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Review

Computer therapy for the anxiety and depression disorders is effective, acceptable and practical health care: An updated meta-analysis

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ABSTRACT

Background: A 2010 meta-analysis of internet-delivered CBT (iCBT) RCTs argued 'computer therapy for the anxiety and depressive disorders was effective, acceptable and practical health care' without data on effectiveness or practicality in routine practice.
Methods: Databases, reviews and meta-analyses were searched for randomised controlled trials of cCBT or iCBT versus a control group (care as usual, waitlist, information control, psychological placebo, pill placebo, etc.) in people who met diagnostic criteria for major depression, panic disorder, social anxiety disorder or generalised anxiety disorder. Number randomised, superiority of treatment versus control (Hedges'g) on primary outcome measure, length of follow-up, follow up outcome, patient adherence and satisfaction/harm were extracted; risk of bias was assessed. A search for studies on effectiveness of iCBT in clinical practice was conducted.
Results: 64 trials were identified. The mean effect size (efficacy) was g = 0.80 (NNT 2.34), and benefit was evident across all four disorders. Improvement was maintained at follow-with good acceptability. Research probity was good, and bias risk low. In addition, nine studies comparing iCBT with traditional face-to-face CBT and three comparing iCBT with bibliotherapy were identified. All three modes of treatment delivery appeared equally beneficial. The results of effectiveness studies were congruent with the results of the efficacy trials.
Limitations: Studies variably measured changes in quality of life and disability, and the lack of comparisons with medications weakens the field.
Conclusions: The conclusions drawn in the original meta-analysis are now supported: iCBT for the anxiety and depressive disorders is effective, acceptable and practical health care.

1. Introduction

Major depression and the anxiety disorders are leading causes of disability worldwide, (Whiteford, Ferrari, Degenhardt, Feigin, & Vos, 2015). Pharmacotherapy and psychotherapy have been the mainstay of treatment for anxiety and depression. CBT is the commonest form of psychotherapy for depression and anxiety and has traditionally been delivered face-to-face. Therapist-delivered CBT is difficult to standardise as factors unique to each therapist-patient interaction can alter how and what treatment is delivered. Central elements of CBT can be omitted and each individual provider can introduce "drift" by administering their own personal version of the intervention (Waller, 2009; Shafran et al., 2009).

Computerised CBT (cCBT) was introduced in 1990, in the form of a CBT manual delivered via CD-ROM (Selmi, 1990). By the end of the decade, it was being delivered over the internet (iCBT). iCBT usually

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takes the form of modules or lessons delivering CBT concepts by desktop, internet or phone app. iCBT has been shown to be equally effective as face-to-face CBT (Andersson, Cuijpers, Carlbring, Riper, & Hedman, 2014), with additional benefits including privacy, convenience and fidelity of treatment. Therapist drift and variability between trial and dissemination in practice is less likely as, once tested and found successful, courses can be distributed exactly as they were designed.

A 2010 meta-analysis, based on 22 randomised controlled trials, argued that computer therapy for the anxiety and depressive disorders was effective, acceptable and practical healthcare (Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010). Since that publication, there have been a number of systematic reviews of this area. Hedman et al. (Hedman, Ljotsson, & Lindefors, 2012) identified iCBT for depression, social anxiety disorder and panic disorder as established treatments. Anderssen et al. (Andersson et al., 2014) identified eight direct comparisons of face to face CBT and iCBT in depression, social anxiety disorder and panic disorder, and found them to be equally efficacious. Olthius, Watt, Bailey, Hayden, and Stewart (2015) (Olthius et al., 2015) did a Cochrane Collaboration of face to face CBT, guided and unguided iCBT and found no differences in efficacy. In addition there have been systematic reviews and meta-analyses looking at trans-diagnostic iCBT for these four disorders (Newby, Twomey, Yuan Li, & Andrews, 2016), and for post-traumatic stress disorder (Sijbrandij, Kunovski, & Cuijpers, 2016).

As the field has matured in the intervening years, we have repeated the Andrews et al. meta-analysis (Andrews et al., 2010) using comparable search terms. We identified studies in which iCBT was compared to a control condition in people who met diagnostic criteria on the basis of structured interviews or above threshold scores on standardised questionnaires. This was done for the same four disorders considered in the 2010 meta-analysis − major depressive disorder (MDD), panic disorder (PD), social anxiety disorder (SAD) or generalised anxiety disorder (GAD). A replication and extension of the original meta-analysis to include an examination of the effect of type of control group and risk of bias on outcome, maintenance of improvement over time, as well as time spent by the therapist, will contribute to the discussion as to whether the original claim that 'computerised therapy for the anxiety and depressive disorders is effective, acceptable and practical health care' remains justified.

2. Method

This review was registered (www.ANZCTR.org.au/ACTRN12610000030077.aspx). The protocol for search, extraction and analysis followed the description in the original paper.

2.1. Study selection

Participants must have been aged 18 or over, and met criteria for either major depressive disorder, generalised anxiety disorder, panic disorder with or without agoraphobia or social anxiety disorder as a primary diagnosis. Diagnosis could be determined by a clinician, telephone interview or by meeting a recognised cut-off on a validated self-report questionnaire. Conditions for inclusion were English language randomised controlled trials of iCBT versus either waitlist control (WLC), information control (IC), care as usual (CAU) or placebo. The outcome of interest was change in symptom severity. All papers analysed were either published or in press, and the investigators had copies of all manuscripts. RCTs that compared iCBT vs face-to-face CBT and iCBT vs bibliotherapy were extracted for separate analysis and effect sizes were calculated. Effectiveness studies were identified and reviewed. In addition, a systematic review of the literature was conducted to identify any harms of iCBT.

2.2. Information sources

Papers identified in the search that were published, or available to the authors, before September 2016 were included. Abstracts were identified by combining terms representative of internet-delivered psychological treatment for major depressive disorder, generalised/generalized anxiety disorder, panic disorder (with or without agoraphobia) or social phobia/social anxiety disorder (both MeSH terms and text words). As in the previous study (Andrews et al., 2010), studies of treatments aimed at a range of diagnoses (transdiagnostic studies) were excluded (see Newby (Newby, Twomey et al., 2016) for a recent review), as were studies of depressive or anxiety symptoms in which no data on the probability of satisfying diagnostic criteria were supplied. An example search strategy for Medline is available from the corresponding author, as per PRISMA guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009). The supplementary search consisted of reference lists of reviews and meta-analyses identified as relevant, as well as reference lists of included studies and papers from conferences and other sources.

Data extracted from each study included: number of subjects randomised, details of treatment condition and control group, pre and post means and standard deviations in the principal outcome measure, Hedges'g (Hedges & Vevea, 1996), number needed to treat (NNT) (Kraemer & Kupfer, 2006), adherence and satisfaction/harm. Data was collected for the primary outcome measure(s) named in the study. Adherence was defined as the percentage of participants randomised who finished the course. To analyse risk of bias using the Cochrane Collaboration tool (Higgins et al., 2011), information about sequence generation, allocation concealment, blinding, missing data and selective reporting was also extracted. The extraction of data and the adequacy of bias minimisation was rated independently by two researchers (AB and LE), with differences resolved following discussion with GA.

2.3. Meta-Analysis

We followed both the PRISMA guidelines (Moher et al., 2009) and the recommendations made in Cuijpers (Cuijpers, 2016). Statistical analysis was done using Comprehensive Meta-Analysis version 3 (Comprehensive Meta-Analysis Software (CMA), 2016). The effect size (Hedges'g) was calculated as the post-test difference between the mean of the treatment condition and the mean of the control condition, divided by the pooled post standard deviation and adjusted for sample size. For ease of clinical interpretation, we also calculated the NNT using both the effect sizes and Z scores (Kraemer & Kupfer, 2006). The NNT represents the number of patients one would expect to treat to have one more successful outcome. Where a study had multiple arms, each relevant arm was treated as a separate trial.

Effect sizes from each trial were pooled according to the random effects model, while differences between study subgroups were pooled according to the mixed effects model. As indicators of heterogeneity of pooled effect sizes, we calculated I^2, which indicates the heterogeneity in percentages. We calculated 95% confidence intervals around I^2 (Ionnidis, Patsopoulos, & Evangelou, 2016), using the non-central chi-squared-based approach within the heterogi module for Stata (Orsini, Bottai, Higgins, & Buchan, 2006). Publication bias was tested by inspecting the funnel plot on the primary outcome measures, and by a trim-and-fill procedure, which yields an estimate of the pooled effect size after accounting for bias (Duval & Tweedie, 2009).

3. Results

3.1. Study selection

A total of 4423 abstracts were examined from the following databases: PubMed (N = 1187), Cinahl (N = 139), PsychINFO (N = 538), Medline (N = 468), Social Sciences Citation Index (N = 1193) and Embase (N = 899). See Fig. 1, below.

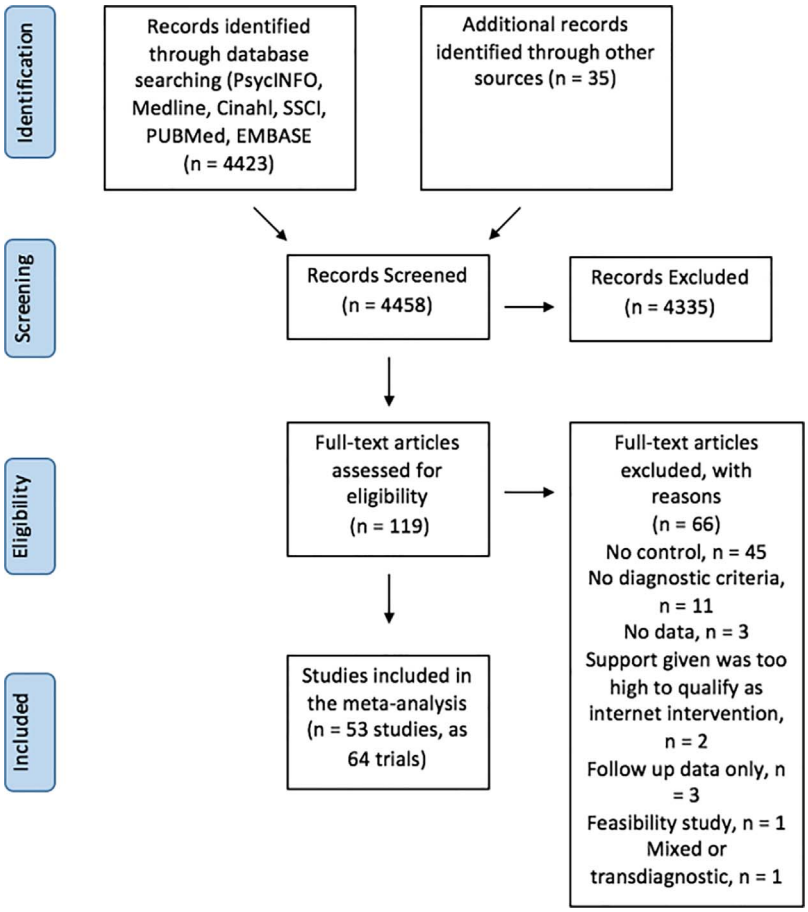

Fig. 1. PRISMA flowchart.

Two of the 22 studies in the original meta-analysis contained multiple relevant arms, which were analysed as separate trials. 31 additional studies were identified following the full-text screen, making 53 randomised controlled studies in total. As studies with multiple relevant arms were treated as separate trials, a total of 64 efficacy trials were analysed. The control conditions varied from wait list in which treatment was deferred for a period (usually three months), to psychological placebos (information and discussion groups about the disorder in question; pseudo-active treatments) to care as usual in which the previous treatment was continued or changed, provided face to face or internet CBT was not introduced. The search also identified nine studies comparing face to face CBT with iCBT, three studies comparing iCBT to bibliotherapy and eight effectiveness studies of the benefits of iCBT when used in routine practice − these were used for separate analyses.

A systematic search of the literature looking for harms was conducted in February 2016, and yielded no results. Both qualitative and quantitative studies were sought, and no study design, date or language limits were imposed on the search. No studies specifically investigated the harms of iCBT. Furthermore, none of the studies examined in this meta-analysis made mention of harm or negative effects experienced by participants. It is the authors' belief that even if the harms of ICBT were not the specific focus of a trial, had they occurred the study would have likely mentioned them. Nevertheless, we recognise that harm-specific research is lacking.

The Cochrane Collaboration tool for assessing risk of bias was used (Higgins et al., 2011). All studies used intention-to-treat methods. Studies with self-report methods precluded blinding, but controlled for investigator bias. 51 trials were judged to have a low risk of bias, while the remaining 13 were unclear. The uncertainty was predominantly due to a lack of information about allocation concealment.

Results of the meta-analysis of the 64 trials (Selmi, 1990; Andersson, 2005; Berger, Hämmerli, Gubser, Andersson, & Caspar, 2011; Choi et al., 2012; Christensen, 2004; de Graaf et al., 2009; Farrer, Christensen, Griffiths, & Mackinnon, 2011; Geraedts et al., 2014; Gilbody et al., 2015; Hallgren et al., 2015; Johansson et al., 2012; Kessler et al., 2009; Kivi et al., 2014; Lintvedt et al., 2011; Newby, Robins et al., 2016; O'Moore et al., 2018; Perini, Titov, & Andrews, 2009; Phillips et al., 2013; Richards et al., 2015; Rosso et al., 2017; Ruwaard et al., 2009; Smith et al., 2017; Titov et al., 2010; Vernmark et al., 2010; Warmerdam, van Straten, Twisk, Riper, & Cuijpers, 2008; Williams, Blackwell, Mackenzie, Holmes, & Andrews, 2013; Wright et al., 2005; Allen et al., 2016; Carlbring, Westling, Ljungstrand, Ekselius, & Andersson, 2001; Carlbring et al., 2006; Klein and Richards, 2001; Klein, Richards, & Austin, 2006; Oromendia, Orrego, Bonillo, & Molinuevo, 2016; Richards, Klein, & Austin, 2006; Ruwaard, Broeksteeg, Schrieken, Emmelkamp, & Lange, 2010; van Ballegooijen et al., 2013; Wims, Titov, Andrews, & Choi, 2010; Andersson et al., 2006; Andersson, Carlbring, & Furmark, 2012; Berger, Hohl, & Caspar, 2009; Botella et al., 2010; Carlbring et al., 2007; Furmark et al., 2009; Titov, Andrews, Schwencke, Drobny, & Einstein, 2008; Titov, Andrews, & Schwencke, 2008; Titov, Andrews, Choi, Schwencke, & Mahoney, 2008; Tulbure et al., 2015; Andersson, Paxling et al., 2012; Christensen et al., 2014a; Jones, Hadjistavropoulos, & Soucy, 2016; Paxling et al., 2011; Robinson et al., 2010; Titov et al., 2009) are displayed in Table 1: grouped by diagnosis, conditions studied, N randomised, outcome measure used, effect size of intervention compared to control condition (Hedges g), NNT, risk of bias, length of follow-up, adherence and patient satisfaction (as a proxy for acceptability). Summary data are in Tables 2–5 and a forest plot of the studies ranked by disorder shows the confidence limits around the effect sizes for each study (Fig. 2).

Table 1
Selected characteristics and results of randomised controlled studies examining the effects of cCBT and iCBT for adult depression and anxiety disorders.

Study	Conditions	N	Outcome Measure	Hedges' g	NNT	Follow Up (Months)	Adherence (%)	Satisfaction (%)	Bias Risk
Major Depressive Disorder									
Anderson (2005)	iCBT + support vs WLC + DG	75	BDI	0.90	2.10	6	65	–	Low
Berger (2011a)	iCBT vs WLC	51	BDI-II	0.72	2.56	6	36	–	Low
Berger (2011b)	iCBT + support vs WLC	51	BDI-II	1.09	1.79	6	56	–	Low
Choi (2012)	iCBT + support vs WLC	63	CBDI	1.51	1.4	3	68	96	Low
Christensen (2004)	CBT + support vs WLC + attention placebo	360	CES-D	0.34	5.26	12	66	–	Unclear
De Graaf (2009)	iCBT vs CAU	203	BDI-II	0.19	9.43	3, 6	–	–	Low
Farrer (2011a)	iCBT vs WLC	73	CES-D	0.57	3.18	–	16	–	Low
Farrer (2011b)	iCBT + support vs WLC	80	CES-D	0.83	2.26	6	18	–	Low
Geraedts (2014)	iCBT + support vs CAU	231	CES-D	0.24	7.46	6, 12	–	–	Low
Gilbody (2015a)	iCBT + support vs CAU	449	PHQ-9	0.02	83.3	12, 24	18	–	Low
Gilbody (2015b)	iCBT + support + CAU vs CAU	481	PHQ-9	0.12	14.71	12, 24	16	–	Low
Hallgren (2015)	iCBT + support vs CAU	629	MADRS	0.42	4.27	3	60	–	Low
Johansson (2012a)	Tailored iCBT + support vs WLC + DG	81	BDI-II	0.92	2.07	6	–	–	Unclear
Johansson (2012b)	Standardised iCBT + support vs WLC + DG	82	BDI-II	0.51	3.55	6	–	–	Unclear
Kessler (2009)	iCBT + CAU vs CAU	297	BDI	0.61	2.99	8	65	–	Low
Kivi (2004)	iCBT + support vs CAU	90	BDI-II	0.06	29.4	–	56	–	Unclear
Lintvedt (2013)	iCBT vs WLC	163	CES-D	0.67	2.75	–	–	83	Low
Newby (2016)	iCBT + support vs CAU	106	PHQ-9	1.08	1.81	3	66	85	Low
O'Moore (2016)	iCBT + support > CAU	69	PHQ-9	1.56	< 1.4	3	84	95	Low
Perini (2009)	iCBT + support vs WLC	48	PHQ-9	0.73	2.54	–	74	82	Low
Phillips (2014)	iCBT + support vs CAU	637	PHQ-9	0.05	35.71	3	90	–	Low
Richards (2015)	iCBT + support vs WLC	262	BDI-II	0.75	2.48	3, 6	38	–	Low
Rosso (2016)	iCBT + support vs attention control	77	PHQ-9	0.89	2.13	–	92	–	Low
Ruwaard (2009)	iCBT + support vs WLC	54	BDI-IA	0.65	2.82	18	–	89	Unclear
Selmi (1990)	cCBT vs WLC	24	BDI	0.97	1.97	2	100	–	Unclear
Smith (2016)	iCBT + support vs WLC	270	PHQ-9	0.91	2.08	3	59	–	Low
Titov (2010a)	iCBT CA vs WLC	94	PHQ-9	1.43	1.45	4	70	87	Low
Titov (2010b)	iCBT TA vs WLC	92	PHQ-9	1.43	1.45	4	80	87	Low
Vernmark (2010)	iCBT + support vs WLC	88	BDI	0.65	2.82	6	59	–	Low
Warmerdan (2008)	iCBT + support vs WLC	263	CES-D	0.04	45.5	–	39	–	Low
Williams (2013)	iCBT + support vs WLC	69	BDI-II	1.05	1.85	–	56	84	Low
Wright (2005)	cCBT + support vs WLC	30	HAM-D	0.93	2.04	3, 6	91	–	Low
Panic Disorder/Agoraphobia									
Allen (2016)	iCBT + support vs WLC	67	PDSS-SR	1.11	1.67	3	63	93	Low
Carlbring (2001)	iCBT + support vs WLC	41	BSQ	1.47	1.42	–	80	85	Low
Carlbring (2006)	iCBT + support vs WLC	60	BSQ	1.90	< 1.4	9	80	97	Low
Klein (2001)	iCBT vs self-monitoring control	23	PDSS	0.39	4.59	–	90	–	Unclear
Klein (2006)	iCBT + support > IC	37	PDSS	3.07	< 1.4	3	–	–	Low
Oromendia (2016a)	iCBT + non-scheduled support vs WLC	52	PDSS-SR	1.21	1.64	6	44	–	Low
Oromendia (2016b)	iCBT + scheduled support vs WLC	50	PDSS-SR	2.08	< 1.4	6	68	–	Low
Richards (2006a)	iCBT + support vs IC	21	PDSS	1.28	1.58	3	–	–	Unclear
Richards (2006b)	iCBT + support + stress modules vs IC	20	PDSS	2.55	< 1.4	3	–	–	Unclear
Ruwaard (2010	iCBT + support vs WLC	58	PDSS-SR	0.41	4.39	36	85	86	Unclear
Van Ballegooijen (2013)	iCBT + support vs WLC	126	PDSS-SR	0.28	6.41	–	6	–	Unclear
Wims (2010)	iCBT + support vs WLC	29	PDSS	0.76	2.44	1	79	–	Low
Social Anxiety Disorder									
Andersson (2006)	iCBT + support vs WLC	64	LSAS-SR	0.83	2.26	12	56	–	Low
Andersson 2012_1	iCBT + support vs WLC	204	LSAS-SR	0.93	2.04	12	55	–	Low
Berger (2009)	iCBT + support vs WLC	52	LSAS-SR	0.61	2.99	–	57	85	Low
Botella (2010)	iCBT vs WLC	91	BFNE	0.45	4	12	48	–	Unclear
Carlbring (2007)	iCBT + support v WLC	57	SPS	1.01	1.91	12	93	–	Unclear
Furmark (2009)	iCBT + support vs WLC	80	SPS	0.82	2.28	12	63	70	Unclear
Titov (2008_1	iCBT + support vs WLC	105	SIAS	0.83	2.26	6	78	100	Low
Titov (2008_2)	iCBT + support vs WLC	88	SIAS	1.27	1.59	6	80	100	Low
Titov (2008_3a	iCBT + support vs WLC	67	SIAS	1.17	1.69	–	77	97	Low
Titov (2008_3b	iCBT vs WLC	66	SIAS	0.40	4.50	–	33	62	Low
Tulbure (2015)	iCBT + support vs WLC	76	LSAS-SR	1.28	1.58	6	39	86	Low
Generalised Anxiety Disorder									
Andersson (2012_2)	iCBT + support vs WLC	54	PSWQ	0.17	10.4	3, 18	–	–	Low
Christensen (2014a)	iCBT vs WLC	222	GAD-7	0.07	25.0	6, 12	–	–	Low
Christensen (2014b)	iCBT + phone support vs WLC	221	GAD-7	0.46	3.91	6, 12	–	–	Low
Christensen (2014c)	iCBT + email support vs WLC	224	GAD-7	0.33	5.43	6, 12	–	–	Low
Jones (2016)	iCBT + support vs WLC	46	GAD-7	0.73	2.54	1	–	77	Low
Paxling (2011)	iCBT + support vs WLC	89	PSWQ	1.17	1.69	12, 36	11	–	Low
Robinson (2010a)	iCBT CA + support vs WLC	100	GAD-7	1.16	1.70	3	74	87	Low
Robinson (2010b)	iCBT TA + support vs WLC	99	GAD-7	1.05	1.85	3	80	87	Low

(*continued on next page*)

Table 1 (*continued*)

Study	Conditions	N	Outcome Measure	Hedges' g	NNT	Follow Up (Months)	Adherence (%)	Satisfaction (%)	Bias Risk
Titov (2009)	iCBT + support vs WLC	48	GAD-7	1.42	1.46	–	75	85	Low

Note: N: number randomised; g: Hedges g; NNT: number needed to treat; Bias risk (low, unclear, high (Ionnidis et al., 2016)); FU: follow up in months; Ad/Sat: percent randomised adhering to whole course/percent satisfied with course; - represents no data; iCBT: internet-delivered CBT; cCBT: computer-delivered CBT via CD-ROM; WLC: waitlist control; CAU: care as usual; CA: clinician-assisted; TA: technician-assisted; IC: information control; DG: discussion group; BDI: Beck Depression Inventory; BDI-II: Beck Depression Inventory II; BDI-IA: Beck Depression Inventory-IA; CBDI: Chinese Beck Depression Inventory; PHQ-9: Patient Health Questionnaire-9; CES-D: Centre for Epidemiologic Studies Depresson Scale ; MADRS: Montgomery-Asberg Depression Rating Scale ; HAM-D: Hamilton Depression Rating; PDSS-SR: Panic Disorder Severity Scale – Self-Rated; BSQ: Body Sensations Questionnaire; PDSS: Panic Disorder Severity Scale; LSAS-SR: Liebowitz Social Anxiety Scale – Self-Rated; SPS: Social Phobia Scale; SIAS: Social Interaction Anxiety Scale ; GAD-7: Generalised Anxiety Disorder-7; PSWQ: Penn State Worry Questionnaire.

Table 2
Summary results of subgroup analyses examining the effects of iCBT and cCBT for depression and anxiety disorders, the type of control group, risk of bias, and maintenance of improvement at follow-up.

	N_{Trials}	$N_{Subjects}$	g	95% CI (g)	p	I^2	95% CI ($I^{2)}$	NNT
All studies	64	8279	0.80	0.68–0.92	.00	84	81–87	2.34
MDD	32	5642	0.67	0.51–0.81	.00	84	79–99	2.78
PD	12	584	1.31	0.85–1.76	.00	84	74–90	1.55
SAD	11	950	0.92	0.76–1.08	.05	35	0–67	2.07
GAD	9	1103	0.70	0.39–1.01	.00	82	67–89	2.63

Note: N_{Trials}: number of trials; $N_{Subjects}$: number of subjects overall; g: Hedge's g effect size of iCBT and cCBT over control conditions; 95% CI (g): 95% confidence interval for Hedge's g results; p: significance of Hedge's g results; I^2: heterogeneity; 95% CI (I^2): 95% confidence interval for I_2; NNT: number needed to treat.

Table 3
Results of subgroup analysis examining the effects of iCBT and cCBT per the type of control group.

Control Condition	N_{Trials}	$N_{Subjects}$	g	95% CI (g)	p	I^2	95% CI ($I^{2)}$	NNT
CAU	10	3192	0.38	0.18–0.59	.00	86	78–91	4.60
WLC	50	5046	0.90	0.74–1.00	.00	74	66–80	2.10

Note: Control condition: control condition used; CAU: care as usual; WLC: waitlist control; N_{Trials}: number of trials; $N_{Subjects}$: number of subjects overall; g: Hedge's g effect size of iCBT and cCBT over control condition; 95% CI (g): 95% confidence interval for Hedge's g results; p: significance of Hedge's g results; I^2: heterogeneity; 95% CI (I^2): 95% confidence interval for I_2; NNT: number needed to treat.

Table 4
Results of subgroup analysis examining the effects of iCBT and cCBT according to the trial's risk of bias.

Risk of Bias	N_{Trials}	$N_{Subjects}$	g	95% CI (g)	p	I^2	95% CI ($I^{2)}$	NNT
Low	50	7112	0.90	0.79–1.10	.00	86	84–89	2.10
Unclear	14	1167	0.74	0.39–0.74	.00	61	18–77	2.51

Note: Risk of bias: classified as per Cochrane Collaboration tool for assessing risk of bias [14]; N_{Trials}: number of trials; $N_{Subjects}$: number of subjects overall; g: Hedge's g effect size of iCBT and cCBT over control condition; 95% CI (g): 95% confidence interval for Hedge's g results; p: significance of Hedge's g results; I^2: heterogeneity; 95% CI (I^2): 95% confidence interval for I_2; NNT: number needed to treat.

3.2. Between-group effect sizes

The overall effect size superiority of iCBT over control groups across all four disorders was 0.80 (95% CI 0.68–0.92). The combined Hedges'g for Major Depression was 0.67 (CI 0.51 − 0.81), for Panic Disorder 1.31 (CI 0.85–1.8), for Generalised Anxiety Disorder 0.70 (CI 0.39–1.0), and for Social Phobia 0.92 (CI 0.75–1.1). All means were above zero and heterogeneity (I^2), as shown in Table 2, was substantial in most groups.

Table 5
Results of subgroup analysis examining the effects of iCBT and cCBT at follow up, compared to immediately after trial completion.

Follow-Up	N_{Trials}	$N_{Subjects}$	g	95% CI (g)	p	I^2	95% CI ($I^{2)}$
3–6 months	29	4630	0.15	0.06–0.23	.05	32	0–56
9–18 months	15	2941	0.22	0.01–0.43	.00	75	51–86

Note: Follow-up: period of time (months) in which follow-up data was collected; N_{Trials}: number of trials; $N_{Subjects}$: number of subjects overall; g: Hedge's g effect size of iCBT and cCBT at follow-up period, compared to immediately after trial completion; 95% CI (g): 95% confidence interval for Hedge's g results; p: significance of Hedge's g results; I^2: heterogeneity; 95% CI (I2): 95% confidence interval for I_2.

3.3. Subgroup analyses

3.3.1. Control group

As seen in Table 3 above, the mean effect size superiority over the control group for studies using a wait list control was higher (0.90) than for care as usual, (0.38, $p < .05$), indicating that the difference in improvement between iCBT and care as usual is less than with wait list controls (Watts, Turnell, Kladnitski, Newby, & Andrews, 2015).

3.3.2. Risk of bias

Risk of bias subgroup analyses were performed (see Table 4). The mean effect size superiority was higher for studies with a low risk of bias (0.90) than those where the risk of bias was deemed unclear (0.74, $p < .05$).

3.3.3. Maintenance of improvement

A majority of trials (51/64) reported follow-up data that ranged from 1 to 36 months post-treatment (median 6 months). Our analysis of the effect size superiority of iCBT over control at follow-up, versus post-treatment, was conducted for two groups (44 trials) – 3–6 months, and 9–18 months (Table 5) with significantly increased benefit at both periods.

3.3.4. Satisfaction and adherence

Adherence and satisfaction are indicators of acceptability of iCBT to patients and 52/64 trials measured one or both. Median adherence was 66% (50/64 trials) and the interquartile range was 29% (Q1 52%, Q3 80%). 24/64 trials provided data on patient satisfaction, with a median of 86% (range 62–100%) of patients reporting that they were satisfied or very satisfied.

3.3.5. Face to face CBT vs iCBT

Nine studies compared computerised CBT to face-to-face therapy (Selmi, 1990; Wright et al., 2005; Botella et al., 2010; Wagner, Horn, & Maercker, 2014; Andersson et al., 2013; Kiropoulos et al., 2008; Carlbring et al., 2005; Andrews, Davies, & Titov, 2011; Bergström et al., 2010), four in MDD, three in PD and two in SP. There were 568 subjects in total, 301 in the iCBT condition and 267 in the face-to-face group. The effect size indicating the difference between iCBT and face-to-face treatments was not significant, g = 0.14 in favour of face-to-face CBT

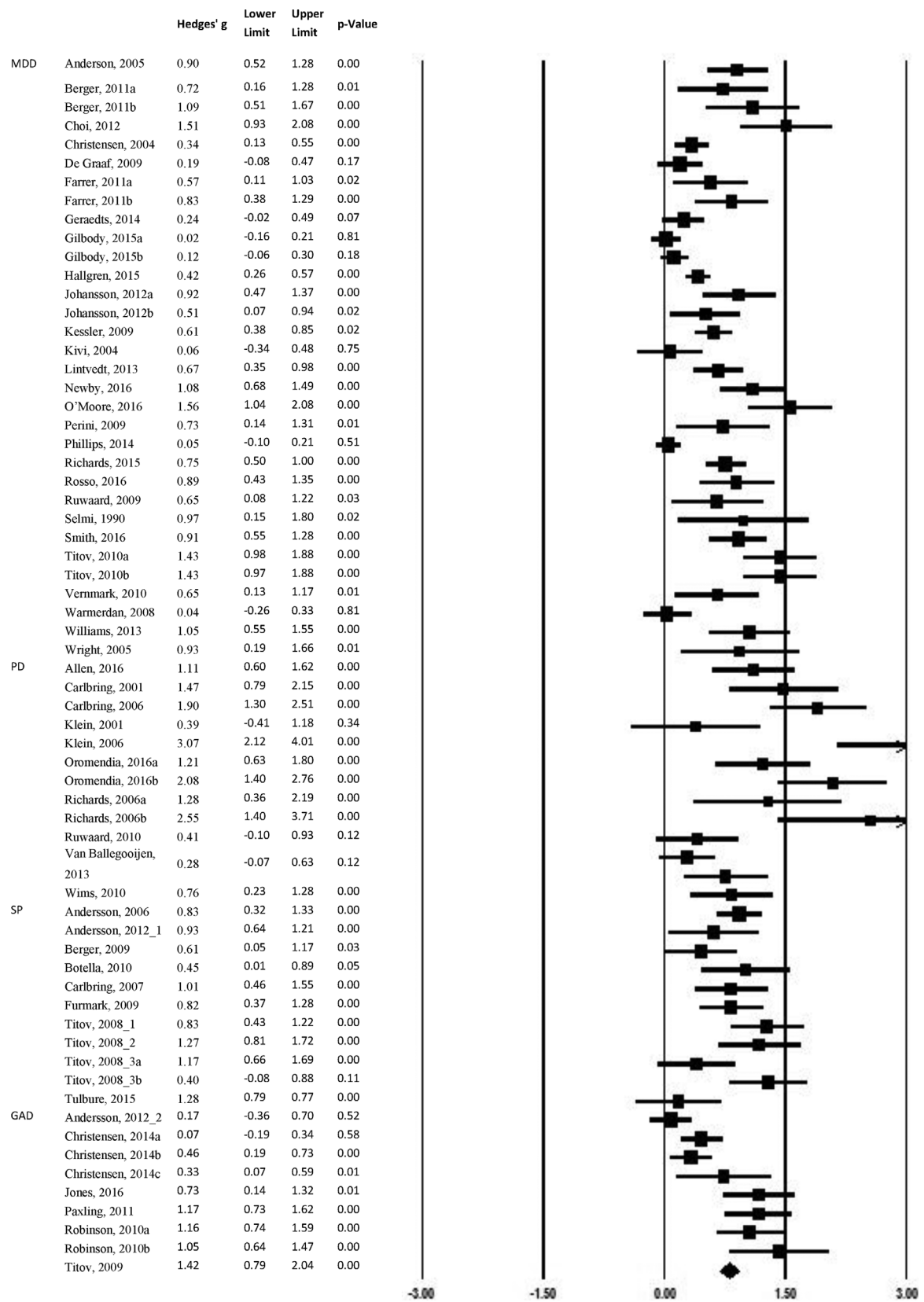

Fig. 2. Effect Sizes of iCBT versus control conditions.

(95% CI: −0.04–0.32).

Five of eight studies reported therapist time (Andersson et al., 2013; Kiropoulos et al., 2008; Carlbring et al., 2005; Andrews et al., 2011; Bergström et al., 2010); on average, therapists spent 7.8 times (SD 4.5) the amount of time on face-to-face subjects than on iCBT participants. The time spent per patient is shown in Table 6, below.

Table 6
Therapist time spent per patient in either iCBT or face-to-face CBT, and between-group effect size significance for primary outcome measure.

Study	Time (iCBT)	SD (iCBT)	Time (F-F)	SD (F-F)	p (Hedge's g)
Andersson et al. (2013)	36	15	290	265	< .05, favouring F-F
Kiropoulos et al. (2008)	352	240	268	255	> .05
Carlbring et al. (2005)	150	–	450–600	–	> .05
Andrews et al. (2011)	18	–	240	–	> .05
Bergström et al., 2010	35	19	360	–	> .05

Note: Time (iCBT): therapist time spent in iCBT condition, in minutes; SD (iCBT): standard deviation of iCBT therapist time, in minutes; Time (F-F): therapist time spent in face to face condition, in minutes; SD (F-F): standard deviation of fact to face therapist time, in minutes; p (Hedge's g): significance of difference in Hedge's g effect size between iCBT condition and face to face condition.

3.3.6. Bibliotherapy CBT vs iCBT

Three studies compared iCBT with bibliotherapy (Smith et al., 2017; Klein et al., 2006; Furmark et al., 2009), one each for MDD, PD and SP, with 255 participants in total – 120 in iCBT and 135 in bibliotherapy. All three had control arms, so were included in the meta-analysis. There was no significant difference overall, with g = 0.12 favouring iCBT (CI −0.12–0.36).

3.3.7. Effectiveness

Eight papers found in the original literature search investigated the effectiveness of iCBT in routine clinical practice (Watts et al., 2015; El Alaoui et al., 2015a; El Alaoui et al., 2015b; Hedman et al., 2014; Hedman et al., 2013; Mewton, Wong, & Andrews, 2012; Ruwaard et al., 2012; Williams and Andrews, 2013). All four disorders were represented in the studies, and the results were congruent with those of efficacy trials, with a pre-post effect size of g = 1.07. Three studies reported the therapist time spent – 11, 11.5 and 12 min per patient per week.

4. Discussion

The results of this study were similar to those of the original meta-analysis. Overall, the mean effect size superiority of iCBT over the control group was 0.88 in the original 22 studies and 0.80 in these 64 studies, with a corresponding rise in NNT from 2.15 to 2.34. Maintenance of improvement at follow-up was demonstrated with small, but significant, effect size superiority at both 3–6 and 9–18 month follow-up. The results are indicative of both short and long term benefit. Efficacy studies suffer from the risk that participants could be unlike patients in routine practice. Computerised treatment automatically generates progress data and this makes studies of effectiveness in routine practice possible. While adherence in practice is lower than in the research trials, the benefits to completers are comparable to those seen in RCTs of the same course, in panic (Carlbring et al., 2001), generalised anxiety disorder (Mewton et al., 2012) depression (Christensen et al., 2014b), or social anxiety disorder (Williams, O'Moore, Mason, & Andrews, 2014), providing further support for the results in the efficacy trials.

The control group was usually a delayed treatment group in which there was no expectation that the delay before treatment would be beneficial. None involved a pill placebo. Nevertheless, the control group did improve – presumably a function of regression to the mean and the natural history of the disorders during the time on the wait list.

Participants showed high rates of satisfaction though only one third of studies measured this. There were acceptable levels of adherence to iCBT. At 6%–100%, the range was large, but only 10/50 trials reported adherence rates below 50%. Adherence in the iCBT and bibliotherapy conditions were comparable, and there was no significant difference between the iCBT and face to face CBT conditions. Although the data was sparse, it appears as though the therapist time required for face to face therapy was, as expected, significantly greater than for iCBT. There is a need for further research in this area, to establish the minimum amount of therapist time required for maximal benefit. This evidence supports the original claim that iCBT is efficacious and acceptable, and provides increased access to treatment for people suffering from anxiety and depression (Andrews et al., 2010).

Control group subgroup analyses showed that iCBT was more effective against waitlist control, versus care as usual. Care as usual has a more significant benefit than being on a waitlist for treatment (Williams & Andrews, 2013).

Risk of bias subgroup analyses showed that the effect size for studies with low bias was higher than those with unclear bias, although the effect size was still large in those with unclear bias.

5. Limitations

Studies variably measured changes in quality of life and disability (for e.g. reduction in work loss days (Mackenzie, Harvey, Mewton, & Andrews, 2014)) with improvement consistent with reduction in primary symptomatology. No systematic analyses of these data were performed.

The mean effect size, indicating the superiority of iCBT over the control group, was 0.80, NNT 2.34. The most common control group was waitlist, with a minority including CAU, informational controls or attention controls. There were no studies comparing iCBT with pill placebo, or iCBT with pharmacotherapy. The original meta-analysis mentioned that iCBT compared to waitlist control resulted in higher effect sizes than when compared to treatment as usual. This finding was confirmed by our results, in which the effect size for studies compared to CAU was 0.38, versus 0.90 against a waitlist control. The lack of comparisons with medication is a serious weakness of the field, for many clinicians will not see iCBT as a bona fide treatment until such comparisons are available. There are three difficulties in doing such research. First, it is not in the interests of pharmaceutical companies to fund or to supply medication for such research. Second, people recruited for a drug trial have to be able to attend the investigators whereas applicants for iCBT trials can live far away, and third, applicants for iCBT trials appear to have a strong aversion to being randomised to medication (Christensen et al., 2014b).

There is evidence, as explained above, that there was no significant difference between iCBT and bibliotherapy in three studies. If the bibliotherapy used is of a high standard this is unsurprising, given the same material is learned − be it from a screen or from a book − it should affect the disorder in a similar manner.

The iCBT courses were diverse. The content varied according to diagnosis (transdiagnostic courses are the topic of a separate meta-analysis (Newby, Twomey et al., 2016)), but even within a diagnosis, the range of CBT topics differed. The form in which the information was presented also varied markedly, i.e. in the use of text, audio, video, cartoon story lines and in the emphasis on field assignments and the use of other supplementary material. The topic has grown to the point where individual iCBT courses should perhaps be treated differently, exactly as different SSRIs are analysed separately. For instance, there are eight trials of the ThisWayUp course for depression in this meta-analysis (mean between group ES = 1.21) (Choi et al., 2012; O'Moore et al., 2018; Perini et al., 2009; Rosso et al., 2017; Smith et al., 2017; Titov et al., 2010; Williams et al., 2013) and four trials of the Andersson depression course (Andersson, 2005; Johansson et al., 2012; Vernmark et al., 2010) (mean between group ES = 0.75). Differences between courses could be of interest.

The Agency for Healthcare Research and Quality have issued a

clinician advisory that in depression, the benefits of CBT and Medication are comparable (Agency for Healthcare Research and Quality, 2016). In other studies medications show a small superiority over CBT (0.34 for MDD 11 studies (Cuijpers & Cristea, 2015), 0.45 for anxiety disorders, 7 studies (Bandelow et al., 2015)). As there are serious side effects with medication, most clinical practice guidelines for anxiety and depressive disorders recommend use of CBT as the first line of treatment. In clinical practice, the number of prescriptions for medication exceed those for CBT because medication is easy to prescribe, relatively cheap, the quality is guaranteed and it is widely available − whereas a referral for face to face CBT means finding a therapist with vacancies, who costs no more than medication, and whose practice is quality assured. iCBT is different − it is easy to prescribe, costs the same as two months of medication, the quality is guaranteed and it is available wherever there is internet or phone access. We therefore contend that iCBT should the treatment of first choice anxiety or depression, used alone, or in combination with medication, as preferred by the patient.

In conclusion, the 64 identified iCBT trials generated large effect size superiority over control groups, with maintenance of benefit at follow-up, acceptable patient adherence and high rates of satisfaction and now with evidence of effectiveness in routine practice.

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