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# Disorder-specific versus transdiagnostic and clinician-guided versus self-guided treatment for major depressive disorder and comorbid anxiety disorders: A randomized controlled trial

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ABSTRACT

Disorder-specific cognitive behavior therapy (DS-CBT) is effective at treating major depressive disorder (MDD) while transdiagnostic CBT (TD-CBT) addresses both principal and comorbid disorders by targeting underlying and common symptoms. The relative benefits of these two models of therapy have not been determined. Participants with MDD ($n = 290$) were randomly allocated to receive an internet delivered TD-CBT or DS-CBT intervention delivered in either clinician-guided (CG-CBT) or self-guided (SG-CBT) formats. Large reductions in symptoms of MDD (Cohen's $d \geq 1.44$; avg. reduction $\geq 45\%$) and moderate-to-large reductions in symptoms of comorbid generalised anxiety disorder (Cohen's $d \geq 1.08$; avg. reduction $\geq 43\%$), social anxiety disorder (Cohen's $d \geq 0.65$; avg. reduction $\geq 29\%$) and panic disorder (Cohen's $d \geq 0.45$; avg. reduction $\geq 31\%$) were found. No marked or consistent differences were observed across the four conditions, highlighting the efficacy of different forms of CBT at treating MDD and comorbid disorders.



## 1. Introduction

Major depressive disorder (MDD) is a chronic and disabling disorder estimated to affect 5% of the world's population each year (Kessler et al., 2009). Both clinical and subclinical levels of depression are associated with considerable burden and economic costs for individuals and to the broader society (Üstün et al., 2004). MDD is frequently comorbid with anxiety disorders and comorbidity is associated with greater distress, disability (Andrews et al., 2002), increased service utilisation (Burgess et al., 2009), and a greater risk of suicide (Norton et al., 2008).

Psychological treatments such as cognitive behavioural therapy (CBT) are effective at treating MDD and anxiety disorders (Butler et al., 2006; Cuijpers et al., 2008; Stewart & Chambless, 2009). CBT interventions are generally designed to be disorder-specific (DS-CBT) and to target the cognitive and behavioural symptoms of the principal disorder with which a patient presents. Although DS-CBT is known to reduce the severity of comorbid anxiety and depressive disorders (Brown et al., 1995; Tsao et al., 2002; Craske et al., 2007; Titov et al., 2009), it is unclear whether this is the most efficient treatment approach.

Several alternative approaches have been developed to address comorbid symptoms, including tailored and transdiagnostic treatments. Tailored approaches modify the treatment according to patient characteristics and comorbidities (Carlbring et al., 2011). The first empirical study of a tailored approach demonstrated treatment superiority over control conditions across several measures of anxiety, depression, and quality of life, in participants with anxiety disorders, with results sustained at two year follow-up (Carlbring et al., 2011). A subsequent study extended these results by demonstrating that a tailored approach produced at least equivalent results to a standard approach in the treatment of depression comorbid with anxiety disorders (Johansson et al., 2012).

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Transdiagnostic CBT (TD-CBT) is an alternative treatment approach that aims to simultaneously address both principal and comorbid disorders by targeting underlying and common symptoms (Mansell et al., 2009; Wilamowska et al., 2010). This approach is based on the notion that many of the common psychological disorders share characteristics including common symptoms, overall course, response to treatment and temperamental antecedents (Barlow et al., 2004; Goldberg, 2010; Murray et al., 2014; Talkovsky & Norton, 2014), and therefore may respond to treatment that is not tailored to each specific diagnosis (McEvoy et al., 2009).

By virtue of involving a single treatment protocol TD-CBT offers advantages of efficiency over DS-CBT. Emerging evidence from uncontrolled trials and randomised controlled trials (RCTs) indicates that TD-CBT is clinically effective (Dear et al., 2011; Johnston et al., 2011; Farchione et al., 2012; Titov et al., 2013) relative to control conditions. However, to date, only one RCT has directly compared TD-CBT with DS-CBT (Norton & Barrera, 2012). In that study, 46 people were randomly allocated to receive a TD-CBT group treatment, or to different DS-CBT treatments specifically for social phobia (SP), generalized anxiety disorder (GAD), or for panic disorder (PD) also administered in group format, with the specific treatment group determined by the person's principal disorder. Using non-inferiority analyses, no differences were found in benefits from either approach at post-treatment, indicating the potential of the TD-CBT approach. Importantly, while these preliminary results are promising, the conclusions that can be drawn from the existing evidence base are constrained by small sample sizes, and limited availability of follow-up data. Large sample sizes will facilitate a more reliable evaluation of the relative impact of TD-CBT and DS-CBT on principal and comorbid disorders, while longer term follow-ups provide the opportunity to explore the stability of gains and the relative benefits of each approach in reducing subsequent vulnerability to emotional disorders.

The present study is the first in a series of RCTs that aim to systematically explore the relative benefits of TD-CBT vs. DS-CBT for people with symptoms of four common mental disorders, by targeting one disorder in each RCT, in the case of the present study, MDD. The disorders of interest in these RCTs include MDD, generalized anxiety disorder (GAD), social anxiety/phobia disorder (SP), and panic disorder (PD). To facilitate comparison, the TD-CBT and DS-CBT interventions were designed to comprise a similar structure, present similar amounts of information, and require a similar amount of therapist contact. However, where the DS-CBT intervention focussed explicitly and solely on treatment of MDD with MDD-specific content, skills, examples and vignettes, the TD-CBT intervention focussed on the management of both anxiety and mood symptoms generally without reference to any specific disorder or symptoms. The secondary aim of the present study was to explore how such interventions may be most efficiently delivered. To date, most studies of TD-CBT interventions have evaluated treatment protocols comprising $\geq$10 treatment sessions. It is questionable, however, whether public health services have the resources and capacity to routinely deliver psychological treatments in this way.

Several lines of research have explored alternate delivery methods for psychological treatments. One line of research has reported that online psychological treatments may be effectively delivered by a technician, who is supervised and supported by a registered therapist. Several studies have empirically evaluated this model, and have found clinically significant improvements when treatment is delivered by technicians in iCBT interventions for depression (Titov et al., 2010), GAD (Robinson et al., 2010), and anxiety disorders (Johnston et al., 2011; Johnston et al., 2013). Another promising line of research has reported that self-guided delivery of TD-CBT and DS-CBT can result in significant clinical improvements (Meyer et al., 2009; Berger et al., 2011; Titov et al., 2013). However, to date, the relative benefits of the therapist and self-guided approaches have not been directly compared. It should be noted that the use of the term self-guided treatment in the present study refers to treatment which is preceded by an initial interview with a therapist, and may involve subsequent interviews, although no planned contact during treatment. There is evidence to indicate that this model of self-guided treatment should be differentiated from fully automated self-guided treatments (Christensen et al., 2006; Klein et al., 2011), which may not include interviews or monitoring, and may result in more modest outcomes (Johansson & Andersson, 2012).

To explore these aims, we compared clinician-guided (CG-CBT) vs. self-guided (SG-CBT) versions of TD-CBT and DS-CBT interventions, delivered over eight weeks. Based on evidence indicating that those seeking treatment via the internet have similar characteristics to people with similar disorders identified in national epidemiological studies (Titov et al., 2010) and evidence indicating that outcomes of internet and face-to-face treatments are similar (Andersson & Hedman, 2013) the recruitment of the sample and delivery of the interventions occurred via the internet with people across Australia. This methodology also reflects growing recognition of the benefits of internet-delivered psychological treatments as evidenced by the public funding of national internet-delivered mental health services (Andrews et al., 2010; Andersson & Titov, 2014; Titov et al., in press). It was hypothesized that TD-CBT and DS-CBT would be associated with significant reductions in principal symptoms of MDD, but that TD-CBT would be superior at reducing symptoms of comorbid GAD, SP and PD at each time point. It was also hypothesised that CG-CBT would be superior to SG-CBT at every time point for symptoms of the four target disorders.

## 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 ACTRN12612000421831. 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, MDD, GAD, PD or SAD. 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 questionnaires, and providing basic demographic information and contact details.

The inclusion criteria for the study were: (i) resident of Australia aged 18–64 years of age; (ii) a principal complaint of depression symptoms; (iii) total score $\geq$5 on the Patient Health Questionnaire-9 (PHQ-9) (Kroenke et al., 2001); 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.

The CONSORT flowchart for this trial is shown in Fig. 1. A total of 568 people applied to participate in the trial and indicated that

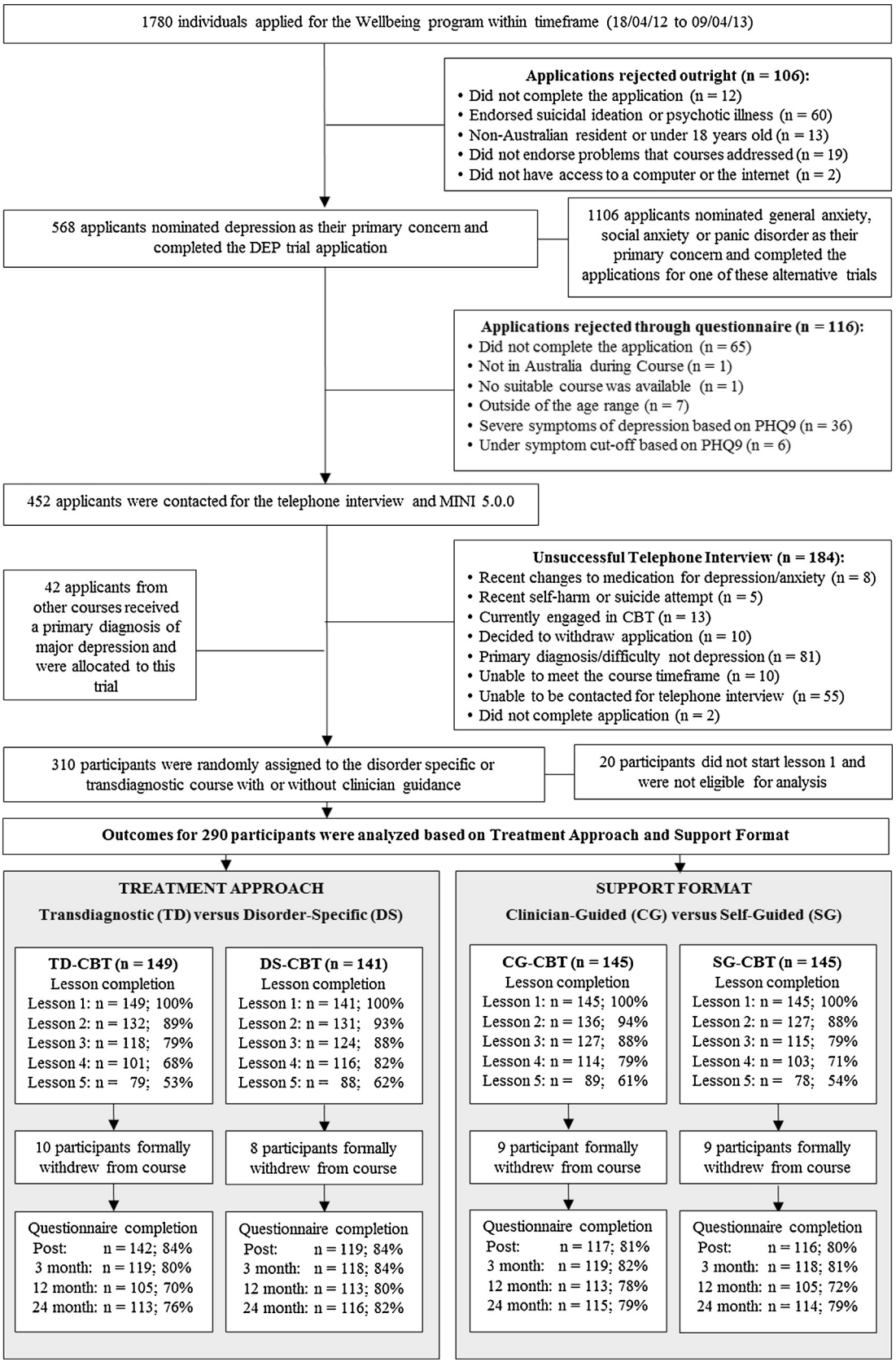


**Fig. 1.** Participant flow from application to 24-month follow-up.

symptoms of MDD were their principal difficulty during the online application process. Of these, 452 met the initial inclusion criteria, 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

42 applicants initially indicated principal difficulties of GAD, SP, or PD during the online application but, upon interview, indicated MDD was their principal difficulty. A total of 310 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 randomised 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 all other time-points. In addition, the GAD-7 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 effect size differences between the arms (i.e., Cohen's *ds* > .35). 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

*2.2.1.1. Patient Health Questionnaire 9-Item Scale (PHQ-9; Kroenke et al., 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 et al., 2011) and is sensitive to change (Kroenke et al., 2010). Scores range from 0 to 27 and Cronbach's α in this study was .82.

#### 2.2.2. Secondary measures

*2.2.2.1. 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., 2010; Dear et al., 2011 Scores range from 0 to 21 and Cronbach's α in the current study was .88.

*2.2.2.2. 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 standardised measures of social anxiety (Weeks et al., 2007; Osório et al., 2010). Scores range from 0 to 12 and Cronbach's α in this study was .87.

*2.2.2.3. 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 α in the current study was .93.

#### 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 0 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 et al., 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 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 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).

#### 2.2.5. Treatment satisfaction and acceptability

Consistent with previous research (Titov et al., 2013; Dear 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 MDD, the Mood Course, or a TD-CBT course, the Wellbeing Course. The Mood Course was developed specifically for this trial and the Wellbeing Course has been previously demonstrated as clinically efficacious in treating symptoms of anxiety and depression (Titov et al., 2012; Titov et al., 2013; Titov et al., 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 eCentreClinic research group, and which is associated with high completion rates, strong clinical outcomes, and high participant satisfaction. 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 protocolised 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. 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), 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 MDD and presented all therapeutic information and skills in the context of MDD and reducing MDD symptoms. Consequently, all vignettes, examples and case stories focussed on MDD 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 from a psychologist using telephone or a secure email messaging system. 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 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 $\leq$10 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 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; Titov et al., 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 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.

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., depression, generalised anxiety, social anxiety and panic) among those meeting MINI diagnostic criteria for the related disorder (i.e., MDD, GAD, SAD and PAN) 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

**Table 1**
Demographic characteristics of the participants.

| | | Treatment Approach | | | Support Format | | |
|---|---|---|---|---|---|---|---|
| | Overall ($n$ = 290) | TD-CBT ($n$ = 149) | DS-CBT (n = 141) | Significance | CG-CBT ($n$ = 145) | SG-CBT ($n$ = 145) | Significance |
| Gender | | | | | | | |
| Male | 82 (28%) | 41 (28%) | 41 (29%) | Wald's $\chi^2$ = .09, $p$ = .768 | 39 (27%) | 43 (30%) | Wald's $\chi^2$ = .27, $p$ = .602 |
| Female | 208 (72%) | 108 (72%) | 100 (71%) | | 106 (73%) | 102 (70%) | |
| Age (years) | | | | | | | |
| Mean (SD) | 44.19 (11.75) | 43.84 (11.71) | 44.55 (11.81) | Wald's $\chi^2$ = .27, $p$ = .605 | 44.87 (11.29) | 43.50 (12.18) | Wald's $\chi^2$ = .99, $p$ = .320 |
| Range | 18–64 | 18–63 | 19–64 | | 18–63 | 19–64 | |
| Marital status | | | | | | | |
| Single/never married | 79 (27%) | 41 (28%) | 38 (27%) | Wald's $\chi^2$ = .35, $p$ = .552 | 34 (23%) | 45 (31%) | Wald's $\chi^2$ = 1.06, $p$ = .302 |
| Married/de facto | 174 (60%) | 92 (62%) | 82 (58%) | | 93 (64.14%) | 81 (56%) | |
| Separated/divorced/widowed | 37 (13%) | 16 (11%) | 21 (15%) | | 18 (12%) | 19 (13%) | |
| Education | | | | | | | |
| High school or less | 46 (16%) | 25 (17%) | 21 (15%) | Wald's $\chi^2$ = .11, $p$ = .738 | 21 (14%) | 25 (17%) | Wald's $\chi^2$ = .11, $p$ = .738 |
| Trade/technical certificate | 57 (20%) | 29 (19%) | 28 (20%) | | 33 (23%) | 24 (17%) | |
| Diploma/degree | 187 (64%) | 95 (64%) | 92 (65%) | | 91 (63%) | 96 (66%) | |
| Employment | | | | | | | |
| Full-time/part-time | 214 (74%) | 107 (72%) | 107 (76%) | Wald's $\chi^2$ = .89, $p$ = .347 | 99 (68%) | 115 (79%) | Wald's $\chi^2$ = 4.47, $p$ = .034 |
| Student | 15 (5%) | 6 (4%) | 9 (6%) | | 9 (6%) | 6 (4%) | |
| Unemployed, retired or disabled | 61 (21%) | 36 (24%) | 25 (18%) | | 37 (26%) | 24 (17%) | |
| Previous mental health treatment | 204 (70%) | 107 (72%) | 97 (69%) | Wald's $\chi^2$ = .32, $p$ = .574 | 99 (68%) | 105 (72%) | Wald's $\chi^2$ = .59, $p$ = .441 |
| Currently taking medication | 107 (37%) | 52 (35%) | 55 (39%) | Wald's $\chi^2$ = .53, $p$ = .469 | 52 (36%) | 55 (38%) | Wald's $\chi^2$ = .11, $p$ = .715 |

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 ($ps \geq .05$). Comparisons exploring differences between participants completing and not completing the questionnaires at post-treatment indicated no differences on the demographic variables reported in Table 1 or in baseline outcome measure scores ($ps \geq .05$).

#### 3.1.2. Clinician time

There were significant differences in clinician contact time between CG-CBT and SG-CBT groups ($F_{1,288}$ = 262.68, $p$ < .001). The mean clinician time per participant in CG-CBT group was 29.51 min (SD = 20.39), which comprised answering and making calls (total calls = 796; range = 0–10 calls; mean time = 20.59; SD = 20.96), as well as reading, sending and responding to secure emails (total emails = 861; range = 0–12 emails; mean time = 8.92; SD = 6.31). The mean total clinician time per participant for SG-CBT was .91 min (SD = 1.982), which comprised answering and making calls (total calls = 3; range = 0–1 call; mean time = .07; SD = .51), as well as reading, sending and responding to secure emails (total emails = 68; range = 0–4 emails; mean time = .84; SD = 1.93). 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 ($F_{1,288}$ = .32, $p$ = .58).

#### 3.1.3. Preliminary test for higher order interactions

The GEE analyses revealed non-significant Treatment Approach by Support Format by Time interactions for all outcomes (GAD-7: Wald's $\chi^2$ = 2.22, $p$ = .649; PHQ-9: Wald's $\chi^2$ = 1.31, $p$ = .859; MINI-SPIN: Wald's $\chi^2$ = 1.86, $p$ = .761; PDSS-SR: Wald's $\chi^2$ = 5.14, $p$ = .273; K10: Wald's $\chi^2$ = 1.01, $p$ = .797; SDS: Wald's $\chi^2$ = 1.00, $p$ = .909) except one (NEO-FFI-N: Wald's $\chi^2$ = 14.34, $p$ = .002). Further analyses revealed that participants receiving self-guided transdiagnostic treatment reported a very small reduction in neuroticism scores from 12-month to 24-month follow-up (exp$\beta$ = 0.865, $p$ = .012), which was not observed in those participants receiving clinician-guided transdiagnostic treatment or self-guided or clinician-guided disorder specific treatment. However, given the very large number of comparisons needed to identify this change and the fact the

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

| | Transdiagnostic Wellbeing Course | | | Disorder-Specific Mood 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 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<br>– Symptom formulation | – Sleep management<br>– What to do in a mental health emergency<br>– Transdiagnostic Case Stories | Education about the prevalence and symptoms of MDD. Introduction of a CBT model and explanation of the functional relationship between physical, thought and behavioural symptoms in MDD. Instructions for identifying their own symptoms and how their symptoms interact. MDD specific vignettes and examples of MDD symptoms provided. | – Symptom identification<br>– Symptom formulation | – Sleep management<br>– What to do in a mental health emergency<br>– MDD 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<br>– Thought challenging | – Structured problem solving<br>– Worry time<br>– Challenging beliefs<br>– Transdiagnostic Case Stories | Introduction to the basic principles of cognitive therapy and importance of managing thoughts to manage MDD. Instructions for monitoring and challenging thoughts. MDD specific vignettes and examples of thoughts provided. | – Thought monitoring<br>– Thought challenging | – Structured problem solving<br>– Challenging beliefs<br>– MDD 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<br>– Pleasant activity scheduling | – Risk Calculation, Coping Calculation and Shifting Attention<br>– 100 pleasant things to do<br>– Transdiagnostic Case Stories | Introduction to the physical symptoms of hypo-arousal and their relationship to MDD. Instructions about controlling physical symptoms by scheduling pleasant activities and light physical activities. MDD specific vignettes and examples of physical symptoms provided. | – Activity scheduling | – 100 pleasant things to do<br>– MDD Case Stories |

Table 2 (*Continued*)

| | Transdiagnostic Wellbeing Course | | | Disorder-Specific Mood Course | | |
|---|---|---|---|---|---|---|
| Lesson | Lesson Content | Primary Skills Taught | Additional Resources | Lesson Content | Primary Skills Taught | Additional Resources |
| 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 | – Assertive communication<br>– Transdiagnostic Case Stories | Introduction to the behavioural symptoms of MDD. Explanation of avoidance and safety behaviours for MDD. Instructions for graded behavioural activation for increasing daily activities. MDD specific vignettes and examples of graded exposure provided. | – Graded behavioural activation for increasing activities | – Assertive communication<br>– MDD 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 MDD. Information about the signs of relapse and managing lapses. Instructions for creating a relapse prevention plan. MDD specific vignettes and examples of lapses and lapse management provided. | – Relapse prevention | - MDD 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 MDD and the materials, vignettes, examples and case stories all focussed on MDD.

change was small and constrained to one time period and to one measure, this higher order interaction was not further analysed.

### 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. Major depressive disorder.* Among those meeting diagnostic criteria for MDD ($n = 217$) the GEE analyses indicated a significant effect for Time (PHQ-9: Wald's $\chi^2 = 468.12$, $p < .001$) but no significant Time by Treatment Approach interaction effect for depressive symptoms (PHQ-9: Wald's $\chi^2 = 3.16$, $p = .532$). Pairwise comparisons indicated that both groups improved similarly from baseline to post-treatment ($p < .001$) with no other significant changes between the other time points.

*3.2.1.2. Generalised anxiety disorder.* Among those meeting diagnostic criteria for GAD ($n = 152$) the GEE analyses indicated a significant effect for Time (GAD-7: Wald's $\chi^2 = 289.44$, $p < .001$) but no significant Time by Treatment Approach interaction for GAD symptoms (GAD-7: Wald's $\chi^2 = 6.98$, $p = .137$). Pairwise comparisons indicated that both groups improved similarly from baseline to post-treatment ($p < .001$) and from post-treatment to 3-month follow-up ($p = .045$). There were no other significant changes between the other time points.

*3.2.1.3. Social anxiety disorder.* Among those meeting diagnostic criteria for SAD ($n = 95$) the GEE analyses indicated a significant effect for Time (MINI-SPIN: Wald's $\chi^2 = 126.03$, $p < .001$) but no significant Time by Treatment Approach interaction for social anxiety symptoms (MINI-SPIN: Wald's $\chi^2 = 5.84$, $p = .211$). Pairwise comparisons indicated that both groups improved similarly from baseline to post-treatment ($p < .001$) and that both group's symptoms worsened slightly from 12-month follow-up to 24-month follow-up ($p = .030$). There were no other significant changes between the other time points.

*3.2.1.4. Panic disorder.* Among those meeting diagnostic criteria for PD ($n = 45$) the GEE analyses indicated a significant effect for Time (PDSS-SR: Wald's $\chi^2 = 34.37$, $p < .001$) and a significant Time by Treatment Approach interaction for panic symptoms (PDSS-SR: Wald's $\chi^2 = 11.10$, $p = .025$). Pairwise comparisons indicated that both groups improved from baseline to post-treatment ($p < .001$) and that the TD-CBT group further improved between 3-month and 12-month follow-up ($p < .001$). However, the pairwise comparisons revealed there were no significant differences between the TD-CBT and DS-CBT groups at any time point ($ps > .05$).

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

Across the whole sample ($n = 290$) the GEE analyses indicated a significant effect for Time (K10: Wald's $\chi^2 = 549.50$, $p < .001$) and a significant Time by Treatment Approach interaction for general psychological distress (K10: Wald's $\chi^2 = 9.27$, $p = .026$). Pairwise comparisons indicated that both groups improved from baseline to post-treatment ($p < .001$) and that the TD-CBT group further improved from post-treatment to 3-month follow-up ($p < .001$). At post-treatment the TD-CBT group reporting slightly lower psychological distress than the DS-CBT group ($p = .011$). However, there were no differences at 3-month or 12-month follow-up ($p > .05$).

Across the whole sample ($n = 290$) there was a significant effect for Time (SDS: Wald's $\chi^2 = 380.54$, $p < .001$) but no significant Time by Treatment Approach interaction for disability (SDS: Wald's $\chi^2 = 9.02$, $p = .061$). Pairwise comparisons indicated that both groups improved from baseline to post-treatment ($p < .001$) and from post-treatment to 3-month follow-up ($p = .025$).

Across the whole sample ($n = 290$) there was a significant effect for Time (NEO-FFI-N: Wald's $\chi^2 = 291.59$, $p < .001$) but no significant Time by Treatment Approach interaction for neuroticism (NEO-FFI-N: Wald's $\chi^2 = 2.42$, $p = .490$). Pairwise comparisons indicated that both groups improved from baseline to post-treatment and from post-treatment to 3-month follow-up ($ps < .001$).

#### 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 the diagnoses (MDE; Wald's $\chi^2 = 206.28$, $p < .001$; GAD: Wald's $\chi^2 = 112.12$, $p < .001$; SAD: Wald's $\chi^2 = 28.505$, $p < .001$) with the exception of panic disorder (PD: Wald's $\chi^2 = 1.22$, $p = .269$). No significant Time by Treatment Approach interactions were observed for any diagnoses (MDE: Wald's $\chi^2 = 0.36$, $p = .546$; GAD: Wald's $\chi^2 = 2.21$, $p = .137$; SAD: Wald's $\chi^2 = 0.01$, $p = .917$; PD: Wald's $\chi^2 = 0.04$, $p = .838$) indicating that the proportion of participants meeting diagnostic criteria, except for PD, significantly reduced across time irrespective of Treatment Approach.

The GEE analyses focusing on average comorbid diagnoses revealed a significant Time effect (Wald's $\chi^2 = 102.94$, $p < .001$) but no Time by Treatment Approach interaction (Wald's $\chi^2 = 3.143$, $p = .076$). 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 a small difference in the number of lessons read by the TD-CBT ($M = 3.89$; SD = 1.21) and DS-CBT groups ($M = 4.26$; SD = 1.43) at post-treatment ($F_{1,288} = 5.61$, $p < .05$). Of the participants that completed the evaluation questions at post- treatment, 92% (100/109) of the TD-CBT group and 96% (108/113) of the DS-CBT group, reported they would recommend the course to others. Moreover, 96% (104/108) of the TD-CBT group and 97% (110/113) 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 reporting finding the course was worth their time ($\chi^2$ range = .20 to 1.38; $p$ range = .240–.656).

### 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 4.

#### 3.3.1. Outcomes across the diagnoses

*3.3.1.1. Major depressive disorder.* Among those meeting diagnostic criteria for MDD ($n = 217$) the GEE analyses indicated a significant effect for Time (PHQ-9: Wald's $\chi^2 = 480.51$, $p < .001$) and a significant Time by Treatment Approach interaction effect for depressive symptoms (PHQ-9: Wald's $\chi^2 = 15.33$, $p = .004$). Pairwise comparisons indicated that both groups improved similarly from baseline to post-treatment ($p < .001$) and that the SG-CBT group further improved from 12-month to 24-month follow-up ($p = .026$). There were also significant differences between the groups at the 3-month ($p = .044$) and 12-month follow-ups ($p < .001$), with the CG-CBT group reporting significantly lower symptoms at each time point. No other significant changes were observed over time or between the two groups.

**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 | | | | | | | | | | | | | | | | | |
| Depression symptoms[a] | | | | | | | | | | | | | | | | | |
| DS-CBT (*n* = 108) | 15.00, (3.78) | 7.36 (4.75) | 6.72 (5.07) | 6.75 (4.64) | 6.86 (4.86) | 51% | 55% | 55% | 54% | 1.78 | 1.85 | 1.95 | 1.87 | −.20 | −.21 | −.18 | −.07 |
| | [14.30, 15.73] | [6.52, 8.31] | [5.83, 7.75] | [5.93, 7.68] | [6.00, 7.84] | [45%, 57%] | [48%, 61%] | [49%, 61%] | [48%, 60%] | [1.46, 2.09] | [1.53, 2.16] | [1.62, 2.27] | [1.54, 2.18] | [−.47, .06] | [−.48, .05] | [−.45, .08] | [−.34, .20] |
| TD-CBT (*n* = 109) | 15.29, (3.62) | 8.40, (5.41) | 7.85 (5.47) | 7.66 (5.22) | 7.21 (5.11) | 45% | 49% | 50% | 53% | 1.50 | 1.60 | 1.70 | 1.82 | | | | |
| | [14.63, 15.99] | [7.45, 9.48] | [6.88, 8.94] | [6.74, 8.71] | [6.32, 8.24] | [38%, 51%] | [42%, 55%] | [43%, 56%] | [46%, 59%] | [1.19, 1.79] | [1.29, 1.90] | [1.38, 2.00] | [1.50, 2.13] | | | | |
| Secondary outcomes | | | | | | | | | | | | | | | | | |
| Generalised anxiety symptoms[b] | | | | | | | | | | | | | | | | | |
| DS-CBT (*n* = 70) | 11.70, (4.25) | 6.67 (4.36) | 5.14 (4.176) | 5.86 (4.05) | 5.20 (3.27) | 43% | 56% | 50% | 56% | 1.17 | 1.56 | 1.41 | 1.71 | .08 | −.30 | .05 | −.02 |
| | [10.75, 12.74] | [5.72, 7.77] | [4.25, 6.22] | [4.98, 6.89] | [4.49, 6.02] | [34%, 51%] | [47%, 64%] | [41%, 57%] | [49%, 62%] | [.80, 1.52] | [1.17, 1.93] | [1.03, 1.77] | [1.32, 2.09] | [-.24, .39] | [-.62, .02] | [-.27, .37] | [-.34, .30] |
| TD-CBT (*n* = 82) | 11.40, (4.28) | 6.35 (4.09) | 6.49 (4.81) | 5.66 (4.33) | 5.29 (4.26) | 44% | 43% | 50% | 54% | 1.21 | 1.08 | 1.33 | 1.43 | | | | |
| | [10.51, 12.37] | [5.53, 7.30] | [5.33, 7.62] | [4.80, 6.68] | [4.44, 6.29] | [36%, 52%] | [33%, 52%] | [41%, 58%] | [45%, 61%] | [.87, 1.53] | [.75, 1.40] | [.99, 1.67] | [1.08, 1.77] | | | | |
| Social anxiety symptoms[c] | | | | | | | | | | | | | | | | | |
| DS-CBT (*n* = 36) | 7.00 (2.74) | 4.71 (2.76) | 4.04 (2.33) | 4.41 (2.92) | 4.95 (3.19) | 33% | 42% | 37% | 29% | .83 | 1.16 | .91 | .69 | −.23 | −.41 | −.07 | −.13 |
| | [6.16, 7.96] | [3.89, 5.70] | [3.35, 4.88] | [3.56, 5.48] | [4.01, 6.11] | [19%, 44%] | [30%, 52%] | [22%, 49%] | [13%, 43%] | [.34, 1.30] | [.65, 1.65] | [.42, 1.39] | [.21, 1.16] | [−.64, .19] | [−.83, .01] | [−.49, .34] | [−.54, .29] |
| TD-CBT (*n* = 59) | 8.05 (2.69) | 5.43 (3.33) | 5.35 (3.59) | 4.64 (3.18) | 5.37 (3.25) | 33% | 34% | 42% | 33% | .87 | .85 | 1.16 | .90 | | | | |
| | [7.39, 8.77] | [4.64, 6.35] | [4.51, 6.35] | [3.89, 5.53] | [4.60, 6.27] | [21%, 42%] | [21%, 44%] | [31%, 52%] | [22%, 43%] | [.48, 1.24] | [.47, 1.22] | [.76, 1.54] | [.51, 1.27] | | | | |
| Panic symptoms[d] | | | | | | | | | | | | | | | | | |
| DS-CBT (*n* = 18) | 8.00 (4.97) | 5.17 (3.93) | 4.65 (4.67) | 5.44 (4.22) | 4.51 (5.40) | 35% | 42% | 32% | 44% | .63 | .69 | .56 | .67 | −.17 | −.30 | .41 | −.03 |
| | [6.01, 10.66] | [3.64, 7.35] | [2.93, 7.40] | [3.80, 7.78] | [2.59, 7.84] | [8%, 54%] | [8%, 63%] | [3%, 53%] | [2%, 68%] | [−.05, 1.29] | [.01, 1.35] | [−.12, 1.21] | [−.01, 1.33] | [−.77, .43] | [−.89, .31] | [−.20, 1.00] | [−.62, .57] |
| TD-CBT (*n* = 27) | 9.45 (6.16) | 6.03 (5.50) | 6.36 (6.36) | 3.68 (4.36) | 4.65 (5.46) | 36% | 33% | 61% | 51% | .58 | .49 | 1.08 | .82 | | | | |
| | [7.39, 12.08] | [4.28, 8.50] | [4.36, 9.27] | [2.36, 5.76] | [2.99, 7.24] | [10%, 55%] | [2%, 54%] | [39%, 75%] | [23%, 68%] | [.03, 1.12] | [-.05, 1.03] | [.50, 1.64] | [.26, 1.37] | | | | |
| Tertiary outcomes | | | | | | | | | | | | | | | | | |
| Disability and functioning (SDS) | | | | | | | | | | | | | | | | | |
| DS-CBT (*n* = 141) | 14.73 (7.92) | 7.79 (6.79) | 7.14 (7.06) | 6.92 (6.59) | 6.08 (6.11) | 47% | 52% | 53% | 59% | .94 | 1.01 | 1.07 | 1.22 | −.20 | −.13 | −.13 | −.17 |
| | [13.48, 16.10] | [6.74, 8.99] | [6.06, 8.40] | [5.91, 8.10] | [5.15, 7.18] | [39%, 54%] | [43%, 59%] | [45%, 60%] | [51%, 65%] | [.69, 1.18] | [.76, 1.26] | [.82, 1.32] | [.97, 1.47] | [−.43, .03] | [−.36, .11] | [−.36, .10] | [−.41, .06] |
| TD-CBT (*n* = 149) | 14.21 (7.97) | 9.24 (7.63) | 8.06 (7.59) | 7.79 (7.13) | 7.22 (6.89) | 35% | 43% | 45% | 49% | .64 | .79 | .85 | .94 | | | | |
| | [12.99, 15.55], | [8.09, 10.55] | [6.93, 9.37] | [6.73, 9.03] | [6.19, 8.41] | [26%, 43%] | [34%, 51%] | [36%, 53%] | [41%, 56%] | [.40, .87] | [.55, 1.02] | [.61, 1.08] | [.70, 1.17] | | | | |
| Psychological distress (K-10) | | | | | | | | | | | | | | | | | |
| DS-CBT (*n* = 141) | 27.65 (7.19) | 19.62(6.72) | 19.26(7.19) | 18.99(6.89) | – | 29% | 30% | 31% | – | 1.15 | 1.17 | 1.23 | – | −.30 | −.07 | −.09 | – |
| | [26.49, 28.87] | [18.55, 20.77] | [18.11, 20.49] | [17.88, 20.16] | | [25%, 33%] | [26%, 35%] | [27%, 35%] | | [.90, 1.40] | [.91, 1.42] | [.97, 1.48] | | [−.53, −.07] | [-.30, .16] | [−.32, .14] | |
| TD-CBT (*n* = 149) | 27.83 (7.16) | 21.68 (6.97) | 19.74 (7.34) | 19.59 (6.90) | – | 22% | 29% | 30% | – | .87 | 1.12 | 1.17 | – | | | | |
| | [26.71, 29.01] | [20.59, 22.83] | [18.60, 20.96] | [18.52, 20.73] | | [18%, 26%] | [25%, 33%] | [26%, 33%] | | [.63, 1.11] | [.87, 1.36] | [.92, 1.41] | | | | | |
| Neuroticism (NEO-FFI-N) | | | | | | | | | | | | | | | | | |
| DS-CBT (*n* = 141) | 31.70 (7.05) | 27.03 (7.50) | 25.25 (7.66) | 25.14 (8.42) | – | 15% | 20% | 21% | – | .64 | .88 | .84 | – | −.36 | −.39 | −.33 | – |
| | [30.55, 32.88] | [25.82, 28.29] | [24.02, 26.55] | [23.79, 26.57] | | [11%, 19%] | [16%, 24%] | [16%, 25%] | | [.40, .88] | [.63, 1.12] | [.60, 1.09] | | [−.59, −.12] | [−.62, −.16] | [−.56, −.10] | |
| TD-CBT (*n* = 149) | 34.02 (6.19) | 29.76 (7.81) | 28.29 (7.94) | 27.82 (7.66) | – | 13% | 17% | 18% | – | .60 | .80 | .89 | – | | | | |
| | [33.04, 35.03] | [28.54, 31.04] | [27.04, 29.59] | [26.62, 29.08] | | [9%, 16%] | [13%, 21%] | [15%, 22%] | | [.37, .84] | [.57, 1.04] | [.65, 1.13] | | | | | |

*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. Depression, generalised anxiety, social anxiety and panic symptoms were measured with the PHQ-9, GAD-7, MINI-SPIN, and PDSS-SR, respectively.

[a] Analyses use the data of participants meeting diagnostic criteria for major depressive disorder at assessment.

[b] Analyses use the data of participants meeting diagnostic criteria for generalised anxiety disorder at assessment.

[c] Analyses use the data of participants meeting diagnostic criteria for social anxiety disorder at assessment.

[d] Analyses use the data of participants meeting diagnostic criteria for panic disorder at assessment.

**Table 4**
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 | | | | | | | | | | | | | | | | | |
| Depression symptoms[a] | | | | | | | | | | | | | | | | | |
| CG-CBT ($n$ = 112) | 15.07 (3.57) | 7.36 (5.04) | 6.59 (4.98) | 6.05 (4.10) | 6.62 (4.79) | 51% | 56% | 60% | 56% | 1.77 | 1.96 | 2.35 | 2.00 | −.21 | −.27 | −.50 | −.17 |
| | [14.43, 15.75] | [6.48, 8.36] | [5.73, 7.58] | [5.33, 6.85] | [5.79, 7.57] | [45%, 57%] | [50%, 62%] | [55%, 65%] | [50%, 62%] | [1.45, 2.07] | [1.63, 2.27] | [2.00, 2.68] | [1.67, 2.31] | [−.48, .06] | [.54, −.01] | [−.77, −.22] | [−.44, .09] |
| SG-CBT ($n$ = 105) | 15.23 (3.85) | 8.44 (5.14) | 8.03 (5.53) | 8.44 (5.47) | 7.49 (5.16) | 45% | 47% | 45% | 51% | 1.50 | 1.51 | 1.44 | 1.70 | | | | |
| | [14.51, 15.98] | [7.51, 9.48] | [7.04, 9.16] | [7.46, 9.56] | [6.56, 8.54] | [38%, 51%] | [40%, 54%] | [37%, 51%] | [44%, 57%] | [1.18, 1.80] | [1.20, 1.81] | [1.13, 1.73] | [1.38 2.01] | | | | |
| Secondary outcomes | | | | | | | | | | | | | | | | | |
| Generalised anxiety symptoms[b] | | | | | | | | | | | | | | | | | |
| CG-CBT ($n$ = 67) | 11.61 (4.38) | 6.47 (4.29) | 5.93 (4.81) | 5.52 (3.93) | 5.32 (3.80) | 44% | 49% | 52% | 54% | 1.19 | 1.23 | 1.46 | 1.53 | −.01 | .02 | −.10 | .03 |
| | [10.61, 12.71] | [5.52, 7.58] | [4.89, 7.20] | [4.65, 6.54] | [4.48, 6.31] | [35%, 52%] | [38%, 58%] | [44%, 60%] | [46%, 61%] | [.81, 1.55] | [.86, 1.60] | [1.07, 1.84] | [1.14, 1.91] | [−.33, .31] | [−.30, .34] | [−.42, .22] | [−.29, .35] |
| SG-CBT ($n$ = 85) | 11.48 (4.18) | 6.52 (4.16) | 5.82 (4.38) | 5.93 (4.41) | 5.19 (3.86) | 43% | 49% | 48% | 55% | 1.19 | 1.32 | 1.29 | 1.56 | | | | |
| | [10.63, 12.41] | [5.69, 7.47] | [4.96, 6.83] | [5.07, 6.95] | [4.43, 6.08] | [35%, 50%] | [41%, 57%] | [39%, 56%] | [47%, 61%] | [.86, 1.51] | [.98, 1.65] | [.96, 1.62] | [1.21, 1.90] | | | | |
| Social anxiety symptoms[c] | | | | | | | | | | | | | | | | | |
| CG-CBT ($n$ = 51) | 7.61 (2.39) | 5.00 (2.76) | 4.47 (2.69) | 4.12 (2.49) | 4.99 (2.69) | 34% | 41% | 46% | 34% | 1.01 | 1.23 | 1.43 | 1.03 | −.11 | −.26 | −.31 | −.15 |
| | [6.98, 8.29] | [4.29, 5.81] | [3.79, 5.28] | [3.49, 4.86] | [4.30, 5.78] | [24%, 44%] | [31%, 50%] | [36%, 54%] | [24%, 43%] | [.59, 1.42] | [.80, 1.65] | [.99, 1.85] | [.61, 1.43] | [−.51, .30] | [−.66, .15] | [−.71, .10] | [−.55, .26] |
| SG-CBT ($n$ = 44) | 7.71 (3.13) | 5.34 (3.53) | 5.30 (3.72) | 5.06 (3.59) | 5.47 (3.75) | 31% | 31% | 34% | 29% | .71 | .70 | .79 | .65 | | | | |
| | [6.83, 8.69] | [4.39, 6.49] | [4.31, 6.52] | [4.10, 6.24] | [4.47, 6.70] | [16%, 43%] | [15%, 44%] | [19%, 47%] | [13%, 42%] | [.27, 1.13] | [.26, 1.13] | [.35, 1.21] | [.21, 1.07] | | | | |
| Panic symptoms[d] | | | | | | | | | | | | | | | | | |
| CG-CBT ($n$ = 22) | 8.27 (4.08) | 5.71 (3.79) | 5.00 (4.22) | 3.87 (3.66) | 3.57 (4.28) | 31% | 40% | 53% | 57% | .65 | .79 | 1.14 | 1.12 | .01 | −.23 | −.23 | −.37 |
| | [6.73, 10.17] | [4.32, 7.53] | [3.51, 7.11] | [2.61, 5.75] | [2.16, 5.89] | [9%, 48%] | [14%, 58%] | [31%, 68%] | [29%, 74%] | [.03, 1.24] | [.16, 1.39] | [.48, 1.75] | [.47, 1.74] | [−.58, .59] | [−.81, .36] | [−.81, .36] | [−.96, .22] |
| SG-CBT ($n$ = 23) | 9.44 (6.95) | 5.67 (5.84) | 6.33 (6.93) | 4.87 (4.95) | 5.57 (6.19) | 40% | 33% | 48% | 41% | .59 | .45 | .76 | .59 | | | | |
| | [6.98, 12.75] | [3.72, 8.64] | [4.05, 9.90] | [3.22, 7.38] | [3.54, 8.78] | [8%, 61%] | [-5%, 57%] | [22%, 66%] | [7%, 62%] | [-.01, 1.17] | [-.14, 1.03] | [.15, 1.34] | [-.01, 1.17] | | | | |
| Tertiary outcomes | | | | | | | | | | | | | | | | | |
| Disability and functioning (SDS) | | | | | | | | | | | | | | | | | |
| CG-CBT ($n$ = 145) | 14.00 (7.91) | 8.17 (6.80) | 7.28 (6.99) | 6.72 (6.53) | 5.81 (6.16) | 42% | 48% | 52% | 59% | .79 | .90 | 1.00 | 1.16 | −.10 | −.09 | −.19 | −.26 |
| | [12.77, 15.35] | [7.13, 9.35] | [6.22, 8.51] | [5.74, 7.87] | [4.89, 6.90] | [33%, 49%] | [39%, 56%] | [44%, 59%] | [51%, 65%] | [.55, 1.03] | [.66, 1.14] | [.76, 1.25] | [.90, 1.40] | [9.33, .13] | [−.32, .14] | [−.42, .04] | [−.49, −.03] |
| SG-CBT ($n$ = 145) | 14.93 (7.96) | 8.89 (7.69) | 7.94 (7.68) | 8.01 (7.16) | 7.52 (6.81) | 40% | 47% | 46% | 50% | .77 | .89 | .91 | 1.00 | | | | |
| | [13.68, 16.28] | [7.73, 10.24] | [6.79, 9.30] | [6.93, 9.27] | [6.49, 8.72] | [31%, 48%] | [38%, 55%] | [38%, 54%] | [42%, 57%] | [.53, 1.01] | [.65, 1.13] | [.67, 1.15] | [.75, 1.24] | | | | |
| Psychological distress (K-10) | | | | | | | | | | | | | | | | | |
| CG-CBT ($n$ = 145) | 27.50 (7.21) | 20.09 (6.81) | 18.96 (7.13) | 18.70 (6.67) | – | 27% | 31% | 32% | – | 1.06 | 1.19 | 1.27 | – | −.17 | −.15 | −.17 | – |
| | [26.35, 28.70] | [19.01, 21.23] | [17.83, 20.15] | [17.64, 19.81] | | [23%, 31%] | [27%, 35%] | [28%, 36%] | | [.81, 1.30] | [.94, 1.44] | [1.01, 1.52] | | [−.40, .06] | [9.38, .08] | [−.40, .06] | |
| SG-CBT ($n$ = 145) | 27.99 (7.13) | 21.27 (6.99) | 20.06 (7.37) | 19.90 (7.07) | – | 24% | 28% | 29% | – | .95 | 1.09 | 1.14 | – | | | | |
| | [26.86, 29.18] | [20.16, 22.44] | [18.90, 21.30] | [18.78, 21.08] | | [20%, 28%] | [24%, 33%] | [25%, 33%] | | [.71, 1.19] | [.84, 1.34] | [.89, 1.38] | | | | | |
| Neuroticism (NEO-FFI-N) | | | | | | | | | | | | | | | | | |
| CG-CBT ($n$ = 145) | 31.93 (6.95) | 27.77 (7.97) | 26.39 (7.99) | 26.39 (8.86) | – | 13% | 17% | 17% | – | .56 | .74 | .70 | – | −.17 | −.11 | −.03 | – |
| | [30.81, 33.08] | [26.50, 29.10] | [25.13, 27.73] | [24.99, 27.87] | | [9%, 17%] | [13%, 21%] | [13%, 22%] | | [.32, .79] | [.50, .98] | [.46, .93] | | [−.40, .06] | [−.34, .12] | [−.26, .20] | |
| SG-CBT ($n$ = 145) | 33.86 (6.34) | 29.10 (7.53) | 27.23 (7.88) | 26.65 (7.38) | – | 14% | 20% | 21% | – | .68 | .93 | 1.05 | – | | | | |
| | [32.84, 34.90] | [27.90, 30.35] | [25.98, 28.55] | [25.47, 27.88] | | [10%, 18%] | [16%, 23%] | [18%, 25%] | | [.45, .92] | [.68, 1.17] | [.80, 1.29] | | | | | |

*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.

Depression, generalised anxiety, social anxiety and panic symptoms were measured with the PHQ-9, GAD-7, MINI-SPIN, and PDSS-SR, respectively.

[a] Analyses use the data of participants meeting diagnostic criteria for major depressive disorder at assessment.

[b] Analyses use the data of participants meeting diagnostic criteria for generalised anxiety disorder at assessment.

[c] Analyses use the data of participants meeting diagnostic criteria for social anxiety disorder at assessment.

[d] 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 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 | | | | | | | | | | | | |
| Major depressive disorder | 73% [65%, 80%] | 77% [69%, 83%] | 10% [6%, 16%] | 9% [5%, 15%] | 86% [78%, 92%] | 88% [80%, 93%] | 77% [70%, 83%] | 72% [65%, 79%] | 8% [4%, 13%] | 12% [7%, 18%] | 90% [83%, 94%] | 84% [75%, 90%] |
| Generalised anxiety disorder | 55% [47%, 63%] | 50% [41%, 58%] | 21% [15%, 28%] | 11% [7%, 18%] | 62% [49%, 73%] | 77% [64%, 86%] | 46% [38%, 54%] | 59% [50%, 66%] | 13% [9%, 20%] | 19% [14%, 27%] | 72% [58%, 82%] | 67% [55%, 77%] |
| Social anxiety disorder | 40% [32%, 48%] | 26% [19%, 33%] | 23% [32%, 48%] | 14% [9%, 21%] | 41% [22%, 56%] | 44% [18%, 63%] | 35% [28%, 43%] | 30% [23%, 38%] | 21% [15%, 29%] | 17% [11%, 24%] | 39% [18%, 56%] | 45% [23%, 63%] |
| Panic disorder | 18% [13%, 25%] | 13% [8%, 19%] | 16% [13%, 25%] | 11% [7%, 17%] | 11% [-26%, 39%] | 17% [-32%, 49%] | 15% [10%, 22%] | 16% [11%, 23%] | 14% [10%, 21%] | 12% [8%, 19%] | 5% [-40%, 36%] | 22% [-19%, 50%] |
| Comorbid diagnoses | | | | | | | | | | | | |
| Average | 1.1 [0.9, 1.3] | 0.9 [0.7, 1.0] | 0.6 [0.5, 0.7] | 0.4 [0.3, 0.5] | 46% [34%, 56%] | 59% [45%, 69%] | 1.0 [0.8, 1.1] | 1.0 [0.9, 1.2] | 0.5 [0.4, 0.6] | 0.5 [0.4, 0.6] | 49% [35%, 60%] | 54% [42%, 64%] |
| Frequency[a] | | | | | | | | | | | | |
| 0 | 18% [13%, 25%] | 17% [12%, 24%] | 65% [57%, 72%] | 74% [66%, 80%] | – | – | 19% [14%, 27%] | 16% [11%, 23%] | 73% [65%, 80%] | 66% [57%, 73%] | – | – |
| 1 | 30% [23%, 37%] | 33% [26%, 42%] | 24% [18%, 32%] | 22% [16%, 30%] | – | – | 31% [24%, 39%] | 32% [25%, 40%] | 20% [14%, 27%] | 26% [20%, 34%] | – | – |
| 2 | 40% [33%, 48%] | 43% [35%, 52%] | 9% [6%, 15%] | 4% [1%, 8%] | – | – | 41% [34%, 50%] | 42% [34%, 50%] | 6% [3%, 11%] | 8% [4%, 13%] | – | – |
| 3 | 12% [8%, 18%] | 6% [3%, 12%] | 1% [0%, 5%] | 1% [0%, 5%] | – | – | 8% [5%, 14%] | 10% [6%, 16%] | 1% [0%, 5%] | 1% [0%, 5%] | – | – |

*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.

*3.3.1.2. Generalised anxiety disorder.* Among those meeting diagnostic criteria for GAD ($n = 152$) the GEE analyses indicated a significant effect for Time (GAD-7: Wald's $\chi^2 = 290.19$, $p < .001$) but no significant Time by Treatment Approach interaction for GAD symptoms (GAD-7: Wald's $\chi^2 = .930$, $p = .920$). Pairwise comparisons indicated that both groups improved similarly from baseline to post-treatment ($p < .001$). There were no other significant changes between the other time points.

*3.3.1.3. Social anxiety disorder.* Among those meeting diagnostic criteria for SAD ($n = 95$) the GEE analyses indicated a significant effect for Time (MINI-SPIN: Wald's $\chi^2 = 128.15$, $p < .001$) but no significant Time by Treatment Approach interaction for social anxiety symptoms (MINI-SPIN: Wald's $\chi^2 = 4.12$, $p = .390$). Pairwise comparisons indicated that both groups improved similarly from baseline to post-treatment ($p < .001$) and that both group's symptoms worsened slightly from 12-month follow-up to 24-month follow-up ($p = .023$).

*3.3.1.4. Panic disorder.* Among those meeting diagnostic criteria for PD ($n = 45$) the GEE analyses indicated a significant effect for Time (PDSS-SR: Wald's $\chi^2 = 36.60$, $p < .001$) but no significant Time by Treatment Approach interaction for panic symptoms (PDSS-SR: Wald's $\chi^2 = 2.64$, $p = .620$). Pairwise comparisons indicated that both groups improved from baseline to post-treatment ($p < .001$). There were no differences between the TD-CBT and DS-CBT groups at any other time points ($ps > .05$).

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

Across the whole sample ($n = 290$) the GEE analyses indicated a significant effect for Time (K10: Wald's $\chi^2 = 547.84$, $p < .001$) but no significant Time by Treatment Approach interaction for general psychological distress (K10: Wald's $\chi^2 = 2.12$, $p = .547$). Pairwise comparisons indicated that both groups improved from baseline to post-treatment ($p < .001$) and from post-treatment to 3-month follow-up ($p = .002$).

Across the whole sample ($n = 290$) there was a significant effect for Time (SDS: Wald's $\chi^2 = 373.41$, $p < .001$) but no significant Time by Treatment Approach interaction for disability (SDS: Wald's $\chi^2 = 3.90$, $p = .419$). Pairwise comparisons indicated that both groups improved from baseline to post-treatment ($p < .001$) and from post-treatment to 3-month follow-up ($p = .021$).

Across the whole sample ($n = 290$) there was a significant effect for Time (NEO-FFI-N: Wald's $\chi^2 = 289.63$, $p < .001$) but no significant Time by Treatment Approach interaction for neuroticism (NEO-FFI-N: Wald's $\chi^2 = 3.05$, $p = .384$). Pairwise comparisons indicated that both groups improved from baseline to post-treatment and from post-treatment to 3-month follow-up ($ps < .001$).

*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 the diagnoses (MDE; Wald's $\chi^2 = 204.97$, $p < .001$; GAD: Wald's $\chi^2 = 224.67$, $p < .001$; SAD: Wald's $\chi^2 = 30.134$, $p < .001$) with the exception of panic disorder (PD: Wald's $\chi^2 = 1.238$, $p = .266$). No significant Time by Treatment Approach interactions were observed for any diagnoses (MDE: Wald's $\chi^2 = 2.483$, $p = .115$; GAD: Wald's $\chi^2 = 0.860$, $p = .353$; SAD: Wald's $\chi^2 = 0.127$, $p = .727$; PD: Wald's $\chi^2 = 0.570$, $p = .450$) indicating that the proportion of participants meeting diagnostic criteria, except for PD, significantly reduced across time irrespective of Treatment Approach.

The GEE analyses focused on average comorbid diagnoses revealed a significant Time effect (Wald's $\chi^2 = 108.26$, $p < .001$) but no Time by Treatment Approach interaction (Wald's $\chi^2 = 0.476$, $p = .490$). 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*

There was no difference in the number of lessons completed by the CG-CBT ($M = 4.21$; SD = 1.21) and SG-CBT ($M = 3.92$; SD = 1.44) groups at post-treatment ($F_{1,288} = 3.59$, $p = .059$). Of the participants who completed the evaluation questions at post- treatment, 93% (102/110) of the CG-CBT group, and 95% (106/112) of the SG-CBT group, reported they *would recommend the course* to others. Further, 96% (106/110) of the CG-CBT group and 97% (108/111) 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: .16–.35; $p = .557$–$.692$).

## 4. Discussion

The present study compared the efficacy of transdiagnostic and disorder-specific CBT for MDD when provided with and without regular clinician contact. The hypotheses were not fully supported. TD- CBT and DS-CBT were both associated with significant improvements in symptoms of MDD as well as significant improvements in comorbid symptoms of GAD, SAD and PD. Gains were maintained at 24-month follow-up. Similarly, the CG-CBT and SG-CBT resulted in significant improvements in symptoms of MDD and significant improvements in comorbid symptoms and again, these improvements were stable at 24-month follow-up. Reflecting this, significant reductions in the proportions of participants meeting diagnostic criteria for MDD, GAD and SAD, but not PD, were observed across all conditions at three month follow-up. There was some evidence of the CG-CBT group reporting marginally lower symptoms than the SG-CBT group at two time points. However, no marked or consistent differences were observed across the outcomes either between TD-CBT or between DS-CBT groups or the CG-CBT or SG-CBT groups. Treatment completion rates were also similar across the groups and satisfaction rates were high.

The large reductions in principal symptoms of MDD (Cohen's $d \geq 1.44$; avg. reduction $\geq 45\%$) and in comorbid symptoms of GAD (Cohen's $d \geq 1.08$; avg. reduction $\geq 43\%$), SAD (Cohen's $d \geq 0.69$; avg. reduction $\geq 29\%$) and PD (Cohen's $d \geq 0.49$; avg. reduction $\geq 32\%$) for both TD-CBT and DS-CBT are consistent with the magnitude of clinical change reported in meta-analyses of the broader transdiagnostic and disorder-specific treatment literature (Butler et al., 2006; McEvoy et al., 2009; Andrews et al., 2010; Reinholt & Krogh, 2014). These improvements were also reflected in significantly reduced proportions of participants meeting diagnostic criteria for MDD (reduction $\geq 86\%$), GAD (reduction $\geq 62\%$), SAD (reduction $\geq 41\%$), but not PD (reduction $\geq 11\%$), at 3-month follow-up when participants again completed a diagnostic interview. The present findings are consistent with an emerging body of literature indicating that different approaches, including transdiagnostic (Titov et al., 2011) and tailored-treatments (Johansson et al., 2012) can be used to treat principal and comorbid symptoms of MDD. The present findings are also consistent with those of the few other existing studies that have directly compared transdiagnostic with disorder- specific treatments, but which also failed to find consistent differences between these models (Norton & Barrera, 2012; Dear et al., in press). Thus, as reported elsewhere (Clark, 2009; Andrews et al., 2010; Norton & Barrera, 2012; Titov et al., 2012; Reinholt & Krogh, 2014), the present findings support the argument that the main benefit of TD-CBT may be in reducing the need for clinicians to be competent in multiple disorder-specific treatments

and may also reduce the need for complex differential diagnoses for the most common and comorbid diagnoses. However, this observation may not apply to all disorders. For example, Craske et al. (2007) reported that a transdiagnostic intervention was less effective than a disorder-specific intervention at treating panic disorder, indicating that the principal disorder may be an important moderating variable in determining choice of treatment. Thus, we note that it is possible that different disorders will respond differently to TD-CBT interventions, and this will be explored further in the studies that are occurring in parallel to the present study, but which target other disorders, including panic disorder.

A surprising finding from the present study was that no consistent differences were observed between the clinical outcomes of participants receiving weekly clinician contact and those who received treatment in a self-guided format. Indeed, large reductions were observed in principal symptoms of MDD (Cohen's $d \geq 1.44$; avg. reduction $\geq 45\%$) as well as comorbid symptoms of GAD (Cohen's $d \geq 1.19$; avg. reduction $\geq 48\%$), SAD (Cohen's $d \geq 0.65$; avg. reduction $\geq 29\%$) and PD (Cohen's $d \geq 0.45$; avg. reduction $\geq 31\%$) across the CG-CBT and SG-CBT groups. These improvements were reflected in significantly reduced proportions of participants meeting diagnostic criteria for MDD (reduction $\geq 84\%$), GAD (reduction $\geq 67\%$), SAD (reduction $\geq 39\%$), but not PD (reduction $\geq 5\%$). These findings are inconsistent with results of reviews that have found that clinician-guided treatment is associated with better adherence and treatment outcomes than self-guided interventions (Richards & Richardson, 2012). This may reflect the increased effectiveness of recently reported self-guided interventions (Berger et al., 2011; Meyer et al., 2015; Dear et al., 2015), which include therapist-administered diagnostic- screening prior to treatment, orientation procedures and high quality treatment materials, factors that have been recognised as important components of effective contemporary self-guided interventions (Andersson & Titov, 2014). Thus, the efficacy of the self-guided groups in the present trial should not be taken to indicate that therapists are not required. Rather, these results indicate that, providing treatment materials are of a high quality, some participants may not require therapist-contact during treatment. In order to provide appropriate clinical governance and to facilitate patient safety in the event of deterioration, we propose that such patients still require initial and post-treatment interviews, as well as monitoring of progress during treatment. This has important implications for the broader implementation of online interventions as it provides support for a cost-effective, yet potentially clinically safer and more clinically effective model than entirely automated self- guided treatments.

Significant improvements were also observed in general psychological distress (Cohen's $d \geq 0.87$; avg. reduction $\geq 22\%$), disability (Cohen's $d \geq 0.64$; avg. reduction $\geq 35\%$) and neuroticism (Cohen's $d \geq 0.56$; avg. reduction $\geq 13\%$) across the TD-CBT and DS-CBT as well as the CG-CBT and SG-CBT groups. This is encouraging and suggests that these treatments not only reduce principal and comorbid symptoms but also several vulnerability factors for psychological disorder. Of note, and consistent with recent reports (Dear et al., in press), we observed significant and sustained reductions in the personality trait of neuroticism, consistent with recent findings that indicate this trait may indeed by modified with treatment (Johansson et al., 2013). In a recent study of transdiagnostic group therapy for anxiety disorders, Talkovsky and Norton (2014) found that negative affect, which is closely related to neuroticism, mediated change in symptoms and that this indirect effect was not moderated by principal diagnosis. Thus, the degree to which an intervention modifies the vulnerability factors of neuroticism or negative affectivity may be crucial in producing symptomatic relief for principal and comorbid disorders, regardless of whether the intervention is diagnosis-specific or transdiagnostic per se. This is important given that neuroticism is a strong predictor of health service use, impairment, and psychiatric morbidity and is associated with considerable economic costs (Lahey, 2009; Cuijpers et al., 2010).

The present study has several important strengths and extends the existing literature in a number of important ways. First, it is the largest study to directly compare TD-CBT and DS-CBT as well as CG-CBT and DS-CBT for MDD and comorbid anxiety disorders. Second, the present study employed two treatment protocols that are similar in structure and format enabling a more direct comparison of the different treatment approaches while controlling for the issue of treatment dose. Thus, the design restricts the differences between the conditions and reduces some potential threats to validity of the results. Third, the present study included long-term follow-up, which enabled detection of potential longer-term differences between the conditions, and it also obtained relatively high response rates providing further confidence in the results. Fourth, the present study examined multiple outcomes (e.g., clinical symptoms, diagnostic assessments, satisfaction and treatment completion) to provide a broad evaluation of the interventions.

Despite these strengths there are some limitations that need to be considered. The first is the absence of a waitlist control group, which would have provided a control for spontaneous remission. A control group was not included within the trial for the reasons that the magnitude of clinical changes of previous control groups using similar methodologies has been negligible (e.g., range of Cohen's $ds < 0.15$; Titov et al., 2011; Titov et al., 2013; Titov et al., 2014; Titov et al., 2015) and withholding treatment would therefore be ethically questionable. Another important limitation is that, despite the relatively large overall sample size, the current trial managed to recruit only a small number of participants ($n = 45$; 15% of the sample) with comorbid PD. Unfortunately, this may have resulted in a floor effect with the result that the present study had relatively low power for detecting improvements in the proportion of participants meeting criteria for PD. Alternatively, it may be that the treatments employed are not effective for comorbid PD; however, this would seem unlikely given the significant reductions in panic symptoms observed among participants with PD. Nevertheless, this is an important issue because, in order to be broadly adopted, TD-CBT treatments need to be at least as effective as DS-CBT treatments for the most common mental disorders and, to date, some trials have suggested that transdiagnostic treatments may not to be as effective as DS-CBT for PD (Craske et al., 2007). Future large scale research is needed to explore this issue and to replicate and build upon the findings of the current trial, especially for SAD and PD. The authors are currently completing trials for these disorders. A third limitation relates to the nature of the therapist-guided condition. It is important to acknowledge that in an attempt to maximize fidelity and to reduce therapist drift, the nature and duration of therapist contact was limited and defined by a carefully developed protocol. This resulted in short weekly contacts, which may have inadvertently reduced the potential benefits of the therapist conditions, although it should be noted that both self and therapist-guided conditions resulted in large and significant improvements in target symptoms.

In conclusion, the present study found large clinical improvements in symptoms of MDD and comorbid GAD, SP and PD in both the TD-CBT and DS-CBT as well as the CG-CBT and SG-CBT groups. These improvements were maintained at 24-month follow-up and were reflected in reductions in the proportions of participants meeting diagnostic criteria for these disorders post-treatment and in reductions in the levels of diagnostic comorbidity. The treatments were associated with satisfactory levels of treatment completion and high levels of treatment satisfaction. It remains to be seen whether the TD-CBT intervention is as effective as DS-CBT for other disorders. The other RCTs we are conducting will help

inform this issue and will help inform clinicians about the potential of TD-CBT.

## 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.

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