Computer-Assisted Cognitive-Behavior Therapy for Depression: A Systematic Review and Meta-Analysis

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ABSTRACT

Objective: To evaluate the efficacy of computer-assisted forms of cognitive-behavior therapy for major depressive disorder (MDD) and examine the role of clinician support and other factors that might affect outcomes.

Data sources: Ovid MEDLINE, PsycINFO, PubMed, and Scopus from their beginnings to July 18, 2016. Keywords were "*randomized, controlled trials of computer-assisted cognitive-behavior therapy for depression*" and "*randomized, controlled trials of mobile apps for cognitive-behavior therapy of depression*."

Study selection: Of 223 studies identified in the search, 183 were excluded yielding a sample of 40 randomized, controlled investigations of computer-assisted cognitive-behavior therapy (CCBT) for depression.

Data extraction: Data were abstracted independently by two authors, and consensus was reached by discussion with a third author.

Results: The overall mean effect size for CCBT compared to control conditions was $g = 0.502$, a moderately large effect. Studies that provided support from a clinician or other person yielded significantly larger effects ($g = 0.673$) than studies in which no support was provided ($g = 0.239$). Completion rate and study setting also influenced outcomes. Lower mean effect sizes were observed in studies with lower completion rates and in studies conducted in primary care practices.

Conclusions: CCBT with a modest amount of support from a clinician or other helping person was found to be efficacious with relatively large mean effect sizes on measures of depressive symptoms. Self-guided CCBT for depression was considerably less effective. Future research should focus on enhancing the implementation of CCBT, including evaluating the amount and type of support needed for effective delivery, methods to improve engagement with computer-assisted therapies, and ways to improve treatment outcome in primary care settings.

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Computer-assisted cognitive-behavior therapy (CCBT) was developed so evidence-based psychotherapy could be delivered to larger numbers of people and broader populations than may be possible with traditional face-to-face therapy.[1–10] Although standard cognitive-behavior therapy (CBT) has been shown to be an effective treatment for depression in many studies,[11–13] there are significant barriers to providing CBT for many people who could benefit from treatment. One of the problems that has limited broader dissemination of CBT is an insufficient number of trained therapists.[8] Other constraints may include the costs of treatment, the usual requirement for 12–20 hours of therapist time for standard CBT,[11–13] lack of access to therapy in rural areas or in other underserved populations, and reticence of people with depression to seek out and accept treatment in clinical settings.[1–4,14,15]

From the beginning of research on CCBT for depression in the late 1980s, reducing cost and improving availability of treatment have been overarching goals.[1–10,16] Other potential contributions of CCBT may be the ability to deliver a consistent therapeutic program on the basics of CBT to each user, enhancement of the therapy experience by offering multimedia learning opportunities, access to therapy at any time or location users may choose, use of interactive learning exercises that build CBT skills, provision of regular feedback to users, promotion of CBT homework completion, and data recording and management.[1,3,5,17]

The majority of studies of CCBT have employed hybrid treatment delivery methods that combine computerized delivery of skill building modules for CBT with clinician support (usually in the range of 1–5 hours).[3,18–39] A smaller number of investigations have used CCBT as a stand-alone treatment method with no clinician support[40–53] or have not provided information on involvement of therapists or other helping persons in treatment.[54–56]

Previous meta-analyses of CCBT[5–8,10] have found evidence for the efficacy of CCBT. However, these reports have not included many

Clinical Points

- Computer-assisted cognitive-behavior therapy (CCBT) offers clinicians the opportunity to leverage their time with patients. By using technology to increase the efficiency of their work, they can deliver evidence-based care to more patients than would be possible with standard cognitive-behavior therapy (CBT).
- Because CCBT programs are designed to offer interactive learning experiences, clinicians can use these programs to help patients build CBT skills for depression.
- By promoting self-help between sessions, CCBT has potential for augmenting the learning process and encouraging application of CBT principles in daily life.

recent trials assessed in the current analysis and often have utilized studies with mixed diagnostic groups. With a greater number of studies now available, it is now possible to more fully assess the importance of human support and other potential moderators of outcomes in CCBT. The aims of the present meta-analysis are to assess the efficacy of CCBT for depression in randomized controlled trials, examine the association between clinician or other helping person involvement in CCBT and outcome, explore other possible treatment moderators (eg, completion rate, study setting, pretreatment severity), and evaluate progress and limitations in CCBT research that may influence adoption of CCBT to address treatment delivery problems.

METHODS

Selection of Randomized Controlled Trials

A computerized search for studies meeting the criteria below was conducted using Ovid MEDLINE, PsycINFO, PubMed, and Scopus from their beginnings to July 18, 2016. The computerized search used the keywords "*randomized, controlled trials of computer-assisted cognitive-behavior therapy for depression*" and "*randomized, controlled trials of mobile apps for cognitive-behavior therapy of depression*." A manual search using other meta-analyses and published reports of CCBT[5–10] also was performed.

The criteria for including studies in the meta-analysis were as follows: (1) the study was a randomized controlled trial (RCT) with control group (ie, wait list, attention control, or treatment as usual) other than standard face-to-face CBT; (2) subjects were depressed as measured by depression rating scales; (3) inclusion criteria specified for depression (ie, clinical diagnosis of depression, diagnosis with standardized assessment [eg, *DSM-IV*,[57] SCID,[58] MINI[59]; see Table 1 for listing and full names of all diagnostic instruments and measures], or assessment with validated measure for depressive symptoms and appropriate cutoff score [eg, PHQ-9,[60] BDI,[61] HDRS,[62] CES-D[63]); (4) participants were 16 years of age or older; (5) the study involved use of a computer program or mobile app that covers core methods of CBT to deliver all or part of the treatment; and (6) the study reported posttreatment mean scores with standard deviation using a psychometrically valid depression rating scale (eg, PHQ-9, BDI, HDRS, CES-D).

Data Extraction

Data were extracted independently by 2 authors (J.H.W., D.R.) and then finalized by discussion with an additional author (M.E.T.) leading to consensus. Extracted data included number of subjects; subject recruitment method (eg, clinical population with advertisements, online only, nonclinical population with advertisements/announcements); type of control group (eg, wait list, attention control, psychoeducational website, treatment as usual); control of other treatments (eg, not controlled, drug-free, no other CBT or psychotherapy allowed); inclusion criteria for depression (eg, *DSM-IV* diagnosis on SCID[58] or other clinical interview, cutoff score on self-report depression scale); type of CCBT program (eg, text, multimedia); pre- and posttreatment means and standard deviations on standard depression rating scale; time spent by clinician or other helping person in treatment/support of CCBT; type of support provided (eg, face-to-face, e-mail or other online asynchronous communication, telephone); treatment completion rate; treatment setting (primary care or non–primary care); and weeks of follow-up data after study completion. When data were not available (eg, pre- and posttreatment means and standard deviations on standard depression rating scale, time spent by clinician or other helping person, intent-to-treat data), corresponding authors of studies were contacted to request these data.

Assessment of Study Integrity/Bias

To assess study quality, we employed the CLEAR NPT,[69] a checklist developed to evaluate reports of nonpharmacological, randomized clinical trials. The CLEAR NPT contains 10 questions, most of which are answered "yes," "no," or "unclear." Question items address the adequacy of the randomization process; how well details of the interventions were described; the degree of care provider experience or skill; whether and how well adherence to treatment protocols was measured; whether caretakers, participants undergoing treatments, and outcome evaluators were or could be blinded and provisions taken if not; the consistency across treatment conditions of follow-up assessments; and whether the intent-to-treat (ITT) principle was followed in conducting analyses. Two of the study authors (T.D.E. and G.K.B.) independently evaluated each study using the CLEAR NPT criteria. Ratings were subsequently compared, and differences were reconciled through discussion leading to consensus.

Statistical Methods

To determine the efficacy of CCBT versus control conditions, we used the DerSimonian-Laird method for the random effect models. We calculated the effect sizes with Hedge's *g*,[70] which is the difference in means at posttreatment or follow-up divided by the pooled standard deviation of both conditions as the estimate of variance. The primary measure of depression was used for these calculations. For

Table 1. Selected Characteristics of Studies of CCBT for Depression

Authors	Subjects, N	Control	Depression Inclusion Criteria	CCBT Program	Name of Computer Program	Support Time	Type of Support	Completion Rate	Setting
Selmi et al 1990[54]	36	Wait list, CBT	Research Diagnostic Criteria	Text, 6 lessons, 6 wk	NR	NR	NR	100%	Non–primary care
Clarke et al 2002[40]	223	TAU	Chart diagnosis of depression	Text, 32 wk, access to website	Odin	0	None	NR	Non–primary care
Proudfoot et al 2004[55]	274	TAU	CIS-R ≥ 12	Multimedia, 8 lessons, 9 wk	Beating the Blues	NR	NR	78%	Primary care
Clarke et al 2005[41]	200	TAU	Chart diagnosis of depression	Text, 16 wk, access to website	NR	0	None	NR	Non–primary care
Wright et al 2005[3]	45	Wait list, CBT	SCID *DSM-IV* MDD	Multimedia, 9 lessons, 8 wk	Good Days Ahead	250 min	Face-to-face	87%	Non–primary care
Spek et al 2007[5]	291	Wait list, group CBT	EPDS ≥ 12 No MDD	Text, 8 lessons, 8 wk	NR	0	NR	48%	Non–primary care
Warmerdam et al 2008[18]	263	Wait list, PST	CES-D ≥ 16	Text, 9 lessons, 12 wk	Coping with Depression	160 min	E-mail	52%	Non–primary care
Clarke et al 2009[43]	109	TAU	Chart diagnosis of depression	Text, 32 wk, access to website	NR	0	None	NR	Non–primary care
Perini et al 2009[19]	45	Wait list	MINI *DSM-IV* MDD	Text, 6 lessons, 8 wk	Sadness Program	111 min	E-mail, online discussion forum	74%	Non–primary care
Ruwaard et al 2009[20]	54	Wait list	BDI ≥ 10	Text	NR	7–14 h	E-mail	92%	Non–primary care
Titov et al 2010[21]	141	Wait list	SCID *DSM-IV* MDD	Text, 6 lessons, 8 wk	Sadness Program	60 min	Telephone, e-mail	70%	Non–primary care
Vernmark et al 2010[22]	88	Wait list, online CBT	SCID *DSM-IV* MDD	Text, 7 lessons, 8 wk	NR	53 min	E-mail	NR	Non–primary care
Berger et al 2011[23]	76	Wait list	MINI *DSM-IV* MDD Dysthymia	Multimedia, 11 lessons, 10 wk	Deprexis	Unsupported (0 min) or Supported (140 min)	NR	Unsupported 36% Supported 56%	Non–primary care
Cooper et al 2011[44]	24	TAU	BDI-II ≥ 14	Multimedia, 8 lessons, 8 wk	Beating the Blues	0	NR	75%	Non–primary care
Farrer et al 2011[24]	155	TAU	KPDS ≥ 22	Multimedia, 5 lessons, 6 wk	MoodGym and Blue Pages	60 min	Telephone	17.8%	Non–primary care
Holländare et al 2011[25]	84	Wait list	MADRS (7–19) No current MDD	Text, 16 Lessons, 10 wk	NR	150 min	E-mail	26.2%	Non–primary care
Titov et al 2011[26]	77	Wait list	MINI *DSM-IV* MDD	Text, 8 lessons, 10 wk	Well-being Program	85 min	Telephone	81%	Non–primary care
van Bastelaar et al 2011[27]	255	Wait list	CES-D ≥ 16	Multimedia, 8 lessons, 14 wk	NR	160–240 min	NR	42.4%	Non–primary care
Choi et al 2012[28]	55	Wait list	SCID *DSM-IV* MDD + subclinical depression	Text, 6 lessons, 8 wk	Sadness Program	97 min	Telephone, e-mail	68%	Non–primary care
Sheeber et al 2012[29]	70	Wait list	CES-D ≥ 21	Multimedia, 8 lessons, 14 wk	Mom-Net	124 min	Face-to-face plus telephone	97.1%	Non–primary care
van der Zanden et al 2012[30]	244	Wait list	CES-D ≥ 10	Text and images, 6 lessons, 6 wk	Master Your Mood	540 min	Chat room texts	20%	Non–primary care
Carlbring et al 2013[31]	80	Wait list	SCID *DSM-IV* MDD	Multimedia, 7 lessons, 8 wk	Depression-Shjälpen	94.8 min	E-mail	27.5%	Non–primary care
Glozier et al 2013[45]	562	Attention control, psychoeducational website	PHQ-9 ≥ 8	Multimedia, 12 lessons, 12 wk	e-couch	0	None	62%	Non–primary care
Høifødt et al 2013[32]	106	Wait list	BDI-II 10–40	Multimedia, 5 lessons, 7 wk	MoodGym	70–506 min	Face-to-face and e-mail	60%	Primary care

(continued)

Table 1 (cont).

Authors	Subjects, N	Control	Depression Inclusion Criteria	CCBT Program	Name of Computer Program	Support Time	Type of Support	Completion Rate	Setting
Lintvedt et al 2013[46]	163	Wait list	KPDS ≥ 20	Multimedia, 5 lessons, 5 wk	MoodGym and Blue Pages	0	None	NR	Non–primary care
Mohr et al 2013[33]	101	Wait list	QIDS > 10	Multimedia, 18 lessons, 12 wk	Mood Manager and Telecoach	60–120 min	Telephone	NR	Primary care
Williams and Andrews, 2013[56]	69	Wait list	MINI *DSM-IV* MDD	6 lessons, 10 wk	Sadness Program	NR	Telephone, e-mail	50%	Non–primary care
Kivi et al 2014[35]	90	TAU	MINI *DSM-IV* MDD	Multimedia, 7 lessons, 12 wk	Depression-Shjälpen	180 min	Telephone and online	56%	Primary care
Phillips et al 2014[48]	637	TAU	PHQ-9 ≥ 2 on ≥ 5 items	Multimedia, 5 lessons, 12 wk	MoodGym	0	None	NR	Non–primary care
Buhrman et al 2015[34]	52	Online discussion group	MADRS ≥ 10	Text with images, 8 lessons, 8 wk	NR	200 min	E-mail	44.4%	Non–primary care
Meyer et al 2015[47]	163	TAU	PHQ-9 ≥ 15	Multimedia + daily texts, 3 mo	Deprexis	0	None	80%	Non–primary care
Buntrock et al 2015[36]	406	TAU	CES-D ≥ 16 MDD excluded	Multimedia, 6 lessons, 6 wk	GET.ON Mood Enhancer	120 min	E-mail	NR	Non–primary care
Gilbody et al 2016[50]	691	TAU	PHQ-9 ≥ 10	Multimedia, 8 lessons w/Beating the Blues or 6 lessons w/Mood Gym, 4 mo	Beating the Blues and MoodGym	< 7 min	Technical support with e-mail reminders	16%–18%	Primary care
Milgrom et al 2016[37]	43	TAU	SCID *DSM-IV* MDD	Multimedia, 6 lessons, 12 wk	MumMood Booster	129 min	Telephone	86%	Non–primary care
Richards et al 2015[39]	96	Wait list	BDI-II 14–29	Multimedia, 7 lessons, 8 wk	Space from Depression	75–105 min	E-mail	38%	Non–primary care
Roepke et al 2015[53]	283	Wait list	CES-D ≥ 16	Mobile app or PC with gaming, daily, 4 wk	SuperBetter	Clinician support (0 min), Tech support (NR)	Technical support, online forum, Facebook	NR	Non–primary care
Pugh et al 2016[38]	50	Wait list	EPDS ≥ 10	Multimedia, 7 lessons, 7–10 wk	Maternal Depression Online	105–200 min	Telephone, e-mail	70%	Non–primary care
Birney et al 2016[49]	300	Education website	PHQ-9 9–19	Mobile app, 6 wk	MoodHacker	0	None	NR	Non–primary care
Hobfoll et al 2016[51]	201	TAU	CES-D ≥ 10	Multimedia, 7 lessons, 6 wk	Vets Prevail	Clinician support (0 min), Peer support (NR)	Peer support, chat online	73%	Non–primary care
Montero-Marin et al 2016[52]	296	TAU	MINI MDD BDI-II 14–28	Multimedia, 10 lessons, 3 mo	Smiling is Fun	0	E-mail: 17 sent to 13 patients	50%	Primary care

Abbreviations: BDI = Beck Depression Inventory,[61] BDI-II = Beck Depression Inventory-2nd Edition, CBT = cognitive-behavior therapy, CCBT = computer-assisted cognitive-behavior therapy, CES-D = Center for Epidemiologic Studies Depression Scale,[63] CIS-R = Clinical Interview Schedule-Revised,[64] EPDS = Edinburgh Postnatal Depression Scale,[65] HDRS = Hamilton Depression Rating Scale,[62] KPDS = Kessler Psychological Distress Scale (K10),[66] MADRS = Montgomery-Asberg Depression Rating Scale,[67] MDD = major depressive disorder, MINI = Mini-International Neuropsychiatric Interview,[59] NR = not reported, PHQ-9 = 9-item Patient Health Questionnaire,[60] PST = problem-solving therapy, QIDS = Quick Inventory of Depressive Symptomatology,[68] SCID = Structured Clinical Interview for *DSM-IV-TR* Axis I Disorders–Patient Edition,[58] TAU = treatment as usual.

some studies (see footnotes in Figure 1), there were multiple comparisons (eg, multiple versions of CCBT or methods of delivery of CCBT vs control conditions); thus, a total of 45 comparisons were made. For the follow-up analysis, we first examined the initial follow-up assessment time point, regardless of timing. The range of time elapsed before the first follow-up assessment was 4 weeks to 6 months, and the longest period of follow-up was 15 months. In addition, we aggregated all of the follow-up assessments per study in order to capture the overall effects of CCBT over time. We used random effects estimates to better generalize beyond the participants in these studies. The heterogeneity of the effects was examined with Q tests and I^2 statistics. We also examined funnel plots to assess symmetry in the findings across studies, and we conducted trim-and-fill analyses to further examine the robustness of the findings.[70]

We tested several potential moderators: (*a*) supported CCBT versus self-guided CCBT; (*b*) completion rates; (*c*) primary care studies versus non–primary care studies; and (*d*) pretreatment severity. For the pretreatment severity moderator analysis, we converted depression rating scales scores to *z*-scores based on norming information for the various measures. The moderator analysis of pretreatment depressive symptom severity required use of a transformation because several different scales were used across the studies. As these highly correlated dependent measures are not usually markedly skewed at pretreatment, we transformed raw scores to *z*-scores instead of a logarithmic transformation.[71]

RESULTS

The electronic search yielded 208 publications; an additional 15 articles were identified from a manual search. Of these 223 publications, 183 were excluded (See PRISMA diagram in Supplementary Figure 1). Principal reasons for exclusion were not an RCT = 60; RCT with active therapy (eg, standard CBT or another psychotherapy) as only control = 9; participants were not depressed = 31; no inclusion criteria for depression = 11; mixed sample including stress and anxiety = 2; participants were less than 16 years of age = 13; did not use computer-delivered therapy = 11; did not use CBT = 4; posttreatment means/SDs with standard depression rating scale were not reported or could not be obtained via author contact = 11; no ITT analysis = 9; duplicate (follow-up or other report on principal study found elsewhere in search) = 22. A total of 40 reports were eligible for inclusion in the meta-analysis. Key characteristics of these studies are shown in Table 1.

A forest plot for the posttreatment effects and 95% confidence intervals, along with numerical effect sizes for each comparison, is displayed in Figure 1. The random effects weighted mean effect size for CCBT versus controls at posttreatment was $g = 0.502$ (SE = 0.057; 95% CI, 0.390 to 0.614; $P < .001$). This effect is moderate to large; however, there was significant heterogeneity in the effects ($Q_{44} = 222.53$, $P < .001$, $I^2 = 80.23$). Examination of the funnel plot (see Appendix 1) of standard errors for posttreatment effects revealed inconsistencies, and the Egger test of asymmetry was significant (intercept = 3.50, SE = 0.615, $P < .001$). A Duval and Tweedie trim-and-fill analysis yielded 13 studies that could have affected the overall g by 0.16. The collective results of these bias tests suggest heterogeneity of studies and the possibility of clinically meaningful moderators of treatment effect.

Follow-Up Analysis

Data were reported for follow-up assessments for CCBT and control conditions (other than standard CBT or other specific active treatment) in 19 of 45 comparisons. The majority of follow-up assessments were performed in comparisons of unsupported CBT (13 of 18). Only 6 of 24 comparisons of supported CBT versus control conditions provided follow-up measures, most likely due to a preponderance of wait-list control groups in these studies. We first examined mean effects based on the initial follow-up assessment time point, regardless of the timing of the follow-up (see Supplementary Figure 2). The random-effects weighted mean effect size for CCBT versus controls at the first follow-up assessment points was $g = 0.386$ (SE = 0.091; 95% CI, 0.207 to 0.565; $P < .001$). There was significant heterogeneity in the effects ($Q_{19} = 124.89$, $P < .001$, $I^2 = 84.79$). We also aggregated the follow-up assessment time points, and the results were similar. The random-effects weighted mean effect size for CCBT versus controls at the aggregated follow-up assessment points was $g = 0.354$ (SE = 0.084; 95% CI, 0.190 to 0.518; $P < .001$).

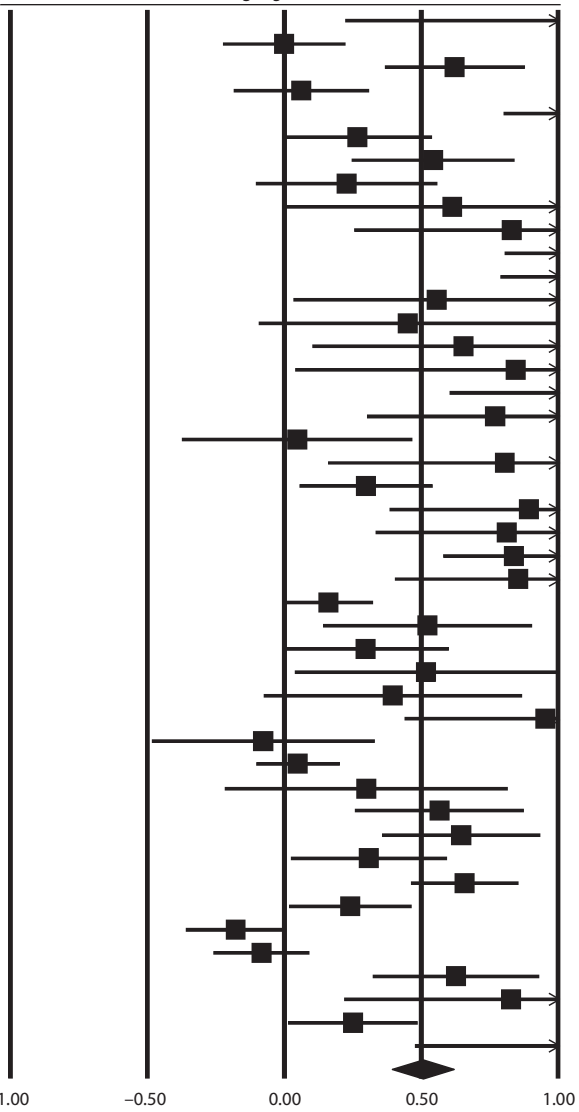
Moderators

Support. We tested whether studies with support from a clinician or other helping person differed from those without any significant support (Figure 2). Among the studies listed in Figure 2, a few provided such minimal support (ie, Gilbody et al[50] reported a mean of less than 7 minutes of technical support via telephone for the entire course of treatment, and Montero-Marín et al[52] sent a total of 17 e-mail messages to 13 of 296 patients) that we considered them to be self-guided CCBT. Also, we found 3 studies[21,24,39] that either compared clinician with technician support or used nonclinicians to provide support. These were included in the category of supported studies. The random-effects weighted mean effect size for clinician or other helping person supported studies was $g = 0.673$ (SE = 0.065; 95% CI, 0.546 to 0.801; $P < .001$). By contrast, CCBT studies that did not include support had a random-effects weighted mean effect size at posttreatment of $g = 0.239$ (SE = 0.063; 95% CI, 0.115 to 0.364; $P < .001$). Thus, studies that had clinician or other helping person support outperformed those without such support by a large margin. An effect size difference of 0.43 on the Hamilton Depression Rating Scale, for example, would correspond to about a 15% difference in response or remission rates.[72]

We also compared the type of clinician support: e-mail (without or with text messaging or other asynchronous online support) versus telephone (without or with e-mail, text messaging, or other asynchronous online support)

Figure 1. Posttreatment Effect Sizes for CCBT Versus Control Condition*

Study	Hedges *g*	Standard Error	Variance	95% CI Lower Limit	95% CI Upper Limit	*Z* Value	*P* Value
Selmi et al 1990	1.046	0.422	0.178	0.219	1.874	2.479	.013
Clarke et al 2002	0.000	0.115	0.013	−0.226	0.226	0.000	1.000
Proudfoot et al 2004	0.623	0.132	0.017	0.364	0.881	4.727	.000
Clarke et al 2005	0.062	0.128	0.016	−0.189	0.313	0.484	.629
Wright et al 2005	1.603	0.411	0.169	0.797	2.409	3.899	.000
Spek et al 2007	0.267	0.141	0.020	−0.009	0.543	1.894	.058
Warmerdam et al 2008	0.543	0.153	0.024	0.243	0.844	3.545	.000
Clarke et al 2009	0.228	0.171	0.029	−0.107	0.562	1.333	.183
Perini et al 2009	0.614	0.311	0.097	0.004	1.223	1.974	.048
Ruwaard et al 2009	0.831	0.296	0.087	0.252	1.410	2.812	.005
Titov et al 2010[a]	1.262	0.235	0.055	0.801	1.722	5.372	.000
Titov et al 2010[b]	1.258	0.241	0.058	0.786	1.731	5.215	.000
Vernmark et al 2010	0.557	0.269	0.072	0.030	1.084	2.070	.038
Berger et al 2011[a]	0.451	0.279	0.078	−0.097	0.998	1.613	.107
Berger et al 2011[c]	0.654	0.283	0.080	0.099	1.209	2.309	.021
Cooper et al 2011	0.845	0.413	0.170	0.037	1.654	2.049	.041
Farrer et al 2011[a]	1.068	0.239	0.057	0.600	1.536	4.475	.000
Farrer et al 2011[c]	0.770	0.240	0.058	0.299	1.241	3.204	.001
Holländare et al 2011	0.047	0.216	0.047	−0.377	0.471	0.219	.827
Titov et al 2011	0.805	0.331	0.110	0.156	1.455	2.432	.015
van Bastelaar et al 2011	0.298	0.126	0.016	0.052	0.544	2.374	.018
Choi et al 2012	0.893	0.261	0.068	0.381	1.406	3.419	.001
Sheeber et al 2012	0.813	0.246	0.061	0.330	1.296	3.302	.001
van der Zanden et al 2012	0.838	0.133	0.018	0.577	1.099	6.292	.000
Carlbring et al 2013	0.855	0.232	0.054	0.401	1.308	3.691	.000
Glozier et al 2013	0.161	0.084	0.007	−0.004	0.327	1.912	.056
Høifødt et al 2013	0.523	0.196	0.038	0.139	0.908	2.667	.008
Lintvedt et al 2013	0.297	0.157	0.025	−0.010	0.604	1.893	.058
Mohr et al 2013[a]	0.517	0.246	0.060	0.036	0.999	2.107	.035
Mohr et al 2013[c]	0.396	0.242	0.059	−0.078	0.871	1.637	.102
Williams and Andrews 2013	0.953	0.264	0.070	0.435	1.472	3.606	.000
Kivi et al 2014	−0.077	0.209	0.044	−0.487	0.333	−0.367	.713
Phillips et al 2014	0.050	0.079	0.006	−0.106	0.205	0.626	.532
Buhrman et al 2015	0.299	0.265	0.070	−0.220	0.819	1.130	.259
Meyer et al 2015	0.567	0.159	0.025	0.255	0.879	3.561	.000
Richards et al 2015	0.646	0.149	0.022	0.354	0.938	4.332	.000
Roepke et al 2015	0.309	0.147	0.022	0.021	0.597	2.103	.035
Buntrock et al 2015	0.658	0.102	0.010	0.459	0.858	6.472	.000
Birney et al 2016	0.241	0.116	0.013	0.015	0.468	2.087	.037
Gilbody et al 2016[BB]	−0.178	0.095	0.009	−0.363	0.008	−1.879	.060
Gilbody et al 2016[MG]	−0.083	0.091	0.008	−0.262	0.095	−0.915	.360
Hobfell et al 2016	0.627	0.157	0.025	0.320	0.934	4.002	.000
Milgrom et al 2016	0.829	0.313	0.098	0.216	1.441	2.651	.008
Montero-Marin et al 2016	0.251	0.122	0.015	0.011	0.491	2.048	.041
Pugh et al 2016	1.058	0.298	0.089	0.474	1.641	3.552	.000
Total	0.502	0.057	0.003	0.390	0.614	8.762	.000



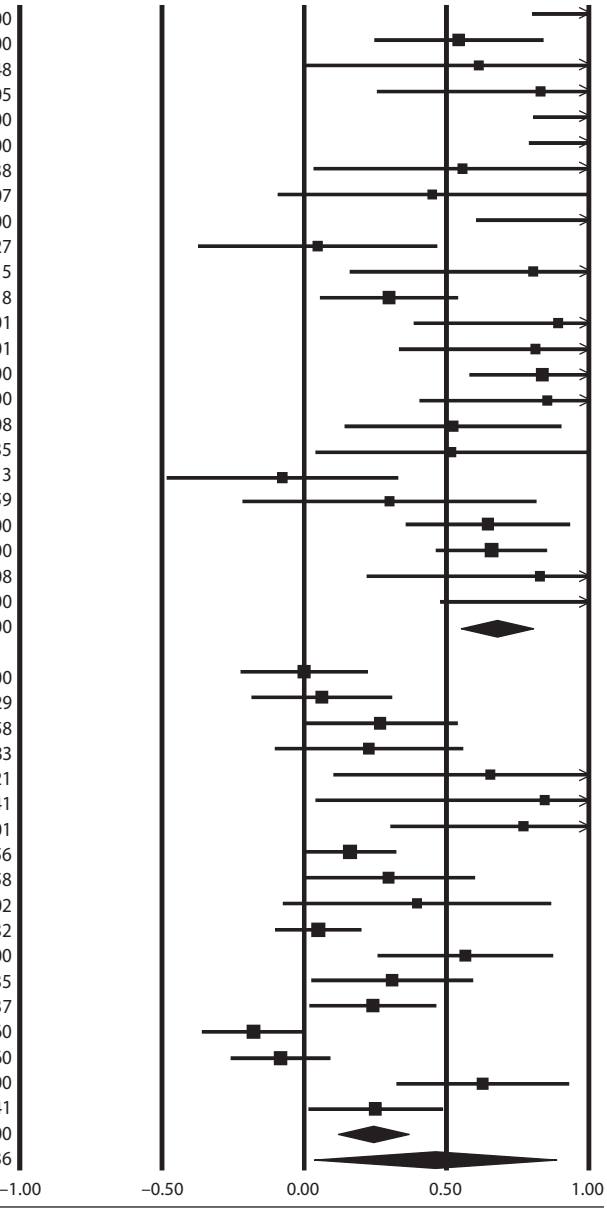
[a]Clinician-assisted CCBT. [b]Technician-assisted CCBT. [c]Unsupported CCBT.
*References to the studies are listed in Table 1.
Abbreviations: BB = Beating the Blues, CCBT = computer-assisted cognitive-behavior therapy, MG = MoodGym.

versus in person (See Supplementary Figure 3). The random-effects weighted mean effect size at posttreatment was lowest for e-mail (without or with text messaging or other asynchronous online support) (n = 9; $g = 0.562$; SE = 0.107; 95% CI, 0.353 to 0.938; $P < .001$), intermediate for telephone (without or with e-mail, text messaging, or other asynchronous online support) (n = 9; $g = 0.782$; SE = 0.114; 95% CI, 0.558 to 1.006; $P < .001$), and largest when face-to-face person support was provided (n = 3; $g = 0.833$ SE = 0.207; 95% CI, 0.427 to 1.24; $P < .001$).

Completion rate. We separated completion rates into quartiles for simplicity and also calculated mean effect sizes for studies that did not report the percentage of patients who completed treatment (Figure 3). The lowest random-effects weighted mean effect size ($g = 0.293$; SE = 0.101; 95% CI, 0.095 to 0.492; $P = .004$) was found for investigations that did not report completion rate. Intermediate mean effect sizes were found for studies with less than 25% completion ($g = 0.410$; SE = 0.155; 95% CI, 0.107 to 0.714; $P = .008$) and for studies with 26%–50% completion rate at posttreatment ($g = 0.451$; SE = 0.122; 95% CI, 0.213 to 0.689; $P < .001$). For studies with 51%–75% completion rate, the random-effects weighted mean effect size at posttreatment was $g = 0.653$ (SE = 0.115; 95% CI, 0.428 to 0.878; $P < .001$). Lastly, the random effects weighted mean effect size for studies with 76%–100% completion rate at posttreatment was $g = 0.818$

Figure 2. Posttreatment Effect Sizes for CCBT Versus Control Condition: Supported Versus Unsupported Therapy*

Study	Hedges *g*	Standard Error	Variance	95% CI Lower Limit	95% CI Upper Limit	*Z* Value	*P* Value
Clinician-Supported CCBT							
Wright et al 2005	1.603	0.411	0.169	0.797	2.409	3.899	.000
Warmerdam et al 2008	0.543	0.153	0.024	0.243	0.844	3.545	.000
Perini et al 2009	0.614	0.311	0.097	0.004	1.223	1.974	.048
Ruwaard et al 2009	0.831	0.296	0.087	0.252	1.410	2.812	.005
Titov et al 2010[a]	1.262	0.235	0.055	0.801	1.722	5.372	.000
Titov et al 2010[b]	1.258	0.241	0.058	0.786	1.731	5.215	.000
Vernmark et al 2010	0.557	0.269	0.072	0.030	1.084	2.070	.038
Berger et al 2011[a]	0.451	0.279	0.078	−0.097	0.998	1.613	.107
Farrer et al 2011[a]	1.068	0.239	0.057	0.600	1.536	4.475	.000
Holländare et al 2011	0.047	0.216	0.047	−0.377	0.471	0.219	.827
Titov et al 2011	0.805	0.331	0.110	0.156	1.455	2.432	.015
van Bastelaar et al 2011	0.298	0.126	0.016	0.052	0.544	2.374	.018
Choi et al 2012	0.893	0.261	0.068	0.381	1.406	3.419	.001
Sheeber et al 2012	0.813	0.246	0.061	0.330	1.296	3.302	.001
van der Zanden et al 2012	0.838	0.133	0.018	0.577	1.099	6.292	.000
Carlbring et al 2013	0.855	0.232	0.054	0.401	1.308	3.691	.000
Høifødt et al 2013	0.523	0.196	0.038	0.139	0.908	2.667	.008
Mohr et al 2013[a]	0.517	0.246	0.060	0.036	0.999	2.107	.035
Kivi et al 2014	−0.077	0.209	0.044	−0.487	0.333	−0.367	.713
Buhrman et al 2015	0.299	0.265	0.070	−0.220	0.819	1.130	.259
Richards et al 2015	0.646	0.149	0.022	0.354	0.938	4.332	.000
Buntrock et al 2015	0.658	0.102	0.010	0.459	0.858	6.472	.000
Milgrom et al 2016	0.829	0.313	0.098	0.216	1.441	2.651	.008
Pugh et al 2016	1.058	0.298	0.089	0.474	1.641	3.552	.000
Total	0.673	0.065	0.004	0.546	0.801	10.385	.000
Unsupported CCBT							
Clarke et al 2002	0.000	0.115	0.013	−0.226	0.226	0.000	1.000
Clarke et al 2005	0.062	0.128	0.016	−0.189	0.313	0.484	.629
Spek et al 2007	0.267	0.141	0.020	−0.009	0.543	1.894	.058
Clarke et al 2009	0.228	0.171	0.029	−0.107	0.562	1.333	.183
Berger et al 2011[c]	0.654	0.283	0.080	0.099	1.209	2.309	.021
Cooper et al 2011	0.845	0.413	0.170	0.037	1.654	2.049	.041
Farrer et al 2011[c]	0.770	0.240	0.058	0.299	1.241	3.204	.001
Glozier et al 2013	0.161	0.084	0.007	−0.004	0.327	1.912	.056
Lintvedt et al 2013	0.297	0.157	0.025	−0.010	0.604	1.893	.058
Mohr et al 2013[c]	0.396	0.242	0.059	−0.078	0.871	1.637	.102
Phillips et al 2014	0.050	0.079	0.006	−0.106	0.205	0.626	.532
Meyer et al 2015	0.567	0.159	0.025	0.255	0.879	3.561	.000
Roepke et al 2015	0.309	0.147	0.022	0.021	0.597	2.103	.035
Birney et al 2016	0.241	0.116	0.013	0.015	0.468	2.087	.037
Gilbody et al 2016[BB]	−0.178	0.095	0.009	−0.363	0.008	−1.879	.060
Gilbody et al 2016[MG]	−0.083	0.091	0.008	−0.262	0.095	−0.915	.360
Hobfell et al 2016		0.157	0.025	0.320	0.934	4.002	.000
Montero-Marin et al 2016	0.251	0.122	0.015	0.011	0.491	2.048	.041
Total	0.239	0.063	0.004	0.115	0.364	3.776	.000
Overall	0.456	0.217	0.047	0.031	0.882	2.102	.036



[a]Clinician-assisted CCBT. [b]Technician-assisted CCBT. [c]Unsupported CCBT.
*References to the studies are listed in Table 1. The studies by Selmi et al, Proudfoot et al, and Williams and Andrews are not included in this analysis because they did not report time of type of support and thus could not be used in a comparison of supported vs unsupported therapy.
Abbreviations: BB = Beating the Blues, CCBT = computer-assisted cognitive-behavior therapy, MG = MoodGym.

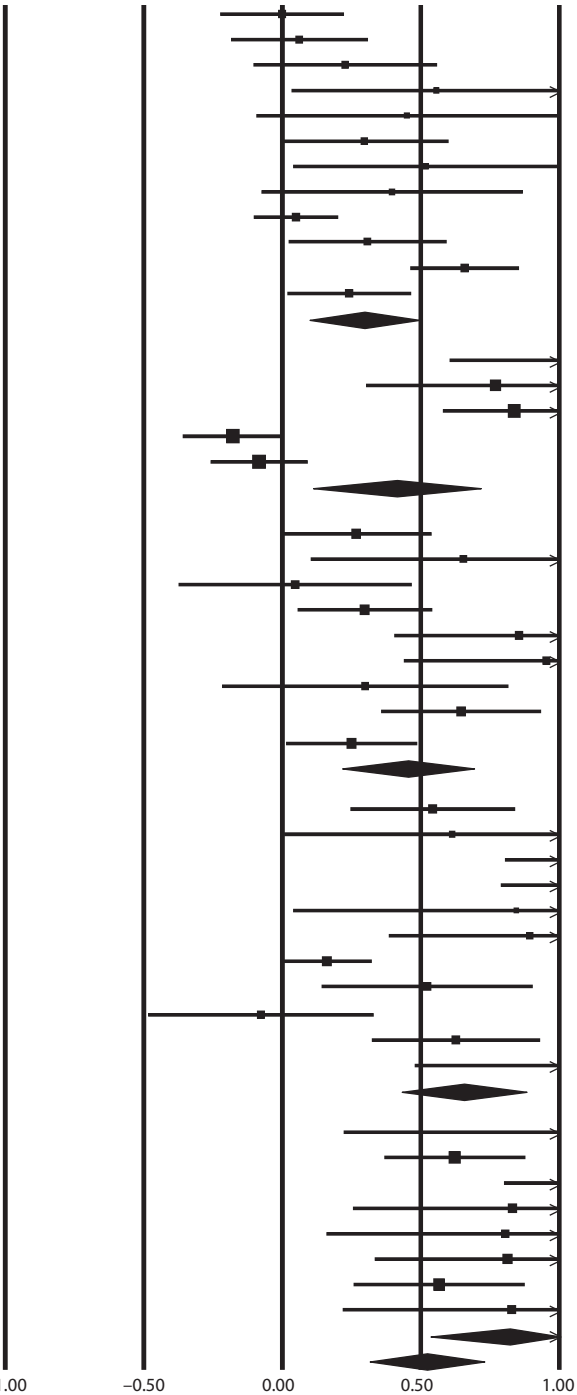
(SE = 0.146; 95% CI, 0.532 to 1.103; $P < .001$). Thus, higher completion rates were associated with larger mean effect sizes.

Primary care. We tested whether the outcomes of studies of CCBT in primary care differed from the other studies. An earlier report[73] had found a random-effects weighted mean effect size for CCBT for depression in primary care that appeared to be lower than reported effect sizes in broader populations. The random-effects weighted mean effect size for the primary care studies at posttreatment was $g = 0.224$ (SE = 0.123; 95% CI, −0.012 to 0.464; $P = .068$). In contrast, studies that were not conducted in primary care sites had a significantly higher random-effects weighted mean effect size at posttreatment of $g = 0.565$ (SE = 0.061; 95% CI, 0.445 to 0.685; $P < .001$). See Supplementary Figure 4 for a forest plot of these mean effect sizes.

Pretreatment severity. The random-effects weighted mean effect size for studies with higher pretreatment severity

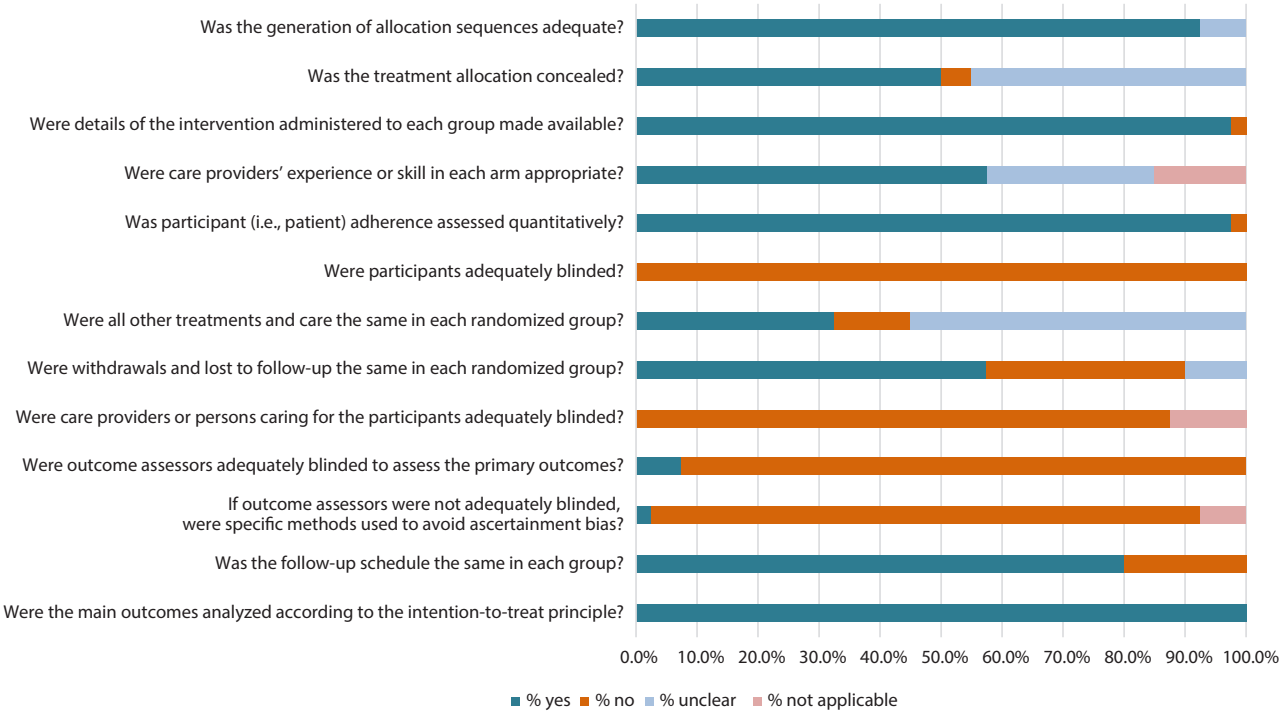
Figure 3. Posttreatment Effect Sizes for CCBT Versus Control Condition: Influence of Completion Rate*

Study	Hedges *g*	Standard Error	Variance	95% CI Lower Limit	95% CI Upper Limit	*Z* Value	*P* Value
Approximate Completion Rate Not Reported							
Clarke et al 2002	0.000	0.115	0.013	−0.226	0.226	0.000	1.000
Clarke et al 2005	0.062	0.128	0.016	−0.189	0.313	0.484	.629
Clarke et a 2009	0.228	0.171	0.029	−0.107	0.562	1.333	.183
Vernmark et al 2010	0.557	0.269	0.072	0.030	1.084	2.070	.038
Berger et al 2011[a]	0.451	0.279	0.078	−0.097	0.998	1.613	.107
Lintvedt et al 2013	0.297	0.157	0.025	−0.010	0.604	1.893	.058
Mohr et al 2013[a]	0.517	0.246	0.060	0.036	0.999	2.107	.035
Mohr et al 2013[c]	0.396	0.242	0.059	−0.078	0.871	1.637	.102
Phillips et al 2014	0.050	0.079	0.006	−0.106	0.205	0.626	.532
Roepke et al 2015	0.309	0.147	0.022	0.021	0.597	2.103	.035
Buntrock et al 2015	0.658	0.102	0.010	0.459	0.858	6.472	.000
Birney et al 2016	0.241	0.116	0.013	0.015	0.468	2.087	.037
Total	0.293	0.101	0.010	0.095	0.492	2.899	.004
Completion Rate 0%–25%							
Farrer et al 2011[a]	1.068	0.239	0.057	0.600	1.536	4.475	.000
Farrer et al 2011[c]	0.770	0.240	0.058	0.299	1.241	3.204	.001
van der Zanden et al 2012	0.838	0.133	0.018	0.577	1.099	6.292	.000
Gilbody et al 2016[BB]	−0.178	0.095	0.009	−0.363	0.008	−1.879	.060
Gilbody et al 2016[MG]	−0.083	0.091	0.008	−0.262	0.095	−0.915	.360
Total	0.410	0.155	0.024	0.107	0.714	2.654	.008
Completion Rate 26%–50%							
Spek et al 2007	0.267	0.141	0.020	−0.009	0.543	1.894	.058
Berger et al 2011[c]	0.654	0.283	0.080	0.099	1.209	2.309	.021
Holländare et al 2011	0.047	0.216	0.047	−0.377	0.471	0.219	.827
van Bastelaar et al 2011	0.298	0.126	0.016	0.052	0.544	2.374	.018
Carlbring et al 2013	0.855	0.232	0.054	0.401	1.308	3.691	.000
Williams and Andrews 2013	0.953	0.264	0.070	0.435	1.472	3.606	.000
Buhrman et al 2015	0.299	0.265	0.070	−0.220	0.819	1.130	.259
Richards et al 2015	0.646	0.149	0.022	0.354	0.938	4.332	.000
Montero-Marin et al 2016	0.251	0.122	0.015	0.011	0.491	2.048	.041
Total	0.451	0.122	0.015	0.213	0.689	3.710	.000
Completion Rate 51%–75%							
Warmerdam et al 2008	0.543	0.153	0.024	0.243	0.844	3.545	.000
Perini et al 2009	0.614	0.311	0.097	0.004	1.223	1.974	.048
Titov et al 2010[a]	1.262	0.235	0.055	0.801	1.722	5.372	.000
Titov et al 2010[b]	1.258	0.241	0.058	0.786	1.731	5.215	.000
Cooper et al 2011	0.845	0.413	0.170	0.037	1.654	2.049	.041
Choi et al 2012	0.893	0.261	0.068	0.381	1.406	3.419	.001
Glozier et al 2013	0.161	0.084	0.007	−0.004	0.327	1.912	.056
Høifødt et al 2013	0.523	0.196	0.038	0.139	0.908	2.667	.008
Kivi et al 2014	−0.077	0.209	0.044	−0.487	0.333	−0.367	.713
Hobfell et al 2016	0.627	0.157	0.025	0.320	0.934	4.002	.000
Pugh et al 2016	1.058	0.298	0.089	0.474	1.641	3.552	.000
Total	0.653	0.115	0.013	0.428	0.878	5.683	.000
Completion Rate 76%–100%							
Selmi et al 1990	1.046	0.422	0.178	0.219	1.874	2.479	.013
Proudfoot et al 2004	0.623	0.132	0.017	0.364	0.881	4.727	.000
Wright et al 2005	1.603	0.411	0.169	0.797	2.409	3.899	.000
Ruwaard et al 2009	0.831	0.296	0.087	0.252	1.410	2.812	.005
Titov et al 2011	0.805	0.331	0.110	0.156	1.455	2.432	.015
Sheeber et al 2012	0.813	0.246	0.061	0.330	1.296	3.302	.001
Meyer et al 2014	0.567	0.159	0.025	0.255	0.879	3.561	.000
Milgrom et al 2016	0.829	0.313	0.098	0.216	1.441	2.651	.008
Total	0.818	0.146	0.021	0.532	1.103	5.610	.000
Overall	0.518	0.106	0.011	0.312	0.725	4.911	.000



[a]Clinician-assisted CCBT. [b]Technician-assisted CCBT. [c]Unsupported CCBT
*References to the studies are listed in Table 1.
Abbreviations: BB = Beating the Blues, CCBT = computer-assisted cognitive-behavior therapy, MG = MoodGym.

Figure 4. Summary of CLEAR Quality Ratings



(*z*-scores from 0.50 to 1.0, indicating higher severity) had a mean posttreatment effect size of $g = 0.865$ (SE = 0.160; 95% CI, 0.551 to 1.180; $P < .001$). The effect sizes for studies with lower severe pretreatment severity scores (*z*-scores less than 0.50) were generally in the moderate range ($g = 0.400$ to 0.481). See Supplementary Figure 5 for a forest plot of these data.

Assessment of Study Quality

As summarized in Figure 4 and detailed in Supplementary Table 1 (a display of quality ratings on all questions for each of the 40 studies in the meta-analysis), the methodological quality ratings were good in general. Ninety percent or more followed adequate randomization processes, described the interventions in sufficient detail, and assessed adherence quantitatively. Consistent with our meta-analysis inclusion criteria, all data were analyzed according to the intent-to-treat principle. Eighty percent adhered to the same follow-up schedule across treatment conditions. Given the nature of the intervention and the reliance on self-report outcome measures, the posttreatment assessments often could not be blinded. Specifically, half either did not conceal treatment assignments such that investigators could not foresee them or did not provide enough information for this question to be evaluated. Several articles did not report whether the proportions of participants receiving other nonstudy treatments (eg, pharmacologic) were the same in each randomized group, and a few did not report the qualifications or training of the care providers for the study interventions. Also, we found that dropout rates among studies or between study conditions varied considerably. Despite these shortcomings, by systematically selecting a group of studies using randomization, minimal contact control conditions, and validated depression scales to measure outcomes, it seems likely that the results of the meta-analysis were not excessively biased by methodological flaws.

DISCUSSION

We confirmed that CCBT has antidepressant effects, as measured by larger mean reductions of scores on validated symptom measures than observed in control conditions. Overall, the magnitude of this effect for supported CCBT, as measured by Hedges *g*, is moderate to large and is comparable to the effects reported in meta-analyses[74–76] of standard treatments of depression, including antidepressant pharmacotherapy and studies of individual psychotherapy. Our meta-analysis included substantially more studies than earlier meta-analyses[5–10,77] and explored a variety of possible moderators of treatment outcome. However, results were largely consistent with previous reports except as noted in the discussion of effects of clinician support that follows. Because available methods of CCBT can substantially reduce clinician time, be more convenient than standard psychotherapy for patients, and offer significant cost savings,[16,77–79] broader implementation of CCBT could have a significant, favorable impact on public health.

The effects of CCBT in our meta-analysis were strongly influenced by support from a clinician or other helping person. Although a few studies of unguided CCBT had moderate to large effects,[23,24,45,53] these were in the minority (4 of 18 comparisons of unguided CCBT vs control

conditions), and many investigations of unguided CCBT had very small effect sizes. We conclude that with current methods, CCBT usually is more effective when supported by a clinician or other helping person. It is not surprising that clinical support can improve the impact of CCBT for depression—a condition that is characterized by fatigue, diminished motivation, pessimism, and difficulties with concentration, memory, and effortful cognition. Other than 1 recent report,[77] other meta-analyses[6–8] also found that effects of CCBT are larger when supported by clinicians or other helping professionals. Ahern and coworkers[77] noted that their meta-analysis of 29 studies of CCBT of depression may not have found differences between supported and unsupported CCBT because of the large heterogeneity of studies they categorized as supported (including trials with negligible amounts of support). In comparing our analysis with that of Ahern and coworkers,[77] we noted that they analyzed only 6 investigations that were listed as providing no support, while our report included 18 such studies.

Most studies that offered support for CCBT utilized clinicians with experience in mental health treatment. However, a few explored the possibility that effective support can be delivered by technicians or trained volunteers.[21,24,39] Their role has been described as providing encouragement, support, and feedback to users or helping participants to use the online intervention. In 1 study[21] that directly compared clinician support with technician support, no statistically significant differences in effectiveness were found. However, more research is needed on provision of support by nonclinicians and the possibility that such methods could be implemented widely, thus influencing the future development of psychotherapy.

At this juncture, it appears that support often can be delivered effectively by telephone or e-mail and other asynchronous online methods. However, the results of our meta-analysis suggest that the mode of delivery can influence outcome. Of the studies reporting a significant amount of support (about 1 hour or more), most (18 of 21) used telephone and/or e-mail or other asynchronous online support with no face-to-face contact. The lowest mean effect sizes were observed in investigations that used only e-mail, text messages, or other online asynchronous support. When telephone or face-to-face support was used, the mean effect sizes were significantly larger. No studies used telemedicine for support—a method that may fit well with delivery of CCBT.

Although we extracted data on the amount of support time in minutes or hours, there was considerable variability in the level of precision of reports. Some studies recorded actual support time, while others noted only the amount of time planned for treatment support or a range of support time that may have been provided. Because of this common lack of precision and other sources of variability noted in this discussion, we did not attempt to assess the relationship between reported amounts of support (except to compare any meaningful support vs no significant support) and mean effect sizes.

Other variations that make it difficult to assess relationships between the amount or type of support and outcome include (1) differences in patient recruitment methods (eg, from mental health or primary care clinical practices, online, advertisements, or combinations of these) and (2) differences in baseline severity, illness complexity, and use of other treatments (eg, mildly depressed persons recruited solely via the Internet; more severely depressed patients who are more representative of those seen in typical clinical settings; drug-free samples in which the only treatments are CCBT vs controls). It is possible that highly motivated persons who seek treatment online may require less support than those who have more severe or chronic depression and seek treatment at providers' offices. The amount and type of support could be a fruitful topic for further study; for example, studies could systematically vary the amount or type of clinical contact (eg, 1 hour vs 4 hours), mode of delivering support, and the level of training of the persons providing support (eg, technician, volunteer, case manager, peer counselor, or psychotherapist) for persons with varied complexity and severity of illness.

Treatment completion rate was found to be an important moderator of treatment effect with the highest mean effect sizes being observed when completion rate was in the top quartile, intermediate mean effect sizes in the next to highest quartile, smaller effects in the lower 2 quartiles, and the lowest mean effect sizes in studies that did not report completion rate. It is likely that completion rate is a complex phenomenon that is affected by a large variety of influences including clinical, sociodemographic, and technical variables. For example, completion rate reported as number of modules accessed does not necessarily account for time spent on modules, which may be a more accurate indicator of completion and adherence. We had suspected that provision of support from a clinician or other helping person would enhance completion rates but found no significant differences in completion rates between supported and nonsupported studies. Potential reasons for difficulties in completing treatment that may be especially relevant in delivery of CCBT could include lack of engagement in computer programs (for example, patients experience the program as too heavily laden with text, onerous to use, not responsive to their specific problems and needs, giving feedback that is off target, not enjoyable or helpful), limited customization or flexibility in treatment, technical problems with reliable access to online programs, and lack of experience in using online resources. Although patients' subjective responses to CCBT have been reported to be positive in aggregate,[80,81] there is room for improvement in the levels of engagement, interactivity, and customization of computer programs used in treatment of depression.

One issue that has received little attention is the use of CCBT in underserved or disadvantaged populations in which educational levels, access to the Internet, or minimal or no prior experience in using computers may present barriers to implementation of a technology-based treatment. Many of the studies in our meta-analysis used subject recruitment

strategies that prevented or reduced the likelihood that such persons would participate (eg, cutoffs on educational level and reading proficiency, recruitment primarily via Internet, requirement to have online access), thus yielding samples of predominately well-educated patients with experience in using online resources. One notable exception is a study with mothers of children enrolled in Head Start in which computer access was provided as a component of study participation.[29] More work needs to be done on designing CCBT methods to overcome obstacles to implementation in patients from disadvantaged populations.

Treatment setting was another potential moderator explored in our meta-analysis. Specifically, we tested whether studies conducted with patients drawn from primary care practices might have smaller effects than those performed elsewhere. Our finding of lower mean effect sizes in studies conducted in primary care settings is consistent with a recent report by Wells and associates.[73] Because there have been a limited number of investigations in primary care settings, it is premature to conclude that CCBT is less effective for such patients. However, there are several possible explanations for the observed difference in treatment outcomes. Recruitment methods that select patients from actual clinical practices may tap a population with more severe or complicated conditions, including comorbidities, which may be less common in Internet-recruited samples. Also, less is known about how to implement CCBT in primary care, and it is possible that further development of methods of delivery, including ways to provide support and overcome barriers to participation, could improve outcomes.[73] Development of service pathways in primary care, underserved populations, and health care in general are among the implementation science and practice issues that are challenges for CCBT. Future research that utilizes implementation science[82] could increase the dissemination of CCBT into routine care.

A final clinically relevant moderator of study outcomes was pretreatment severity. If one presumes that CCBT is not a robust treatment and should be used primarily for milder forms of depression, it would be expected that studies that enrolled more severely depressed persons would observe poorer outcomes than those that enrolled persons with less severe illness. To the contrary, we observed the largest mean effect sizes in studies with the highest mean pretreatment severity scores. In this regard, CCBT is similar to other active treatments of depression, including pharmacotherapy and individual psychotherapy.[83] Evidence that CCBT is as effective as a standard treatment for severe depression was reported recently in a direct comparison of clinician-supported CCBT with a full course of up to 20 sessions of standard CBT in drug-free patients with major depressive disorder.[84] These findings should lay to rest the notion that CCBT should be limited to patients with milder depressions.

There are several limitations to our review and meta-analysis. First, less than half of the comparisons of CCBT versus a control condition performed follow-up assessments, and studies that did include follow-up measurements were heavily weighted toward unsupported CCBT. Because many supported studies utilized wait-list control groups and did not compare CCBT with other active treatments, their research designs precluded meaningful longer-term evaluations. The single study[3] that compared supported CCBT to standard, individual CBT found that both active treatments had sustained effects across 6 months of follow-up. Also, a recent investigation[84] of CCBT versus standard CBT showed no loss of effect 6 months after completion of treatment. However, further research is needed to assess the durability of CCBT in comparison to other effective treatments for depression. Second, we were not able to determine if the effectiveness of CCBT is influenced by recruitment method and the education and previous computer experience of study participants. We think that such influences are likely. Third, many studies were performed with persons from nonclinical samples, thus raising questions about generalizability for treatment of depression in clinical practice.

Fourth, many studies reported low completion rates for persons who participated in CCBT. Although some studies had completion rates of 80% or higher, the factors affecting retention of participants have not been adequately investigated. Fifth, we did not assess the quality of the computer programs used and are not aware of any rating system for doing so. However, it could be worthwhile to determine if the programs with multimedia formats and higher production values are associated with better outcomes than more bare-bones programs that rely primarily on reading text for delivery of program content. We suspect that advances in program quality (eg, engagement, interactivity, mobile components, integration of clinician support with computer delivery) could improve adherence and effectiveness of CCBT. Sixth, there has been less study of CCBT in comparison to conventional individual therapy than wait lists or treatment as usual. Furthermore, the benefit of CCBT has not been compared to well-monitored, guideline-concordant pharmacotherapy for depression. Only 2[3,54] of the 40 studies in our meta-analysis compared CCBT with standard CBT in addition to a wait list or other nonstandard CBT control condition, and only 1 of these[3] was in drug-free patients with documented major depressive disorder. Nevertheless, there have been a growing number of studies that have directly examined the effects of CCBT versus standard CBT, and such studies have not found significant differences in treatment outcome.[85]

Seventh, without access to individual-level data from participants, we could not determine if the effects of CCBT were comparable for patients with more extensive treatment histories, such as those who had not obtained adequate benefit from at least 1 trial of antidepressant medication or had comorbid conditions. Eighth, a variety of rating scales were used to measure symptom severity. Although we used *z*-scores to account for this variability, greater consistency in use of rating scales would promote higher confidence in analyses of the influence of treatment severity on outcome. Finally, the majority of CCBT studies reviewed here used desktop, laptop, or notebook computers for treatment

delivery instead of fully mobile applications. Smartphones would appear to have considerable potential for CCBT because of their convenience, accessibility, and widespread use. However, most mobile apps developed to date have been geared toward specific self-help methods such as relaxation or breathing training, increased activity levels, or spotting negative thoughts instead of the comprehensive CBT programs employed in CCBT.[86–89] There have been a limited number of RCTs of these methods for treating patients with well-documented depression, and concerns have been raised about the quality, reliability, and security of mobile apps.[89] Also, it is not known whether CCBT will be more effective if delivered with skill-building modules that involve sustained effort for time periods (eg, 20–40 minutes) that approximate traditional therapy, as in most studies reported here; with smartphones in shorter bursts throughout the day; or with a combination of these methods.

A sufficient number of studies of CCBT for depression have been conducted to conclude that this method, when combined with modest amounts of clinician support, offers potential for delivery of evidence-based treatment at greater efficiency and lower cost than standard CBT. Future development of CCBT for depression should address issues such as refining and improving methods for integrating clinician and computer elements of therapy; enhancing program customization, engagement, and interactivity; increasing completion rates; overcoming barriers to implementation, especially in disadvantaged populations and in primary care settings; and taking advantage of newer technologies as they become available.

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Supplementary Material

Article Title: Computer-Assisted Cognitive-Behavioral Therapy for Depression: A Systematic Review and Meta-Analysis

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List of Supplementary Material for the article

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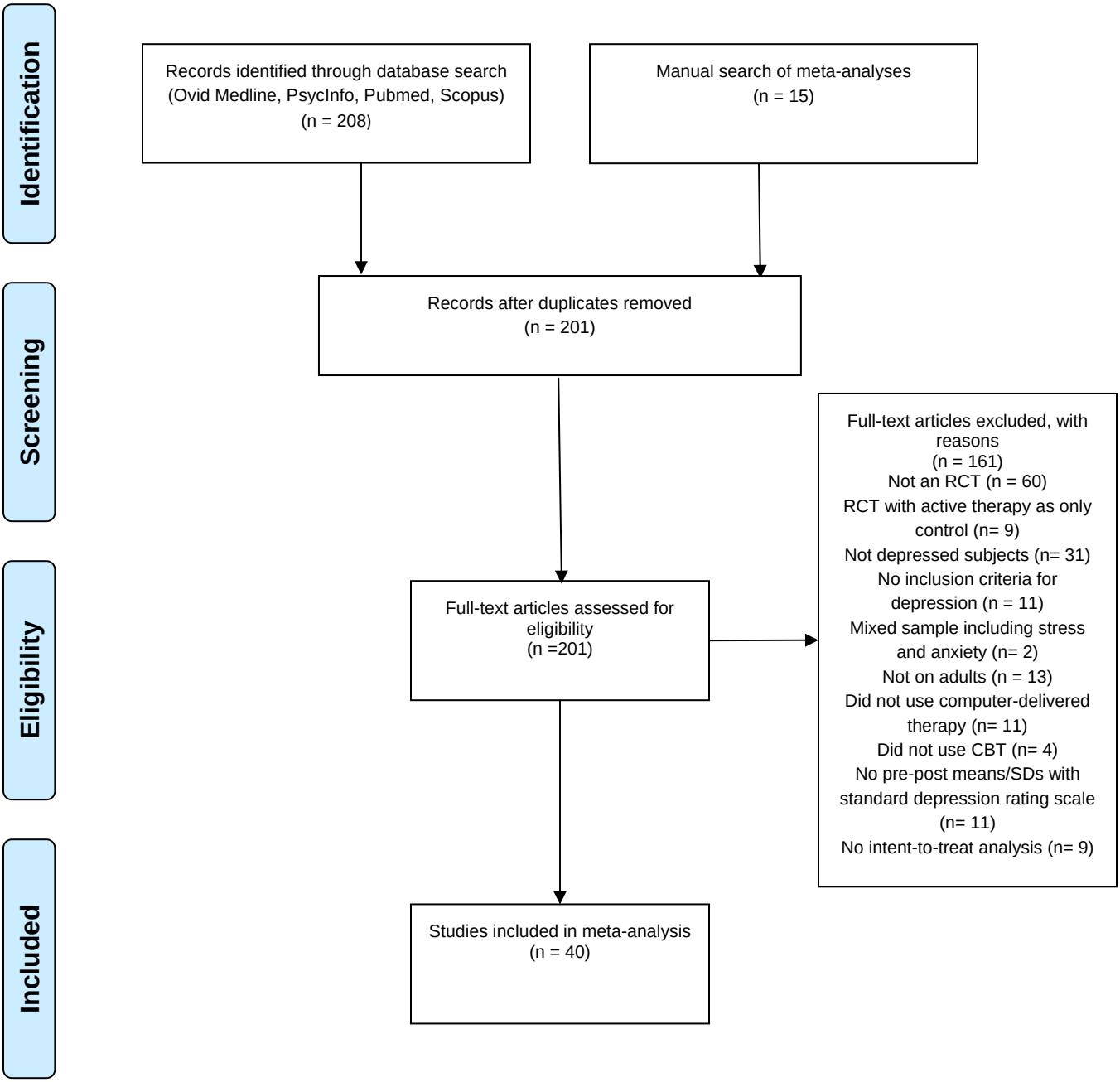
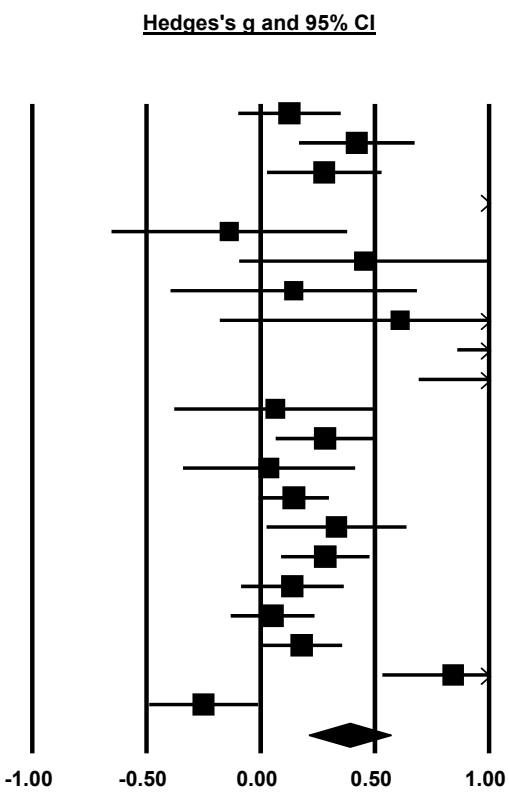
Supplementary Figure 1. PRISMA Flowchart



Supplementary Figure 2. Effect Sizes for CCBT versus Control Condition: Follow-up Analysis

Study	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
			Statistics for each study				
Clarke et al. 2002	0.125	0.116	0.013	-0.102	0.351	1.081	0.280
Proudfoot et al. 2004	0.420	0.130	0.017	0.165	0.675	3.231	0.001
Clarke et al. 2005	0.278	0.128	0.017	0.026	0.529	2.161	0.031
Clarke et al. 2009	2.115	0.197	0.039	1.729	2.501	10.740	0.000
Vernmark et al .2010	-0.138	0.264	0.070	-0.656	0.379	-0.524	0.600
Berger et al. 2011a	0.451	0.279	0.078	-0.097	0.998	1.613	0.107
Berger et al. 2011c	0.144	0.276	0.076	-0.397	0.686	0.522	0.601
Cooper et al. 2011	0.610	0.404	0.163	-0.181	1.402	1.511	0.131
Farrer et al. 2011a	1.342	0.247	0.061	0.858	1.827	5.432	0.000
Farrer et al. 2011c	1.183	0.252	0.063	0.690	1.676	4.700	0.000
Hollandare et al. 2011	0.064	0.227	0.051	-0.381	0.508	0.281	0.779
Calbring 2013	0.281	0.112	0.012	0.063	0.500	2.524	0.012
Hoifodt et al. 2013	0.036	0.193	0.037	-0.342	0.414	0.187	0.852
Phillips et al. 2014	0.145	0.079	0.006	-0.011	0.300	1.827	0.068
Meyer et al. 2015	0.332	0.157	0.025	0.024	0.640	2.110	0.035
Buntrock et al. 2015	0.282	0.100	0.010	0.087	0.478	2.836	0.005
Birney et al. 2016	0.138	0.115	0.013	-0.088	0.364	1.199	0.231
Gilbody et al. 2016BB	0.051	0.094	0.009	-0.134	0.237	0.545	0.586
Gilbody et al. 2016MG	0.179	0.091	0.008	0.001	0.357	1.970	0.049
Hobfoll et al. 2016	0.842	0.159	0.025	0.530	1.155	5.292	0.000
Montero-Marin et al 2016	-0.251	0.122	0.015	-0.491	-0.011	-2.050	0.040
	0.386	0.091	0.008	0.207	0.565	4.228	0.000

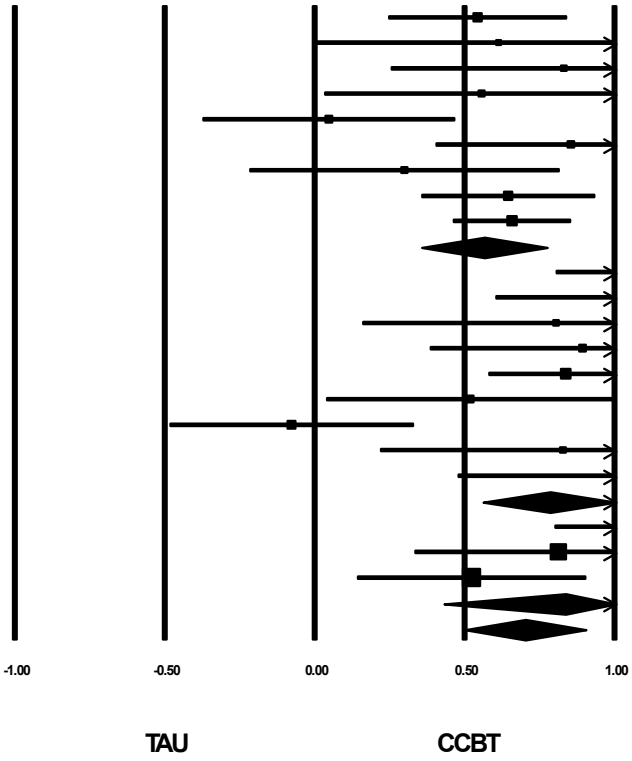


a = Clinician-assisted CCBT; b = Technician-assisted CCBT; c = Unsupported CCBT

MG = MoodGym; BB = Beating the Blues

Supplementary Figure 3. Effect Sizes for CCBT versus Control Condition: Type of Clinician Support

	Study	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
***E-mail/online alone	Warmerdam et al. 2008	0.543	0.153	0.024	0.243	0.844	3.545	0.000
***E-mail/online alone	Perini et al. 2009	0.614	0.311	0.097	0.004	1.223	1.974	0.048
***E-mail/online alone	Ruwaard et al. 2009	0.831	0.296	0.087	0.252	1.410	2.812	0.005
***E-mail/online alone	Vernmark et al .2010	0.557	0.269	0.072	0.030	1.084	2.070	0.038
***E-mail/online alone	Hollandare et al. 2011	0.047	0.216	0.047	-0.377	0.471	0.219	0.827
***E-mail/online alone	Calbring et al. 2013	0.855	0.232	0.054	0.401	1.308	3.691	0.000
***E-mail/online alone	Buhrman et al. 2015	0.299	0.265	0.070	-0.220	0.819	1.130	0.259
***E-mail/online alone	Richards et al. 2015	0.646	0.149	0.022	0.354	0.938	4.332	0.000
***E-mail/online alone	Buntrock et al. 2015	0.658	0.102	0.010	0.459	0.858	6.472	0.000
***E-mail/online alone	Overall	0.562	0.107	0.011	0.353	0.772	5.255	0.000
**Telephone alone or with e-mail	Titov et al. 2010a	1.262	0.235	0.055	0.801	1.722	5.372	0.000
**Telephone alone or with e-mail	Farrer et al. 2011	1.068	0.239	0.057	0.600	1.536	4.475	0.000
**Telephone alone or with e-mail	Titov et al. 2011	0.805	0.331	0.110	0.156	1.455	2.432	0.015
**Telephone alone or with e-mail	Choi et al. 2012	0.893	0.261	0.068	0.381	1.406	3.419	0.001
**Telephone alone or with e-mail	van der Zanden et al 2012	0.838	0.133	0.018	0.577	1.099	6.292	0.000
**Telephone alone or with e-mail	Mohr et al., 2013	0.517	0.246	0.060	0.036	0.999	2.107	0.035
**Telephone alone or with e-mail	Kivi et al., 2014	-0.077	0.209	0.044	-0.487	0.333	-0.367	0.713
**Telephone alone or with e-mail	Milgrom et al. 2016	0.829	0.313	0.098	0.216	1.441	2.651	0.008
**Telephone alone or with e-mail	Pugh et al. 2016	1.058	0.298	0.089	0.474	1.641	3.552	0.000
**Telephone alone or with e-mail	Overall	0.782	0.114	0.013	0.558	1.006	6.842	0.000
*Face-to-face, either alone or with telephone and/or email	Wright et al. 2005	1.603	0.411	0.169	0.797	2.409	3.899	0.000
*Face-to-face, either alone or with telephone and/or email	Sheeber et al. 2012	0.813	0.246	0.061	0.330	1.296	3.302	0.001
*Face-to-face, either alone or with telephone and/or email	Hoifodt et al. 2013	0.523	0.196	0.038	0.139	0.908	2.667	0.008
*Face-to-face, either alone or with telephone and/or email	Overall	0.833	0.207	0.043	0.427	1.239	4.024	0.000
Overall		0.699	0.103	0.011	0.498	0.901	6.808	0.000

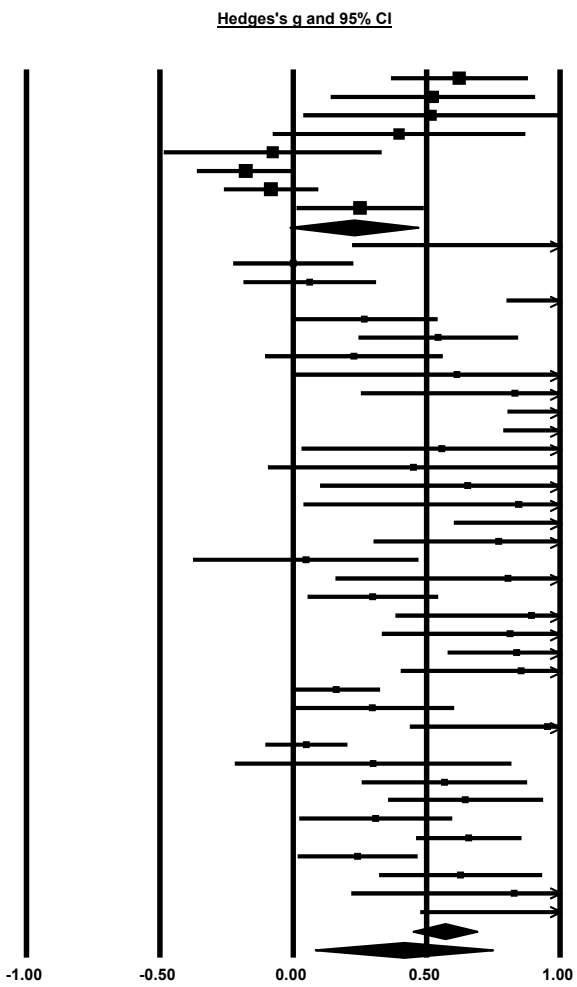


a = Clinician-assisted CCBT; b = Technician-assisted CCBT; c = Unsupported CCBT

MG = MoodGym; BB = Beating the Blues

Supplementary Figure 4. Post-treatment Effect Sizes for CCBT versus Control Condition: Primary Care Compared to Other Settings

	Study	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
				Statistics for each study				
~Primary Care Settings	Proudfoot et al. 2004	0.623	0.132	0.017	0.364	0.881	4.727	0.000
~Primary Care Settings	Hoifodt et al. 2013	0.523	0.196	0.038	0.139	0.908	2.667	0.008
~Primary Care Settings	Mohr et al., 2013a	0.517	0.246	0.060	0.036	0.999	2.107	0.035
~Primary Care Settings	Mohr et al., 2013c	0.396	0.242	0.059	-0.078	0.871	1.637	0.102
~Primary Care Settings	Kivi et al., 2014	-0.077	0.209	0.044	-0.487	0.333	-0.367	0.713
~Primary Care Settings	Gilbody et al., 2016BB	-0.178	0.095	0.009	-0.363	0.008	-1.879	0.060
~Primary Care Settings	Gilbody et al., 2016MG	-0.083	0.091	0.008	-0.262	0.095	-0.915	0.360
~Primary Care Settings	Montero-Marin et al 2016	0.251	0.122	0.015	0.011	0.491	2.048	0.041
~Primary Care Settings		0.224	0.123	0.015	-0.016	0.464	1.827	0.068
Other Settings	Selmi et al. 1990	1.046	0.422	0.178	0.219	1.874	2.479	0.013
Other Settings	Clarke et al. 2002	0.000	0.115	0.013	-0.226	0.226	0.000	1.000
Other Settings	Clarke et al. 2005	0.062	0.128	0.016	-0.189	0.313	0.484	0.629
Other Settings	Wright et al. 2005	1.603	0.411	0.169	0.797	2.409	3.899	0.000
Other Settings	Spek et al. 2007	0.267	0.141	0.020	-0.009	0.543	1.894	0.058
Other Settings	Warmerdam et al. 2008	0.543	0.153	0.024	0.243	0.844	3.545	0.000
Other Settings	Clarke et al. 2009	0.228	0.171	0.029	-0.107	0.562	1.333	0.183
Other Settings	Perini et al. 2009	0.614	0.311	0.097	0.004	1.223	1.974	0.048
Other Settings	Ruwaard et al. 2009	0.831	0.296	0.087	0.252	1.410	2.812	0.005
Other Settings	Titov et al. 2010a	1.262	0.235	0.055	0.801	1.722	5.372	0.000
Other Settings	Titov et al. 2010b	1.258	0.241	0.058	0.786	1.731	5.215	0.000
Other Settings	Vernmark et al .2010	0.557	0.269	0.072	0.030	1.084	2.070	0.038
Other Settings	Berger et al. 2011a	0.451	0.279	0.078	-0.097	0.998	1.613	0.107
Other Settings	Berger et al. 2011c	0.654	0.283	0.080	0.099	1.209	2.309	0.021
Other Settings	Cooper et al. 2011	0.845	0.413	0.170	0.037	1.654	2.049	0.041
Other Settings	Farrer et al. 2011a	1.068	0.239	0.057	0.600	1.536	4.475	0.000
Other Settings	Farrer et al. 2011c	0.770	0.240	0.058	0.299	1.241	3.204	0.001
Other Settings	Hollandare et al. 2011	0.047	0.216	0.047	-0.377	0.471	0.219	0.827
Other Settings	Titov et al. 2011	0.805	0.331	0.110	0.156	1.455	2.432	0.015
Other Settings	Van Bastelaar et al., 2011	0.298	0.126	0.016	0.052	0.544	2.374	0.018
Other Settings	Choi et al. 2012	0.893	0.261	0.068	0.381	1.406	3.419	0.001
Other Settings	Sheeber et al. 2012	0.813	0.246	0.061	0.330	1.296	3.302	0.001
Other Settings	van der Zanden et al 2012	0.838	0.133	0.018	0.577	1.099	6.292	0.000
Other Settings	Calbring et al. 2013	0.855	0.232	0.054	0.401	1.308	3.691	0.000
Other Settings	Glozier et al. 2013	0.161	0.084	0.007	-0.004	0.327	1.912	0.056
Other Settings	Lintvedt et al. 2013	0.297	0.157	0.025	-0.010	0.604	1.893	0.058
Other Settings	Williams et al. 2013	0.953	0.264	0.070	0.435	1.472	3.606	0.000
Other Settings	Phillips et al. 2014	0.050	0.079	0.006	-0.106	0.205	0.626	0.532
Other Settings	Buhrman et al. 2015	0.299	0.265	0.070	-0.220	0.819	1.130	0.259
Other Settings	Meyer et al. 2015	0.567	0.159	0.025	0.255	0.879	3.561	0.000
Other Settings	Richards et al. 2015	0.646	0.149	0.022	0.354	0.938	4.332	0.000
Other Settings	Roepke et al. 2015	0.309	0.147	0.022	0.021	0.597	2.103	0.035
Other Settings	Buntrock et al. 2015	0.658	0.102	0.010	0.459	0.858	6.472	0.000
Other Settings	Birney et al., 2016	0.241	0.116	0.013	0.015	0.468	2.087	0.037
Other Settings	Hobfell et al. 2016	0.627	0.157	0.025	0.320	0.934	4.002	0.000
Other Settings	Milgrom et al. 2016	0.829	0.313	0.098	0.216	1.441	2.651	0.008
Other Settings	Pugh et al. 2016	1.058	0.298	0.089	0.474	1.641	3.552	0.000
Other Settings		0.565	0.061	0.004	0.445	0.685	9.241	0.000
Overall		0.411	0.170	0.029	0.078	0.744	2.421	0.015

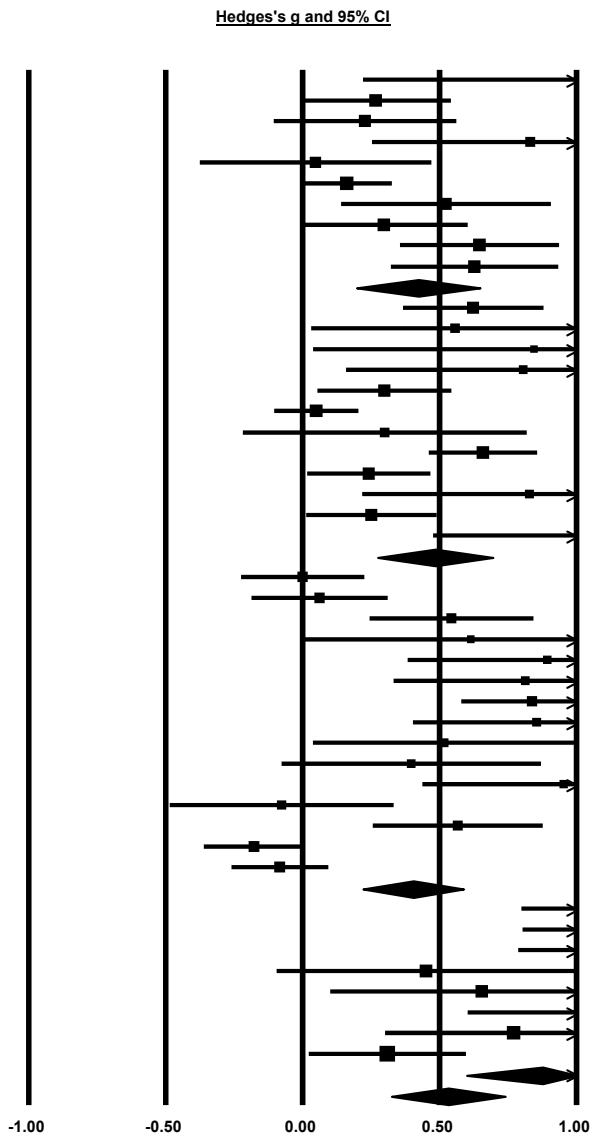


a = Clinician-assisted CCBT; b = Technician-assisted CCBT; c = Unsupported CCBT

MG = MoodGym; BB = Beating the Blues

Supplementary Figure 5. Post-treatment Effect Sizes for CCBT versus Control Condition: Influence of Baseline Severity of Depression

	Study	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
				Statistics for each study				
I. -0.5 or lower	Selmi et al. 1990	1.046	0.422	0.178	0.219	1.874	2.479	0.013
I. -0.5 or lower	Spek et al. 2007	0.267	0.141	0.020	-0.009	0.543	1.894	0.058
I. -0.5 or lower	Clarke et al. 2009	0.228	0.171	0.029	-0.107	0.562	1.333	0.183
I. -0.5 or lower	Ruwaard et al. 2009	0.831	0.296	0.087	0.252	1.410	2.812	0.005
I. -0.5 or lower	Hollandare et al. 2011	0.047	0.216	0.047	-0.377	0.471	0.219	0.827
I. -0.5 or lower	Glozier et al. 2013	0.161	0.084	0.007	-0.004	0.327	1.912	0.056
I. -0.5 or lower	Hoifodt et al. 2013	0.523	0.196	0.038	0.139	0.908	2.667	0.008
I. -0.5 or lower	Lintvedt et al. 2013	0.297	0.157	0.025	-0.010	0.604	1.893	0.058
I. -0.5 or lower	Richards et al. 2015	0.646	0.149	0.022	0.354	0.938	4.332	0.000
I. -0.5 or lower	Hobfell et al. 2016	0.627	0.157	0.025	0.320	0.934	4.002	0.000
I. -0.5 or lower		0.419	0.115	0.013	0.193	0.644	3.638	0.000
II. 0 to -0.5	Proudfoot et al. 2004	0.623	0.132	0.017	0.364	0.881	4.727	0.000
II. 0 to -0.5	Vernmark et al .2010	0.557	0.269	0.072	0.030	1.084	2.070	0.038
II. 0 to -0.5	Cooper et al. 2011	0.845	0.413	0.170	0.037	1.654	2.049	0.041
II. 0 to -0.5	Titov et al. 2011	0.805	0.331	0.110	0.156	1.455	2.432	0.015
II. 0 to -0.5	Van Bastelaar et al., 2011	0.298	0.126	0.016	0.052	0.544	2.374	0.018
II. 0 to -0.5	Phillips et al. 2014	0.050	0.079	0.006	-0.106	0.205	0.626	0.532
II. 0 to -0.5	Buhrman et al. 2015	0.299	0.265	0.070	-0.220	0.819	1.130	0.259
II. 0 to -0.5	Buntrock et al. 2015	0.658	0.102	0.010	0.459	0.858	6.472	0.000
II. 0 to -0.5	Birney et al., 2016	0.241	0.116	0.013	0.015	0.468	2.087	0.037
II. 0 to -0.5	Milgrom et al. 2016	0.829	0.313	0.098	0.216	1.441	2.651	0.008
II. 0 to -0.5	Montero-Marin et al 2016	0.251	0.122	0.015	0.011	0.491	2.048	0.041
II. 0 to -0.5	Pugh et al. 2016	1.058	0.298	0.089	0.474	1.641	3.552	0.000
II. 0 to -0.5		0.481	0.107	0.012	0.271	0.691	4.482	0.000
III. 0 to 0.5	Clarke et al. 2002	0.000	0.115	0.013	-0.226	0.226	0.000	1.000
III. 0 to 0.5	Clarke et al. 2005	0.062	0.128	0.016	-0.189	0.313	0.484	0.629
III. 0 to 0.5	Warmerdam et al. 2008	0.543	0.153	0.024	0.243	0.844	3.545	0.000
III. 0 to 0.5	Perini et al. 2009	0.614	0.311	0.097	0.004	1.223	1.974	0.048
III. 0 to 0.5	Choi et al. 2012	0.893	0.261	0.068	0.381	1.406	3.419	0.001
III. 0 to 0.5	Sheeber et al. 2012	0.813	0.246	0.061	0.330	1.296	3.302	0.001
III. 0 to 0.5	van der Zanden et al 2012	0.838	0.133	0.018	0.577	1.099	6.292	0.000
III. 0 to 0.5	Calbring et al. 2013	0.855	0.232	0.054	0.401	1.308	3.691	0.000
III. 0 to 0.5	Mohr et al., 2013a	0.517	0.246	0.060	0.036	0.999	2.107	0.035
III. 0 to 0.5	Mohr et al., 2013c	0.396	0.242	0.059	-0.078	0.871	1.637	0.102
III. 0 to 0.5	Williams et al. 2013	0.953	0.264	0.070	0.435	1.472	3.606	0.000
III. 0 to 0.5	Kivi et al., 2014	-0.077	0.209	0.044	-0.487	0.333	-0.367	0.713
III. 0 to 0.5	Meyer et al. 2015	0.567	0.159	0.025	0.255	0.879	3.561	0.000
III. 0 to 0.5	Gilbody et al., 2016BB	-0.178	0.095	0.009	-0.363	0.008	-1.879	0.060
III. 0 to 0.5	Gilbody et al., 2016MG	-0.083	0.091	0.008	-0.262	0.095	-0.915	0.360
III. 0 to 0.5		0.400	0.094	0.009	0.216	0.584	4.269	0.000
IV. 0.5 to 1	Wright et al. 2005	1.603	0.411	0.169	0.797	2.409	3.899	0.000
IV. 0.5 to 1	Titov et al. 2010a	1.262	0.235	0.055	0.801	1.722	5.372	0.000
IV. 0.5 to 1	Titov et al. 2010b	1.258	0.241	0.058	0.786	1.731	5.215	0.000
IV. 0.5 to 1	Berger et al. 2011a	0.451	0.279	0.078	-0.097	0.998	1.613	0.107
IV. 0.5 to 1	Berger et al. 2011c	0.654	0.283	0.080	0.099	1.209	2.309	0.021
IV. 0.5 to 1	Farrer et al. 2011a	1.068	0.239	0.057	0.600	1.536	4.475	0.000
IV. 0.5 to 1	Farrer et al. 2011c	0.770	0.240	0.058	0.299	1.241	3.204	0.001
IV. 0.5 to 1	Roepke et al. 2015	0.309	0.147	0.022	0.021	0.597	2.103	0.035
IV. 0.5 to 1		0.872	0.141	0.020	0.595	1.149	6.176	0.000
Overall		0.528	0.106	0.011	0.320	0.736	4.980	0.000



a = Clinician-assisted CCBT; b = Technician-assisted CCBT; c = Unsupported CCBT **MG = MoodGym; BB = Beating the Blues**

Supplementary Table 1. CLEAR Ratings for Individual Studies

Study Reference	CLEAR-NPT Checklist Item														
	1	2	3	4	5	6	6.11	6.12	7	7.11	7.12	8	8.1	9	10
Selmi et al. 1990	3	3	0	0	0	1	3	0	1	3	0	0	na	0	0
Clarke et al. 2002	0	3	0	3	0	1	0	3	1	0	3	1	1	0	0
Proudfoot et al. 2004	0	3	0	3	1	1	0	0	1	0	0	1	1	0	0
Clarke et al. 2005	0	3	0	3	0	1	0	1	1	0	1	1	1	0	0
Warmerdam et al. 2005	0	3	0	0	0	1	3	1	1	3	1	1	1	0	0
Wright et al. 2005	3	3	0	0	0	1	0	0	1	0	0	0	na	0	0
Spek et al. 2007	0	0	0	0	0	1	3	1	1	3	1	1	1	0	0
Clarke et al. 2009	0	3	0	3	0	1	0	0	1	0	0	1	1	0	0
Perini et al. 2009	0	3	0	0	0	1	1	1	1	1	1	1	1	0	0
Ruwaard et al. 2009	0	3	0	0	0	1	0	0	1	0	0	1	1	1	0
Titov et al. 2010	0	3	0	0	0	1	1	1	1	1	1	1	1	1	0
Vernmark et al. 2010	0	3	0	0	0	1	3	0	1	3	0	0	na	0	0
Berger et al. 2011	0	3	0	0	0	1	3	3	1	3	3	1	1	0	0
Cooper et al. 2011	0	0	1	3	0	1	0	0	1	0	0	1	1	0	0
Farrer et al. 2011	0	3	0	3	0	1	3	1	1	3	1	1	1	0	0
Hollandre et al. 2011	0	3	0	0	0	1	3	0	1	3	0	2	0	0	0
Titov et al. 2011	0	3	0	0	0	1	0	0	1	0	0	1	1	1	0
Van Bastelaar et al. 2011	0	3	0	0	0	1	3	1	1	3	1	1	1	1	0
Choi et al. A12012	0	0	0	0	0	1	3	0	1	3	0	1	1	1	0
Sheeber et al. 2012	0	0	0	0	0	1	3	0	1	3	0	1	1	0	0
ver der Zanden et al. 2012	0	0	0	3	0	1	3	0	1	3	0	1	1	0	0
Carlbring et al 2013	0	0	0	0	0	1	0	0	1	0	0	1	1	1	0
Glozier et al., 2013	0	0	0	na	0	1	3	3	na	3	3	1	1	0	0
Hoifodt et al. 2013	0	1	0	3	0	1	3	1	1	3	1	1	1	0	0
Lintvedt et al. 2013	0	0	0	na	0	1	3	1	na	3	1	1	1	0	0
Mohr et al. 2013	0	0	0	0	0	1	3	0	1	3	0	1	1	1	0
Williams et al. 2013	0	3	0	na	0	1	3	3	na	3	3	1	1	0	0
Kivi et al. 2014	3	0	0	0	0	1	1	0	1	1	0	1	1	0	0
Phillips et al. 2014	0	0	0	na	0	1	3	0	1	3	0	1	1	0	0
Buhrman et al. 2015	0	0	0	0	0	1	3	0	1	3	0	1	1	0	0
Meyer et al, 2015	0	0	0	na	0	1	0	0	na	0	0	1	1	0	0
Richards et al. 2015	0	0	0	0	0	1	0	1	1	0	1	1	1	1	0
Roepke et al. 2015	0	0	0	na	0	1	3	1	na	3	1	1	1	0	0
Buntrock et al. 2015	0	0	0	3	0	1	1	1	1	1	1	1	1	0	0
Gilbody et al. 2015	0	1	0	0	0	1	0	0	1	0	0	1	1	0	0
Birney et al. 2016	0	0	0	3	0	1	3	0	2	3	0	1	1	0	0
Hobfell et al. 2016	0	3	0	0	0	1	3	1	1	3	1	1	1	0	0
Milgrom et al. 2016	0	0	0	0	0	1	1	0	1	1	0	1	1	0	0
Montero-Martin et al 2016	0	0	0	3	0	1	0	0	1	0	0	1	1	0	0
Pugh et al. 2016	0	0	0	0	0	1	3	0	1	3	0	1	1	0	0

Note.

CLEAR NPT Item Number

1	Was the generation of allocation sequences adequate? Yes (0); No (1); Unclear (3)
2	Was the treatment allocation concealed? Yes (0); No (1); Unclear (3)
3	Were details of the intervention administered to each group made available? Yes (0); No (1); Unclear (3)
4	Were care providers' experience or skill in each arm appropriate? Yes (0); No (1); Unclear (3)
5	Was participant (i.e., patients) adherence assessed quantitatively? Yes (0); No (1); Unclear (3)
6	Were participants adequately blinded? Yes (0); No, because blinding is not feasible (1); No, although blinding is feasible (2); Unclear (3)
6.1	If participants were not adequately blinded
6.11	Were all other treatments and care (i.e., cointerventions) the same in each randomized group? Yes (0); No (1); Unclear (3)
6.12	Were withdrawals and lost to follow-up the same in each randomized group? Yes (0); No (1); Unclear (3)
7	Were care providers or persons caring for the participants adequately blinded? Yes (0); No, because blinding is not feasible (1); No, although blinding is feasible (2); Unclear (3)
7.1	If care providers were not adequately blinded
7.11	Were all other treatments and care (i.e., cointerventions) the same in each randomized group? Yes (0); No (1); Unclear (3)
7.12	Were withdrawals and lost to follow-up the same in each randomized group? Yes (0); No (1); Unclear (3)
8	Were outcome assessors adequately blinded to assess the primary outcomes? Yes (0); No, because blinding is not feasible (1); No, although blinding is feasible (2); Unclear (3)
8.1	If outcome assessors were not adequately blinded, were specific methods used to avoid ascertainment bias (systematic differences in outcome assessment)? Yes (0); No (1); Unclear (3)
9	Was the follow-up schedule the same in each group? Yes (0); No (1); Unclear (3)
10	Were the main outcomes analyzed according to the intention-to-treat principle? Yes (0); No (1); Unclear (3)