Cognitive-Behavioral Therapy for Adult Anxiety Disorders: A Meta-Analysis of Randomized Placebo-Controlled Trials

Stefan G. Hofmann, Ph.D., and Jasper A. J. Smits, Ph.D.

Objective: Cognitive-behavioral therapy (CBT) is frequently used for various adult anxiety disorders, but there has been no systematic review of the efficacy of CBT in randomized placebo-controlled trials. The present study meta-analytically reviewed the efficacy of CBT versus placebo for adult anxiety disorders.

Data Sources: We conducted a computerized search for treatment outcome studies of anxiety disorders from the first available date to March 1, 2007. We searched MEDLINE, PsycINFO, PubMed, Scopus, the Institute of Scientific Information, and Dissertation Abstracts International for the following terms: *random**, *cognitive behavior*therap**, *cognitive therap**, *behavior*therap**, *GAD*, *generalized anxiety disorder*, *OCD*, *obsessive compulsive disorder*, *social phobia*, *social anxiety disorder*, *specific phobia*, *simple phobia*, *PTSD*, *post-traumatic stress disorder*, and *acute stress disorder*. Furthermore, we examined reference lists from identified articles and asked international experts to identify eligible studies.

Study Selection: We included studies that randomly assigned adult patients between ages 18 and 65 years meeting DSM-III-R or DSM-IV criteria for an anxiety disorder to either CBT or placebo. Of 1165 studies that were initially identified, 27 met all inclusion criteria.

Data Extraction: The 2 authors independently identified the eligible studies and selected for each study the continuous measures of anxiety severity. Dichotomous measures reflecting treatment response and continuous measures of depression severity were also collected. Data were extracted separately for completer (25 studies for continuous measures and 21 studies for response rates) and intent-to-treat (ITT) analyses (6 studies for continuous measures and 8 studies for response rates).

Data Synthesis: There were no significant differences in attrition rates between CBT and placebo. Random-effects models of completer samples yielded a pooled effect size (Hedges' g) of 0.73 (95% CI = 0.88 to 1.65) for continuous anxiety severity measures and 0.45 (95% CI = 0.25 to 0.65) for depressive symptom severity measures. The pooled odds ratio for completer treatment response rates was 4.06 (95% CI = 2.78 to 5.92). The strongest effect sizes were observed in obsessive-compulsive disorder and acute stress disorder, and the weakest effect size was found in panic disorder. The advantage of CBT over placebo did not depend on placebo modality, number of sessions, or study year.

Conclusions: Our review of randomized placebo-controlled trials indicates that CBT is efficacious for adult anxiety disorders. There is, however, considerable room for improvement. Also, more studies need to include ITT analyses in the future.

(J Clin Psychiatry 2008;69:621–632)

Received July 17, 2007; accepted Sept. 5, 2007. *From the Department of Psychology, Boston University, Mass. (Dr. Hofmann); and the Department of Psychology, Southern Methodist University, Dallas, Tex. (Dr. Smits).*

Acknowledgments appear at the end of the article.

Dr. Hofmann has been a consultant to Organon and has received grant/research support from the National Institute of Mental Health. Dr. Smits reports no additional financial or other relationships relevant to the subject of this article.

Corresponding author and reprints: Stefan G. Hofmann, Ph.D., Department of Psychology, Boston University, 648 Beacon Street, 6th Floor, Boston, MA 02215 (e-mail: shofmann@bu.edu).

Epidemiologic studies indicate that anxiety disorders are the most prevalent class of mental disorders, with 12-month and lifetime prevalence rates of 18.1% and 28.8%, respectively.[1,2] Numerous studies have examined the efficacy of cognitive-behavioral therapy (CBT) for adult anxiety disorders. CBT here refers to the class of interventions that are based on the basic premise that emotional disorders are maintained by cognitive factors and that psychological treatment leads to changes in these factors through cognitive (cognitive restructuring) and behavioral (e.g., exposure, behavioral experiments, relaxation training, social skills training) techniques.[3]

Meta-analytic reviews of these studies have generally yielded large effect sizes for the majority of treatment studies.[4] However, these existing meta-analyses are not without limitations.[5–10] One of the most concerning weaknesses of meta-analyses involving psychotherapy research is related to the quality of the original studies. In particular, a number of frequently-cited meta-analyses of CBT for anxiety disorders have included studies that vary greatly with respect to control procedures, which range from wait-list, alternative treatments, and placebo inter-

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ventions that were evaluated with or without randomization. Other studies fail to include any control groups.[8] Therefore, it has been argued that the results of most existing meta-analyses of CBT for anxiety disorders are of limited validity because the quality and rigor of meta-analyses are directly related to the quality and rigor of the studies that are included in these analyses.[8,10]

The gold standard design in clinical outcome research is the randomized placebo-controlled trial. Although not without problems, this design has been used as the primary test of the direct effects of the treatment on outcome in clinical research.[11] Clinicians in pharmacotherapy trials typically administer a sugar pill to individuals in the placebo condition. Instead of including a pill placebo, a number of psychotherapy trials have employed psychological placebo conditions to control for nonspecific factors. Although it is difficult, if not impossible, to protect the blind in placebo-controlled psychotherapy trials, the randomized placebo-controlled design is still the most rigorous and conservative test of the effects of an active treatment.

The primary aim of this study was to determine the acute efficacy of CBT as compared to placebo for adult anxiety disorders. In contrast to existing meta-analyses of CBT for anxiety disorders, we limited our selection to randomized placebo-controlled trials of DSM-III-R or DSM-IV anxiety disorders that directly compared the treatment efficacy of CBT with a placebo condition. We further expanded our search to all types of anxiety disorders in order to compare the effects of CBT among the various anxiety disorders and explored the potential moderating effects of number of treatment sessions, placebo modality (pill vs. psychological placebo), and publication year.

METHOD

Data Sources

Several approaches were used to identify studies. First, we searched MEDLINE, PsycINFO, PubMed, Scopus, the Institute of Scientific Information, and Dissertation Abstracts International. We searched for treatment outcome studies of anxiety disorders from the first available date to March 1, 2007. We used the search term *random** in order to identify randomized controlled studies, and we used the following terms to identify studies that included a CBT condition: *cognitive behavior*therap**, *cognitive therap**, or *behavior*therap**. In order to identify studies targeting specific anxiety disorders, we used the following search terms: *GAD*, *generalized anxiety disorder*, *OCD*, *obsessive compulsive disorder*, *social phobia*, *social anxiety disorder*, *specific phobia*, *simple phobia*, *PTSD*, *post-traumatic stress disorder*, and *acute stress disorder*. Second, we asked colleagues from Germany, Japan, Korea, Netherlands, Portugal, and Spain to identify randomized controlled CBT trials that were published in their respective languages. Finally, we conducted manual searches in the lists of references from empirical studies, meta-analyses, and review articles.

Selection and Study Characteristics

We selected studies that met the following criteria. First, patients had to be between ages 18 and 65 years and meet DSM-III-R or DSM-IV diagnostic criteria for an anxiety disorder as determined by a psychometrically sound and structured diagnostic instrument. Studies with children and adolescents or geriatric individuals were excluded because the CBT approaches differ greatly among these age groups. Furthermore, an inspection of the literature suggested that the number of randomized placebo-controlled studies with children and geriatric samples was insufficient for a comparison with adult samples.[12] Second, patients had to be randomly assigned to either CBT or placebo. The psychological placebo had to involve interventions to control for nonspecific factors (e.g., regular contact with a therapist, reasonable rationale for the intervention, discussions of the psychological problem). Placebo interventions that included active treatment ingredients for the target problem (e.g., an intervention that specifically instructs participants to engage in exposure exercises to test certain predictions or to challenge a maladaptive thinking style) were not included. Third, the clinical severity of the anxiety disorder had to be assessed by means of psychometrically sound clinician-rated or self-report measures. Finally, reports had to provide sufficient information to calculate effect sizes (i.e., means and standard deviations, t or F values, change scores, frequencies, or probability levels).[1] Studies that reported on secondary or subanalyses of a larger, more complete, or earlier study were excluded from the analysis.

Data Extraction

The 2 authors independently selected for each study the continuous interviewer and self-report measures that have shown to be valid and reliable for the assessment of clinical severity of the anxiety disorder of interest (i.e., symptom severity, symptom frequency, and quality of life). For those studies that reported dichotomous outcomes, we selected the most conservative measure of treatment response. We collected measures of depressive symptom severity to study the specificity of CBT for the target problem. For each of these decisions, disagreement between the 2 authors was resolved through discussion, and consensus was obtained. Two other individuals independently extracted the numerical data from completer and, if available, intent-to-treat ([ITT] last-observation-carried-forward method) samples.

Data Synthesis

Effect size estimates of continuous measures. The first step involved calculating for each study the effect

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sizes for the differences in treatment effects between CBT and placebo. For continuous measures, we calculated the Hedges' g effect size and its 95% CI. This effect size is a variation on Cohen's d that corrects for biases due to small sample sizes[13] and is calculated using the following formula:

$$g = \frac{\overline{\Delta}_{CBT} - \overline{\Delta}_{PLA}}{\sqrt{\frac{(n_{CBT}-1)SD^2_{CBT} + (n_{PLA}-1)SD^2_{PLA}}{(n_{total}-2)}}} \times \left(1 - \frac{3}{4(n_{CBT}+n_{PLA})-9}\right)$$

, where $\overline{\Delta}$ is the mean pretreatment to posttreatment change, *SD* is the standard deviation of posttreatment scores, *n* is the sample size, *CBT* refers to the CBT condition, and *PLA* refers to the placebo condition. These controlled effect sizes may be conservatively interpreted with Cohen's[14] convention of small (0.2), medium (0.5), and large (0.8) effects. We calculated an average Hedges' g effect size for studies that included multiple continuous measures of anxiety disorder severity and separate Hedges' g effect sizes for measures of depressive symptom severity.

Effect size estimates of dichotomous measures. For dichotomous measures, we calculated the odds ratio (OR) and its 95% CI using the Cox-Hinkley-Miettinen-Nurminen method.[15] The OR is a measure of the effect size that is defined as the ratio of the odds of an event (i.e., attrition and treatment response) occurring in 1 group (patients in the CBT condition) to the ratio of the event in another group (patients in the placebo condition). Thus, OR was calculated using the following formula:

$$OR = \frac{p/(1-p)}{q/(1-q)}$$

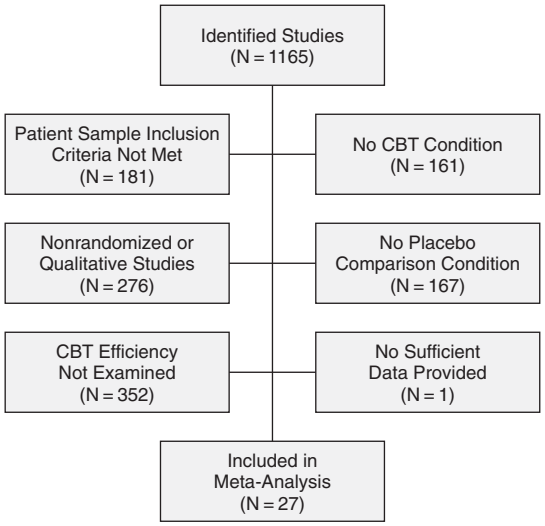
, where *p* refers to the percentage of responders or dropouts in the CBT condition and *q* to the percentage of responders or dropouts in the placebo condition. An OR of 1 indicates that the event is equally likely in both groups. If necessary, we reversed signs to ensure that a positive OR for treatment response indicated an advantage of CBT over placebo.

Pooled effect size estimates. The effect size estimates (Hedges' g and OR, separately) were combined across studies to obtain a summary statistic. We adopted random-effects models[16,17] instead of fixed-effects models because random-effects models are more appropriate when the aim is to generalize beyond the observed studies.[16] Average effect sizes for the primary outcome measures (i.e., anxiety disorder severity and treatment response) were computed for ITT data in addition to completer data.

Publication bias. It has been argued that meta-analyses may overestimate the overall effect size because studies with nonsignificant findings are often not published, a bias that is also known as the file-drawer problem.[18] A conservative method often employed to address this issue involves calculating the fail-safe N, which reflects the number of unretrieved studies required to reduce the overall effect size to a nonsignificant level.[19] According to Rosenthal,[20] effect sizes are robust if the fail-safe N exceeds $5k + 10$, where *k* reflects the number of studies included in the meta-analysis. For the present study, we computed the fail-safe N for the major analyses. All effect size calculations and publication bias analyses were completed using the program Comprehensive Meta-Analysis, version 2.[21]

Moderator analyses. To explore the potential impact of study characteristics (study year, placebo modality) or clinical characteristics (anxiety disorder, number of treatment sessions) on outcome, we used generalized linear models. Separate analyses were completed for the effect sizes for anxiety and depression (using data from completer samples). In each analysis, the study weight was entered as the weight variable and the respective moderator variable as the factor or covariate. Significant effects of factors were followed up with pairwise comparisons using Bonferroni correction.

Figure 1. Study Selection and Reasons for Exclusions



Abbreviation: CBT = cognitive-behavioral therapy.

RESULTS

Study Selection

Figure 1 presents a flow diagram illustrating the study selection process. Our search strategy yielded 1165 potentially eligible studies, of which 27 met all inclusion criteria. Among the 27 studies, the most commonly studied disorder was social anxiety disorder ([SAD] N = 7), followed by posttraumatic stress disorder ([PTSD] N = 6), panic disorder (N = 5), acute stress disorder ([ASD] N = 4), obsessive-compulsive disorder ([OCD]

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J Clin Psychiatry 69:4, April 2008

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Table 1. Characteristics of Studies Included in the Meta-Analysis

Study	Target Disorder	CBT Type	Placebo Type	N (CBT plus placebo)	No. of Sessions	Anxiety Measure	Depression Measure	Analysis	Jadad Score
Bryant et al[22] 1998	Acute stress disorder	CBT	Supportive counseling	24	5	Impact of Event Scale[23]	Beck Depression Inventory[24]	Completer	1
Bryant et al[25] 1999	Acute stress disorder	CBT	Supportive counseling	38	6	Impact of Event Scale	Beck Depression Inventory	Completer	2
Bryant et al[26] 2003	Acute stress disorder	CBT	Supportive counseling	24	5	Impact of Event Scale	Beck Depression Inventory	Completer	3
Bryant et al[27] 2005	Acute stress disorder	CBT	Supportive counseling	57	6	Impact of Event Scale	Beck Depression Inventory	Completer, intention to treat	3
Borkovec and Costello[28] 1993	Generalized anxiety disorder	CBT	Nondirective therapy	43	12	HAM-A,[29] ADIS-R-severity,[30] STAI-T,[32] ZSRA,[33] PSWQ[34]	Beck Depression Inventory, HAM-D[31]	Completer	2
Wetherell et al[35] 2003	Generalized anxiety disorder	CBT	Discussion group	52	12	ADIS-IV-severity,[36] HAM-A, PSWQ, Beck Anxiety Inventory[37]	Beck Depression Inventory, HAM-D	Completer	2
Foa et al[38] 2005	Obsessive-compulsive disorder	Exposure and response prevention	Pill placebo	55	15	CGI-S[39], YBOCS,[40] NIMH Global Obsessive-Compulsive Scale[41]	…	Completer	3
Greist et al[42] 2002	Obsessive-compulsive disorder	Behavior therapy	Systematic relaxation	167	10	YBOCS, Work and Social Adjustment Scale[43]	HAM-D	Completer	1
Lindsay et al[46] 1997	Obsessive-compulsive disorder	Exposure and response prevention	Anxiety management	18	15	YBOCS, The Padua Inventory,[44] MOCI,[45] Interference Rating Scale[46]	Beck Depression Inventory	Completer	1
Bakker et al[47] 1999	Panic disorder	Cognitive therapy	Pill placebo	67	12	CGI-S, MSPS,[48] Patient Global Evaluation,[48] panic frequency, Overall Phobia Score, Anticipatory Anxiety Score	MADRS[49]	Completer, intention to treat	2
Barlow et al[50] 2000	Panic disorder	CBT	Pill placebo	101	12	Panic Disorder Severity Scale[51]	…	Completer, intention to treat	3
Black et al[52] 1993	Panic disorder	Cognitive therapy	Pill placebo	50	8	CGI-S, Clinical Anxiety Scale,[53] Panic Attack Severity Score,[51] Sheehan Disability Scale[48]	MADRS	Completer, intention to treat	2
Craske et al[54] 1995	Panic disorder	CBT	Nondirective-supportive therapy	30	4	ADIS-R-severity, Anxiety Sensitivity Index,[55] Fear Questionnaire,[56] FDAS,[57] Subjective Symptoms Scale[58]	…	Completer	2
Sharp et al[59] 1996	Panic disorder	CBT	Pill placebo	80	10	…	MADRS	Intention to treat	2
Blanchard et al[60] 2003	Posttraumatic stress disorder	CBT	Supportive counseling	73	12	CAPS-2,[61] Brief Symptom Inventory,[62] Impact of Event Scale, LIFE,[63] PCL[64]	Beck Depression Inventory	Completer	2

(continued)

Table 1 (continued). Characteristics of Studies Included in the Meta-Analysis

Study	Target Disorder	CBT Type	Placebo Type	N (CBT plus placebo)	No. of Sessions	Anxiety Measure	Depression Measure	Analysis	Jadad Score
Bryant et al[65] 2003	Posttraumatic stress disorder	CBT	Supportive counseling	38	8	CAPS-2, Impact of Event Scale, Catastrophic Cognitions Questionnaire[66]	Beck Depression Inventory	Completer	3
Foa et al[67] 1991	Posttraumatic stress disorder	Prolonged exposure	Supportive counseling	28	9	Posttraumatic Stress Disorder Symptom Scale[68]	Beck Depression Inventory	Completer	2
Marks et al[69] 1998	Posttraumatic stress disorder	CBT	Relaxation	45	10	Posttraumatic Stress Disorder Symptom Scale, Impact of Event Scale	Beck Depression Inventory	Completer	2
McDonagh et al[70] 2005	Posttraumatic stress disorder	CBT	Problem-solving therapy	51	14	CAPS-2, Quality of Life Inventory[71]	Beck Depression Inventory	Completer, intention to treat	2
Neuner et al[72] 2004	Posttraumatic stress disorder	Narrative exposure therapy	Supportive counseling	31	4	Posttraumatic Stress Diagnostic Scale,[73] SF-12[74]	…	Completer	2
Clark et al[75] 2003	Social anxiety disorder	Cognitive therapy	Pill placebo	43	16	ADIS-R-severity, SPS,[76] SIAS,[76] LSAS,[77] FQ-SP,[56] FNE,[78] SPWSS[75]	Beck Depression Inventory	Completer	2
Cottraux et al[79] 2000	Social anxiety disorder	CBT	Supportive therapy	63	8	LSAS, Quality of Life Scale,[79] Fear Questionnaire, SISST[80]	Beck Depression Inventory	Completer	3
Davidson et al[81] 2004	Social anxiety disorder	CCBT	Pill placebo	120	14	CGI-S, Brief Social Phobia Scale,[82] Social Phobia and Anxiety Inventory[83]	…	Completer, intention to treat	3
Heimberg et al[84] 1998	Social anxiety disorder	Cognitive-behavioral group therapy	Educational-supportive group therapy, pill placebo	69	12	ADIS-R-severity, SPDS,[85] LSAS, FNE, SAD,[78] SPS, SCL-90-R-IS,[86] SCL-90-R-PA,[86] impromptu speech task	SCL-90-R-depression[86]	Completer	3
Lucas[87] 1994	Social anxiety disorder	Cognitive-behavioral group therapy	Educational-supportive group therapy	44	12	Social Phobia and Anxiety Inventory, SIAS, SPS, SISST	Beck Depression Inventory	Completer	2
Smits et al[88] 2006	Social anxiety disorder	Behavior therapy	Psychological placebo	38	3	LSAS-SR,[89] impromptu speech task	…	Completer	2
Turner et al[90] 1994	Social anxiety disorder	Behavior therapy	Pill placebo	47	20	…	…	Completer	2

Abbreviations: ADIS-IV = Anxiety Disorder Interview Schedule for DSM-IV; ADIS-R = Anxiety Disorder Interview Schedule-Revised; CAPS-2 = Clinician-Administered Posttraumatic Stress Disorder Scale, version 2; CBT = cognitive-behavioral therapy; CCBT = comprehensive cognitive-behavioral therapy; CGI-S = Clinical Global Impressions-Severity of Illness scale; FDAS = Four Dimensional Anxiety Scale; FNE = Fear of Negative Evaluation scale; FQ-SP = Fear Questionnaire-Social Phobia scale; HAM-A = Hamilton Rating Scale for Anxiety; HAM-D = Hamilton Rating Scale for Depression; LIFE = Longitudinal Interval Follow-up Evaluation; LSAS = Liebowitz Social Anxiety Scale; LSAS-SR = Liebowitz Social Anxiety Scale-Self Report; MADRS = Montgomery-Asberg Depression Rating Scale; MOCI = Maudsley Obsessive Compulsive Inventory; MSPS = Marks-Sheehan Phobia Scale; NIMH = National Institute of Mental Health; PCL = Posttraumatic Stress Disorder Checklist; PGE = Patient Global Evaluation; PSWQ = Penn State Worry Questionnaire; SAD = Social Avoidance and Distress scale; SCL-90-R-PA = Symptom Checklist-90-Revised-Phobic Anxiety; SCL-90-R-IS = Symptom Checklist-90-Revised-Interpersonal Sensitivity; SF-12 = 12-item Short Form Health Survey; SIAS = Social Interaction Anxiety Scale; SISST = Social Interaction Self-Statement Test; SPDS = Social Phobic Disorder Severity and Change Form; SPS = Social Phobia Scale; SPWSS = Social Phobia Weekly Summary Scale; STAI-T = State Trait Anxiety Inventory-Trait subscale; YBOCS = Yale-Brown Obsessive Compulsive Scale; ZSRA = Zung Self-Rating of Anxiety Scale.
Symbol: … = no measures administered.

N = 3), and generalized anxiety disorder ([GAD] N = 2). We did not identify any studies that compared CBT to placebo for the treatment of specific phobia. Table 1 lists the characteristics for each of the studies included in the meta-analysis. In order to quantify the quality of the study design, the following scores were assigned (1 if present, 0 if not) to the clinical trials using modified Jadad criteria[91]: (1) the study was described as randomized, (2) participants were randomly assigned in an adequate manner (e.g., adequate randomization procedure; the study reported withdrawals and dropouts), (3) participants and evaluators were blinded to treatment condition (i.e., participants and evaluators were not aware whether they received active treatment or placebo intervention), (4) the evaluators were blinded to treatment conditions (i.e., evaluators were not aware which treatment condition participants had received), and (5) the description of dropouts was provided.

Unfortunately, few studies provided data that were corrected for attrition (i.e., ITT analysis using last-observation-carried-forward method). Six studies (1 on ASD, 2 on PTSD, and 3 on panic disorder) with an aggregate of 364 patients provided ITT data for continuous measures of anxiety disorder severity, and 8 studies (N = 524) reported ITT response rates (1 study on ASD, 1 on GAD, 1 on OCD, 2 on panic disorder, 2 on PTSD, and 1 on SAD). Our attempts to obtain ITT data from authors who did not include these in the original reports were unsuccessful. As shown in Table 1, 25 studies provided completer data for continuous measures of anxiety disorder severity (N = 1108). Response rates for completer samples were reported in 21 studies (N = 971), and 20 studies provided completer data for measures of depressive symptoms (N = 881).

Data Synthesis

Pooled analyses. There were no differences in attrition rates between CBT and placebo (OR = 1.19, 95% CI = 0.88 to 1.65, z = 1.13, p = .26). The weighted mean attrition rate was 23% for CBT and 22% for the placebo conditions. The random-effects meta-analysis of completer samples yielded mean effect sizes for the main outcome measures that were in the medium to large range, each reflecting an advantage of CBT over placebo (Figures 2 and 3). The overall Hedges' g for anxiety disorder severity was 0.73 (95% CI = 0.56 to 0.90, z = 8.62, p < .001), and the pooled OR for treatment response was 4.06 (95% CI = 2.78 to 5.92, z = 7.26, p < .001). As reflected by a mean Hedges' g of 0.45 (95% CI = 0.25 to 0.65, z = 4.52, p < .001), the effect of CBT relative to placebo on measures of depressive symptom severity was in the small to medium range.

Pooled analyses using data from ITT samples yielded smaller effect sizes. The Hedges' g for anxiety disorder severity was 0.33 (95% CI = 0.11 to 0.54, z = 2.99, p < .001), and the OR for treatment response was 1.84 (95% CI = 1.17 to 2.91, z = 2.63, p < .05).

Publication bias. The effect size observed for measures of anxiety disorder severity corresponded to a z value of 11.45. Therefore, it would require 829 failed trials for the combined 2-tailed p value to exceed .05. Fail-safe Ns for the response and measures of depression severity analyses were 411 and 183, respectively. These findings suggest that the effect sizes observed in the present study are likely to be robust.

Comparison between diagnostic groups. As can be seen in Figure 4, the effect size for continuous measures of anxiety disorder severity was largest for OCD (Hedges' g = 1.37, 95% CI = 0.64 to 2.20, z = 3.23, p < .001) followed by ASD (Hedges' g = 1.31, 95% CI = 0.93 to 1.69, z = 6.71, p < .001), SAD (Hedges' g = 0.62, 95% CI = 0.39 to 0.86, z = 5.28, p < .001), PTSD (Hedges' g = 0.62, 95% CI = 0.28 to 0.96, z = 3.59, p < .001), GAD (Hedges' g = 0.51, 95% CI = 0.05 to 0.97, z = 2.16, p = .03), and panic disorder (Hedges' g = 0.35, 95% CI = 0.04 to 0.65, z = 2.24, p = .03). Results of generalized linear models analyses revealed that the difference among anxiety disorders was significant. ($\chi^2[5] = 29.31$, p < .001). Pairwise comparisons indicated that the effect size for ASD was significantly greater relative to those observed for all other disorders with the exception of OCD (all p values < .05). In addition, the difference between OCD and panic disorder was significant (p < .05).

Differences in Hedges' g for measures of depressive symptom severity among anxiety disorders were not significant ($\chi^2[5] = 3.78$, p = .58; see Figure 4). Significant effect sizes were observed for PTSD (Hedges' g = 0.59, 95% CI = 0.20 to 0.98, z = 2.97, p < .001) and OCD (Hedges' g = 0.34, 95% CI = 0.04 to 0.65, z = 2.19, p = .03). Effects sizes approached significance for ASD (Hedges' g = 0.32, 95% CI = –0.03 to 0.66, z = 1.79, p = .07) and SAD (Hedges' g = 0.66, 95% CI = –0.10 to 1.42, z = 1.42, p = .09). Nonsignificant effect sizes were observed for GAD (Hedges' g = 0.38, 95% CI = –0.23 to 0.98, z = 1.22, p = .22) and panic disorder (Hedges' g = 0.14, 95% CI = –0.21 to 0.49, z = 0.78, p = .43).

A comparison of the ORs of treatment response showed a similar pattern of results. As shown in Figure 5, the largest OR was observed for OCD (OR = 12.24, 95% CI = 2.91 to 51.55, z = 3.42, p < .001) and ASD (OR = 8.07, 95% CI = 1.96 to 33.21, z = 2.89, p < .001), followed by SAD (OR = 4.21, 95% CI = 2.07 to 8.98, z = 3.90, p < .001), PTSD (OR = 3.06, 95% CI = 1.54 to 6.07, z = 3.19, p < .001), and panic disorder (OR = 2.52, 95% CI = 1.18 to 5.39, z = 2.38, p < .002). The OR did not reach statistical significance for GAD (OR = 2.27, 95% CI = 0.49 to 10.56, z = 1.04, p = .30).

Moderator analyses. The Hedges' g for anxiety disorder severity was not moderated by the number of sessions (β = –.02, SE = .02, p = .47), publication year (β = .02,

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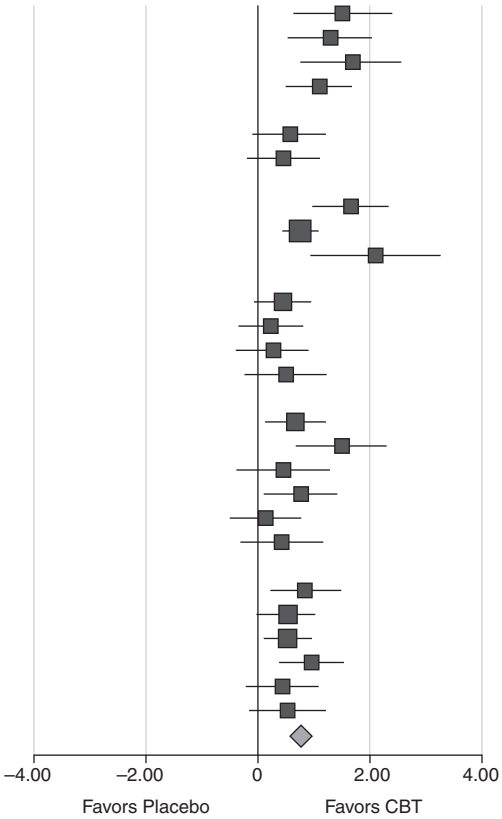
Figure 2. Effect Size Estimates (Hedges' g) and the Statistical Tests of the Acute Treatment Efficacy of CBT Compared to Placebo on the Primary Continuous Anxiety Measures for the Identified Studies[a]

Study	Statistic: Hedges' g	95% CI	z Value	p Value
Acute Stress Disorder				
Bryant et al[22] (1998)	1.49	0.60 to 2.38	3.29	.00
Bryant et al[25] (1999)	1.28	0.52 to 2.04	3.29	.00
Bryant et al[26] (2003)	1.66	0.75 to 2.58	3.57	.00
Bryant et al[27] (2005)	1.08	0.47 to 1.69	3.47	.00
Generalized Anxiety Disorder				
Borkovec and Costello[28] (1993)	0.57	–0.08 to 1.21	1.71	.09
Wetherell et al[35] (2003)	0.44	–0.21 to 1.10	1.34	.18
Obsessive-Compulsive Disorder				
Foa et al[38] (2005)	1.65	0.95 to 2.35	4.62	.00
Greist et al[42] (2002)	0.74	0.40 to 1.08	4.32	.00
Lindsay et al[46] (1997)	2.08	0.91 to 3.26	3.48	.00
Panic Disorder				
Bakker et al[47] (1999)	0.43	–0.09 to 0.96	1.62	.11
Barlow et al[50] (2000)	0.23	–0.35 to 0.81	0.77	.44
Black et al[52] (1993)	0.26	–0.40 to 0.92	0.78	.44
Craske et al[54] (1995)	0.49	–0.25 to 1.22	1.29	.20
PTSD				
Blanchard et al[60] (2003)	0.65	0.11 to 1.20	2.35	.02
Bryant et al[65] (2003)	1.48	0.68 to 2.29	3.61	.00
Foa et al[67] (1991)	0.44	–0.39 to 1.28	1.05	.30
Marks et al[69] (1998)	0.75	0.11 to 1.40	2.28	.02
McDonagh et al[70] (2005)	0.13	–0.50 to 0.77	0.41	.68
Neuner et al[72] (2004)	0.41	–0.32 to 1.14	1.10	.27
Social Anxiety Disorder				
Clark et al[75] (2003)	0.89	0.25 to 1.53	2.72	.01
Cottreaux et al[79] (2000)	0.51	–0.02 to 1.04	1.89	.06
Davidson et al[81] (2004)	0.52	0.09 to 0.96	2.36	.02
Heimberg et al[84] (1998)	0.94	0.36 to 1.52	3.15	.00
Lucas[87] (1994)	0.43	-0.23 to 1.09	1.28	.20
Smits et al[88] (2006)	0.53	–0.15 to 1.21	1.52	.13
Overall	0.73	0.56 to 0.90	8.62	.00



[a]With the exception of the Barlow et al.[50] trial, all effect size estimates are based on the combination of the main outcome measures. The Barlow et al.[50] trial was based on the Panic Disorder Severity Scale.[51]
Abbreviation: CBT = cognitive-behavioral therapy.

SE = .02, p = .37), or placebo modality (i.e., psychological vs. pill placebo; β = 0.14, SE = .20, p = .46). Similarly, the effect sizes for continuous measures of depression symptom severity did not depend on the number of sessions (β = 0.24, SE = .03, p = .41), publication year (β = –0.13, SE = .02, p = .59), or placebo modality (β = 0.21, SE = .26, p = .42).

DISCUSSION

A number of meta-analyses support the efficacy of CBT for anxiety disorders. However, existing meta-analyses of CBT focused on only 1 or a few selected disorders and included a heterogeneous number of studies ranging from randomized placebo-controlled trials to small uncontrolled, open-label studies. This led some authors to question the validity of the findings from these analyses.[8] Limiting a meta-analysis to only randomized placebo-controlled studies circumvents some of these methodological problems.

The goal of the present study was to estimate the efficacy of CBT compared to psychological or pharmacologic placebo conditions, to compare the efficacy of CBT for DSM-III-R or DSM-IV anxiety disorders, and to examine whether the number of treatment sessions, the placebo modality, and publication year moderates treatment outcome. To answer these questions, we screened 1165 studies and identified 27 randomized placebo-controlled trials totaling 1496 patients. As reflected by medium to large effect sizes for measures of anxiety disorder severity, CBT yields significantly greater benefits than placebo treatments. The results revealed that the effects were significantly greater for ASD relative to all other disorders with exception of OCD. Moreover, CBT for OCD was more effective than CBT for panic disorder. This pattern of result is somewhat surprising and runs counter to the

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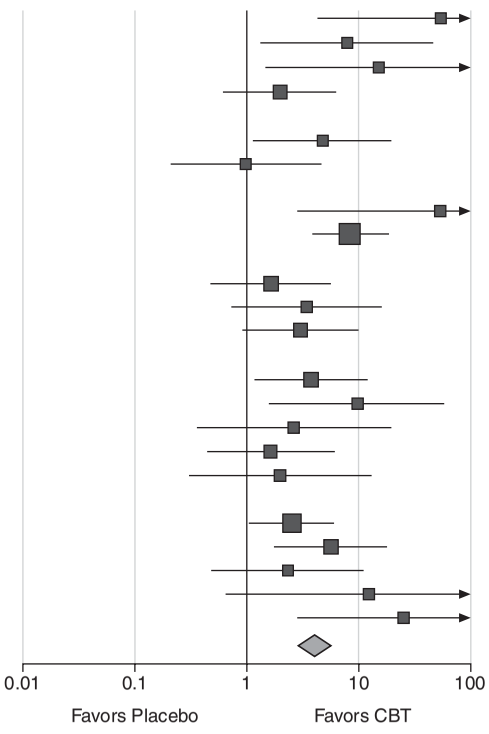
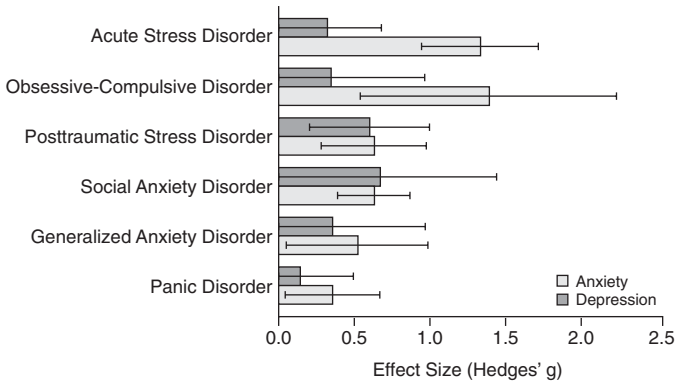
Figure 3. Odds Ratios and Statistical Tests of the Acute Treatment Response to CBT Versus Placebo for the Identified Studies

Study	Outcome	Statistic: Odds Ratio	95% CI	z Value	p Value
Acute Stress Disorder					
Bryant et al[22] (1998)	CIDI = No PTSD Diagnosis	55.00	4.30 to 703.43	3.08	.00
Bryant et al[25] (1999)	CAPS-2 = No PTSD Diagnosis	8.00	1.33 to 48.18	2.27	.02
Bryant et al[26] (2003)	CAPS-2 = No PTSD Diagnosis	15.40	1.47 to 160.97	2.28	.02
Bryant et al[27] (2005)	CAPS-2 = No PTSD Diagnosis	2.02	0.62 to 6.55	1.17	.24
Generalized Anxiety Disorder					
Borkovec and Costello[28] (1993)	6 Outcome Measures > 20% Improvement	4.81	1.14 to 20.25	2.14	.03
Wetherell et al[35] (2003)	3 Outcome Measures > 20% Improvement	1.00	0.21 to 4.81	0.00	1.00
Obsessive-Compulsive Disorder					
Foa et al[38] (2005)	CGI-I = 1	53.95	2.88 to 1009.80	2.67	.01
Greist et al[42] (2002)	CGI-I < 3	8.52	3.83 to 18.96	5.25	.00
Panic Disorder					
Barlow et al[50] (2000)	CGI-I < 3 and CGI-S < 4	1.67	0.48 to 5.81	0.80	.42
Black et al[52] (1993)	CGI-I < 3	3.47	0.73 to 16.53	1.56	.12
Sharp et al[59] (1996)	SRT[92] = CSC[93]	3.07	0.91 to 10.30	1.81	.07
PTSD					
Blanchard et al[60] (2003)	CAPS-2 = No PTSD Diagnosis	3.77	1.16 to 12.27	2.20	.03
Bryant et al[65] (2003)	CAPS-2 = No PTSD Diagnosis	9.75	1.59 to 59.70	2.46	.01
Foa et al[67] (1991)	PTSD Symptom Scale = CSC	2.67	0.36 to 19.71	0.96	.34
McDonagh et al[70] (2005)	CAPS-2 = No PTSD Diagnosis	1.65	0.44 to 6.20	0.74	.46
Neuner et al[72] (2004)	SRQ-20[94] > 10	2.00	0.30 to 13.26	0.72	.47
Social Anxiety Disorder					
Davidson et al[81] (2004)	CGI-I < 3	2.55	1.05 to 6.21	2.07	.04
Heimberg et al[84] (1998)	SPDS-S < 3 and SPDS-C[85] < 3	5.67	1.75 to 18.38	2.89	.00
Lucas[87] (1994)	2 Outcome Measures = Reliable Change[93]	2.33	0.48 to 11.40	1.05	.30
Smits et al[88] (2006)	LSAS-SR > 50% Improvement	12.63	0.64 to 250.04	1.66	.10
Turner et al[90] (1994)	CGI-I < 3	25.33	2.84 to 226.07	2.89	.00
Overall		4.06	2.78 to 5.92	7.26	.00



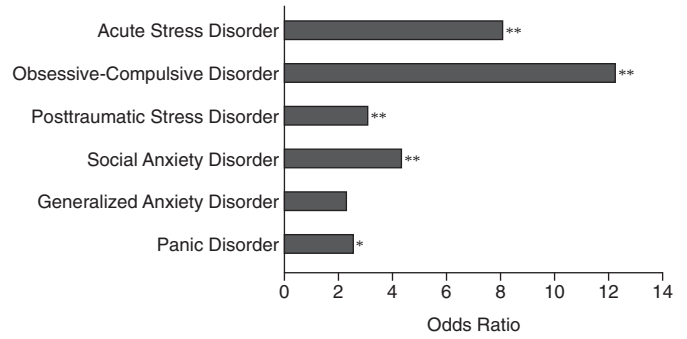
Abbreviations: CAPS-2 = Clinician-Administered PTSD Scale, version 2; CBT = cognitive-behavioral therapy; CGI-I = Clinical Global Impressions-Improvement scale; CGI-S = Clinical Global Impressions-Severity of Illness scale; CIDI = Composite International Diagnostic Interview; CSC = clinically significant change; LSAS-SR = Liebowitz Social Anxiety Scale-Self Report; PTSD = posttraumatic stress disorder; SPDS-C = Social Phobic Disorders Severity and Change Form; SPDS-S = Social Phobic Disorder Severity and Change Form-Severity; SRQ-20 = Self-Reporting Questionnaire 20; SRT = Symptom Rating Test.

Figure 4. Mean Effect Size Estimates (Hedges' g) and Corresponding 95% CIs of the Acute Treatment Efficacy of CBT as Compared to Placebo on the Various Anxiety Disorders for the Primary Continuous Anxiety and Depression Measures



Abbreviation: CBT = cognitive-behavioral therapy.

Figure 5. Mean Odds Ratios of Acute Treatment Response to CBT as Compared to Placebo and Statistical Tests for the Various Anxiety Disorders



*p < .05.
**p < .001.
Abbreviation: CBT = cognitive-behavioral therapy.

general notion that OCD is the most treatment-resistant anxiety disorder. Obviously, a strong effect size based on a large number of patients in clinical trials does not rule out the possibility of encountering a highly treatment-resistant case in clinical practice. This disjunction between clinical experience and empirical data may be particularly evident in disorders with a wide range of symptomatology and severity, as is the case in OCD-spectrum disorders.

The overall effect size findings are generally in line with more recent meta-analyses that examined only single disorders using considerably less stringent inclusion criteria for the original studies.[95–99] These studies reported effect sizes for CBT that were in the medium to large range. Moreover, we observed no difference between the pill placebo and the psychological placebo condition, and the psychological placebo conditions were structurally equivalent to the respective CBT intervention. Therefore, it is unlikely that the effect sizes found in the present study were systematically biased by the choice or the structure and duration of the placebo control condition.[100] Finally, the publication bias is unlikely to account for the observed effects.

In order to examine the specificity of the CBT intervention for reducing anxiety, we explored the treatment effects on depression in addition to the targeted anxiety disorder. We chose to examine the effects on depression because of the high comorbidity between anxiety and depression and because CBT for anxiety disorders was originally derived from the CBT approach for depression. Although the pooled effect size was statistically significant (Hedges' $g = 0.45$, $p < .001$), a comparison between CBT and placebo by the diagnostic groups showed that CBT significantly outperformed placebo in reducing depression only in PTSD and OCD. These findings support the specificity of CBT for most of the anxiety disorders.

Although we avoided many of the potential methodological problems of meta-analytic studies, there remain a number of notable weaknesses. First, although the majority of studies included in the analyses were of generally high quality as assessed by the Jadad criteria,[91] a surprisingly large number of these studies failed to report ITT data. Despite our attempts to obtain these data from the investigators, it was not possible to gather enough information to compare the ITT effect sizes between the specific anxiety disorders. The pooled ITT effect size for continuous anxiety severity measures and the OR for treatment response were small (Hedges' $g = 0.33$; $OR = 1.84$) but statistically significant. Because of the small number of studies, the results of these analyses should be interpreted with caution (6 studies for the analyses of the continuous measures and 8 studies for the dichotomous response rate estimate). It is, however, interesting that the completer analyses yielded greater effect sizes than the ITT analyses. The dropout rates in CBT were relatively small and, therefore, are unlikely to account for this difference. A plausible explanation is the fact that the ITT analyses included mostly studies with panic disorder samples, which in the completer analyses were associated with relatively small effect sizes (see Figure 4).

Despite recent findings indicating that effect sizes for ITT samples may not differ from those observed with completer samples,[98] it is quite possible that the effect sizes of the completer analyses are biased. Given the status of CBT as the gold standard psychosocial intervention for treating anxiety disorders, it is very surprising and concerning that after more than 20 years of CBT treatment research, we were able to identify only 6 high-

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quality randomized placebo-controlled CBT trials that provided ITT analyses for continuous measures and only 8 trials for ITT response rate analyses. In our opinion, this is an unacceptable situation that will have to change for psychosocial intervention to become a viable alternative to pharmacotherapy in the medical community.

Second, most of the trials that were selected also included combined-treatment conditions, such as a combination of CBT and pharmacotherapy or a combination of CBT and pill placebo. These conditions were not included in the present analyses because the objective of this study was to examine the efficacy of CBT as monotherapy compared to placebo as monotherapy. Third, CBT refers to a family of interventions that share basic therapeutic principles and treatment rationale. However, the specific treatment techniques and emphasis on the various treatment components differ from disorder to disorder. These differences might have accounted for some of the differences in treatment efficacy. Similarly, there was some variation in the nature of the placebo conditions, and it is possible that some placebo conditions were more efficacious than others. However, we did not find any systematic differences between the trials in placebo conditions, and there was no difference between psychological and pill placebos. Finally, although we limited the diagnoses to DSM-III-R and DSM-IV criteria, we were unable to estimate the effect size of panic disorder with agoraphobia separate from panic disorder without agoraphobia because most of the clinical trials on panic disorder did not distinguish these 2 diagnostic groups.

Despite these weaknesses, our quantitative literature review of randomized placebo-controlled trials provides strong support for the efficacy of CBT as an acute intervention for adult anxiety disorders. At the same time, the results also suggest that there is still considerable room for further improvement. As suggested by recent findings, pharmacologic augmentation strategies designed to enhance the learning that occurs with CBT approaches for anxiety disorders may hold particular promise.[93,101]

Acknowledgments: The authors thank Angela Berry (Southern Methodist University, Dallas, Tex.), Erik Müller and Christiane Suttner (University of Marburg, Germany), and Kristina Korte (Boston University, Mass.) for their assistance with data extraction as well as Mark Powers, Ph.D. (University of Amsterdam, the Netherlands) for his comments on an earlier version of this manuscript and David Rosenfield, Ph.D. (Southern Methodist University, Dallas, Tex.) for his statistical advice. The authors also wish to thank the many authors of the original studies included in these analyses for their valuable support. None of the acknowledged individuals report any financial or other relevant relationships related to the article.

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