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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,

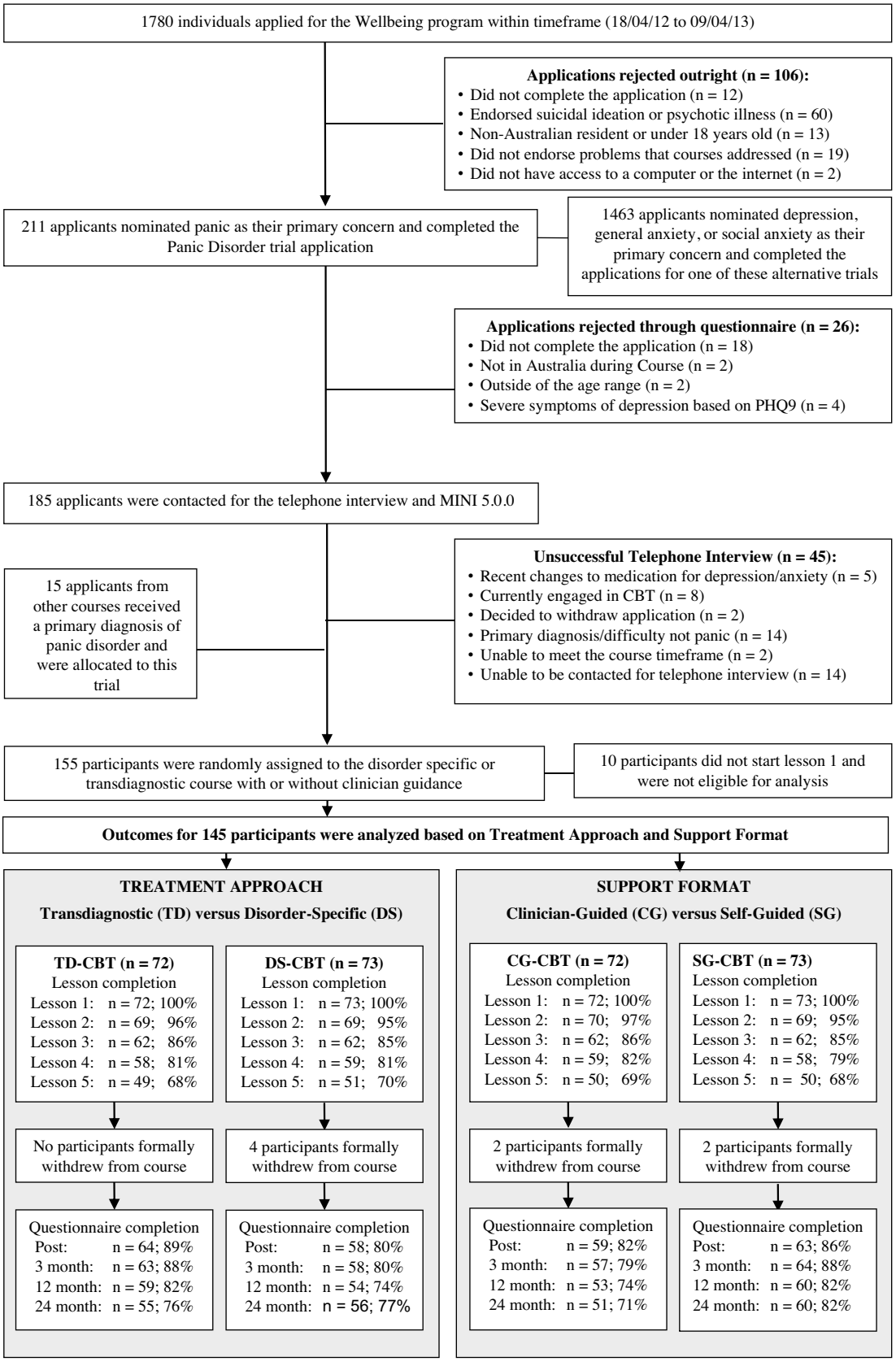

Fig. 1. Participant flow from application to 24-month follow-up.

Table 1
Demographic characteristics of the participants.

		Treatment Approach			Support Format		
	Overall (n = 145)	TD-CBT (n = 72)	DS-CBT (n = 73)	Significance	CG-CBT (n = 72)	SG-CBT (n = 73)	Significance
Gender							
Male	30 (21%)	19 (26%)	11 (15%)	Wald's X^2 2.77 $p = .096$	19 (26%)	11 (15%)	Wald's $X^2 = 2.77, p = .096$
Female	115 (79%)	53 (74%)	62 (85%)		53 (74%)	62 (85%)	
Age (years)							
Mean (SD)	41.40 (11.28)	43.40 (11.23)	39.42 (11.05)	Wald's $X^2 = 4.23 p = .040$	39.42 (11.05)	43.40 (11.23)	Wald's $X^2 = 2.04, p = .153$
Range	18–62	18–62	18–58		18–58	18–62	
Marital Status							
Single/Never Married	79 (27%)	13 (18%)	20 (27%)	Wald's $X^2 = 1.11 p = .293$	19 (26%)	14 (19%)	Wald's $X^2 = .62$, $p = .432$
Married/De Facto	174 (60%)	51 (71%)	45 (62%)		45 (63%)	51 (70%)	
Separated/Divorced/Widowed	37 (13%)	8 (11%)	8 (11%)		8 (11%)	8 (11%)	
Education							
High School or less	38 (26%)	14 (19%)	24 (33%)	*Wald's* $X^2 = 4.70 p = .030$	20 (28%)	18 (25%)	*Wald's* $X^2 = .01$, $p = .927$
Trade/Technical Certificate	25 (17%)	11 (15%)	14 (19%)		11 (15%)	14 (19%)	
Diploma/Degree	82 (57%)	47 (65%)	35 (48%)		41 (57%)	41 (56%)	
Employment							
Full-time/Part-time	109 (75%)	60 (83%)	49 (67%)	*Wald's* $X^2 = 5.58 p = .018$	72 (100%)	37 (51%)	*Wald's* $X^2 < .01$, $p = .997$
Student	7 (5%)	4 (6%)	3 (4%)		0 (0%)	7 (10%)	
Unemployed, retired or disabled	29 (20%)	8 (11%)	21 (29%)		0 (0%)	29 (40%)	
Previous Mental Health Treatment	108 (75%)	53 (74%)	55 (75%)	*Wald's* $X^2 = .06$, $p = .811$	46 (64%)	62 (85%)	*Wald's* $X^2 = 8.03$, $p = .005$
Currently Taking Medication	58 (40%)	30 (42%)	28 (38%)	*Wald's* $X^2 = .17$, $p = .684$	25 (35%)	33 (45%)	*Wald's* $X^2 = 1.65$, $p = .199$

Note: TD = transdiagnostic, DS = disorder-specific, CG = clinician-guided, SG = self-guided, CBT = cognitive behaviour therapy.

which were assessed via the online application, and then participated in a telephone interview during which the Mini International Neuropsychiatric Interview Version 5 (MINI) (Lecrubier et al., 1997) was administered and the inclusion criteria re-assessed. A further 15 applicants initially indicated principal difficulties of MDD, GAD or SAD, during the online application but, upon interview, indicated PD was their principal difficulty. A total of 155 applicants met all inclusion criteria following the telephone interview.

2.2. Design and measures

The study employed a CONSORT-revised compliant RCT where participants were randomized to receive one of two treatment approaches (Treatment Approach: TD-CBT vs DS-CBT) and one of two support formats (Support Format: CG-CBT vs SG-CBT). All participants completed questionnaires at initial assessment, pre-treatment, post-treatment and at 3, 12, and 24-month follow-up. The primary and secondary measures were administered at each time point with the exception of the PDSS-SR, which due to an administrative error was not administered at initial assessment but was administered at pre-treatment and all other time-points. Consequently, pre-treatment PDSS-SR scores were used as baseline in the current study. In addition, the PDSS-SR and PHQ-9 were also administered weekly during the treatment. To reduce burden on participants the tertiary outcomes were not administered at initial assessment and the K-10 and NEO-FF-N were not administered at 24-month follow-up. All analyses, except those for the PDSS-SR and the tertiary measures, used the initial assessment scores as baseline. Unblinded MINI diagnostic assessments were conducted via telephone at initial assessment and again at 3-month follow-up. The study was powered for comparisons between the two treatment approaches and between the two delivery formats. The researchers sought to recruit at least 102 participants for each comparison arm (i.e., TD-CBT vs DS-CBT and CG-CBT vs SG-CBT) which, with alpha set at 0.05 and power set at 0.80, would enable the detection of small-to-moderate (i.e., Cohen's *ds* > .35) effect size differences between the arms. Unfortunately, recruitment difficulties meant that only 132 participants with principal PD were recruited, providing sufficient power to detect a moderate-to-large (i.e., Cohen's *ds* > .50) effect size difference between the arms on the primary outcome of panic symptoms.

2.2.1. Primary measure

2.2.1.1. Panic Disorder Severity Scale-Self Report (PDSS-SR) (Houck, Spiegel, Shear, & Rucci, 2002).. The PDSS-SR is a 7-item measure of panic disorder symptoms. Psychometric evaluations suggest that it has high internal consistency, good test-retest reliability and is sensitive to treatment-related change in panic symptoms (Houck et al., 2002). Scores range from 0 to 28 and Cronbach's α in the current study was. 93.

2.2.2. Secondary measures

2.2.2.1. Patient Health Questionnaire-9 Item (PHQ-9) (Kroenke, Spitzer, & Williams, 2001).. The PHQ-9 is a 9-item measure of symptoms of depression based on the DSM-IV diagnostic criteria for major depressive disorder (Kroenke et al., 2001). The PHQ-9 has good internal consistency (Titov, Dear, McMillan et al., 2011; Titov, Dear, Schwencke et al., 2011) and is sensitive to change (Kroenke, Spitzer, Williams, & Lowe, 2010). Scores range from 0 to 27 and Cronbach's α in this study was .82.

2.2.2.2. Generalized Anxiety Disorder 7-Item Scale (GAD-7) (Spitzer, Kroenke, Williams, & Löwe, 2006).. The GAD-7 is a 7-item measure of the symptoms and severity of general anxiety, which is based on the DSM-IV diagnostic criteria for GAD (Löwe et al., 2008). The GAD-7 has good internal consistency and good convergent and divergent validity with other anxiety and disability scales (Kroenke et al., 2010; Dear, Titov, Schwencke et al., 2011; Dear, Titov, Sunderland et al., 2011). Scores range from 0 to 21 and Cronbach's α in the current study was .88.

2.2.2.3. Mini-Social Phobia Inventory (MINI-SPIN) (Connor, Kobak, Churchill, Katzelnick, & Davidson, 2001).. The 3-item MINI-SPIN is a measure of social anxiety symptoms based on DSM-IV criteria for social anxiety disorder (Connor et al., 2001; Weeks, Spokas, & Heimberg, 2007). The MINI-SPIN has good internal consistency and adequate convergent validity with other standardised measures of social anxiety (Weeks et al., 2007; Osório et al., 2010). Scores range from 0 to 15 and Cronbach's α in this study was .87.

2.2.3. Tertiary measures

2.2.3.1. Kessler 10-item scale (K-10) (Kessler et al., 2002).. The K-10 is a ten-item measure of general psychological distress with total

scores ≥ 22 associated with a diagnosis of anxiety and depressive disorders (Andrews & Slade, 2001). Scores range from 10 to 50 and Cronbach's α in the current study was .89.

2.2.3.2. Sheehan Disability Scale (SDS) (Sheehan, 1983).. The SDS is a 3-item measure of disability with high internal consistency (Leon, Olfson, Portera, Farber, & Sheehan, 1997). Scores range from 0 to 30 and Cronbach's α in the present study was .89.

2.2.3.3. NEO-Five Factor Inventory—Neuroticism Subscale (NEO-FFI-N) (Costa & McCrae, 1985).. The Neuroticism subscale of the NEO is a 12-item measure of a general tendency to experience negative emotional states and sensitivity to stress (Clark, Watson, & Mineka, 1994; Griffith et al., 2010), which is considered a higher-order risk factor for anxiety and depression (Cuijpers, van Straten, & Donker, 2005; Spinhoven, de Rooij, Heiser, Smit, & Penninx, 2009). Scores range from 0 to 48 and Cronbach's α in the current study was .75.

2.2.4. Other measures

2.2.4.1. Mini International Neuropsychiatric Interview Version 5.0.0 (MINI) (Lecrubier et al., 1997).. The MINI is a brief diagnostic interview developed to determine the presence of current Axis-I disorders using DSM-IV diagnostic criteria. It has excellent inter-rater reliability and adequate concurrent validity with the Composite International Diagnostic Interview (World Health Organization, 1990).

2.2.4.2. Treatment satisfaction and acceptability. Consistent with previous research (Titov et al., 2013; Dear, Gandy et al., 2015; Dear, Staples et al., 2015; Dear, Zou et al., 2015), treatment satisfaction and acceptability was assessed at post-treatment via two questions: (1) 'Would you feel confident in recommending this treatment to a friend?' and (2) 'Was it worth your time doing the Course?'. Participants responded to these questions with a 'Yes' or 'No' response.

2.3. Interventions

All participants received access to either a DS-CBT course for PD, the *Panic Course*, or a TD-CBT course, the *Wellbeing Course*. The *Panic Course* was developed specifically for this trial to target symptoms of PD and the *Wellbeing Course* has been previously demonstrated as clinically efficacious in treating symptoms of anxiety and depression (Titov, Dear, Johnston, & Terides, 2012; Titov et al., 2013, 2014). Consistent with the previous trials in this series of 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), the two courses comprised a similar structure and similar amounts and forms of content to facilitate comparisons. Both include five lessons delivered online over eight weeks, lesson summaries and homework assignments for each lesson, a similar number of detailed case stories, and a similar number of additional resources targeting symptoms such as sleep problems and communication skills. Based on the content and previous results (Titov, Dear, Staples, Bennett-Levy et al., 2015; Titov, Dear, Staples, Terides et al., 2015), it is expected that reading the first four lessons of each course will provide an adequate therapeutic dose. Each lesson is presented in a slide format combining text and images, with approximately 60 slides per lesson and 50 words per slide. Participants are instructed to read lessons in order over 8 weeks. Lessons 1, 2, 3, 4, and 5 are available at the beginning of weeks 1, 2, 4, 5, and 7, respectively. This timetable provides participants with additional time for the most complex components of the intervention; namely skills for managing cognitive and behavioural symptoms.

Consistent with standard definitions (McEvoy et al., 2009) and the other trials in this series of trials (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 TD-CBT intervention was the same for all participants and was not designed to treat any specific psychological disorder and rather aimed to present a broad range of therapeutic information and skills relevant to the cognitive, physical and behavioural symptoms of psychological distress generally. Reflecting this, the TD-CBT intervention did not mention specific diagnoses and all vignettes, examples and case stories were presented to cover a broad range of situations and types of psychological distress (e.g., excessive worry, low mood, social anxieties, and panic and strong physical sensations). In contrast, the DS-CBT treatment was specifically designed to target symptoms of PD and presented all therapeutic information and skills in the context of PD and reducing PD symptoms. Consequently, all vignettes, examples and case stories focussed on PD and the management of associated symptoms, and no specific mention of other diagnoses or the broader application of therapeutic skills was made. The content and differences between the TD-CBT and DS-CBT interventions are summarised in Table 2.

Participants in the clinician-guided condition (CG-CBT) received weekly contact via telephone or a secure email messaging system. Three accredited and nationally registered psychologists and one CBT-trained counsellor provided treatment. Based on the findings of previous studies (Craske et al., 2009; Johnston, Titov, Andrews et al., 2011; Johnston, Titov, Spence et al., 2011) and to minimise therapist drift (Waller, 2009), the nature of the contact was protocolised and key aims included (1) reinforcing the main messages of each lesson, (2) answering questions, (3) reinforcing progress and skills practice, (4) problem solving the use of skills, (5) normalising the challenges of recovery, and (6) obtaining feedback about the participant's perception and engagement with the course. Each contact was designed to take ≤ 10 min, but more time was provided when clinically indicated. The clinicians received training in online interventions via the training program at the eCentreClinic and received supervision from BFD and NT during weekly individual and group supervision sessions. Participants in the self-guided condition did not receive weekly contact, but were monitored throughout treatment by the clinicians and were able to contact the clinic if technical assistance was required, or if they were experiencing a mental health crisis. A research assistant provided technical support for all participants in the trial.

All participants received an email at the start of the intervention with guidelines about the course and a recommended timetable for working through the materials. Consistent with previous research (Titov et al., 2013, 2014), participants also received automated emails at the beginning of each week to inform them about additional resources and to recommend activities for that week. All participants also received automatic emails that reinforced their progress, congratulated them on the completion of lessons, and reminded them about the availability of new materials when they had not viewed the lesson within a week of it becoming available.

2.4. Statistical analyses

All analyses were conducted using SPSS version 21. Group differences in demographic variables and diagnostic variables were analysed using binomial and multinomial logistic regression and general linear models analyses. The alpha significance level for the preliminary analyses was adjusted from 0.05 to 0.01 as a partial control for the large number of analyses conducted. Participants who did not start the interventions were not included in any analyses.

Table 2
Therapeutic content and skills included within the Transdiagnostic Wellbeing Course and Disorder-Specific Panic Course.

Lesson	Transdiagnostic Wellbeing Course			Disorder-Specific Panic Course		
	Lesson Content	Primary Skills Taught	Additional Resources	Lesson Content	Primary Skills Taught	Additional Resources
1	Education about the general prevalence and symptoms of anxiety and low mood without mention of specific disorders. Introduction of a CBT model and explanation of the functional relationship between physical, thought and behavioural symptoms in psychological distress. Instructions for identifying their own symptoms and how their symptoms interact. Transdiagnostic vignettes and examples of anxiety and low mood symptoms provided.	- Symptom identification - Symptom formulation	- Sleep management - What to do in a mental health emergency - Transdiagnostic case stories	Education about the prevalence and symptoms of PD. Introduction of a CBT model and explanation of the functional relationship between physical, thought and behavioural symptoms in PD. Instructions for identifying their own symptoms and how their symptoms interact. PD specific vignettes and examples of PD symptoms provided.	- Symptom identification - Symptom formulation	- Sleep management - What to do in a mental health emergency - PD case stories
2	Introduction to the basic principles of cognitive therapy and importance of managing thoughts to manage anxiety and low mood. Instructions for monitoring and challenging thoughts related to anxiety and low mood. Transdiagnostic vignettes and examples of thoughts provided.	- Thought monitoring - Thought challenging	- Structured problem solving - Worry Time - Challenging beliefs - Transdiagnostic case stories	Introduction to the basic principles of cognitive therapy and importance of managing thoughts to manage PD. Instructions for monitoring and challenging thoughts. PD specific vignettes and examples of thoughts provided.	- Thought monitoring - Thought challenging	- Structured problem solving - Challenging beliefs - PD case stories
3	Introduction to the physical symptoms of hyper-arousal and hypo-arousal and their relationship to anxiety and low mood. Instructions about controlling physical symptoms using de-arousal strategies such as controlled breathing and scheduling pleasant activities. Transdiagnostic vignettes and examples of physical symptoms provided.	- Controlled breathing - Pleasant activity scheduling	- Risk calculation, coping calculation and shifting attention - 100 pleasant things to do - Transdiagnostic case stories	Introduction to the physical symptoms of hyper-arousal and their relationship to PD. Instructions about controlling physical symptoms using de-arousal strategies such as controlled breathing. PD specific vignettes and examples of physical symptoms provided.	- Controlled breathing	- Risk calculation, coping calculation and shifting attention - PD case stories
4	Introduction to the behavioural symptoms of anxiety and low mood. Explanation of avoidance and safety behaviours and their relationship to ongoing distress. Instructions for graded exposure for safely confronting fears and increasing activity levels. Transdiagnostic vignettes and examples of graded exposure provided.	- Graded exposure - Behavioural activation	- Assertive communication - Transdiagnostic case stories	Introduction to the behavioural symptoms of PD. Explanation of avoidance and safety behaviours for PD. Instructions for graded behavioural activation for increasing daily activities. PD specific vignettes and examples of graded exposure provided.	- Graded exposure	- Assertive communication - PD case stories
5	Information about the occurrence of lapses and the process of recovery from anxiety and low mood. Information about the signs of relapse and managing lapses. Instructions for creating a relapse prevention plan. Transdiagnostic vignettes and examples of lapses and lapse management provided.	- Relapse prevention	- Transdiagnostic case stories	Information about the occurrence of lapses and the process of recovery from PD. Information about the signs of relapse and managing lapses. Instructions for creating a relapse prevention plan. PD specific vignettes and examples of lapses and lapse management provided.	- Relapse prevention	- PD case stories

Note: The transdiagnostic course was designed in such a way that no specific anxiety or depressive disorder was mentioned throughout the materials, vignettes, examples and case stories. The disorder specific course made specific mention of PD and the materials, vignettes, examples and case stories all focussed on PD.

The generalised estimation model (GEE) modelling technique was employed to examine changes in the symptom measures over time. GEE emphasizes the modelling of change in an average group effect over time while accounting for within-subject variance with the specification of a working correlation structure. Rather than creating conditional interpretation with the use of individual intercepts or random slopes, as in traditional mixed linear models, the primary emphasis in GEE is to directly model the average group-related change over time (Hubbarb et al., 2010). An exchangeable working correlation structure and maximum likelihood estimation was selected, coupled with a robust error estimation for the purposes of model parsimony, for all GEE analyses. All GEE models also specified a gamma distribution with a log link response scale to address positive skewness in the dependent variable distributions. Importantly, in the GEE analyses, the model coefficients represent multiplicative change in the dependent variable from baseline; these coefficients result in a change factor (i.e., $\exp(\beta)$), which can be used to calculate the average percentage change of symptoms from baseline. Consistent with the principles of intention-to-treat analyses, separate GEE models utilising random intercepts were employed to impute missing data. The same approach was used for the imputation of the missing binary diagnostic values. Specifically, probability values were imputed based on an individual's initial diagnostic status combined with time by treatment condition estimates and cases demonstrating higher cumulative probability than the baseline value being imputed as having a diagnosis.

To maximise power and the interpretability of results, the two treatment approaches and the two support formats were analysed separately; however, to ensure these analyses did not obscure important patterns within the data, all higher order interactions were explored first. Following these initial explorations, a systematic series of analyses were employed to comprehensively compare the two treatment approaches (TD-CBT vs. DS-CBT) and the two support formats (CG-CBT vs. SG-CBT). First, to explore efficacy across symptom domains, GEE analyses were conducted on the primary and secondary outcome variables from baseline to 24-month follow-up focussed on the four symptom domains (i.e., panic, depression, generalised anxiety, and social anxiety) among those meeting MINI diagnostic criteria for the related disorder (i.e., PD, MDD, GAD and SAD) at assessment. Second, to explore efficacy in terms of general psychological distress, disability and neuroticism, GEE analyses were conducted on the tertiary outcomes from baseline to 24-month follow-up using the overall sample data. Third, for the binary outcome variable of diagnostic status, GEE analyses were conducted using a binary scale and logit link function implementing quasi-likelihood probability estimates at each time point between groups. Fourth, to examine the overall cumulative reduction in comorbid diagnoses, the average count of comorbid diagnoses was analysed over time and between groups with a negative binomial probability distribution and a log link function. Finally, to explore acceptability and satisfaction, one-way factorial ANOVAs and chi-square analyses were conducted on the lesson completion and treatment satisfaction data. For comparison and benchmarking purposes, Cohen's *d* effect sizes and 95% confidence intervals were calculated for the within-group and between-group effects based on the estimated marginal means derived from the GEE models. The average percentage change across time was also calculated from the GEE analyses for each of the outcome variables with 95% confidence intervals. Importantly, to accurately reflect percentage change, a constant of 10 was subtracted from K10 scores when calculating percentage change scores.

3. Results

3.1. Preliminary analyses

3.1.1. Baseline differences

Demographic characteristics of the sample are shown in Table 1. Specific details of participant flow, treatment attrition, lesson completion and questionnaire response are shown in Fig. 1. There were no differences between the TD-CBT and DS-CBT or the CG-CBT and SG-CBT groups on the demographic variables ($ps > .01$) with the exception that a slightly higher proportion of participants in SG-CBT group reported a history of mental health treatment compared to participants in the CG-CBT group. Comparisons exploring differences between participants completing and not completing the questionnaires at post-treatment indicated that those not completing questionnaires were younger (M diff = 8.12, *Wald's* $X^2 = 11.37$, $p = .001$). No other differences were found for any of the demographic variables in Table 1 or in baseline outcome measure scores ($ps \geq .01$).

3.1.2. Clinician time

There were significant differences in clinician contact time between CG-CBT and SG-CBT groups ($F_{1,143} = 208.75$, $p < .001$). The mean clinician time per participant in CG-CBT group was 36.79 minutes (SD = 21.35), which comprised answering and making calls (total calls = 453; range = 0–14 calls; mean time = 26.13; SD = 23.67), as well as reading, sending and responding to secure emails (total emails = 768; range = 0–12 emails; mean time = 10.67; SD = 8.57). The mean total clinician time per participant for SG-CBT was. 55 min (SD = 1.88), which comprised answering and making calls (total calls = 2; range = 0–1 call; mean time = .11; SD = .83), as well as reading, sending and responding to secure emails (total emails = 10; range = 0–2 emails; mean time = .44 SD = 1.60). This contact was focused on assessing and managing mental health crises rather than the provision of treatment or course-related clinical support. No significant differences were found between the TD-CBT and DS-CBT in the amount of clinician time required ($F_{1,143} = .86$, $p = .356$).

3.1.3. Preliminary test for higher order interactions

The GEE analyses revealed significant Treatment Approach by Support Format by Time interactions for symptoms of panic (PDSS-SR: *Wald's* $X^2 = 19.05$, $p = .001$) and depression (PHQ-9: *Wald's* $X^2 = 9.86$, $p = .043$) as well as general psychological distress (K10: *Wald's* $X^2 = 9.10$, $p = .028$) and disability (SDS: *Wald's* $X^2 = 10.78$, $p = .029$), but no other outcomes (GAD-7: *Wald's* $X^2 = 9.43$, $p = .051$; MINI-SPIN: *Wald's* $X^2 = 5.77$, $p = .217$; NEO-FFI-N: *Wald's* $X^2 = 6.36$, $p = .095$). Closer examination of these interactions revealed that they were driven by small differences between conditions at one time point or changes between two time points, which were not maintained and did not reflect a pattern of difference over time. For example, pairwise comparisons revealed no significant differences between the conditions in panic symptoms until 24-month follow-up, where the disorder-specific clinician-guided condition reported lower symptoms than both the transdiagnostic clinician-guided condition (M diff = 3.89; $p = .009$) and the disorder-specific self-guided condition (M diff = 3.19; $p = .015$), while the transdiagnostic self-guided condition reported lower symptoms than the transdiagnostic clinician-guided condition (M diff = 3.18; $p = .033$). Similarly, despite a significant interaction effect, no differences were found between the conditions on depression symptoms or general distress at any time point; however, giving rise to the higher order interaction, some minor changes were observed between follow-up time points within some conditions, which were not observed in the other conditions. Importantly, given the very small sample sizes per cell (all ns ≤ 30) in these higher order analyses, the

associated risk of spurious findings and the fact these changes were not reflective of a pattern of difference between conditions over time, these higher order interactions were not further considered.

3.2. Transdiagnostic CBT (TD-CBT) versus disorder-specific CBT (DS-CBT)

The means, percentage reductions and effect sizes for the TD-CBT and DS-CBT groups are shown in Table 3.

3.2.1. Outcomes across the diagnoses

3.2.1.1. Panic disorder. Among those meeting diagnostic criteria for PD (n = 132) the GEE analyses indicated a significant effect for Time (PDSS-SR: *Wald's* $X^2 = 260.55$, $p < .001$). There was no significant Time by Treatment Approach interaction for panic symptoms (PDSS-SR: *Wald's* $X^2 = 1.62$, $p = .806$). Pairwise comparisons indicated that both groups improved from baseline to post-treatment ($p < .001$) and from post-treatment to 3-month follow-up ($p < .001$). There were no significant differences between the groups at any time point.

3.2.1.2. Major depressive disorder. Among those meeting diagnostic criteria for MDD (n = 38) the GEE analyses indicated a significant effect for Time (PHQ-9: *Wald's* $X^2 = 76.57$, $p < .001$), and a significant Time by Treatment Approach interaction effect for depressive symptoms (PHQ-9: *Wald's* $X^2 = 14.59$, $p = .006$). Pairwise comparisons indicated that both groups improved from baseline to post-treatment ($p < .001$), and that the TD-CBT group significantly improved from post-treatment to 3-month follow-up ($p = .004$). There was a significant difference between the two groups at 3-month follow-up ($p = .032$) but not at any other time point.

3.2.1.3. Generalised anxiety disorder. Among those meeting diagnostic criteria for GAD (n = 47), GEE analyses indicated a significant effect for Time (GAD-7: *Wald's* $X^2 = 73.51$, $p < .001$) but no significant Time by Treatment Approach interaction for GAD symptoms (GAD-7: *Wald's* $X^2 = 5.17$, $p = .270$). Pairwise comparisons indicated that both groups improved from baseline to post-treatment ($p < .001$). There were no significant differences between the groups at any time point.

3.2.1.4. Social anxiety disorder. Among those meeting diagnostic criteria for SAD (n = 39), analyses indicated a significant effect for Time (MINI-SPIN: *Wald's* $X^2 = 53.46$, $p < .001$) but no significant Time by Treatment Approach interaction for social anxiety symptoms (MINI-SPIN: *Wald's* $X^2 = 4.79$, $p = .310$). Both groups improved from baseline to post-treatment ($p < .001$) and from post to 3-month follow-up ($p = .003$). There were no significant differences between the groups at any time point.

3.2.2. Outcomes for disability, general psychological distress, and neuroticism

Across the whole sample (n = 145) there were significant main effects for Time on measures of disability (SDS: *Wald's* $X^2 = 166.20$, $p < .001$), general psychological distress (K-10: *Wald's* $X^2 = 135.57$, $p < .001$), and neuroticism (NEO-FFI-N: *Wald's* $X^2 = 93.37$, $p < .001$), but no significant Time by Treatment Approach interactions (SDS: *Wald's* $X^2 = 1.06$, $p = .900$; K-10: *Wald's* $X^2 = 0.62$, $p = .890$; NEO-FFI-N: *Wald's* $X^2 = 5.63$, $p = .131$). Pairwise comparisons indicated that, on all measures, both groups improved from baseline to post-treatment ($ps < .001$) and from post-treatment to 3-month follow-up ($ps < .01$). There was also a further significant improvement to 12-month follow-up on neuroticism ($ps < .001$). However, there were no differences between the groups at any time point.

3.2.3. Changes in diagnostic status

The numbers and changes in the proportion of participants meeting formal diagnostic criteria at initial assessment and 3-month follow-up are shown in Table 4. The GEE analyses of diagnoses revealed a significant effect for Time across the diagnoses (PD: *Wald's* $X^2 = 67.32$, $p < .001$; MDE; *Wald's* $X^2 = 16.50$, $p < .001$; GAD: *Wald's* $X^2 = 24.88$, $p < .001$; SAD: *Wald's* $X^2 = 22.83$, $p < .001$). No significant Time by Treatment Approach interactions were observed for any diagnoses (PD: *Wald's* $X^2 = 0.15$, $p = .697$; MDE: *Wald's* $X^2 = 0.67$, $p = .411$; GAD: *Wald's* $X^2 = 0.04$, $p = .835$; SAD: *Wald's* $X^2 < 0.01$, $p = .989$) indicating that the proportion of participants meeting diagnostic criteria reduced across both groups.

The GEE analyses focusing on average comorbid diagnoses revealed a significant Time effect (*Wald's* $X^2 = 103.72$, $p < .001$) but no Time by Treatment Approach interaction (*Wald's* $X^2 = 0.30$, $p = .581$). These analyses indicated significant reductions in comorbid diagnoses amongst both groups over time.

3.2.4. Treatment completion and satisfaction rates

There was no difference in the number of lessons read by the TD-CBT ($M = 4.32$; SD = 1.24) and DS-CBT groups ($M = 4.30$; SD = 1.16) at post-treatment ($F_{1,143} = .01$, $p = .928$). Of the participants that completed the evaluation questions at post-treatment, 98% (60/61) of the TD-CBT group and 98% (56/57) of the DS-CBT group, reported they *would recommend the course* to others. Moreover, 93% (57/61) of the TD-CBT group and 95% (54/57) of the DS-CBT group reported participating in the course was *worth their time*. There were no significant differences between the groups in the proportions of participants who reported they would recommend the course or found the course was worth their time (X^2 range = .00 to .09; p range = .766 to .961).

3.3. Clinician-guided CBT (CG-CBT) versus self-guided CBT (DS-CBT)

The means, standard deviations and effect sizes for the CG-CBT and SG-CBT groups are shown in Table 5.

3.3.1. Outcomes across the diagnoses

3.3.1.1. Panic disorder. Among those meeting diagnostic criteria for PD (n = 132), GEE analyses indicated a significant effect for Time (PDSS-SR: *Wald's* $X^2 = 260.87$, $p < .001$) but no significant Time by Support Format interaction for panic symptoms (PDSS-SR: *Wald's* $X^2 = 3.11$, $p = .540$). Pairwise comparisons indicated that both groups improved from baseline to post-treatment and from post-treatment to 3-month follow-up ($ps < .001$). There were no differences between the groups at any time points.

3.3.1.2. Major depressive disorder. Among those meeting diagnostic criteria for MDD (n = 38), there was a significant effect for Time (PHQ-9: *Wald's* $X^2 = 56.36$, $p < .001$), but no significant Time by Support Format interaction effect for depressive symptoms (PHQ-9: *Wald's* $X^2 = 3.16$, $p = .531$). Pairwise comparisons indicated that both groups improved from baseline to post-treatment ($p < .001$). There were no differences between the groups at any time points.

3.3.1.3. Generalised anxiety disorder. Among those meeting diagnostic criteria for GAD (n = 47), GEE analyses indicated a significant effect for Time (GAD-7: *Wald's* $X^2 = 67.18$, $p < .001$) but no significant Time by Support Format interaction for GAD symptoms (GAD-7: *Wald's* $X^2 = .6.90$, $p = .142$). Both groups improved from baseline to post-treatment ($p < .001$). There were no differences between the groups at any time points.

3.3.1.4. Social anxiety disorder. Among those meeting diagnostic criteria for SAD (n = 39), there was a significant effect for Time

Table 3
Means, percentage change and effect sizes: transdiagnostic (TD-CBT) versus disorder specific (DS-CBT).

	Estimated Marginal Means					% Change from baseline				Within Group Cohen's d from baseline				Between Group Cohen's d			
	Baseline	Post	3mth	12mth	24mth	Post	3mth	12mth	24mth	Post	3mth	12mth	24mth	Post	3mth	12mth	24mth
Principal Outcome																	
Panic Symptoms[a]																	
DS-CBT (n = 68)	11.77 (5.05)	7.36 (5.94)	5.82 (4.97)	5.41 (4.85)	5.44 (5.62)	37%	50%	54%	54%	.79	1.17	1.27	1.17	.02	−.03	−.04	−.11
	[10.63, 13.02]	[6.08, 8.92]	[4.76, 7.14]	[4.37, 6.70]	[4.25, 6.96]	[24%, 48%]	[39%, 60%]	[43%, 63%]	[41%, 64%]	[.43, 1.13]	[.80, 1.53]	[.89, 1.63]	[.80, 1.53]	[−.32, .36]	[−.37, .32]	[-.38, .30]	[-.45, .23]
TD-CBT (n = 64)	12.95 (5.96)	7.23 (5.79)	5.94 (4.17)	5.63 (5.84)	6.10 (6.10)	44%	54%	57%	53%	.97	1.36	1.24	1.14				
	[11.57, 14.50]	[5.94, 8.79]	[5.00, 7.05]	[4.36, 7.26]	[4.77, 7.79]	[32%, 54%]	[46%, 61%]	[44%, 66%]	[40%, 63%]	[.60, 1.33]	[.97, 1.74]	[.85, 1.61]	[.76, 1.50]				
Secondary Outcomes																	
Depression Symptoms[b]																	
DS-CBT (n = 24)	12.96 (5.05)	7.82 (5.00)	8.17 (5.98)	7.46 (5.00)	8.53 (5.49)	40%	37%	42%	34%	1.02	.87	1.09	.84	.02	.63	.38	.56
	[11.08, 15.15]	[6.06, 10.09]	[6.10, 10.94]	[5.71, 9.76]	[6.60, 11.04]	[22%, 53%]	[16%, 53%]	[25%, 56%]	[15%, 49%]	[.41, 1.61]	[.26, 1.44]	[.47, 1.68]	[.24, 1.42]	[−.64, .68]	[−.06, 1.29]	[−.30, 1.03]	[−.13, 1.21]
TD-CBT (n = 14)	13.43 (4.08)	7.70 (4.75)	4.92 (3.37)	5.69 (4.12)	5.43 (5.72)	43%	63%	58%	60%	1.29	2.27	1.89	1.61				
	[11.46, 15.74]	[5.57, 10.64]	[3.43, 7.05]	[3.90, 8.31]	[3.13, 9.41]	[21%, 59%]	[48%, 74%]	[38%, 71%]	[30%, 77%]	[.45, 2.07]	[1.27, 3.15]	[.95, 2.72]	[.72, 2.41]				
Generalised Anxiety Symptoms[c]																	
DS-CBT (n = 26)	12.85 (4.54)	8.46 (4.84)	8.00 (4.90)	6.48 (5.30)	8.42 (5.15)	34%	38%	50%	34%	.94	1.03	1.29	.91	.30	.29	.10	.38
	[11.22, 14.71]	[6.79, 10.55]	[6.31, 10.13]	[4.74, 8.87]	[6.66, 10.65]	[18%, 47%]	[21%, 51%]	[31%, 63%]	[17%, 48%]	[.35, 1.49]	[.43, 1.59]	[.68, 1.87]	[.33, 1.47]	[−.28,	[−.29,	[−.48,	[.−21,
TD-CBT (n = 21)	13.91 (3.85)	6.94 (5.32)	6.66 (4.17)	5.99 (4.95)	6.56 (4.58)	50%	52%	57%	53%	1.50	1.81	1.79	1.74	.87]	.87]	.67]	.95]
	[12.36, 15.64]	[4.99, 9.64]	[5.09, 8.71]	[4.21, 8.54]	[4.87, 8.84]	[31%, 64%]	[37%, 63%]	[39%, 70%]	[36%, 65%]	[.79, 2.15]	[1.06, 2.49]	[1.04, 2.46]	[1.00, 2.41]				
Social Anxiety Symptoms [d]																	
DS-CBT (n = 21)	8.43 (2.25)	6.46 (2.57)	5.48 (3.12)	5.03 (2.57)	4.81 (3.25)	23%	35%	40%	43%	.82	1.08	1.41	1.30	.28	.26	.09	−.23
	[7.52, 9.44]	[5.45, 7.65]	[4.30, 6.98]	[4.05, 6.26]	[3.60, 6.42]	[9%, 35%	[17%, 49%]	[26%, 52%]	[24%, 57%]	[.17, 1.43]	[.42, 1.71]	[.71, 2.05]	[.61, 1.93]	[−.36,	[−.38,	[−.54,	[−.86,
TD-CBT (n = 18)	8.22 (2.63)	5.60 (3.61)	4.69 (2.93)	4.75 (3.65)	5.62 (3.78)	32%	43%	42%	32%	.83	1.27	1.09	.80	.90]	.89]	.72]	.41]
	[7.09, 9.54]	[4.15, 7.54]	[3.52, 6.26]	[3.33, 6.77]	[4.12, 7.67]	[8%, 50%]	[24%, 57%]	[18%, 60%]	[7%, 50%]	[.13, 1.49]	[.53, 1.95]	[.37, 1.76]	[.10, 1.46]				
Tertiary Outcomes																	
Disability and Functioning (SDS)																	
DS-CBT (n = 73)	11.92 (7.35)	7.81 (7.01)	6.22 (6.24)	5.56 (6.41)	5.58 (6.84)	34%	48%	53%	53%	.57	.84	.92	.89	−.01	.11	.00	.03
	[10.35, 13.72]	[6.36, 9.59]	[4.94, 7.82]	[4.27, 7.24]	[4.22, 7.39]	[20%, 47%]	[34%, 59%]	[39%, 64%]	[38%, 65%]	[.24, .90]	[.49, 1.17]	[.58, 1.26]	[.55, 1.23]	[−.34, .32]	[−.22, .43]	[−.33, .32]	[−.30, .35]
TD-CBT (n = 72)	11.95 (8.99)	7.88 (7.55)	5.56 (5.85)	5.57 (6.53)	5.40 (7.21)	34%	53%	53%	55%	.49	.84	.82	.80				
	[10.04, 14.21]	[6.31, 9.84]	[4.36, 7.09]	[4.25, 7.31]	[3.96, 7.36]	[18%, 47%]	[41%, 64%]	[39%, 64%]	[38%, 67%]	[.16 to.82]	[.50, 1.18]	[.48, 1.16]	[.46, 1.14]				
Psychological Distress (K−10)[e]																	
DS-CBT (n = 73)	23.14 (6.92)	19.52 (6.15)	18.57 (7.01)	17.51 (6.49)	–	28%	35%	43%	–	.55	.66	.84	–	.18	.25	.17	–
	[21.61, 24.78]	[18.17, 20.98]	[17.03, 20.26]	[16.08, 19.05]		[16%, 38%]	[22%, 47%]	[31%, 54%]		[.22, .88]	[.32 to.99]	[.50, 1.17]		[−.15, .50]	[−.08, .58]	[−.16, .49]	
TD-CBT (n = 72)	21.81 (7.72)	18.38 (6.79)	16.94 (5.85)	16.45 (6.11)	–	29%	41%	45%	–	.47	.71	.77	–				
	[20.09, 23.67]	[16.88, 20.01]	[15.63, 18.35]	[15.10, 17.93]		[15%, 42%]	[29%, 52%]	[33%, 57%]		[.14, .80]	[.37, 1.04]	[.43, 1.10]					
Neuroticism (NEO-FFI-N)																	
DS-CBT (n = 73)	29.06 (8.54)	27.53 (8.46)	25.48 (8.71)	23.23 (8.54)	–	5%	12%	20%	–	.18	.42	.68	–	.23	.08	−.04	–
	[27.16, 31.08]	[25.65, 29.54]	[23.55, 27.56]	[21.36, 25.27]		[−2%, 12%]	[5%, 19%]	[13%, 26%]		[−.15, .50]	[.08, .74]	[.35, 1.01]		[−.09,	[−.25,	[−.37,	
TD-CBT (n = 72)	27.92 (8.15)	25.56 (8.40)	24.83 (8.40)	23.60 (8.74)	–	8%	11%	15%	–	.29	.37	.51	–	.56]	.40]	.28]	
	[26.10, 29.87]	[23.69, 27.58]	[22.96, 26.85]	[21.67, 25.71]		[1%, 15%]	[4%, 18%]	[8%, 22%]		[−.04, .61]	[.04, .70]	[.18, .84]					

Note: Standard deviations are shown in rounded parentheses for the means and 95% confidence intervals are shown in square parentheses. Percentage reductions derived from the model change factor (i.e., $1 - \exp(\beta)$) in the model. Panic, depression, generalised anxiety, and social anxiety symptoms were measured with the PDSS-SR, PHQ-9, GAD-7, and MINI-SPIN, respectively.

[a] Analyses use the data of participants meeting diagnostic criteria for Panic Disorder at assessment.

[b] Analyses use the data of participants meeting diagnostic criteria for Major Depressive Disorder at assessment.

[c] Analyses use the data of participants meeting diagnostic criteria for Generalised Anxiety Disorder at assessment.

[d] Analyses use the data of participants meeting diagnostic criteria for Social Anxiety Disorder at assessment.

[e] To accurately reflect percentage change, a constant of 10 was subtracted from K10 scores when calculating percentage change scores.

Table 4
Proportions meeting diagnostic criteria over time for each of the groups.

	TD-CBT versus DS-CBT						CG-CBT versus SG-CBT					
	Baseline		3mth		% Change from Baseline		Baseline		3mth		% Change from Baseline	
	TD-CBT	DS-CBT	TD-CBT	DS-CBT	TD-CBT	DS-CBT	CG-CBT	SG-CBT	CG-CBT	SG-CBT	CG-CBT	SG-CBT
Diagnosis												
Panic Disorder	89% [79%,94%]	93% [85%,97%]	40% [30%,52%]	47% [36%,59%]	55% [42%,67%]	49% [37%,61%]	90% [81%,95%]	92% [83%,96%]	39% [28%,51%]	49% [37%,60%]	57% [44%,69%]	47% [35%,59%]
Major Depressive Disorder	19% [12%,30%]	33% [23%,44%]	1% [0%,9%]	7% [3%,16%]	93% [53%,99%]	79% [53%,91%]	32% [22%,44%]	21% [13%,31%]	7% [3%,16%]	1% [0%,9%]	78% [51%,91%]	93% [55%,99%]
Generalised Anxiety Disorder	29% [20%,41%]	36% [26%,47%]	11% [6%,21%]	16% [9%,26%]	62% [29%,81%]	56% [28%,75%]	33% [23%,45%]	32% [22%,43%]	11% [6%,21%]	16% [9%,26%]	67% [38%,83%]	50% [18%,71%]
Social Anxiety Disorder	25% [16%,36%]	29% [20%,40%]	10% [5%,19%]	11% [6%,21%]	61% [24%,81%]	60% [27%,79%]	32% [22%,44%]	22% [14%,33%]	14% [8%,24%]	7% [3%,16%]	57% [25%,76%]	67% [28%,85%]
Comorbid Diagnoses												
Average	1.62	1.90	0.62	0.80	62% [50%,71%]	58% [46%,67%]	1.87	1.65	0.70	0.72	62% [51%,71%]	56% [43%,66%]
Frequency[a]												
0	8% [4%,17%]	1% [0%,9%]	51% [40%,63%]	44% [33%,56%]	–	–	4% [1%,12%]	5% [2%,14%]	49% [37%,60%]	47% [36%,59%]	–	–
1	40% [30%,52%]	42% [32%,54%]	36% [26%,48%]	35% [25%,46%]	–	–	39% [28%,51%]	44% [33%,55%]	35% [25%,46%]	36% [26%,48%]	–	–
2	36% [26%,48%]	29% [20%,40%]	11% [6%,21%]	17% [10%,27%]	–	–	31% [21%,42%]	34% [24%,46%]	14% [8%,24%]	14% [8%,24%]	–	–
3	11% [6%,21%]	19% [12%,30%]	1% [0%,9%]	4% [1%,12%]	–	–	18% [11%,29%]	12% [7%,22%]	3% [1%,10%]	3% [1%,10%]	–	–

Note: 95% confidence intervals of estimates are shown in parentheses both for estimates of proportions of participants meeting diagnostic criteria and for percentage change.

[a] The frequency of comorbid diagnoses over time was estimated employing binary logistic regressions to provide estimates of frequency with 95% confidence intervals rather than simple raw counts.

Table 5
Means, percentage change and effect sizes: clinician-guided (CG-CBT) versus self-guided (SG-CBT).

	Estimated Marginal Means					% Change from baseline				Within Group Cohen's d from baseline				Between Group Cohen's d			
	Baseline	Post	3mth	12mth	24mth	Post	3mth	12mth	24mth	Post	3mth	12mth	24mth	Post	3mth	12mth	24mth
Principal Outcome																	
Panic Symptoms[a]																	
CG-CBT (n = 65)	12.32 (5.80)	7.94 (6.45)	6.08 (4.76)	5.53 (5.80)	5.70 (6.21)	36%	51%	55%	54%	.71	1.18	1.17	1.10	.22	.08	.01	−.02
	[10.98, 13.83]	[6.51, 9.67]	[5.02, 7.36]	[4.28, 7.14]	[4.38, 7.42]	[22%, 47%]	[40%, 59%]	[42%, 65%]	[40%, 65%]	[.36, 1.06]	[.80, 1.54]	[.79, 1.54]	[.73, 1.46]	[−.13, .56]	[−.26, .43]	[−.34, .35]	[−.36, .32]
SG-CBT (n = 67)	12.36 (5.24)	6.68 (5.16)	5.69 (4.42)	5.50 (4.83)	5.81 (5.57)	44%	54%	57%	53%	1.09	1.38	1.36	1.21				
	[11.17, 13.68]	[5.55, 8.04]	[4.73, 6.85]	[4.45, 6.80]	[4.63, 7.30]	[35%, 55%]	[45%, 62%]	[45%, 64%]	[41%, 63%]	[.72, 1.45]	[.99, 1.74]	[.98, 1.73]	[.84, 1.57]				
Secondary Outcomes																	
Depression Symptoms[b]																	
CG-CBT (n = 23)	13.13 (4.70)	7.87 (5.13)	6.65 (5.23)	6.48 (3.93)	6.46 (5.73)	40%	49%	51%	51%	1.07	1.30	1.54	1.27	.05	−.15	−.18	−.37
	[11.34, 15.21]	[6.02, 10.27]	[4.81, 9.18]	[5.05, 8.31]	[4.86, 8.57]	[225,54%]	[30%, 63%]	[37%, 62%]	[35%, 63%]	[.43, 1.67]	[.65, 1.92]	[.85, 2.16]	[.62, 1.88]	[−.60, .70]	[−.80, .50]	[−.83, .48]	[−1.02, .29]
SG-CBT (n = 15)	13.13 (4.76)	7.64 (4.49)	7.47 (5.58)	7.33 (5.73)	8.82 (7.09)	42%	43%	44%	33%	1.19	1.09	1.10	.71				
	[10.94, 15.77]	[5.67, 10.29]	[5.12, 10.90]	[4.93, 10.90]	[5.87, 13.24]	[22%, 57%]	[17%, 61%]	[17%, 62%]	[−1%, 55%]	[.38, 1.93]	[.30, 1.83]	[.31, 1.84]	[−.04, 1.43]				
Generalised Anxiety Symptoms[c]																	
CG-CBT (n = 24)	13.67 (4.31)	8.35 (5.05)	7.07 (4.80)	6.70 (5.00)	6.77 (4.46)	39%	48%	51%	50%	1.13	1.45	1.49	1.57	.23	−.14	.17	−.34
	[12.05, 15.51]	[6.55, 10.64]	[5.40, 9.27]	[4.97, 9.04]	[5.20, 8.82]	[22%, 52%]	[32%, 61%]	[34%, 64%]	[35%, 62%]	[.51, 1.72]	[.79, 2.06]	[.83, 2.11]	[.90, 2.19]	[−.35,	[−.71,	[−.40,	[−.91,
SG-CBT (n = 23)	12.96 (4.17)	7.19 (5.13)	7.74 (4.46)	5.81 (5.28)	8.44 (5.32)	44%	40%	55%	35%	1.23	1.21	1.50	.95	.80]	.43]	.74]	.24]
	[11.36, 14.78]	[5.38, 9.63]	[6.11, 9.81]	[4.01, 8.41]	[6.52, 10.93]	[26%, 59%]	[24%, 53%]	[35%, 69%]	[16%, 50%]	[.58, 1.84]	[.56, 1.82]	[.83, 2.13]	[.32, 1.54]				
Social Anxiety Symptoms [d]																	
CG-CBT (n = 23)	8.31 (2.49)	5.32 (3.21)	4.29 (2.93)	4.41 (3.26)	4.23 (3.26)	36%	48%	47%	49%	1.04	1.48	1.34	1.41	−.60	−.70	−.39	−.70
	[7.35, 9.38]	[4.16, 6.81]	[3.25, 5.67]	[3.26, 5.95]	[3.09, 5.78]	[18%, 50%]	[32%, 61%]	[28%, 61%]	[30%, 63%]	[.41, 1.64]	[.80, 2.10]	[.68, 1.96]	[.74, 2.03]	[−1.24, .06]	[−1.34, −.03]	[−1.03, .26]	[−1.34, −.03]
SG-CBT (n = 16)	8.38 (2.36)	7.12 (2.64)	6.31 (2.84)	5.61 (2.76)	6.56 (3.48)	15%	25%	33%	22%	.50	.79	1.08	.61				
	[7.29, 9.62]	[5.93, 8.54]	[5.06, 7.86]	[4.41, 7.14]	[5.06, 8.51]	[−2%, 29%]	[6%, 40%]	[15%, 47%]	[−2%, 40%]	[−.21, 1.19]	[.05 t 01.49]	[.31, 1.79]	[−.11, 1.30]				
Tertiary Outcomes																	
Disability and Functioning (SDS)																	
CG-CBT (n = 72)	12.07 (8.65)	8.01 (7.98)	6.28 (6.53)	5.59 (6.36)	5.65 (7.04)	34%	48%	54%	53%	.49	.76	.85	.81	.05	.13	.01	.05
	[10.23, 14.25]	[6.36, 10.09]	[4.94, 7.99]	[4.29, 7.28]	[4.25, 7.53]	[16%, 47%]	[34%, 59%]	[40%, 64%]	[38%, 65%]	[.15, .82]	[.41, 1.09]	[.51, 1.19]	[.47, 1.15]	[−.28, .37]	[−.20, .45]	[−.32, .33]	[−.28, .37]
SG-CBT (n = 73)	11.80 (7.69)	7.68 (6.49)	5.50 (5.47)	5.54 (6.58)	5.33 (7.09)	35%	53%	53%	55%	.58	.94	.87	.87				
	[10.16, 13.69]	[6.33, 9.32]	[4.38, 6.91]	[4.22, 7.26]	[3.93, 7.22]	[21%, 46%]	[41%, 63%]	[38%, 64%]	[39%, 67%]	[.24, .91]	[.60, 1.28]	[.53, 1.21]	[.53, 1.21]				
Psychological Distress (K−10)[e]																	
CG-CBT (n = 72)	22.03 (7.30)	18.93 (6.62)	17.32 (6.19)	16.62 (6.02)	–	26%	39%	45%	–	.44	.57	.70	–	−.01	−.13	−.11	–
	[20.41, 23.78]	[17.46, 20.53]	[15.95, 18.82]	[15.29, 18.07]		[12%, 38%]	[27%, 51%]	[33%, 56%]		[.10, .77]	[.23, .90]	[.36, 1.03]		[−.33, .32]	[−.46, .19]	[−.44, .21]	
SG-CBT (n = 73)	22.92 (7.43)	18.98 (6.32)	18.19 (6.84)	17.34 (6.58)	–	31%	37%	43%	–	.57	.66	.80	–				
	[21.28, 24.68]	[17.58, 20.48]	[16.69, 19.83]	[15.89, 18.91]		[19%, 41%]	[24%, 48%]	[31%, 54%]		[.24, .90]	[.33, .99]	[.45, 1.13]					
Neuroticism (NEO-FFI-N)																	
CG-CBT (n = 72)	28.17 (7.72)	25.85 (7.98)	23.92 (8.65)	22.31 (8.49)	–	8%	15%	21%	–	.30	.52	.72	–	−.16	−.29	−.26	–
	[26.45 30.00]	[24.07 27.75]	[22.01 26.00]	[20.44 24.35]		[1%, 15%]	[8% to22%]	[14%, 27%]		[−.03, .62]	[.18, .85]	[.38, 1.06]		[−.49, .16]	[−.61, .04]	[−.58, .07]	
SG-CBT (n = 73)	28.81 (8.97)	27.24 (8.97)	26.37 (8.37)	24.51 (8.63)	–	5% [−2%, 12%]	8%	15%	–	.18	.28	.49	–				
	[26.82 30.94]	[25.27 29.37]	[24.52 28.36]	[22.60 26.58]			[2%,15%]	[8%, 22%]		[−.15, .50]	[−.05, .61]	[.16 to.82]					

Note: Standard deviations are shown in rounded parentheses for the means and 95% confidence intervals are shown in square parentheses. Percentage reductions derived from the model change factor (i.e., 1 − exp(β)) in the model. Panic, depression, generalised anxiety, and social anxiety symptoms were measured with the PDSS-SR, PHQ-9, GAD-7, and MINI-SPIN, respectively.

[a] Analyses use the data of participants meeting diagnostic criteria for Panic Disorder at assessment.

[b] Analyses use the data of participants meeting diagnostic criteria for Major Depressive Disorder at assessment.

[c] Analyses use the data of participants meeting diagnostic criteria for Generalised Anxiety Disorder at assessment.

[d] Analyses use the data of participants meeting diagnostic criteria for Social Anxiety Disorder at assessment.

[e] To accurately reflect percentage change, a constant of 10 was subtracted from K10 scores when calculating percentage change scores.

(MINI-SPIN: *Wald's* $X^2 = 56.05$, $p < .001$), and a significant Time by Support Format interaction for social anxiety symptoms (MINI-SPIN: *Wald's* $X^2 = 10.40$, $p = 0.034$). Pairwise comparisons indicated that both groups improved from baseline to post-treatment ($p < .001$) and that the CG-CBT group further improved to 3-month follow-up ($p = .03$). Pairwise comparisons revealed the CG-CBT group reported slightly lower symptoms at 3-month (M diff = 2.02; $p = .031$) and 24-month follow-up (M diff = 2.33; $p = .034$) compared with the SG-CBT group.

3.2.2. Outcomes for disability, general psychological distress, and neuroticism. Across the whole sample (n = 145) there were significant main effects for Time on measures of disability (SDS: *Wald's* $X^2 = 164.64$, $p < .001$), general psychological distress (K-10: *Wald's* $X^2 = 138.17$, $p < .001$), and neuroticism (NEO-FFI-N: *Wald's* $X^2 = 95.26$, $p < .001$), but no significant Time by Treatment Approach interactions (SDS: *Wald's* $X^2 = .90$, $p = .924$; K-10: *Wald's* $X^2 = 1.04$, $p = .793$; NEO-FFI-N: *Wald's* $X^2 = 4.93$, $p = .177$). Pairwise comparisons indicated that, on all measures, both groups improved from baseline to post-treatment ($ps < .001$) and from post-treatment to 3-month follow-up ($ps < .01$). There was also a further significant improvement to 12-month follow-up on neuroticism ($ps < .001$). However, there were no differences between the groups at any time point.

3.3.3. Changes in diagnostic status. The numbers and changes in the proportion of participants meeting formal diagnostic criteria at initial assessment and 3-month follow-up are shown in Table 4. The GEE analyses of diagnoses revealed a significant effect for Time across the diagnoses (PD: *Wald's* $X^2 = 68.74$, $p < .001$; MDE; *Wald's* $X^2 = 18.48$, $p < .001$; GAD: *Wald's* $X^2 = 25.86$, $p < .001$; SAD: *Wald's* $X^2 = 23.15$, $p < .001$). No significant Time by Support Format interactions were observed for any diagnoses (PD: *Wald's* $X^2 = 0.11$, $p = .731$; MDE: *Wald's* $X^2 = 0.95$, $p = .328$; GAD: *Wald's* $X^2 = 1.12$, $p = .290$; SAD: *Wald's* $X^2 = 0.17$, $p = .676$) indicating that the proportion of participants meeting diagnostic criteria reduced across both groups.

The GEE analyses focusing on average comorbid diagnoses revealed a significant Time effect (*Wald's* $X^2 = 105.26$, $p < .001$) but no Time by Support Format interaction (*Wald's* $X^2 = 0.70$, $p = .401$). These analyses indicated significant reductions in comorbid diagnoses amongst both groups over time.

3.3.4. Treatment completion and satisfaction rates. There was no difference in the number of lessons completed by the CG-CBT ($M = 4.35$; SD = 1.15) and SG-CBT ($M = 4.27$; SD = 1.25) groups at post-treatment ($F_{1,145} = .13$, $p = .714$). Of the participants who completed the evaluation questions at post-treatment, 96% (54/56) of the CG-CBT group, and 100% (62/62) of the SG-CBT group, reported they *would recommend the course* to others. Further, 93% (52/56) of the CG-CBT group and 95% (59/62) of the SG-CBT group reported the course was *worth their time*. There were no significant differences in the proportions of participants willing to recommend the course or finding the course was worth their time (X^2 range: .28–2.25; $p = .133$–$.597$).

4. Discussion

The present study is one of four in a series of RCTs designed to compare internet-delivered TD-CBT and DS-CBT as well as CG-CBT and SG-CBT for several common mental disorders. The current study focused on comparing these two treatment approaches and support formats for adults with principal PD and several common comorbid disorders. It was hypothesised that both TD-CBT and DS-CBT would result in significant reductions in principal symptoms of PD, but that TD-CBT would be superior at reducing symptoms of comorbid MDD, GAD and SAD 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 PD and symptoms of comorbid disorders. These hypotheses were only partially supported. All conditions were associated with large improvements in principal PD symptoms and moderate-to-large improvements on comorbid symptoms of MDD, GAD and SAD. However, no marked or consistent differences were found across the post-treatment, 3, 12 or 24-months follow-up time points between TD-CBT and DS-CBT groups or the CG-CBT and SG-CBT groups. The present study provides support for both treatment approaches and support formats in the treatment of principal PD and the comorbid disorders of interest.

The findings of the present study are consistent with the findings of the other three RCTs in this series of studies comparing TD-CBT and DS-CBT (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), but extends these results to PD. Encouragingly, the present study found evidence of large overall reductions in symptoms of PD (Cohen's $d \geq 0.71$; avg. reduction $\geq$ 36%) and moderate-to-large reductions in symptoms of comorbid MDD (Cohen's $d \geq 0.71$; avg. reduction $\geq$ 33%), GAD (Cohen's $d \geq 0.91$; avg. reduction $\geq$ 34%) and SAD (Cohen's $d \geq 0.50$; avg. reduction $\geq$ 15%). These reductions were reflected in marked reductions in the percentages of participants meeting diagnostic criteria for PD (i.e., $\geq$ 47%), MDD (i.e., $\geq$ 78%), GAD (i.e., $\geq$ 50%) and SAD (i.e., $\geq$ 57%) across the groups. These findings are broadly consistent with those observed in other internet-delivered trials of CBT for PD (Klein et al., 2006; Richards, Klein, & Austin, 2006; Kiropoulos et al., 2008) as well as face-to-face trials of CBT for PD (Butler et al., 2006; Stewart & Chambless, 2009; Sánchez-Meca et al., 2010; Hoffman et al., 2012). Importantly, sustained improvements were also found across all groups on measures of neuroticism, psychological distress, and disability, indicating the benefits of treatment generalised to other domains. The findings of the present study therefore highlight the potential of both treatment approaches and support formats for the internet-delivered CBT treatment of principal PD.

The present study is the largest (n = 135) to the authors' knowledge to compare TD-CBT and DS-CBT for principal PD and it is noteworthy that it found the two treatment approaches to be associated with similar improvements in panic symptoms. The few other studies to compare these treatment approaches have involved relatively small numbers (n < 15) of participants with PD (e.g., (Ellard et al., 2010; Farchione et al., 2012; Norton & Barrera, 2012) and, in contrast to the current study, the next largest study (n = 65) found evidence supporting the superiority of a more disorder-specific approach (Craske et al., 2007). However, there are key differences between the transdiagnostic approach used in that study and most other studies to date. Specifically, that study (Craske et al., 2007) allowed clinicians to 'stray' from targeting the principal PD diagnosis by applying a second disorder-specific treatment protocol to the most severe comorbid disorder; thus, in effect, applying two disorder-specific treatments. In contrast, the current study used a single and broader transdiagnostic treatment protocol that was provided to all participants irrespective of their diagnostic profile. One possibility is that having clinicians use multiple disorder-specific treatment protocols to form a more transdiagnostic treatment 'dilutes' therapeutic effects; that is, compared to learning one treatment protocol and set of treatment principles, which can be applied regardless of the nature of the emotional problem. If replicated, the findings of the current study are important given the pragmatic advantages of TD-CBT in attempts to disseminate effective psychological treatments (McHugh, Murray, & Barlow, 2009). Yet, it has to be noted that the current findings

also support the longstanding observation that disorder-specific treatments also have substantial transdiagnostic treatment effects (Brown, Antony, & Barlow, 1995; Tsao, Mystkowski, Zucker, & Craske, 2002). Thus, as mentioned elsewhere, the key criteria used to inform the decisions between using TD-CBT and DS-CBT may be more pragmatic than clinical when it comes to the treatment of common and highly comorbid mental disorders.

The findings of the current study are also consistent with the other studies in this series, which found clinician-guided and self-guided iCBT result in similar clinical outcomes for principal MDD, GAD and 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). These findings are also consistent with the few other studies in the literature to directly compare newer-generation clinician-guided and self-guided iCBT interventions, and which have found similar outcomes for both support formats (Berger, Caspar, et al., 2011; Berger, Hämmerli, et al., 2011; Titov et al., 2013; Dear, Gandy et al., 2015; Dear, Staples et al., 2015; Dear, Zou et al., 2015). However, these findings are inconsistent with those of meta-analyses in the area that have compared across studies and that have found clinician-guided iCBT to be associated with higher completion rates and greater clinical outcomes (Andersson & Cuijpers, 2009; Cuijpers et al., 2009). Unfortunately, there is still very limited empirical data about the essential components and clinical processes required for efficacious, safe and acceptable internet-delivered treatment, which makes it difficult to explain discrepancies in findings between studies. However, it is important to note that studies finding self-guided iCBT to be equally efficacious have typically employed highly developed treatment protocols (i.e., developed over numerous clinical trials), been conducted by specialised clinical research units (i.e., with significant experience in internet-delivered treatment), have involved some kind of therapist-administered screening assessment prior to treatment (i.e., to orient patients to the treatment) and have included measures, such as regular automatic emails, aimed at engaging patients throughout treatment. More research is needed to identify the essential components and clinical processes required for effective, safe and acceptable clinician-guided and self-guided iCBT treatments. This is a critical area for future research which will likely explain some of the differences currently being observed between studies whilst also informing the development and use of optimally effective clinician-guided and self-guided internet-delivered treatments. However, the present findings add to emerging studies in highlighting the potential of carefully designed and delivered iCBT treatments for increasing access to effective treatment and reducing the burden of common mental health disorders (Kazdin, 2015).

As with all studies the present study has a number of limitations and design features that need to be carefully considered when interpreting its findings. The main limitations of the current study are the absence of a control group, the use of a superiority trial design and the difficulties experienced in recruiting the target number of participants with principal PD and comorbid MDD, GAD and SAD. The absence of a control group means that it is not possible to control for the general effects of time and spontaneous remission. The use of a superiority trial design means that significant caution is needed in considering any statistical findings from the current as supporting true clinical equivalence, which requires the use of specific analyses. The failure to recruit the target number of participants (target n = 200; actual n = 135) means that the present study was only powered to detect moderate to large differences on the primary outcome of PD symptoms and large differences on comorbid symptoms of MDD, GAD and SAD. It also means that estimates of clinical effects are unlikely to be as accurate or reliable as those observed in the larger studies in this series of 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). It is important to bear in mind that, although a study may have a sufficient sample size to detect a difference of a certain magnitude, much larger sample sizes are often needed to obtain stable estimates of effects that are not disproportionately influcenced by positive or negative outliers. Indeed, potentially reflecting this, several significant higher order interactions were observed in the current study that were not observed in the other larger studies in this series and yet, on closer examination, did not reflect marked or sustained differences between the conditions; that is, they emerged at only one or two time points. However, previous literature has noted the unique challenge of obtaining sufficient sample sizes to comprehensively compare transdiagnostic and disorder-specific treatments, given that these clinical trials require sufficient participants with both the principal disorder of interest as well as any comorbid disorders of interest (Titov et al., 2012).

Other limitations include resource constraints that meant it was not possible to blind the diagnostic assessments as well as the limited clinician time spent supporting patients in the clinician-guided treatment group. It is possible that differences between the clinician-guided and self-guided treatment groups may have emerged had the clinicians had more time to support patients; however, it is important to note there was significant variability in the amount of clinician time participants wanted and the clinicians were permitted to spend more time with participants where clinically indicated. It is also possible that differences would have been observed had the current study not employed a newer-generation self-guided iCBT treatment and, for example, participants were provided with a more basic self-guided iCBT treatment that did not involve an initial assessment, patient safety monitoring, the availability of technical support or the use of automatic emails to guide and engage patients throughout treatment. It is also important to note that, as with most studies, a meaningful proportion of participants continued to experience clinical-level symptoms and to meet diagnostic criteria for disorders following treatment. One interesting avenue for future research could be to examine stepped-care models of internet-delivered treatment where participants start with more self-guided and lower-intensity treatments initially and, with the goal of improving clinical outcomes, are 'stepped up' to more intensitve and clinician-guided internet-delivered treatments based on clinical need. Nevertheless, the current study has a number of notable strengths including employing the largest sample of participants with principal PD to date as well as high retention rates, long-term follow-up and the use of multiple outcomes (e.g., clinical symptoms, diagnostic assessments, satisfaction rates and treatment completion) to compare the two treatment approaches and two support formats.

The present study found significant clinical improvements and high levels of treatment satisfaction among adults with principal PD for both transdiagnostic and disorder-specific CBT delivered with and without clinician contact during treatment. Clinical improvements were observed in panic symptoms as well as symptoms of MDD, GAD and SAD immediately post-treatment and were maintained at 3, 12 and 24-month follow-up. Clinical improvements in symptoms were also reflected in reduced proportions of participants meeting diagnostic criteria for PD, MDD, GAD and SAD at 3-month follow-up. No marked or consistent differences were observed in the clinical outcomes, satisfaction rates or treatment completion rates whether participants received TD-CBT or DS-CBT or whether they received CG-CBT or SG-CBT. Thus, the present study joins the other studies in this series, in highlighting the public health potential of carefully designed and delivered transdiagnostic and disorder-specific treatments delivered for principal PD as well

as the potential to successfully provide internet-delivered treatment in clinician-guided and self-guided formats.

Declaration of interest

N Titov and B Dear are funded by the Australian Government to develop and provide the MindSpot Clinic, a national online assessment and treatment service for Australian adults with anxiety and depression. N Titov and B Dear are also authors of the treatment programs employed in the current research but derive no financial benefit from them.

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References

Allen, L. B., White, K. S., Barlow, D. H., Shear, K., Gorman, J. M., & WS, W. (2010). Cognitive-behavior therapy (CBT) for panic disorder: relationship of anxiety and depression comorbidity with treatment outcome. *Journal of Psychopathology and Behavioral Assessment*, *32*(2), 185–192.

American Psychiatric Association, (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Washington, D.C.

Andersson, G., & Cuijpers, P. (2009). Internet-based and other computerized psychological treatments for adult depression: a meta-analysis. *Cognitive Behaviour Therapy*, *38*(4), 196–205.

Andersson, G., & Titov, N. (2014). Advantages and limitations of Internet-based interventions for common mental disorders. *World Psychiatry*, *13*, 4–11.

Andrews, G., Cuijpers, P., Craske, M. G., McEvoy, P., & Titov, N. (2010). Computer therapy for the anxiety and depressive disorders is effective, acceptable and practical health care: a meta-analysis. *PLoS One*, *5*(10), e13196.

Andrews, G., & Slade, T. (2001). Interpreting scores on the kessler psychological distress scale (K10). *Australian and New Zealand Journal of Public Health*, *25*(6), 494–497.

Barlow, D. H., Allen, L. B., & Choate, M. L. (2004). Toward a unified treatment for emotional disorders. *Behavior Therapy*, *35*, 205–230.

Berger, T., Caspar, F., Richardson, R., Kneubuhler, B., Sutter, D., & Andersson, G. (2011). Internet-based treatment of social phobia: a randomised controlled trial comparing unguided with two types of guided self-help. *Behaviour Research and Therapy*, *49*(3), 158–169.

Berger, T., Hämmerli, K., Gubser, N., & Caspar, F. (2011). Internet-based treatment of depression: a randomised controlled trial comparing guided with unguided self-help. *Behaviour Research and Therapy*, *40*, 251–266.

Bergstrom, J., Andersson, G., Ljotsson, B., Ruck, C., Andreewitch, S., Karlsson, A., et al. (2010). Internet-versus group-administered cognitive behaviour therapy for panic disorder in a psychiatric setting: a randomised trial. *BMC Psychiatry*, *10*, 54.

Brown, T. A., Antony, M. M., & Barlow, D. H. (1995). Diagnostic comorbidity in panic disorder: effect on treatment outcome and course of comorbid diagnoses following treatment. *Journal of Consulting and Clinical Psychology*, *63*(3), 408–418.

Butler, A. C., Chapman, J. E., Forman, E. M., & Beck, A. T. (2006). The empirical status of cognitive-behavioral therapy: a review of meta-analyses. *Clinical Psychology Review*, *26*(1), 17–31.

Carlbring, P., Nilsson-Ihrfelt, E., Waara, J., Kollenstam, C., Buhrman, M., Kaldo, V., & Andersson, G. (2005). Treatment of panic disorder: live therapy vs. self-help via the Internet. *Behaviour Research and Therapy*, *43*(10), 1321–1333.

Clark, L., Watson, D., & Mineka, S. (1994). Temperament, personality, and the mood and anxiety disorders. *Journal of Abnormal Psychology*, *103*(1), 103–116.

Connor, K. M., Kobak, K. A., Churchill, L. E., Katzelnick, D., & Davidson, J. R. (2001). Mini-SPIN: a brief screening assessment for generalized social anxiety disorder. *Depression and Anxiety*, *14*(2), 137–140.

Costa, P. T., & McCrae, R. R. (1985). The NEO personality inventory. *PAR Psychological Assessment Resources*,

Craske, M. G., Farchione, T. J., Allen, L. B., Barrios, V., Stoyanova, M., & Rose, R. (2007). Cognitive behavioral therapy for panic disorder and comorbidity: more of the same or less of more? *Behaviour Research and Therapy*, *45*(6), 1095–1109.

Craske, M. G., Roy-Byrne, P. P., Stein, M. B., Sullivan, G., Sherbourne, C., & Bystritsky, A. (2009). Treatment for anxiety disorders: efficacy to effectiveness to implementation. *Behaviour Research and Therapy*, *47*(11), 931–937.

Cuijpers, P., Marks, I. M., van Straten, A., Cavanagh, K., Gega, L., & Andersson, G. (2009). Computer-aided psychotherapy for anxiety disorders: a meta-analytic review. *Cognitive Behaviour Therapy*, *38*(2), 66–82.

Cuijpers, P., van Straten, A., & Donker, M. (2005). Personality traits of patients with mood and anxiety disorders. *Psychiatry Research*, *133*(2), 229–237.

Dear, B. F., Titov, N., Schwencke, G., Andrews, G., Johnston, L., Craske, M. G., et al. (2011). An open trial of a Brief transdiagnostic internet treatment for anxiety and depression. *Behaviour Research and Therapy*, *49*(12), 830–837.

Dear, B. F., Titov, N., Sunderland, M., McMillan, D., Anderson, T., Lorian, C., et al. (2011). Psychometric comparison of the generalized anxiety disorder scale-7 and the penn state worry questionnaire for measuring response during treatment of generalised anxiety disorder. *Cognitive Behaviour Therapy*, *40*(3), 216–227.

Dear, B., Gandy, M., Karin, E., Staples, L. G., Johnston, L., Fogliati, V. J., et al. (2015). The Pain Course: a randomised controlled trial examining an internet delivered pain management program when provided with different levels of clinician support. *Pain*, *156*(10), 1920–1935.

Dear, B. F., Staples, L. G., Terides, M. D., Karin, E., Zou, J., Johnston, L., et al. (2015). Transdiagnostic versus disorder-specific and clinician-guided versus self-guided internet-delivered treatment for generalized anxiety disorder and comorbid disorders: a randomized controlled trial. *Journal of Anxiety Disorders*, *36*, 63–77.

Dear, B. F., Zou, J. B., Ali, S., Lorian, C. N., Johnston, L., Sheehan, J., et al. (2015). Clinical and cost-effectiveness of therapist-guided internet-delivered cognitive behavior therapy for older adults with symptoms of anxiety: a randomized controlled trial. *Behavior Therapy*, *46*(2), 206–217.

Dear, B.F., Staples, L.G., Terides, M.D., Fogliati, V.J., Sheehan, J., Johnston, L., Kayrouz, R., Dear, R., McEvoy, P. and Titov, N. (submitted). Transdiagnostic versus disorder-specific and clinician-guided versus self-guided internet-delivered treatment for Social Anxiety Disorder and comorbid disorders: A randomized controlled trial.

Ellard, K. K., Fairholme, C. P., Boisseau, C. L., Farchione, T. J., & Barlow, D. H. (2010). Unified protocol for the transdiagnostic treatment of emotional disorders: protocol development and initial outcome data. *Cognitive and Behavioral Practice*, *17*(1), 88–101.

Farchione, T. J., Fairholme, C. P., Ellard, K. K., Boisseau, C. L., Thompson-Hollands, J., Carl, J. R., et al. (2012). Unified protocol for transdiagnostic treatment of emotional disorders: a randomized controlled trial. *Behavior Therapy*, *43*(3), 666–678.

Goldberg, D., (2010). Should our major classifications of mental disorders be revised?

Griffith, J. W., Zinbarg, R. E., Craske, M. G., Mineka, S., Rose, R. D., Waters, A. M., et al. (2010). Neuroticism as a common dimension in the internalizing disorders. *Psychological Medicine*, *40*, 1125–1136.

Hedman, E., Ljótsson, B., Kaldo, V., Hesser, H., Alaoui, S., Kraepelien, M., et al. (2013). Effectiveness of Internet-based cognitive behaviour therapy for depression in routine psychiatric care. *Journal of Affective Disorders*, *155*, 49–58.

Hedman, E., Ljótsson, B., Rück, C., Bergström, J., Andersson, G., Kaldo, V., et al. (2013). Effectiveness of Internet-based cognitive behaviour therapy for panic disorder in routine psychiatric care. *Acta Psychiatrica Scandinavica*, *128*(6), 457–467.

Hoffman, S. G., Asnaani, A., Vonk, I. J., Sawyer, A. T., & Fang, A. (2012). The efficacy of cognitive behavioral therapy: a review of meta-analyses. *Cognitive Therapy and Research*, *36*(5), 427–440.

Houck, P. R., Spiegel, D. A., Shear, M. K., & Rucci, P. (2002). Reliability of the self-report version of the Panic Disorder Severity Scale. *Depression and Anxiety*, *15*(4), 183–185.

Hubbarb, A., Ahern, J., Fleisher, N., Vean Der Laan, M., Lippman, S., Jewell, N., et al. (2010). To GEE or not to GEE: comparing population average and mixed models for estimating the associations between neighborhood risk factors and health. *Epidemiology*, *21*, 467–474.

Johnston, L., Titov, N., Andrews, G., Spence, J., & Dear, B. F. (2011). A RCT of a transdiagnostic internet-delivered treatment for three anxiety disorders: examination of support roles and disorder-specific outcomes. *PLoS One*, *6*(11), e28079.

Johnston, L., Titov, N., Spence, J., Andrews, G., & Dear, B. (2011). A RCT of a transdiagnostic internet-delivered treatment for three anxiety disorders: examination of support roles and disorder-specific outcomes. *PLoS One*, e28079.

Kazdin, A. (2015). Evidence-based psychotherapies II: changes in models of treatment and treatment delivery. *South African Journal of Psychology*, *45*(1), 3–21.

Kessler, R. C., Andrews, G., Colpe, L. J., Hiripi, E., Mroczek, D. K., Normand, S.-L., et al. (2002). Short screening scales to monitor population prevalences and trends in non-specific psychological distress. *Psychological Medicine*, *32*(06), 959–976.

Kessler, R. C., Chiu, W., Demler, O., & Walters, E. E. (2005). Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the national comorbidity survey replication. *Archives of General Psychiatry*, *62*(6), 617–627.

Kiropoulos, L. A., Klein, B., Austin, D. W., Gilson, K., Pier, C., Mitchell, J., et al. (2008). Is internet-based CBT for panic disorder and agoraphobia as effective as face-to-face CBT? *Journal of Anxiety Disorders*, *22*(8), 1273–1284.

Klein, B., Austin, D., Pier, C., Kiropoulos, L., Shandley, K., Mitchell, J., et al. (2009). Internet-based treatment for panic disorder: does frequency of therapist contact make a difference? *Cognitive Behaviour Therapy*, *38*(2), 100–113.

Klein, B., Richards, J. C., & Austin, D. W. (2006). Efficacy of internet therapy for panic disorder. *Journal of Behavior Therapy and Experimental Psychiatry*, *37*(3), 213–238.

Kroenke, K., Spitzer, R. L., & Williams, J. B. (2001). The PHQ-9: validity of a Brief depression severity measure. *Journal of General Internal Medicine*, *16*(9), 606–613.
Kroenke, K., Spitzer, R. L., Williams, J. B., & Lowe, B. (2010). The patient health questionnaire somatic, anxiety, and depressive symptom scales: a systematic review. *General Hospital Psychiatry*, *32*(4), 345–359.
Löwe, B., Decker, O., Müller, S., Brähler, E., Schellberg, D., Herzog, W., et al. (2008). Validation and standardization of the generalized anxiety disorder screener (GAD-7) in the general population. *Medical Care*, *46*(3), 266–274.
Lecrubier, Y., Sheehan, D., Weiller, E., Amorim, P., Bonora, I., Harnett Sheehan, K., et al. (1997). The Mini International Neuropsychiatric Interview (MINI). A short diagnostic structured interview: reliability and validity according to the CIDI. *European Psychiatry*, *12*(5), 224–231.
Leon, A. C., Olfson, M., Portera, L., Farber, L., & Sheehan, D. V. (1997). Assessing psychiatric impairment in primary care with the Sheehan Disability Scale. *The International Journal of Psychiatry in Medicine*, *27*(2), 93–105.
Mansell, W., Allison, H., Ed, W., & Roz, S. (2009). Conceptual foundations of the transdiagnostic approach to CBT. *Journal of Cognitive Psychotherapy*, *23*(1), 6–19.
McEvoy, P., Grove, R., & Slade, T. (2011). Epidemiology of anxiety disorders in the australian general population: findings of the 2007 australian national survey of mental health and wellbeing. *Australian and New Zealand Journal of Psychiatry*, *45*, 957–967.
McEvoy, P. M., Nathan, P., & Norton, P. J. (2009). Efficacy of transdiagnostic treatments: a review of published outcome studies and future research directions. *Journal of Cognitive Psychotherapy*, *23*(1), 20–33.
McHugh, R. K., Murray, H. W., & Barlow, D. H. (2009). Balancing fidelity and adaptation in the dissemination of empirically-supported treatments: the promise of transdiagnostic interventions. *Behaviour Research and Therapy*, *47*(11), 946–953.
McQuaid, J. R., Stein, M. B., McCahill, M., Laffaye, C., & Ramel, W. (2000). Use of brief psychiatric screening measures in a primary care sample. *Depression and Anxiety*, *12*, 21–29.
Mewton, L., Wong, N., & Andrews, G. (2012). The effectiveness of internet cognitive behavioural therapy for generalized anxiety disorder in clinical practice. *Depress Anxiety*, *29*(10), 843–849.
Murray, L. K., Dorsey, S., Haroz, E., Lee, C., Alsiary, M. M., Haydary, A., et al. (2014). A common elements treatment approach for adult mental health problems in low-and middle-income countries. *Cognitive and Behavioral Practice*, *212*, 111–123.
Newby, J., Mackenzie, A., Williams, A., McIntyre, K., Watts, S., Wong, N., et al. (2013). Internet cognitive behavioural therapy for mixed anxiety and depression: a randomized controlled trial and evidence of effectiveness in primary care. *Psychological Medicine*, *43*, 2635–2648.
Norton, P. J., & Barrera, T. L. (2012). Transdiagnostic versus diagnosis-specific CBT for anxiety disorders: a preliminary randomized controlled noninferiority trial. *Depression and Anxiety*, *29*(10), 874–882.
Osório, F. d. L., Crippa, J. A. S., & Loureiro, S. R. (2010). Further study of the psychometric qualities of a brief screening tool for social phobia (MINI-SPIN) applied to clinical and nonclinical samples. *Perspectives in Psychiatric Care*, *46*(4), 266–278.
Otto, M. W., & Deveney, C. (2005). Cognitive-behavioral therapy and the treatmentof panic disorder: efficacy and strategies. *The Journal of Clinical Psychiatry*, *66*(Suppl. 4), 28–32.
Richards, J. C., Klein, B., & Austin, D. W. (2006). Internet cognitive behavioural therapy for panic disorder: does the inclusion of stress management information improve end-state functioning? *Clinical Psychologist*, *10*(1), 2–15.
Ruwaard, J., Lange, A., Schrieken, B., Dolan, C. V., & Emmelkamp, P. (2012). The effectiveness of online cognitive behavioral treatment in routine clinical practice. *PLoS One*, *7*(7), e40089.
Sánchez-Meca, J., Rosa-Alcázar, A. I., Marín-Martínez, F., & Gómez-Conesa, A. (2010). Psychological treatment of panic disorder with or without agoraphobia: a meta-analysis. *Clinical Psychology Review*, *30*, 37–50.
Salkovskis, P. M. (2004). Cognitive-behavioural treatment for panic. *Psychiatry*, *3*(5), 39–42.
Sheehan, D. V. (1983). *The anxiety disease*. New York: Scribner.
Spinhoven, P., de Rooij, M., Heiser, W., Smit, J. H., & Penninx, B. W. (2009). The role of personality in comorbidity among anxiety and depressive disorders in primary care and specialty care: a cross-sectional analysis. *General Hospital Psychiatry*, *31*(5), 470–477.
Spitzer, R. L., Kroenke, K., Williams, J. B., & Löwe, B. (2006). A Brief measure for assessing generalized anxiety disorder: the GAD-7. *Archives of Internal Medicine*, *166*(10), 1092–1097.
Stewart, R. E., & Chambless, D. L. (2009). Cognitive–behavioral therapy for adult anxiety disorders in clinical practice: a meta-analysis of effectiveness studies. *Journal of Consulting and Clinical Psychology*, *77*(4), 595.
Tsao, J. C. I., Mystkowski, J. L., Zucker, B. G., & Craske, M. G. (2002). Effects of cognitive-behavioral therapy for panic disorder on comorbid conditions: replication and extension. *Behavior Therapy*, *33*(4), 493–509.
Titov, N., Dear, B., McMillan, D., Anderson, T., Zou, J., & Sunderland, M. (2011). Psychometric comparison of the PHQ-9 and BDI-II for measuring response during treatment of depression. *Cognitive Behaviour Therapy*, *40*(2), 126–136.
Titov, N., Dear, B. F., Schwencke, G., Andrews, G., Johnston, L., Craske, M. G., et al. (2011). Transdiagnostic internet treatment for anxiety and depression: a randomised controlled trial. *Behaviour Research and Therapy*, *49*(8), 441–452.
Titov, N., Dear, B., Johnston, L., & Terides, M. D. (2012). Transdiagnostic internet treatment for anxiety and depression. *Spanish Journal of Clinical Psychology*, *17*(3), 237–260.
Titov, N., Dear, B., Johnston, L., Lorian, C., Zou, J., Wootton, B., et al. (2013). Improving adherence and clinical outcomes in self-guided internet treatment for anxiety and depression: randomised controlled trial. *PLoS One*, *8*(7), e62873.
Titov, N., Dear, B. F., Johnston, L., McEvoy, P., Wootton, B., Terides, M. D., et al. (2014). Improving adherence and clinical outcomes in self-guided internet treatment for anxiety and depression: a 12 month follow-up of a randomised controlled trial. *PLoS One*, *9*(2), e89591.
Titov, N., Dear, B., Staples, L. G., Bennett-Levy, J., Klein, B., Rapee, R., et al. (2015). MindSpot Clinic: an accessible, efficient and effective online treatment service for anxiety and depression. *Psychiatric Services*, *66*(10), 1043–1050.
Titov, N., Dear, B., Staples, L. G., Terides, M. D., Karin, E., Sheehan, J., et al. (2015). Disorder-specific versus transdiagnostic and clinician-guided versus self-guided treatment for major depressive disorder and comorbid anxiety disorders: a randomized controlled trial. *Journal of Anxiety Disorders*, *35*, 88–102.
Waller, G. (2009). Evidence-based treatment and therapist drift. *Behaviour Research and Therapy*, *47*(2), 119–127.
Wang, P., Aguilar-Gaxiola, S., Alonso, J., Angermeyer, M., Borges, G., Bromet, E., et al. (2007). Use of mental health services for anxiety mood, and substance disorders in 17 countries in the WHO world mental health surveys. *Lancet*, *370*, 841–850.
Weeks, J. W., Spokas, M. E., & Heimberg, R. G. (2007). Psychometric evaluation of the mini-social phobia inventory (Mini-SPIN) in a treatment-seeking sample. *Depression and Anxiety*, *24*(6), 382–391.
World Health Organization, 1990. Composite International Diagnostic Interview, Version 1.0. Geneva, World Health Organization.