

Contents lists available at ScienceDirect

## Journal of Anxiety Disorders



## Transdiagnostic versus disorder-specific and clinician-guided versus self-guided internet-delivered treatment for generalized anxiety disorder and comorbid disorders: A randomized controlled trial



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#### ARTICLE INFO

Article history: Received 27 May 2015 Received in revised form 25 August 2015 Accepted 7 September 2015 Available online 11 September 2015

Keywords: Generalized anxiety disorder Anxiety disorders Treatment Transdiagnostic Disorder-specific Self-guided Clinician-guided Internet 24-Month follow-up Randomized controlled trial

## ABSTRACT

Generalized anxiety disorder (GAD) can be treated effectively with either disorder-specific cognitive behavior therapy (DS-CBT) or transdiagnostic CBT (TD-CBT). The relative benefits of DS-CBT and TD-CBT for GAD and the relative benefits of delivering treatment in clinician guided (CG-CBT) and self-guided (SG-CBT) formats have not been examined. Participants with GAD (n = 338) were randomly allocated to receive an internet-delivered TD-CBT or DS-CBT intervention delivered in either CG-CBT or SG-CBT formats. Large reductions in symptoms of GAD (Cohen's  $d \ge 1.48$ ; avg. reduction  $\ge 50\%$ ) and comorbid major depressive disorder (Cohen's  $d \ge 1.64$ ; avg. reduction  $\ge 45\%$ ), social anxiety disorder (Cohen's  $d \ge 0.80$ ; avg. reduction  $\ge 29\%$ ) and panic disorder (Cohen's  $d \ge 0.55$ ; avg. reduction  $\ge 33\%$ ) were found across the conditions. No substantive differences were observed between DS-CBT and TD-CBT and SG-CBT.

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## 1. Introduction

Generalized anxiety disorder (GAD) is a common anxiety disorder characterized by chronic and uncontrollable worry (American Psychiatric Association, 2013). The 12-month prevalence of GAD in Australia and the United States is 2.7% and 3.1%, respectively, (Kessler et al., 2008; Slade et al., 2009) and GAD has a projected lifetime prevalence of 9.1% (McEvoy et al., 2011). However, large numbers of people experience subclinical levels of worry that significantly interferes with daily functioning (Whiteford et al., 2013) and GAD is frequently comorbid with other anxiety disorders and depression (Hoffman et al., 2008).

GAD can be treated effectively with psychological treatments such as cognitive behavioural therapy (CBT), which can be adminis-

tered face-to-face (Butler et al., 2006a; Cuijpers et al., 2008; Stewart & Chambless, 2009; Cuijpers et al., 2014a) and via the internet and workbooks (Titov et al., 2009a; Robinson et al., 2010; Paxling et al., 2011; Andersson et al., 2012; Andersson & Titov, 2014; Titov et al., 2014a,b; Dear et al., 2015b; Titov et al., 2015a; Titov et al., in press). CBT aims to reduce vulnerability to emotional dysregulation by helping patients understand the antecedents, consequences, and patterns of cognitive and behavioral symptoms of psychological disorders, and teaches skills designed to reduce the prevalence of unhelpful patterns of thought and behavior.

CBT interventions are typically designed to target symptoms of one disorder at a time (i.e., disorder-specific CBT) (McEvoy et al., 2009; McManus et al., 2010; Titov et al., 2012). However, it is unclear whether this is the optimal approach given the high comorbidity between anxiety and depressive disorders. Several alternative treatment approaches, such as tailored and transdiagnostic treatments, have recently emerged with the aim of simultaneously treating both principal and comorbid disorders. Tailored approaches modify the treatment according to patient

http://dx.doi.org/10.1016/j.janxdis.2015.09.003

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symptom characteristics and comorbidities (Carlbring et al., 2011) and there is now some emerging evidence of their equivalence to disorder-specific approaches (Berger, Boettcher, & Caspar, 2014). In contrast, transdiagnostic approaches are designed to target common underlying symptoms and predisposing psychological factors for anxiety and depression without tailoring (Barlow et al., 2004; McEvoy et al., 2009; McHugh et al., 2009; Titov et al., 2012). The conceptual basis of transdiagnostic treatments is informed by evidence that anxiety and depressive disorders share several characteristics including common symptoms, overall course, response to treatment, and temperamental antecedents (Barlow et al., 2004; Goldberg, 2010). Transdiagnostic treatments also offer potential pragmatic advantages over disorder-specific treatments including simplified treatment planning for both clinicians and patients and increased cost efficiencies (McHugh et al., 2009; Titov et al., 2012).

Results from several clinical trials indicate that internetdelivered transdiagnostic CBT is clinically effective for GAD (Johnston et al., 2011; Titov et al., 2013; Dear et al., 2015b) and traditional face-to-face transdiagnostic CBT is effective for comorbid anxiety and depressive disorders (Ellard, Fairholme, Boisseau, Farchione, & Barlow, 2010; Norton & Barrera, 2012; Norton et al., 2013; Farchione et al., 2012). However, despite their potential, few studies have directly compared the clinical efficacy or acceptability of transdiagnostic with disorder-specific CBT treatments. One recent study (n=46) randomly allocated participants to receive either a single transdiagnostic CBT treatment or to one of three disorder-specific treatments for social anxiety, GAD, and panic disorder with allocation determined by the participant's principal disorder (Norton & Barrera, 2012). All treatments were administered in a face-to-face group format and, while both treatments were effective, non-inferiority analyses did not reveal significant differences between the two approaches. Similarly, a recent randomized controlled trial (RCT) allocated participants (n = 290) with depression to receive either disorder-specific or transdiagnostic CBT and to receive treatment with or without clinician guidance (Titov et al., in press). Each treatment comprised 5 online lessons, which were delivered over 8 weeks, and all participants reported significant improvements in symptoms of depression, GAD, social anxiety and panic disorder, which were maintained at 24-month follow-up (Titov et al., in press). Importantly, no substantive differences were observed between participants who received either the disorder-specific or transdiagnostic treatment, or between those who did or did not receive clinician guidance, at post-treatment, 3-month follow-up, 12-month follow-up or 24-month follow-up. The findings of these recent studies provide support for the transdiagnostic approach but additional large trials are required to determine the reliability and clinical benefits of this approach compared with disorder-specific treatments for a broad range of anxiety and depressive disorders.

The present study extends this work by exploring the relative clinical efficacy and acceptability of transdiagnostic and disorderspecific CBT for GAD when provided in both clinician-guided and self-guided formats. Participants (n=338) were randomized to receive either transdiagnostic treatment (TD-CBT) or disorder specific (DS-CBT) treatment for symptoms of GAD, in either a clinician-guided format (CG-CBT) or self-guided format (SG-CBT). Both treatment options consisted of 5 lessons of internet-delivered CBT (iCBT) delivered over 8 weeks. Participants were assessed prior to treatment, immediately post-treatment, and at 3, 12, and 24months after treatment. It was hypothesized that both TD-CBT and DS-CBT would result in significant reductions in symptoms of GAD, but that TD-CBT would be superior at reducing symptoms of comorbid depression, social anxiety and panic at each time point. It was also hypothesized that CG-CBT would be superior to SG-CBT at every time point for both symptoms of generalized anxiety and comorbid depression, social anxiety, and panic symptoms.

#### 2. Method

#### 2.1. Participants

Participants read about the study and applied to participate via the website of the eCentreClinic (www.ecentreclinic.org), which is a specialist research unit that provides information about common mental health disorders and offers free psychological treatment via participation in clinical trials. The study was promoted via advertisements in major newspapers across Australia and via unpaid general advertisements by a broad range of non-governmental organizations 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, GAD, major depression, panic disorder or social anxiety disorder. Interested individuals were invited to submit an online application to participate in the trial, which involved completing several symptom questionnaires, and providing basic demographic information and contact details.

Five-hundred and twenty-five people applied online to participate in the trial and indicated that symptoms of GAD were their principal difficulty. Four-hundred and thirty-six of these applicants met the initial inclusion criteria 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 assessed. A further 70 applicants indicated principal difficulties of depression, social anxiety, or panic during the online application but, upon interview, indicated GAD was their principal difficulty. The inclusion criteria for the study were: (i) resident of Australia aged 18–64 years of age; (ii) a principal complaint of GAD symptoms; (iii) total score >5 on the GAD-7 indicating at least mild symptoms (Spitzer et al., 2006); 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 within the last 12 months; and (iv) currently participating in CBT. The CONSORT flowchart for this trial is shown in Fig. 1.

A total of 366 applicants met the inclusion criteria and were randomly allocated to receive one of the two treatment approaches: Transdiagnostic CBT (TD-CBT) or disorder-specific CBT (DS-CBT). Participants were also randomly allocated to receive one of the two delivery formats: clinician-guided CBT (CG-CBT) or self-guided CBT (SG-CBT). Randomization involved a permuted block randomization sequence, with interviewers blind to randomization until participants were accepted into the study. The demographic characteristics of the resultant sample are shown in Table 1. 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 ACTRN12612000433808.

#### 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, pretreatment, 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 all other time-points. In addition, the



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

Demographic characteristics of the participants.

		Treatment app	proach		Support format					
	Overall ( <i>n</i> = 338)	TD-CBT DS-CBT ( <i>n</i> = 170) ( <i>n</i> = 168)		Significance	CG-CBT ( <i>n</i> = 168)	SG-CBT ( <i>n</i> = 170)	Significance			
Gender Male Female	82 (24%) 256 (76%)	43 (25%) 127 (75%)	39 (23%) 129 (77%)	Wald's $\chi^2 = .20$ , p = .656	40 (24%) 128 (76%)	42 (25%) 128 (75%)	Wald's $\chi^2 = .04$ , <i>p</i> = .848			
Age (years) Mean (SD) Range	43.78 (11.29) 19,65	44.33 (10.71) 19,63	43.22 (11.86) 19,65	Wald's $\chi^2 = .83$ , p = .363	44.53 (11.73) 19,65	43.04 (10.83) 18,63	Wald's $\chi^2 = 1.47$ , p = .224			
Marital status Single/never married Married/ De Facto Separated/divorced/widowed	66 (20%) 227 (67%) 45 (13%)	36 (21%) 114 (67%) 20 (12%)	30 (18%) 113 (67%) 25 (15%)	Wald's $\chi^2 = .1.06$ , <i>p</i> = .301	34 (20%) 115 (68%) 19 (11%)	32 (19%) 112 (66%) 26 (15%)	Wald's $\chi^2$ = .72 <i>p</i> = .395			
Education High school or less Trade/technical certificate Diploma/degree	39 (12%) 59 (17%) 240 (71%)	27 (16%) 34 (20%) 109 (64%)	12 (7%) 25 (15%) 131 (78%)	Wald's $\chi^2 = 8.59$ , <i>p</i> = .003	22 (13%) 29 (17%) 117 (70%)	17 (10%) 30 (18%) 123 (72%)	Wald's $\chi^2$ = .43, <i>p</i> = .511			
Employment Full time/part time Student Unemployed, retired or disabled	249 (76%) 17 (5%) 240 (71%)	129 (76%) 7 (4%) 34 (20%)	120 (71%) 10 (6%) 38 (23%)	Wald's $\chi^2 = .75$ , <i>p</i> = .385	115 (68%) 7 (4%) 46 (27%)	134 (79%) 10 (6%) 26 (15%)	Wald's $\chi^2$ = 5.46, <i>p</i> = .019			
Previous mental health treatment Currently taking medication	227 (67%) 90 (27%)	117 (69%) 50 (29%)	110 (65%) 40 (24%)	Wald's $\chi^2$ = .43, p = .512 Wald's $\chi^2$ = 1.35, p = .245	112 (67%) 40 (24%)	115 (68%) 50 (29%)	Wald's $\chi^2$ = .037, <i>p</i> = .848 Wald's $\chi^2$ = 1.35, <i>p</i> = .245			

GAD-7 and PHQ-9 were also administered weekly during 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. 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 effect size differences between the arms (i.e., Cohen's ds > .35). Specifically, 204 participants were sought for the TD-CBT and DS-CBT comparisons and for the CG-CBT and SG-CBT comparisons. However, more participants were recruited to address both expected treatment withdrawal and questionnaire non-response at post-treatment time points.

#### 2.2.1. Primary measure

# Generalized anxiety disorder 7-Item scale (GAD-7; Spitzer et al., 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., 2010a; Dear et al., 2011). Scores range from 0 to 21 and Cronbach's  $\alpha$  in the current study was .87.

#### 2.2.2. Secondary measures

Patient health questionnaire-9 Item scale (PHQ-9; Kroenke et al., 2001a)

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., 2001b). The PHQ-9 has good internal consistency (Titov et al., 2011) and is sensitive to change (Kroenke et al., 2010b). Scores range from 0 to 27 and Cronbach's  $\alpha$  in this study was .84.

Mini-social phobia inventory (MINI-SPIN; Connor et al., 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 et al., 2007). The MINI-SPIN has good internal consistency and adequate convergent validity with other standardized measures of social anxiety (Weeks et al., 2007; Osório et al., 2010). Scores range from 0 to 12 and Cronbach's  $\alpha$  in this study was .88.

Panic disorder severity scale—self report (PDSS-SR; Houck et al.,

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 (Houck et al., 2002). Scores range from 0 to 28 and Cronbach's  $\alpha$  in the current study was .92.

#### 2.2.3. Tertiary measures

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  $\geq$ 22 associated with a diagnosis of anxiety and depressive disorders (Andrews & Slade, 2001). Scores range from 0 to 50 and Cronbach's  $\alpha$  in the current study was .87.

Sheehan disability scale (SDS; Sheehan, 1983).

The SDS is a 3-item measure of disability with high internal consistency (Leon et al., 1997). Scores range from 0 to 30 and Cronbach's  $\alpha$  in the present study was .85.

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 et al., 1994; Griffith et al., 2010), which is considered a higher-order risk factor for anxiety and depression (Cuijpers et al., 2005; Spinhoven et al., 2009). Scores range from 0 to 48 and Cronbach's  $\alpha$  in the current study was .77.

#### 2.2.4. Other measures

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).

#### 2.2.5. Treatment satisfaction and acceptability

Consistent with previous research (Titov et al. 2013; Dear et al. 2015a), 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 GAD, the Worry Course, or a TD-CBT course, the Wellbeing Course. The Worry Course was developed specifically for this trial. The Wellbeing Course has been previously demonstrated as clinically efficacious in treating symptoms of anxiety and depression (Titov et al. 2012, 2013, 2014). The two courses were based on the Macquarie University Model (MUM) of internet-delivered CBT, which was developed over a large number of clinical trials by the eCentre-Clinic research group, and which is associated with high completion rates, strong clinical outcomes, and high participant satisfaction (e.g., Titov et al., 2013, 2014, 2015; Dear et al., 2015a,b; Titov et al., in press). Characteristics of this model include a high level of treatment structure, a combination of didactic teaching methods with detailed clinical case narratives, scaffolded content which builds in detail over the course of treatment, homework assignments designed to facilitate skill acquisition, systematic release of materials over a pre-defined period of treatment, and regular and protocolized support provided by a combination of clinician contact via telephone or email as well as via automated emails and short message service prompts that encourage the practice of skills and their adoption into day-to-day routines.

To facilitate comparisons the two courses comprise a similar structure and similar amounts and forms of content. Both include 5 lessons delivered online over 8 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. Each lesson is presented in a slide format combining text and images, with approximately 60 slides per lesson and 50 words per slide. Automated analyses of readability indicate the required reading age of the text is 9-10 years of age (Titov et al., 2013, 2014). Participants are instructed to read lessons in order over 8 weeks. Lessons 1–5 are available at the beginning of weeks 1–7, respectively. This timetable provides participants with additional time for the most complex components of the intervention; namely skills for managing cognitive and behavioral symptoms. Consistent with standard definitions (McEvoy et al., 2009), the TD-CBT intervention 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 behavioral symptoms of psychological distress generally. Reflecting this, the TD-CBT treatment 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 GAD and presented all therapeutic information and skills in the context of GAD and reducing GAD symptoms. Consequently, all vignettes, examples and case stories focussed on GAD and the management of associated symptoms and no specific mention of other diagnoses or the broader application of therapeutic skills was made. Thus, the core difference between the transdiagnostic and disorder-specific treatment courses was the way in which the content was presented and taught rather than the actual skills taught. The content and differences between the TD-CBT and DS-CBT interventions are summarized in Table 2.

Participants in the clinician-guided condition (CG-CBT) received weekly contact from a psychologist using telephone or a secure email messaging system, based on the preferences of the participant. Three accredited and nationally registered psychologists provided treatment and all had either Masters Degrees or Doctoral Degrees in clinical psychology. Based on the findings of previous studies (Craske et al., 2009; Johnston et al., 2011) and to minimize therapist drift (Waller, 2009), the nature of the contact was protocolized 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) normalizing the challenges of recovery, and (6) obtaining feedback about the participant's perception and engagement with the course. Each contact was designed to take  $\leq 10 \text{ min}$ , but more time was provided when clinically indicated. The psychologists 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. Participants were not explicitly informed their participation would be closely monitored throughout treatment. However, they were informed that they 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), all 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 them within a week of them 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 these preliminary analyses was adjusted from 0.05 to 0.01 as a partial control for the very large number of analyses conducted. However, all of the subsequent analyses employed a 0.05 alpha significance level. Participants who did not start the interventions were not included in any analyses.

The generalized 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.

Therapeutic content and skills covered within the transdiagnostic Wellbeing Course and disorder-specific Worry Course.

	Trees diama stis Marille size Courses			Disorder-specific Worry Course						
	Iransdiagnostic Weilbeing Course			Disorder-specific worry Course						
Lesson	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 behavioral 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 GAD. Introduction of a CBT model and explanation of the functional relationship between physical, thought and behavioural symptoms in GAD. Instructions for identifying their own symptoms and how their symptoms interact. GAD specific vignettes and examples of GAD symptoms provided.	- Symptom identification - Symptom formulation	- Sleep management - What to do in a mental health emergency - GAD 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 GAD. Instructions for monitoring and challenging thoughts related to GAD. GAD specific vignettes and examples of thoughts provided.	- Thought monitoring - Thought challenging	- Structured problem solving - Worry time - Challenging beliefs - GAD 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 relaxation - Pleasant activity scheduling	<ul> <li>Risk calculation,</li> <li>coping calculation and</li> <li>shifting attention</li> <li>100 pleasant things to</li> <li>do</li> <li>Transdiagnostic case</li> <li>stories</li> </ul>	Introduction to the physical symptoms of hyper-arousal and hypo-arousal and their relationship to GAD. Instructions about controlling physical symptoms using de-arousal strategies such as controlled breathing and scheduling pleasant activities. GAD specific vignettes and examples of physical symptoms provided.	- Controlled relaxation - Pleasant activity scheduling	- Risk calculation, coping calculation and shifting attention - 100 pleasant things to do - GAD case stories				
4	Introduction to the behavioral symptoms of anxiety and low mood. Explanation of avoidance and safety behaviors 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	- Assertive communication - Transdiagnostic case stories	Introduction to the behavioral symptoms of GAD. Explanation of avoidance and safety behaviors and their relationship to GAD. Instructions for graded exposure for safely confronting fears and managing excessive worries. GAD specific vignettes and examples of graded exposure provided.	- Graded exposure	- Assertive communication - GAD 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 GAD. Information about the signs of relapse and managing lapses. Instructions for creating a relapse prevention plan. GAD specific vignettes and examples of lapses and lapse management provided.	- Relapse prevention	- GAD case stories				

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

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 utilizing 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 maximize power and the interpretability of results, the two treatment approaches and the two support formats were analyzed separately; however, to ensure these analyses did not obscure higher order 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., generalized anxiety, social anxiety, panic and depression) among those meeting MINI diagnostic criteria for the related disorder (i.e., GAD, SAD, PAN and MDE) 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.

#### 3. Results

## 3.1. Preliminary analyses

## 3.1.1. Baseline differences

Demographic and diagnostic 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. Preliminary analyses did not reveal any differences between the TD-CBT and DS-CBT groups or the CG-CBT and SG-CBT groups at baseline ( $ps \ge .01$ ). The only exception was a difference in the proportions with different levels of education between the TD-CBT and DS-CBT, where the TD-CBT group had a marginally higher proportion of participants with lower levels of educational achievement (p = .003). Comparisons exploring differences between participants completing and not completing the questionnaires at post-treatment indicated that those not completing questionnaires were slightly younger (M diff=4.76, Wald's  $\chi^2 = 8.05$ , p = .004) and had marginally higher symptoms of depres-

sion (PHQ: M diff=2.51, Wald's  $\chi^2$  = 8.05, *p* = .005) and higher levels of psychological distress (K10: M diff=2.91, Wald's  $\chi^2$  = 7.36, *p* = .007). No other differences were found.

#### 3.1.2. Clinician time

Consistent with the design, there was a significant difference in clinician contact time between CG-CBT and SG-CBT groups  $(F_{1,336} = 563.75, p < .001;$  Cohen's d = 2.58). The mean clinician time per participant in CG-CBT group was 33.54 min (SD = 18.07), which comprised answering and making calls (total calls = 918; range = 0-11 calls; mean time = 22.06; SD = 18.87), as well as reading, sending and responding to secure emails (total emails = 873; range 0-10 messages; mean time = 11.48; SD = 9.20). The mean total clinician time per participant for SG-CBT was .48 min (SD=1.62), which comprised answering and making calls (total calls = 2; range = 0-2 calls; mean time = .02; SD = 17.27), as well as reading, sending and responding to secure emails (total emails = 32; range 0-4 messages; mean time = .48; SD = 1.62). However, this contact was primarily concerned with 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 ( $F_{1,336} = .68, p = .41$ ).

## 3.1.3. Preliminary test for higher order interactions

The GEE analyses did not reveal any significant treatment approach by support format by time interactions (GAD-7: Wald's  $\chi^2$  = 4.35, *p* = .629; PHQ-9: Wald's  $\chi^2$  = 4.72, *p* = .580; MINI-SPIN: Wald's  $\chi^2$  = 3.56, *p* = .735; PDSS-SR: Wald's  $\chi^2$  = 5.38, *p* = .371). The GEE analyses also did not reveal any significant treatment approach by support format by time interactions for the tertiary outcomes (K10: Wald's  $\chi^2$  = 2.75, *p* = .601; SDS: Wald's  $\chi^2$  = 9.92, *p* = .078; NEO-FFI-N: Wald's  $\chi^2$  = 1.92, *p* = .589).

# 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. Generalized anxiety disorder. Among those who met diagnostic criteria for GAD (n=291) the GEE analyses indicated a significant effect for time (GAD-7: Wald's  $\chi^2$ =834.15, p<.001) and a significant time by treatment approach interaction for GAD symptoms (GAD-7: Wald's  $\chi^2$ =18.54, p=.001). Pairwise comparisons indicated there were no differences between the TD-CBT and DS-CBT groups at post-treatment (p=.701), 3-month follow-up (p=.803) or 12-month follow-up (p=.132), but did indicate a difference at 24-month follow-up (p<.001) with the TD-CBT group reporting fewer symptoms. These comparisons also indicated that both groups improved from baseline to post-treatment (p<.001) and from post-treatment to 3-month follow-up (ps=.022–.040) and that the TD-CBT group's symptoms improved slightly from 12-month to 24-month follow-up (p=.013).

3.2.1.2. Major depressive disorder. Among those who met diagnostic criteria for MDD (n=157) the GEE analyses indicated a significant effect for time (PHQ-9: Wald's  $\chi^2 = 510.69$ , p < .001) and a significant time by treatment approach interaction for depressive symptoms (PHQ-9: Wald's  $\chi^2 = 15.65$ , p = .004). Pairwise comparisons indicated there were no differences between the TD-CBT and DS-CBT groups at 3-month follow-up (p = .435), but did indicate significant differences at post-treatment (p = .019), 12-month (p = .016) and 24-month follow-up (p = .001) with the TD-CBT

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

	Estimated mar	ginal means	,	% Change from baseline				Within group Cohen's d from baseline				Between group Cohen's d					
	Baseline	Post	3 month	12 month	24 month	Post	3 month	12 month	24 month	Post	3 month	12 month	24 month	Post	3 month	12 month	24 month
<b>Principal outcome</b> Generalized anxiety s DS-CBT ( <i>n</i> = 140)	symptoms <sup>a</sup> 12.69 (4.45)	6.25 (3.99)	5.56 (4.14)	5.48 (3.89)	5.95 (4.30)	51%	56%	57%	53%	1.52	1.66	1.73	1.54	.04	.03	.18	.48
TD-CBT ( <i>n</i> = 151)	12.36 (4.31) [11.69, 13.06]	[5.05, 6.55] 6.07 (4.03) [5.46, 6.75]	5.44 (4.05) [.83, 6.12]	4.83 (3.37) [4.32, 5.40]	4.17, (3.07) [3.70, 4.69]	[45%, 56%] [45%, 56%]	[50%, 61%] [50%, 61%]	[51%, 62%] 61% [56%, 65%]	[47%, 30%] 66% [62%, 70%]	1.51 [1.24, 1.76]	1.66 [1.39, 1.91]	1.95 [1.66, 2.21]	2.19 [1.89, 2.46]	[ .13, .27]	[ .20, .20]	[ .05, .41]	[.24,.71]
Secondary outcomes	s																
Depression symptom DS-CBT (n = 69)	15 <sup>D</sup> 14.47 (3.80) [13.60, 15.39]	7.94 (4.15) [7.02, 8.99]	6.96 (4.50) [5.98, 8.11]	7.01 (4.64) [5.99, 8.19]	7.76 (5.00) [6.66, 9.03]	45% [38%, 51%]	52% [44%, 59%]	52% [43%, 59%]	46% [38%, 54%]	1.64 [1.24, 2.02]	1.80 [1.40, 2.19]	1.76 [1.36, 2.14]	1.51 [1.12, 1.88]	.38 [.06, .70]	.13 [19, .44]	.40 [.08, .72]	.56 [.24, .88]
TD-CBT $(n = 88)$	14.10 (4.00) [13.29, 14.96]	6.41 (3.93) [5.64, 7.29]	6.41 (4.28) [5.58, 7.37]	5.42 (3.31) [4.77, 6.16]	5.40 (3.42) [4.73, 6.17]	55% [48%, 60%]	55% [48%, 60%]	62% [56%, 66%]	62% [56%, 66%]	1.94 [1.57, 2.29]	1.86 [1.50, 2.20]	2.37 [1.97, 2.74]	2.34 [1.94, 2.71]				
Social anxiety sympto	oms <sup>c</sup>																
DS-CBT (n = 59)	7.97 (2.44) [7.37, 8.61]	5.69 (2.90) [5.00, 6.48]	4.98 (3.14) [4.24, 5.85]	4.67 (2.84) [4.00, 5.45]	4.71 (2.57) [4.10, 5.41]	29% [19%, 37%]	37% [27%, 47%]	41% [32%, 50%]	41% [32%, 49%]	.85 [.47, 1.22]	1.06 [.67, 1.44]	1.25 [.85, 1.63]	1.30 [.90, 1.69]	.16 [19, .52]	.20 [–.15, .56]	.12 [24, .48]	.32 [.04, .68]
TD-CBT ( <i>n</i> = 63)	7.79 (2.55) [7.19, 8.45]	5.22 (2.82) [4.57, 5.96]	4.36 (2.96) [3.69, 5.16]	4.33 (2.80) [3.69, 5.08]	3.82 (2.92) [3.16, 4.61]	33% [23%, 41%]	44% [34%, 53%]	44% [35%, 53%]	51% [41%, 59%]	.96 [.59, 1.32]	1.24 [.86, 1.62]	1.29 [.90, 1.67]	1.45 [1.05, 1.84]				
Panic symptoms <sup>d</sup> DS-CBT (n = 50)	9.83 (6.23) [8.25, 11.72]	6.33 (6.61) [4.74, 8.45]	5.05 (6.91) [3.46, 7.38]	4.47 (5.89) [3.10, 6.44]	4.10 (5.49) [2.83, 5.94]	36% [14%, 52%]	49% [25%, 65%]	55% [35%, 68%]	58% [40%, 71%]	.55 [.14, .94]	.73 [.47, 1.13]	.89 [.47, 1.29]	.98 [.556, 1.38]	.07 [34, .48]	02 [43, .39]	.09 [32, .50]	.05 [–.36, .46]
TD-CBT $(n = 42)$	10.06 (4.71) [8.73, 11.59]	5.91 (4.17) [4.78, 7.32]	5.16 (4.21) [4.03, 6.60]	4.02 (3.39) [3.12, 5.19]	3.83 (4.41) [2.71, 5.42]	41% [27%, 53%]	49% [34%, 60%]	60% [48%, 69%]	62% [46%, 73%]	.93 [.47, 1.37]	1.10 [.63, 1.55]	1.47 [.98, 1.94]	1.37 [.88, 1.83]				
<b>Tertiary outcomes</b> Disability and function DS-CBT ( <i>n</i> = 168)	oning (SDS) 12.40 (7.00) [11.38, 13.51]	7.86 (6.91) [6.87, 8.98]	6.13 (6.31) [5.25, 7.17]	5.99 (6.08) [5.13, 6.99]	4.93 (6.88) [5.24, 7.35]	37% [28%, 45%]	51% [42%, 58%]	52% [44%, 59%]	50% [41%, 58%]	.65 [.43, .87]	.94 [.71, 1.17]	.98 [.75, 1.20]	1.08 [.84, 1.30]	.07 [14, .29]	.06 [15, .28]	.08 [14, .29]	.12 [09, .34]
TD-CBT ( <i>n</i> = 170)	13.28 (7.64) [12.18, 14.48]	7.36 (6.42) [6.45, 8.39]	5.77 (5.45) [5.00, 6.65]	5.53 (5.95) [4.70, 6.50]	4.20 (4.93) [3.52, 5.01]	45% [37%, 51%]	57% [50%, 62%]	58% [51%, 65%]	68% [62%, 74%]	.84 [.62, 1.06]	1.13 [.90, 1.36]	1.13 [.90, 1.36]	1.41 [1.17, 1.65]				
Psychological distress DS-CBT (n = 168)	s (K-10) 25.98 (6.80) [24.97, 27.04]	19.70 (647) [18.73, 20.70]	17.98 (5.83) [17.11, 18.88]	17.73 (5.71) [16.88, 18.62]	-	24% [20%, 28%]	31% [27%, 34%]	32% [28%, 35%]	-	.95 [.72, 1.17]	1.26 [1.03, 1.49]	1.31 [1.07, 1.55]	-	.06 [15, .28]	05 [26, .16]	–.04 [–.18, .25]	-
TD-CBT ( <i>n</i> = 170)	26.05 (7.23) [24.98, 27.16]	19.30 (6.48) [18.35, 20.30]	18.27 (6.00) [17.39, 19.19]	17.51 (5.93) [16.65, 18.43]	-	26% [22%, 30%]	30% [26%, 33%]	33% [29%, 36%]	-	.98 [.76, 1.21]	1.17 [.94, 1.40]	1.29 [1.05, 1.52]	-				
Neuroticism (NEO-FF DS-CBT (n = 168)	FI-N) 31.63 (7.27) [30.55, 32.76]	27.28 (8.52) [26.01, 28.61]	26.17 (8.25) [24.95, 27.46]	24.88 (8.50) [23.62, 26.21]	-	14% [10%, 18%]	17% [13%, 21%]	21% [17%, 25%]	-	.55 [.33, .77]	.70 [.48, .92]	.85 [.63, 1.07]	-	17 [38, .05]	.03 [19, .24]	03 [25, .18]	-
TD-CBT (n = 170)	32.64 (7.12) [31.59, 33.73]	28.63 (7.76) [27.48, 29.82]	25.95 (8.23) [24.74, 27.22]	25.13 (7.58) [24.02, 26.30]	-	12% [9%, 16%]	21% [17%, 24%]	23% [19%, 26%]	-	.54 [.32, .75]	.87 [.65, 1.09]	1.02 [.79, 1.25]	-		-		

Note: Standard deviations are shown in round 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. Generalized anxiety, depression, social anxiety and panic symptoms were measured with the GAD-7, PHQ-9, MINI-SPIN, and PDSS-SR, respectively.

<sup>a</sup> Analyses use the data of participants meeting diagnostic criteria for generalized anxiety disorder at assessment.

<sup>b</sup> Analyses use the data of participants meeting diagnostic criteria for major depressive disorder at assessment.

<sup>c</sup> Analyses use the data of participants meeting diagnostic criteria for social anxiety disorder at assessment.

<sup>d</sup> Analyses use the data of participants meeting diagnostic criteria for panic disorder at assessment.

group reporting fewer symptoms at each time point. These comparisons revealed that both groups improved from baseline to post-treatment (p < .001) and that the TD-CBT group's symptoms improved slightly from 3-month to 12-month follow-up (p = .003).

3.2.1.3. Social anxiety disorder. Among those who met diagnostic criteria for SAD (n = 122) the GEE analyses indicated a significant effect for time (MINI-SPIN: Wald's  $\chi^2 = 190.55$ , p < .001) but no significant time by treatment approach interaction for social anxiety symptoms (MINI-SPIN: Wald's  $\chi^2 = 4.17$ , p = .383). Pairwise comparisons indicated that both groups improved similarly from baseline to post-treatment (p < .001) and from post-treatment to 3-month follow-up (p < .001).

3.2.1.4. Panic disorder. Among those who met diagnostic criteria for PD (n=92) the GEE analyses indicated a significant effect for time (PDSS-SR: Wald's  $\chi^2 = 115.24$ , p < .001) but no significant time by treatment approach interaction for panic symptoms (PDSS-SR: Wald's  $\chi^2 = .89$ , p = .925). Pairwise comparisons indicated that both groups improved from baseline to post-treatment (p < .001) and from post-treatment to 3-month follow-up (p = .015).

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

Across the whole sample (n = 338) the GEE analyses indicated a significant effect for Time (K10: Wald's  $\chi^2 = 906.10$ , p < .001) but no significant time by treatment approach interaction for general psychological distress (K10: Wald's  $\chi^2 = 1.79$ , p = .616). 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).

Across the whole sample (n = 338) there was a significant effect for time (SDS: Wald's  $\chi^2 = 512.51$ , p < .001) and a significant time by treatment approach interaction for disability (SDS: Wald's  $\chi^2 = 16.28$ , p = .003). Pairwise comparisons indicated there were no differences between the TD-CBT and DS-CBT groups at posttreatment (p = .493), 3-month follow-up (p = .568) or 12-month follow-up (p = .482), but did indicate a difference at 24-month follow-up (p = .002) with the TD-CBT group reporting less disability. The comparisons indicated that both groups improved from baseline to post-treatment (p < .001) and from post-treatment to 3month follow-up (p < .001), and that the TD-CBT group's symptoms improved slightly from 12-month to 24-month follow-up (p = .002).

Across the whole sample (n = 338) there was a significant effect for time (NEO-FFI-N: Wald's  $\chi^2 = 400.35$ , p < .001) but no significant time by treatment approach interaction for neuroticism (NEO-FFI-N: Wald's  $\chi^2 = 5.94$ , p = .115). These comparisons also indicated that both groups improved from baseline to post-treatment (p < .001), from post-treatment to 3-month follow-up (p < .001), and from 3month follow-up to 12-month follow-up (p = .002).

#### 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 5. The GEE analyses of diagnoses revealed a significant effect for time across all of the diagnoses (GAD: Wald's  $\chi^2 = 224.67$ , p < .001; MDE; Wald's  $\chi^2 = 114.71$ , p < .001; SAD: Wald's  $\chi^2 = 78.52$ , p < .001; PD: Wald's  $\chi^2 = 41.27$ , p < .001) and no significant time by treatment approach effects (GAD: Wald's  $\chi^2 = 0.860$ , p = .353; MDE: Wald's  $\chi^2 = 0.02$ , p = .882; SAD: Wald's  $\chi^2 = 0.63$ , p = .425) with the exception of panic disorder (PD: Wald's  $\chi^2 = 6.04$ , p = .013). Pairwise comparisons revealed that the proportion of participants meeting diagnostic criteria for GAD, MDE, SP and PD reduced significantly across both groups and that the TD-CBT group reported significantly fewer diagnoses of PD at 3-month follow-up.

The GEE analyses focusing on average comorbid diagnoses revealed a significant time effect (Wald's  $\chi^2$  = 122.9, *p* < .001) but no time by treatment approach interaction (Wald's  $\chi^2$  = 3.291, *p* = .070). These analyses indicated significant reductions in comorbid diagnoses amongst both the TD-CBT and DS-CBT 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 = 4.28; SD = 1.16) and DS-CBT groups (M = 4.32; SD = 1.18) at post-treatment ( $F_{1,336}$  = .07, p = .795). Of the participants that completed the evaluation questions at post-treatment, 99% (138/140) of the TD-CBT group and 97% (133/137) of the DS-CBT group, reported they *would recommend the course* to others. Moreover, 97% (136/140) of the TD-CBT group and 98% (134/137) 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 willing to recommend the course or finding the course was worth their time ( $\chi^2$  range = .21–.73; p range = .394–.646).

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

The means, percentage reductions and effect sizes for the CG-CBT and SG-CBT groups are shown in Table 4.

## 3.3.1. Outcomes across the diagnoses

3.3.1.1. Generalized anxiety disorder. Among those who met diagnostic criteria for GAD (n=291) the GEE analyses indicated a significant effect for time (GAD-7: Wald's  $\chi^2$ =811.87, p<.001) but no significant time by support format interaction for GAD symptoms (GAD-7: Wald's  $\chi^2$ =7.17, p=.127). Pairwise comparisons indicated that there were no significant differences between the groups at any time point (p range=.066–.919). These comparisons also indicated that both groups improved from baseline to post-treatment (p<.001) and that the SG-CBT group's scores also improved from post-treatment to 3-month follow-up (p<.001), while the CG-CBT group's scores improved from 3-month follow-up to 12-month follow-up (p=.019).

3.3.1.2. Major depressive disorder. Among those who met diagnostic criteria for MDD (n=157) the GEE analyses indicated a significant effect for time (PHQ-9: Wald's  $\chi^2$  = 475.66, p < .001) and a significant time by support format interaction for depressive symptoms (PHQ-9: Wald's  $\chi^2$  = 14.45, p = .006). Pairwise comparisons indicated there were no differences between the groups at any time point (p range = .081–.926). These comparisons indicated that both groups improved from baseline to post-treatment (p<.001) and that the SG-CBT group also improved between post-treatment and 3-month follow-up (p=.004), while the CG-CBT group improved between 12-month and 24-month follow-up (p=.026).

3.3.1.3. Social anxiety disorder. Among those who met diagnostic criteria for SAD (n=122) indicated a significant effect for time (MINI-SPIN: Wald's  $\chi^2 = 189.99$ , p < .001) but no significant time by support format interaction for social anxiety symptoms (MINI-SPIN: Wald's  $\chi^2 = 2.38$ , p = .666). These comparisons also indicated that both groups improved similarly from baseline to post-treatment (p < .001) and from post-treatment to 3-month follow-up (p < .001).

3.3.1.3. Panic disorder. Among those who met diagnostic criteria for PD (n = 92) the GEE analyses revealed a significant effect for time

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	3 month	12 month	24 month	Post	3 month	12 month	24 month	Post	3 month	12 month	24 month	Post	3 month	12 month	24 month
Principal outcome Generalized anxiety	symptoms <sup>a</sup>																
CG-CBT ( <i>n</i> = 144)	12.61 (4.40) [11.93, 13.33]	6.09 (3.96) [5.49, 6.75]	5.94 (4.63) [5.24, 6.73]	5.16 (3.55) [4.63, 5.76]	5.23 (4.36) [4.58, 5.97]	52% [46%, 57%]	53% [47%, 58%]	59% [54%, 63%]	59% [53%, 64%]	1.56 [1.29, 1.82]	1.48 [1.21, 1.73]	1.86 [1.58, 2.13]	1.68 [1.41, 1.95]	–.03 [–.26, .19]	.22 [–.02, .45]	.01 [22, .24]	.10 [12, .33]
SG-CBT (n = 147)	12.42 (4.34) [11.72, 13.16]	6.23 (4.05) [5.60, 6.94]	5.06 (3.48) [4.51, 5.67]	5.12, (3.72) [4.54, 5.77]	4.83 (3.24) [4.32, 5.39]	50% [44%, 55%]	59% [54%, 64%]	59% [54%, 63%]	61% [57%, 65%]	1.47 [1.21, 1.73]	1.87 [1.59, 2.14]	1.81 [1.53, 2.07]	1.98 [1.70 2.26]				
Secondary outcomes																	
Depression sympton	ns <sup>D</sup>	6 72 (2 00)	7.17(4.50)	C 00 (2 77)	7.02 (4.00)	52%	50%	5.0%	510/	1.00	1.00	0.17	1.61	10	25	02	20
CG-CBI(n=81)	[13.63, 15.31]	6.73 (3.88) [5.97, 7.59]	[6.29, 8.18]	[5.35, 6.93]	7.02 (4.90) [6.06, 8.12]	53% [47%, 59%]	50% [43%, 56%]	58% [52%, 63%]	51% [44%, 58%]	[1.63, 2.28]	[1.36, 1.98]	2.17 [1.82, 2.49]	[1.30, 1.92]	18 [49, .13]	.25 [–.07, .56]	–.02 [–.33, .30]	.28 [04, .59]
SG-CBT (n = 76)	14.07 (3.78) [13.20, 14.99]	7.46 (4.23) [6.53, 8.53]	6.10 (4.18) [5.19, 7.17]	6.1 (4.22) [5.23, 7.23]	5.82 (3.66) [5.02, 6.75]	47% [39%, 54%]	57% [49%, 63%]	56% [49%, 63%]	59% [52%, 64%]	1.65 [1.27, 2.01]	2.00 [1.60, 2.38]	1.98 [1.58, 2.35]	2.22 [1.80, 2.61]				
Social anxiety symp	toms <sup>c</sup>																
CG-CBT(n=62)	7.79 (2.36) [7.23, 8.39]	5.22 (2.63) [4.61, 5.91]	4.72 (3.22) [3.99, 5.58]	4.45 (3.00) [3.77, 5.25]	4.19 (2.82) [3.55, 4.95]	33% [24%, 41%]	39% [28%, 49%]	43% [33%, 52%]	46% [36%, 54%]	1.03 [.65, 1.40]	1.09 [.70, 1.46]	1.24 [.85, 1.61]	1.38 [.98, 1.77]	–.16 [–.52, .19]	.04 [32, .39]	–.04 [–.39, .32]	04 [40, .31]
SG-CBT $(n = 60)$	7.97 (2.62) [7.33, 8.67]	5.69 (3.07) [4.95, 6.52]	4.61 (2.90) [3.93, 5.41]	4.55 (2.63) [3.92, 5.27]	4.31 (2.77) [3.65, 5.07]	29% [18%, 38%]	42% [32%, 51%]	43% [34%, 51%]	46% [36%, 54%]	.80 [.42, 1.17]	1.22 [.82, 1.60]	1.30 [.90, 1.69]	1.36 [.95, 1.75]				
Panic symptoms <sup>d</sup>																	
CG-CBT(n=44)	10.18 (4.60) [8.88, 11.67]	6.83 (4.73) [5.54, 8.42]	5.78 (5.25) [4.39, 7.61]	4.86 (4.80) [3.60, 6.55]	5.04 (5.75) [3.57, 7.12]	33% [17%, 46%]	43% [25%, 57%]	52% [36%, 65%]	50% [30%, 65%]	.72 [.28, 1.14]	.89 [.45, 1.32]	1.13 [.67, 1.57]	.98 [.53, 1.41]	.27 [15, .67]	.24 [17, .65]	.27 [14, .68]	.44 [02, .85]
SG-CBT (n = 48)	9.75 (6.09) [8.20, 11.60]	5.43 (5.71) [4.06, 7.27]	4.49 (5.57) [3.18, 6.33]	3.65 (4.21) [2.65, 5.02]	2.95 (3.59) [2.11, 4.14]	44% [25%, 58%]	54% [35%, 67%]	63% [48%, 73%]	70% [58%, 78%]	.73 [.31, 1.14]	.90 [.47, 1.31]	1.17 [.72, 1.59]	1.36 [.91, 1.79]				
Tertiary outcomes																	
Disability and functi	ioning (SDS)	7.52 (6.40)	6 52 (6 12)	5 70 (5 02)	611(704)	4.40/	50%	<b>57</b> 0/	<b>FF0</b> /	07	1.05	1.17	1.04	00	10	01	20
CG-CBI(n = 168)	[12.43, 14.58]	[6.61, 8.57]	[5.66, 7.51]	5.79 (5.92) [4.96, 6.75]	[5.14, 7.27]	44% [36%, 51%]	52% [44%, 58%]	57% [50%, 63%]	55% [46%, 62%]	.87 [.64, 1.09]	[.81, 1.27]	1.17 [.94, 1.40]	1.04 [.81, 1.26]	–.02 [–.24, .19]	.19 [02, .41]	.01 [20, .22]	.30 [.09, .52]
SG-CBT (n = 170)	12.22 (7.47) [11.14, 13.42]	7.68 (6.84) [6.71, 8.79]	5.38 (5.62) [4.59, 6.31]	5.72 (6.11) [4.86, 6.73]	4.29 (4.81) [3.61, 5.08]	37% [28%, 45%]	56% [48%, 62%]	53% [45%, 60%]	65% [58%, 70%]	.64 [.42, .85]	1.04 [.81, 1.26]	.95 .73, 1.18]	1.26 [1.03, 1.49]				
Psychological distres	ss (K-10)																
CG-CBT (n = 168)	26.53 (7.21) [25.46, 27.64]	19.48 (6.26) [18.56, 20.44]	18.90 (6.35) [17.97, 19.88]	17.73 (6.08) [16.84, 18.66]	-	27% [23%, 30%]	29% [25%, 32%]	33% [30%, 37%]	-	1.04 [.81, 1.27]	1.12 [.89, 1.35]	1.32 [1.08, 1.55]	-	01 [22, .21]	.26 [05, .48]	.04 [18, .25]	-
SG-CBT ( <i>n</i> = 170)	25.51 (6.76) [24.50, 26.56]	19.52 (6.68) [18.53, 20.56]	17.36 (5.37) [16.56, 18.19]	17.52 (5.56) [16.69, 18.38]	-	23% [19%, 27%]	32% [29%, 35%]	31% [28%, 35%]	-	.89 [.67, 1.11]	1.34 [1.10, 1.57]	1.29 [1.05, 1.52]	-				
Neuroticism (NEO-F	FI-N)																
CG-CBT ( <i>n</i> = 168)	32.57 (7.08) [31.52, 33.65]	28.0 (8.01) [26.90, 29.31]	26.86 (8.54) [25.60, 28.17]	25.31 (7.88) [24.15, 26.52]	-	14% [10%, 17%]	18% [13%, 21%]	22% [19%, 26%]	-	.59 [.37, .81]	.73 [.51, .95]	.97 [.74, 1.19]	-	.03 [18, .24]	.19 [–.02, .41]	.07 [14, .29]	-
SG-CBT (n = 170)	31.72 (7.31) [30.63, 32.85]	27.83 (8.33) [26.59, 29.13]	25.27 (7.86) [24.10, 26.50]	24.71 (8.20) [23.50, 25.99]	-	12% [8%, 16%]	20% [16%, 24%]	22% [18%, 26%]	-	.50 [.28, .71]	.85 [.63, 1.07]	.90 [.68, 1.12]	-				

Note: Standard deviations are shown in round 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. Generalized anxiety, depression, social anxiety and panic symptoms were measured with the GAD-7, PHQ-9, MINI-SPIN, and PDSS-SR, respectively.

<sup>a</sup> Analyses use the data of participants meeting diagnostic criteria for generalized anxiety disorder at assessment.

<sup>b</sup> Analyses use the data of participants meeting diagnostic criteria for major depressive disorder at assessment.

<sup>c</sup> Analyses use the data of participants meeting diagnostic criteria for social anxiety disorder at assessment.

<sup>d</sup> Analyses use the data of participants meeting diagnostic criteria for panic disorder at assessment.

## Table 5 Proportions meeting diagnostic criteria over time for each of the groups.

	TD-CBT versus	S DS-CBT				CG-CBT versus SG-CBT							
	Baseline		3 month		% Change from	% Change from baseline		Baseline		3 month		% 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													
Generalized anxiety disorde Major depressiv disorder Social anxiety disorder Panic disorder <b>Comorbid diag</b> Average	89% r [83%, 93%] /e 52% [44%, 59%] 37% [30%, 45%] 29% [23%, 37%] moses 1.18	83% [77%, 88%] 41% [34%, 49%] 35% [28%, 43%] 25% [19%, 32%] 1.01	31% [24%, 38%] 11% [7%, 17%] 8% [5%, 13%] 6% [3%, 11%] 0.39	28% [22%, 35%] 7% [4%, 12%] 10% [6%, 16%] 13% [8%, 18%] 0.46	58% [50%, 66%] 41% [33%, 49%] 29% [21%, 36%] 24% [16%, 31%] 66%	53% [44%, 62%] 34% [26%, 42%] 25% [18%, 32%] 13% [5%, 20%] 54%	86% [80%, 90%] 48% [41%, 56%] 37% [30%, 44%] 26% [20%, 33%]	86% [80%, 91%] 45% [37%, 52%] 35% [35%, 43%] 28% [22%, 35%] 1.08	32% [26%, 40%] 8% [5%, 14%] 10% [6%, 15%] 10% [6%, 15%] 0.46	26% [20%, 34%] 10% [6%, 15%] 9% [5%, 14%] 9% [5%, 14%] 0.39	54% [46%, 60%] 40% [32%, 48%] 27% [20%, 35%] 17% [10%, 24%] 58%	60% [53%, 66%] 35% [27%, 43%] 26% [19%, 34%] 19% [12%, 27%]	
nverage	[1.05, 1.32]	[0.88, 1.15]	[0.30, 0.51]	[0.36, 0.58]	[56%, 74%	[42%, 64%]	[0.98, 1.26]	[0.95, 1.22]	[0.36, 0.59]	[0.30, 0.51]	[46%, 68%]	[53%, 72%]	
Frequency <sup>a</sup>													
0	26% [20%, 33%]	32% [26%, 40%]	81% [74%, 86%]	76% [69%, 82%]	-	-	29% [23%, 36%]	29% [23%, 36%]	80% [74%, 86%]	76% [70%, 82%]	-	-	
1	38% [31%, 46%]	41% [34%, 49%]	14% [10%, 20%]	20% [14%, 26%]	-	-	37% [31%, 45%]	42% [35%, 49%]	13% [9%, 19%]	21% [15%, 27%]	-	-	
2	28% [21%, 35%]	20% [15%, 27%]	5% [2%, 9%]	2% [1%, 6%]	-	-	26% [20%, 33%]	22% [16%, 29%]	5% [3%, 10%]	2% [1%, 5%]	-	-	
3	8% [5%, 13%]	7% [4%, 11%]	1% [0%, 4%]	2% [1%, 5%]	-	-	7% [4%, 12%]	8% [4%, 13%]	1% [0%, 5%]	1% [0%, 5%]	-	-	

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

<sup>a</sup> The frequency of comorbid diagnoses over time was estimated employing binary logistic regressions, provide estimates of frequency with 95% confidence intervals rather than simple raw counts.

(PDSS-SR: Wald's  $\chi^2$  = 129.85 *p* < .001) but no significant time by support format interaction for panic symptoms (PDSS-SR: Wald's  $\chi^2$  = 5.93, *p* = .205). Pairwise comparisons revealed that both groups improved similarly from baseline to post-treatment (*p* < .001) and from post-treatment to 3-month follow-up (*p* = .016).

# 3.3.2. Outcomes for general psychological distress, disability, and neuroticism

Across the whole sample (n=338) the GEE analyses indicated a significant effect for time (K10: Wald's  $\chi^2 = 906.32$ , p < .001) but no significant time by support format interaction for general psychological distress (K10: Wald's  $\chi^2 = 10.12$ , p = .018). Pairwise comparisons indicated there were no differences between the CG-CBT and SG-CBT groups at post-treatment (p = .956) and 12-month follow-up (p = .743), but there was a difference at 3-month followup (p = .016) with the SG-CBT group reporting marginally less disability. The comparisons indicated that both groups improved from baseline to post-treatment (p < .001) and that the SG-CBT group's symptoms improved slightly from post-treatment to 3month follow-up (p < .001), while the CG-CBT group's symptoms improved slightly from 3-month to 12-month follow-up (p = .006).

Across the whole sample (n=338) there was a significant effect for time (SDS: Wald's  $\chi^2 = 490.62$ , p < .001) and a significant time by support format interaction for disability (SDS: Wald's  $\chi^2 = 13.41$ , p = .009). Pairwise comparisons indicated there were no differences between the CG-CBT and SG-CBT groups at post-treatment (p = .835), 3-month follow-up (p = .076) or 12-month follow-up (p = .005), with the SG-CBT group reporting less disability. The comparisons indicated that both groups improved from baseline to post-treatment (p < .001) and from post-treatment to 3-month follow-up (p < .021), and the SG-CBT group's symptoms also improved from 12-month to 24-month follow-up (p < .001).

Across the whole sample (n = 338) there was a significant effect for Time (NEO-FFI-N: Wald's  $\chi^2 = 398.59$ , p < .001) but no significant time by support format effect for neuroticism (NEO-FFI-N: Wald's  $\chi^2 = 5.01$ , p = .171). Pairwise comparisons indicated that both groups improved from baseline to post-treatment (p < .001), from post-treatment to 3-month follow-up (p < .001), and from 3month follow-up to 12-month follow-up (p = .002).

## 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 5. The GEE analyses of diagnoses revealed a significant effect for time across all of the diagnoses (GAD: Wald's  $\chi^2 = 228.35$ , p < .001; MDE; Wald's  $\chi^2 = 117.83$ , p < .001; SAD: Wald's  $\chi^2 = 78.82$ , p < .001; PD: Wald's  $\chi^2 = 41.38$ , p < .001) and no significant time by treatment approach effects (GAD: Wald's  $\chi^2 = 0.888$ , p = .346; MDE: Wald's  $\chi^2 = 0.741$ , p = .389; SAD: Wald's  $\chi^2 = 0.001$ , p = .971; PD: Wald's  $\chi^2 = 0.212$ , p = .645). Pairwise comparisons revealed that the proportion of participants meeting diagnostic criteria for GAD, MDE, SP and PD reduced significantly from pre-treatment to 3-month follow-up for both the CG-CBT and SG-CBT groups.

The GEE analyses focused on average comorbid diagnoses revealed a significant time effect (Wald's  $\chi^2$  = 123.6, *p* < .001) but no time by treatment approach interaction (Wald's  $\chi^2$  = 0.620, *p* = .431). These analyses indicated significant reductions in comorbid diagnoses amongst both the CG-CBT and SG-CBT groups over time.

#### 3.3.4. Treatment completion and satisfaction rates

The CG-CBT group (M = 4.45; SD = .98) completed slightly more lessons on average than the SG-CBT group (M = 4.15; SD = 1.32) at

the post-treatment time point ( $F_{1,336}$  = 5.84, p = .016). Of the participants that completed the evaluation questions at post-treatment, 97% (134/138) of the CG-CBT group, and 99% (137/138) of the SG-CBT group, reported they *would recommend the course* to others. Further, 97% (133/137) of the CG-CBT group and 99% (137/138) 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 ( $\chi^2$  range = .69–1.86; p range = .404–.173).

## 4. Discussion

The aim of the current study was to compare the clinical efficacy and acceptability of transdiagnostic CBT and disorder-specific CBT for GAD when provided in both clinician-guided and selfguided formats. It was hypothesized that both TD-CBT and DS-CBT would result in significant improvements on principal symptoms of GAD, but that TD-CBT would be associated with superior improvements to DS-CBT on comorbid symptoms of depression, social anxiety, and panic at each time point. It was also hypothesized that CG-CBT would be superior to SG-CBT on both principal and comorbid symptoms at each time point. These hypotheses were not fully supported. All conditions resulted in significant improvements across the outcome measures and these corresponded to significant reductions in the proportions of participants meeting diagnostic criteria. Some statistically significant differences were found between the TD-CBT and DS-CBT groups at longer-term follow-up, with the TD-CBT group reporting slightly lower levels of symptoms of generalised anxiety and depression. There was also some evidence of a greater reduction in PD diagnoses among the TD-CBT group compared with the DS-CBT group. However, the differences were relatively small in magnitude and were not consistently observed across the outcome domains or diagnoses. Finally, no differences were found between participants who received CG-CBT or SG-CBT either in terms of symptom scores or changes in diagnostic status. Treatment completion and satisfaction was high amongst all groups.

The results of the current trial indicate that TD-CBT and DS-CBT are both effective at reducing symptoms of GAD with gains sustained for at least 24 months. The magnitude of reductions seen in the current trial were large (Cohen's  $d \ge 1.51$ ; avg. reduction  $\ge 51\%$ ) and consistent with those reported in face-to-face treatments (Butler et al., 2006b; Stewart & Chambless, 2009; Cuijpers et al., 2014b) and internet-delivered treatments for GAD (Andrew et al., 2010). The findings also indicate that both TD-CBT and DS-CBT result in large reductions in comorbid symptoms of major depressive disorder (Cohen's  $d \ge 1.64$ ; avg. reduction  $\ge 45\%$ ), social anxiety disorder (Cohen's  $d \ge 0.85$ ; avg. reduction  $\ge 29\%$ ) and panic disorder (Cohen's  $d \ge 0.55$ ; avg. reduction  $\ge 36\%$ ). Importantly, these results were maintained across the follow-up period and are consistent with the magnitude of improvements reported for disorder-specific interventions for these conditions (Butler et al., 2006b; Andrews et al., 2010; Reinholt & Krogh, 2014).

There was some evidence of lower levels of generalized anxiety, depression and disability at the 24-month follow-up point among the TD-CBT group compared with the DS-CBT group. This may suggest that transdiagnostic treatments increase long-term resilience to psychological distress and common internalizing disorders. Importantly, while the mechanism by which this would occur is not clear based on existing data, one conceivable possibility is that the transdiagnostic approach increases long-term resilience by encouraging the broad application of therapeutic skills across a range of symptoms and in the context of a broad range of triggers of psychological distress. Thus, when new symptoms or psychological distress arise, patients who have received transdiagnostic treatment are more able to employ previously learnt skills than patients who received disorder specific treatments and who only learnt to apply therapeutic skills to specific symptoms. Further research is needed to examine whether this is the case but it is broadly consistent with the rationale and theories supporting transdiagnostic treatment (Barlow et al., 2004; Titov et al., 2012). However, it should also be noted that the clinical differences between TD-CBT and DS-CBT were relatively minor and both treatments were associated with significant reductions in symptoms and diagnoses as well as high levels of treatment completion and treatment satisfaction. Thus, the results of the current study are consistent with studies that have compared transdiagnostic and disorder specific treatment, and that have not found marked or consistent clinical outcome differences between the two forms of treatment (Norton & Barrera, 2012; Titov et al., in press).

The findings of the current study suggest that the benefits of transdiagnostic treatment may not emerge until long after treatment and, thus, the choice of transdiagnostic treatment may be primarily pragmatic over the short term. For example, as highlighted elsewhere (Clark, 2009; Andrews et al., 2010; Norton & Barrera, 2012; Titov et al., 2012), transdiagnostic interventions remove the requirement for clinical services to offer multiple disorder-specific treatments as well as the requirement for therapists to be competent in administering multiple and highly specific disorder-specific treatments. Moreover, because they are suitable for multiple disorders, transdiagnostic treatments have the potential to remove the requirement for detailed differential diagnosis prior to treatment, which can take considerable time and may delay the commencement of effective treatment. Thus, as has also been highlighted elsewhere, the use of transdiagnostic treatments may significantly assist in efforts to disseminate and increase access to evidenced based psychological treatment (McHugh et al., 2009). The findings of the current study support the use of transdiagnostic treatment for adults with principal symptoms of GAD and symptoms of other comorbid anxiety and depressive disorders.

In the present study, similar clinical outcomes, treatment completion and satisfaction levels were obtained when the treatment was provided in either clinician-guided or self-guided formats. These results are consistent with an emerging number of studies that indicate self-guided internet-delivered interventions can be developed to a point where they result in large clinical effects consistent with clinician-guided interventions (Berger et al., 2011a,b; Titov et al., 2013; Dear et al., 2015a). These findings highlight the public health potential of carefully designed self-guided interventions for reducing the burden of common mental health conditions, which is unlikely to be addressed via traditional treatment approaches (Kazdin, 2015). However, it is important to note that participants in the current trial received a comprehensive telephone assessment prior to treatment, which, while brief, allowed participants to ask questions about the treatment and allowed clinicians to orient the participant to treatment. It is also important to note that all participants received automated emails throughout treatment, which were carefully designed to guide their progress and that have been found to be important in other trials (Titov et al., 2013, 2014). Participants' symptoms were also monitored daily throughout treatment and contact was initiated to ensure participants' safety in the event of significant deteriorations in symptoms or self-reported safety. These processes, in combination, are likely to have built therapeutic alliance, confidence, engagement and adherence with the intervention, which are all known to be important in facilitating clinical outcomes (Martin et al., 2000).

It is also important to note that significant reductions in general psychological distress (Cohen's  $d \ge 0.89$ ; avg. reduction  $\ge 23\%$ ), disability (Cohen's  $d \ge 0.64$ ; avg. reduction  $\ge 37\%$ ) and neuroticism (Cohen's  $d \ge 0.50$ ; avg. reduction  $\ge 12\%$ ) were observed and sustained at follow-up across all conditions. The changes observed

in neuroticism are consistent with an emerging body of literature indicating that internet-delivered psychological interventions can reduce the expression of personality traits associated with emotional vulnerability (Hedman et al., 2014; Titov et al., in press). Clinical changes in vulnerability factors, such as neuroticism, are important because they are a strong predictor of impairment, health service use and psychiatric morbidity and are associated with considerable economic costs (Lahey, 2009; Cuijpers et al., 2010). Unfortunately, to date, very little research has examined the mechanisms through which internet-delivered treatments operate to reduce psychological disorder and distress. However, the current findings suggest that neuroticism may be a worthwhile factor for further study.

The present study has a number of strengths and limitations that should be borne in mind when considering its findings. The main limitation of the current trial is the absence of a control group, which limits the ability to control for general time effects and spontaneous remission. However, it is important to note that previous trials have shown that control groups of people with a diagnosis of GAD do not improve significantly over time without intervention (Titov et al., 2009b; Robinson et al., 2010). It is also important to note that the current trial was designed and conducted as a superiority trial and consequently caution is needed in concluding any statistical findings as supporting clinical equivalence, which requires the use of equivalence trial analyses. The current trial also used the internet as a method for delivering treatment and, although there is emerging evidence of their equivalennt efficacy (Andersson, Titov, & Null, 2014), some caution is needed in generalizing the findings of the current study to treatments delivered face-to-face. An important strength of the research design was the similarity of the disorder-specific and transdiagnostic treatments with respect to format and structure, which substantially reduces the number of key variables that could account for any differential outcomes. Other notable strengths include the use of a large sample size, high retention rates, the long-term follow-up of participants as well as the use of multiple outcomes to comprehensively evaluate the intervention (e.g., clinical symptoms, diagnostic assessments, satisfaction and treatment completion).

The present trial found large clinical improvements and high levels of treatment satisfaction for both transdiagnostic and disorder-specific treatment for GAD when delivered in both clinician-guided and self-guided formats. Clinical improvements were observed across a broad range of clinical domains and were largely maintained from post-treatment until 24-month follow-up. There was some evidence favoring transdiagnostic treatment over disorder-specific treatment, but the differences were relatively small in magnitude, were not consistently observed across measures, and were only observed at long-term follow-up. No marked or consistent differences were observed between groups who received treatment in clinician-guided and self-guided formats. Thus, together with the results of a similar trial evaluating transdiagnostic and disorder-specific treatment for depression (Titov et al., in press), the present study highlights the public health potential of internet-delivered transdiagnostic treatments in either clinicianguided or self-guided formats. However, it remains to be seen whether the findings of the current trial generalize to other common mental disorders, such as panic disorder and social anxiety disorder. Those questions will be addressed in future trials.

## **Conflict 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.

#### Acknowledgements

The authors gratefully acknowledge the participants for their involvement and helpful comments. This research was enabled by funding from the Australian National Health and Medical Research Council (NHMRC) Project Grant No. 630560. B.F.D. was supported by an NHMRC Australian Public Health Fellowship.

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