic CBT (TD-CBT) approach, which aims to simultaneously target the underlying cognitive and behavioural processes common across the anxiety and depressive disorders (Barlow, Allen, & Choate, 2004; Mansell, Allison, Ed, & Roz, 2009; Goldberg, 2010; Murray et al., 2014). There is considerable evidence from clinical trials of the more established DS-CBT approach to the treatment for PD (Butler et al., 2006; Hoffman et al., 2012; Sánchez-Meca et al., 2010;

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Stewart & Chambless, 2009) and the results from emerging trials of TD-CBT for PD have been encouraging (Ellard, Fairholme, Boisseau, Farchione, & Barlow, 2010; Dear, Titov, Schwencke et al., 2011; Dear, Titov, Sunderland et al., 2011; Dear, Titov, Schwencke et al., 2011; Dear, Titov, Sunderland et al., 2011; Johnston, Titov, Andrews, Spence, & Dear, 2011; Johnston, Titov, Spence, Andrews, & Dear, 2011; Titov, Dear, McMillan et al., 2011; Titov, Dear, Schwencke et al., 2011; Farchione et al., 2012; Norton & Barrera, 2012). However, with the exception of several recent studies (Dear, Gandy et al., 2015; Dear, Staples et al., 2015; Dear, Zou et al., 2015; Titov, Dear, Staples, Bennett-Levy et al., 2015; Titov, Dear, Staples, Terides et al., 2015; Dear et al., submitted), studies of TD-CBT have involved relatively small numbers of participants (e.g., < 10) with PD to date. Moreover, one of the only studies to focus on principal PD (n = 65) found evidence supporting the superiority of a more disorder-specific approach to PD over more transdiagnostic approaches trying to also address comorbid disorders (Craske et al., 2007). However, where other studies of transdiagnostic treatment have relied on a single treatment protocol, it is important to note that this study employed a slightly different approach where, in the transdiagnostic condition, clinicians could employ another disorder-specific treatment protocol targeting the next most severe comorbid symptoms (Craske et al., 2007). Thus, further research is needed to examine the relative benefits of TD-CBT and DS-CBT for panic disorder and panic symptoms ideally using larger samples.

One overarching issue facing efforts to reduce the burden of panic disorder and other common mental health disorders is that relatively few people seek or receive treatment (Wang et al., 2007). This has led to recent calls for innovation in the treatment of common mental health disorders (Kazdin, 2015), and one such innovative approach is the delivery of treatment via the internet (Andersson & Titov, 2014). Internet-delivered CBT (iCBT) employs all of the same principles and, apart from being delivered via the internet, provides the same therapeutic information and skills as traditional face-to-face CBT treatments (Andersson & Titov, 2014). Reflecting the growing evidence for iCBT (e.g., (Andersson & Cuijpers, 2009; Cuijpers et al., 2009; Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010), there are now major efforts to explore the potential of iCBT for anxiety and depression as a part of routine care and mental health service provision (Mewton, Wong, & Andrews, 2012; Ruwaard, Lange, Schrieken, Dolan, & Emmelkamp, 2012; Hedman, Ljótsson, Kaldo et al., 2013; Hedman, Ljótsson, Rück et al., 2013; Newby et al., 2013; Titov, Dear, Staples, Bennett-Levy et al., 2015; Titov, Dear, Staples, Terides et al., 2015). Notwithstanding the potential of iCBT, very little is known empirically about what components are necessary for iCBT to be effective, safe and acceptable. Meta-analyses indicate that clinician-guided iCBT is associated with higher completion rates and greater clinical outcomes than self-guided iCBT (Andersson & Cuijpers, 2009; Cuijpers et al., 2009). However, several recent trials of newer-generation self-guided iCBT treatments have found similar clinical outcomes with and without clinician-guidance (Berger, Caspar et al., 2011; Berger, Hämmerli, Gubser, & Caspar, 2011; Titov et al., 2013; Dear, Gandy et al., 2015; Dear, Staples et al., 2015; Dear, Zou et al., 2015; Titov, Dear, Staples, Bennett-Levy et al., 2015; Titov, Dear, Staples, Terides et al., 2015). These newer-generation self-guided treatments have typically been carefully developed over multiple clinical trials to work in a self-guided format and often involve some kind of screening assessment, patient safety monitoring and other measures, such as automatic emails, aimed at engaging patients throughout treatment. Safe, acceptable and effective self-guided iCBT treatments arguably have even more potential than clinician-guided iCBT programs for improving access to treatment. Unfortunately, although some studies have shown good outcomes can be obtained with very little clinician contact (Klein et al., 2009), no studies have directly compared the acceptability or efficacy of self-guided and clinician-guided iCBT for PD.

The present study is one of four large randomized controlled trials (RCTs) that explore the relative clinical efficacy and acceptability of internet-delivered transdiagnostic CBT and disorder-specific CBT, when provided in both clinician-guided and self-guided formats (Dear, Gandy et al., 2015; Dear, Staples et al., 2015; Dear, Zou et al., 2015; Titov, Dear, Staples, Bennett-Levy et al., 2015; Titov, Dear, Staples, Terides et al., 2015; Dear et al., submitted). The present study employed the same design as these other trials in the series and specifically sought to examine the relative clinical efficacy and acceptability of transdiagnostic (TD-CBT) and disorder-specific (DS-CBT) for principal PD, when provided in both clinician-guided (CG-CBT) and self-guided (SG-CBT) formats. It was hypothesised that both TD-CBT and DS-CBT would result in significant reductions in symptoms of PD, but that, by targeting underlying cognitive and behavioural processes, TD-CBT would be superior at reducing symptoms of comorbid depression, generalised anxiety and social anxiety at each time point. It was also hypothesised that CG-CBT would be superior to SG-CBT at every time point for both symptoms of SAD and comorbid depression, generalised anxiety, and social anxiety.

## 2. Method

### 2.1. Participants

The study was approved by the Human Research Ethics Committee (HREC) of Macquarie University, Sydney, Australia, and the trial was registered on the Australian and New Zealand Clinical Trials Registry (ANZCTR) as ACTRN12612000431820. The study was promoted via advertisements in major newspapers across Australia and via unpaid general advertisements by a broad range of non-governmental organisations providing services to people with mental health difficulties. This study was advertised alongside three other studies with the same design, with each RCT targeting people with one of four principal diagnoses, that is, Panic Disorder (PD), Major Depressive Disorder (MDD), Generalised Anxiety Disorder (GAD), or Social Anxiety Disorder (SAD) (Dear, Gandy et al., 2015; Dear, Staples et al., 2015; Dear, Zou et al., 2015; Titov, Dear, Staples, Bennett-Levy et al., 2015; Titov, Dear, Staples, Terides et al., 2015; Dear et al., submitted). Participants read about the study and applied to participate via the website of the eCentreClinic (www.ecentreclinic.org), which is a specialist research unit offering the opportunity to receive free treatment via the internet. Interested individuals were invited to submit an online application to participate in the trial, which involved completing several symptom and demographic questionnaires.

The inclusion criteria for the study were: (i) resident of Australia aged 18–64 years of age; (ii) principal symptoms consistent with Panic Disorder; (iii) total score ≥ 1 on the Anxiety Sensitivity Questionnaire (ANSQ) (McQuaid, Stein, McCahill, Laffaye, & Ramel, 2000), and (iv) if taking medication for anxiety or depression, being on a stable dose for at least one month. The exclusion criteria were: (i) experiencing an unmanaged psychotic illness; (ii) experiencing very severe symptoms of depression (i.e., defined as a total score > 22 or endorsing a score > 2 to item 9 of the Patient Health Questionnaire 9-item (PHQ9); (iii) having a history of self-harm or suicide attempts within the last 12 months; or (iv) currently participating in CBT. Table 1 shows the demographic characteristics of the resultant sample.

The CONSORT flowchart for this trial is shown in Fig. 1. A total of 211 people applied to participate in the trial and indicated that symptoms of PD were their principal difficulty during the online application process. Of these, 185 met the initial inclusion criteria,