

**COGNITIVE-BEHAVIORAL THERAPY FOR ADULT ANXIETY DISORDERS:
A META-ANALYSIS OF RANDOMIZED PLACEBO-CONTROLLED TRIALS**

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ABSTRACT

Objective: Cognitive-behavioral therapy (CBT) is frequently used for various adult anxiety disorders, but there has been no systematic review of 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 of treatment outcome studies of anxiety disorders between the 1st available year and March 1, 2007. 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 meeting DSM-III-R or DSM-IV criteria for an anxiety disorder to either CBT or placebo. Of 1,165 studies that were initially identified, 27 met all inclusion criteria

Data Extraction: The two 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 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 effect models of completer samples yielded a pooled effect size (Hedges' g) of 0.73 (95% confidence interval, 0.88-1.65) for continuous anxiety severity measures and 0.45 (90% confidence interval, 0.25-0.65) for depressive symptom severity measures. The pooled odds ratio for completer treatment response rates was 4.06 (95% confidence interval, 2.78-5.92). The strongest effect sizes were observed for obsessive-compulsive disorder and acute stress

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 intent-to-treat analyses in the future.

INTRODUCTION

Epidemiological studies indicate that anxiety disorders are the most prevalent class of mental disorders with a 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 ^{5,6,7,8,9,10}. 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 waitlist, alternative treatments, and placebo interventions 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 is 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. 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 for 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 used the search terms *random** in order to identify randomized controlled studies and we used 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*, *Generalised 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: (1) patients had to be between ages 18 and 65 and met 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 samples¹²; (2) 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; (3) the clinical severity of the anxiety disorder had to be assessed by means of psychometrically sound clinician-rated or self-report measures; and (4) 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 sub-analyses of a larger, more complete, or earlier study were excluded from the analysis.

DATA EXTRACTION

The two 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. Measures of depressive symptom severity were also collected to study the specificity of CBT for the target problem. For each of these decisions, disagreement between the two 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 sizes for the difference between CBT and placebo. For continuous measures, we calculated the Hedges' g effect size and its 95% confidence interval. This effect size is a variation on Cohen's d that corrects for biases due to small sample sizes¹³ and is calculated using the following formula:

$$g = \frac{\bar{\Delta}_{CBT} - \bar{\Delta}_{PLA}}{\sqrt{\frac{(n_{CBT} - 1)SD_{CBT}^2 + (n_{PLA} - 1)SD_{PLA}^2}{(n_{total} - 2)}}} \times \left(1 - \frac{3}{4(n_{CBT} + n_{PLA}) - 9}\right), \text{ where } \bar{\Delta} \text{ is the mean pre- to}$$

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 (1988) 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% confidence interval using the Cox–Hinkley–Miettinen–Nurminen method ¹⁴. The odds ratio 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 one group (patients in the CBT group) to the ratio of the event in another group (patients in the placebo condition). Thus, OR was calculated using the following formula:

$$OR = \frac{p/(1-p)}{q/(1-q)}, \text{ where } p \text{ refers to the percent responders or drop-outs in the CBT}$$

condition and q to the percent responders or drop-outs in the placebo condition. An odds ratio 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 ^{15,16} instead of fixed-effects models, because random-effects models are more appropriate when the aim is to generalize beyond the observed studies ¹⁵. 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 non-significant findings are often not published, a bias that is also known as the *File Drawer Problem* ¹⁷. 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 non-significant level ¹⁸. According to Rosenthal ¹⁹, 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 ²⁰.

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.

RESULTS

STUDY SELECTION

Figure 1 presents a flow diagram illustrating the study selection process. Our search strategy yielded 1,165 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 (PD; $n=5$), acute stress disorder (ASD; $n=4$), obsessive-compulsive disorder (OCD; $n=3$), and generalized anxiety disorder (GAD; $n=2$). We did not identify any studies that compared CBT to a 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 ²¹: (a) The study was described as randomized; (b) Participants were adequately randomized (e.g., adequate randomization procedure; the study reported withdrawals and dropouts); (c) Participants and evaluators were blinded to treatment condition (i.e., participants and evaluators were not aware whether they received active treatment or placebo intervention); (d) The evaluators were blinded to treatment conditions (i.e., evaluators were not aware which treatment condition participants had received; and (e) the description of drop-outs was provided.

Unfortunately, only few studies provided data that was corrected for attrition (i.e., ITT using last observation carried forward method). Only 6 studies provided ITT data for continuous measures of anxiety disorder severity from an aggregate of 364 patients (1 study on ASD, 2 on PTSD, and 3 on PD), and 8 studies ($n=524$) reported ITT response rates (1 study on ASD, 1 on GAD, 1 on OCD, 2 on PD, 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 ($n = 1,108$). 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: 0.88-1.65, $z = 1.13$, $P = .26$). 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 (see Figures 2 and 3). The overall Hedges' g for anxiety disorder severity was 0.73 (95% CI: 0.56-0.90, $z = 8.62$, $P < .001$), and the pooled OR for treatment response was 4.06 (95% CI: 2.78-5.92, $z = 7.26$, $P < .001$). As reflected by a mean Hedges' g of 0.45 (95% CI: 0.25-0.65, $z = 4.52$, $P < .001$) 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: 0.11-0.54, $z = 2.99$, $P < .001$), and the OR for treatment response was 1.84 (95% CI: 1.17-2.91, $z = 2.63$, $P < .05$).

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 two-tailed p -value to exceed .05. Fail-safe N s 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: 0.64-2.20, $z = 3.23$, $P < .001$) followed by ASD (Hedges' $g = 1.31$, 95% CI: 0.93-1.69, $z = 6.71$, $P < .001$), SAD (Hedges' $g = 0.62$, 95% CI: 0.39-0.86, $z = 5.28$, $P < .001$), PTSD (Hedges' $g = 0.62$, 95% CI: 0.28-0.96, $z = 3.59$, $P < .001$), GAD (Hedges' $g = 0.51$, 95% CI: 0.05-0.97, $z = 2.16$, $P = .03$), and PD (Hedges' $g = 0.35$, 95% CI: 0.04-0.65, $z = 2.24$, $P = .03$). 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 s < .05). In addition, the difference between OCD and PD 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: 0.20-0.98, $z = 2.97$, $P < .001$) and OCD (Hedges' $g = 0.34$, 95% CI: 0.04-0.65, $z = 2.19$, $P = .03$). Effects sizes approached significance for ASD (Hedges' $g = 0.32$, 95% CI: -0.03-0.66, $z = 1.79$, $P = .07$) and SAD (Hedges' $g = 0.66$, 95% CI: -0.10-1.42, $z = 1.42$, $P = .09$). Non-significant effect sizes were observed for GAD (Hedges' $g = 0.38$, 95% CI: -0.23-0.98, $z = 1.22$, $P = .22$) and PD (Hedges' $g = 0.14$, 95% CI: -0.21-0.49, $z = 0.78$, $P = .43$).

A comparison of the odds ratios of treatment response showed a similar pattern of results. As shown in Figure 5, the largest odds ratio was observed for OCD ($OR = 12.24$, 95% CI: 2.91-51.55, $z = 3.42$, $P < .001$) and ASD ($OR = 8.07$, 95% CI: 1.96-33.21, $z = 2.89$, $P < .001$), followed by SAD ($OR = 4.21$, 95% CI: 2.07-8.98, $z = 3.90$, $P < .001$), PTSD ($OR = 3.06$, 95% CI: 1.54-6.07, $z = 3.19$, $P < .001$), and PD ($OR = 2.52$, 95% CI: 1.18-5.39, $z = 2.38$, $P < .002$). The odds ratio did not reach statistical significance for GAD ($OR = 2.27$, 95% CI: 0.49-10.56, $z = 1.04$, $P = .03$).

Moderator analyses

The Hedges' g for anxiety disorder severity was not moderated by the number of sessions ($B = -.02$, $SE = .02$, $P = .47$), publication year ($B = .02$, $SE = .02$, $P = .37$), or placebo modality (i.e., psychological vs. pill placebo; $B = 0.14$, $SE = .20$, $P = .46$). Similarly, the effect sizes for continuous measures of depression symptom severity did not depend on the number of sessions

($B = 0.24$, $SE = .03$, $P = .41$), publication year ($B = -0.13$, $SE = .02$, $P = .59$), or placebo modality ($B = 0.21$, $SE = .26$, $P = .42$).

CONCLUSIONS

A number of meta-analyses support the efficacy of CBT for anxiety disorders. However, existing meta-analyses of CBT have focused on only one 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 analyses⁸. 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 pharmacological 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 1,165 studies and identified 27 randomized placebo-controlled trials totaling 1,496 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 PD. This pattern of result is somewhat surprising and runs counter the 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 only examined single disorders using considerably less stringent inclusion criteria for the original studies^{90,91,92,93,94}. 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 condition⁹⁵. 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 only significantly outperformed placebo in reducing depression 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 that were included in the analyses were of generally high quality as assessed by the Jadad criteria²¹, 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, surprising 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 effects sizes for ITT samples may not differ from those observed with completer samples⁹³, 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 only able to identify 6 high-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 between CBT and pharmacotherapy, or a combination between CBT and pill placebo. These conditions were not included in the present analyses because the objective of this study was to only examine the efficacy of CBT as monotherapy as

compared to placebo as monotherapy. Third, CBT refers to a family of interventions that share the 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 sizes of panic disorder with agoraphobia separate from panic disorder without agoraphobia because most of the clinical trials on panic disorder did not distinguish these two 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, pharmacological augmentation strategies designed to enhance the learning that occurs with CBT approaches for anxiety disorders may hold particular promise^{96,97}.

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Table 1: Characteristics of Studies Included in the Meta-analysis.

Disorder/ Study	Target Disorder	CBT Type	Placebo Type	Sample Size (CBT plus Placebo)	Number of Sessions	Anxiety Measures	Depression Measures	Analyses	Jadad Score
Bryant et al., 1998 ²²	ASD	CBT	Supportive Counseling	24	5	IES	BDI	Completer	1
Bryant et al., 1999 ²⁵	ASD	CBT	Supportive Counseling	38	6	IES	BDI	Completer	2
Bryant et al., 2003 ²⁶	ASD	CBT	Supportive Counseling	24	5	IES	BDI	Completer	3
Bryant et al., 2005 ²⁷	ASD	CBT	Supportive Counseling	57	6	IES	BDI	Completer, ITT	3
Borkovec & Costello, 1997 ²⁸	GAD	CBT	Nondirective Therapy	43	12	HAM-A, ADIS-R Severity, STAI-T, ZSRA, PSWQ	BDI; HAM-D	Completer	2
Wetherell et al., 2003 ³⁵	GAD	CBT	Discussion Group	52	12	ADIS-IV Severity, HAM-A, PSWQ, BAI	BDI; HAM-D	Completer	2
Foa et al., 2005 ³⁸	OCD	ERP	Pill Placebo	55	15	CGI-S, YBOCS NIMH Global OC Scale		Completer	3
Greist et al., 2002 ⁴¹	OCD	BT	Systematic Relaxation	167	10	YBOCS, WSAS	HAM-D	Completer	1

Lindsay et al., 1997 ⁴⁵	OCD	ERP	Anxiety Management	18	15	YBOCS, PADUA, MOCI: Interference Rating Scale	BDI	Completer	1
Bakker et al., 1999 ⁴⁶	PD	CT	Pill Placebo	67	12	CGI-S, MSPS, PGE; Panic Frequency, Overall Phobia Score, Anticipatory Anxiety Score	MADRS	Completer, ITT	2
Barlow et al., 2000 ⁴⁹	PD	CBT	Pill Placebo	101	12	PDSS		Completer, ITT	3
Black et al., 1993 ⁵¹	PD	CT	Pill Placebo	50	8	CGI-S, CAS, Panic Attack Severity Score, SDS	MADRS	Completer, ITT	2
Craske et al., 1995 ⁵³	PD	CBT	Nondirective-Supportive Therapy	30	4	ADIS-R – Severity, ASI, FQ, FDAS, Subjective Symptoms Scale		Completer	2
Sharp et al., 1996 ⁵⁷	PD	CBT	Pill Placebo	80	10		MADRS	ITT	2
Blanchard et al., 2003 ⁵⁸	PTSD	CBT	Supportive Counseling	73	12	CAPS-2, BSI, IES, LIFE, PCL	BDI	Completer	2
Bryant et al., 2003 ⁶³	PTSD	CBT	Supportive Counseling	38	8	CAPS-2, IES, CCQ	BDI	Completer	3

Foa et al., 1991 ⁶⁵	PTSD	PE	Supportive Counseling	28	9	PTSD symptom scale	BDI	Completer	2
Marks et al., 1998 ⁶⁷	PTSD	CBT	Relaxation	45	10	PTSD symptom scale, IES	BDI	Completer	2
McDonagh et al., 2005 ⁶⁸	PTSD	CBT	Problem- Solving Therapy	51	14	CAPS-2, QOLI	BDI	Completer, ITT	2
Neuner et al., 2004 ⁷⁰	PTSD	NET	Supportive Counseling	31	4	PDS, MOS		Completer	2
Clark et al., 2003 ⁷³	SAD	CT	Pill Placebo	43	16	ADIS- Severity, SPS, SIAS, LSAS, FQ-SP, FNE; SPWWS	BDI	Completer	2
Cottraux et al., 2000 ⁷⁷	SAD	CBT	Supportive Therapy	63	8	LSAS, QOL, FQ, SISST	BDI	Completer	3
Davidson et al., 2004 ⁷⁹	SAD	CCBT	Pill Placebo	120	14	CGI-S, BSPS, SPAI			3
Heimberg et al., 1998 ⁸²	SAD	CBGT	Educational Supportive Group Therapy; Pill Placebo*	69	12	ADIS-R- Severity, SPDS-S, LSAS, FNE, SAD, SPS, SCL-90-R-IS, SCL-90-R- PA, Impromptu Speech Task	SCL-90-R- Depression	Completer	3

Lucas, 1994 ⁸⁵	SAD	CBGT	Educational- Supportive Group Therapy	44	12	SPAI; SIAS; SPS, SISST	BDI	Completer	2
Smits et al., 2006 ⁸⁶	SAD	BT	Psychological Placebo	38	3	LSAS-SR, Impromptu Speech Task		Completer	2
Turner et al., 1994 ⁸⁸	SAD	BT	Pill Placebo	47	20			Completer	2

Note: ASD = Acute Stress Disorder; GAD = Generalized Anxiety Disorder; OCD = Obsessive Compulsive Disorder; PD = Panic Disorder; PTSD = Post Traumatic Stress Disorder; SAD = Social Anxiety Disorder. BT = Behavior Therapy; CT = Cognitive Therapy; CBGT = Cognitive-Behavioral Group Therapy; CBT = Cognitive-Behavioral Therapy; CCBT = Comprehensive Cognitive-Behavioral Therapy; ERP = Exposure and Response Prevention; NET = Narrative Exposure Therapy; PE = Prolonged Exposure. ADIS-IV = Anxiety Disorder Interview Schedule for DSM-IV ³⁶; ADIS-R = Anxiety Disorder Interview Schedule Revised ³⁰; ASI = Anxiety Sensitivity Index ⁵⁴; BAI = Beck Anxiety Inventory ³⁷; BDI = Beck Depression Inventory ²⁴; BSI = Brief Symptom Inventory ⁶⁰; BSPS = Brief Social Phobia Scale ⁸⁰; CAPS-2 = Clinician Administered PTSD Scale, version 2 ⁵⁹; CAS = Clinical Anxiety Scale ⁵²; CCQ = Catastrophic Cognitions Questionnaire ⁶⁴; CGI - S = Clinical Global Impressions Scale – Severity ³⁹; FDAS = Four Dimensional Anxiety Scale ⁵⁶; FNE = Fear of Negative Evaluation Scale ⁷⁶; FQ = Fear Questionnaire ⁵⁵; FQ – SP = Fear Questionnaire – Social Phobia scale ⁵⁵; HAM-A = Hamilton Anxiety Rating Scale ²⁹; HAM – D = Hamilton Depression Rating Scale ³¹; IES = Impact of Event Scale ²³; LIFE = The LIFE Base ⁶¹; LSAS = Liebowitz Social Anxiety Scale ⁷⁵; LSAS-SR = Liebowitz Social Anxiety Scale – Self Report ⁸⁷; MADRS = Montgomery-Asberg Depression Rating Scale ⁴⁸; MOCI = Maudsley Obsessional-Compulsive Inventory ⁴⁴; MSPS = Marks-Sheehan Phobia Scale ⁴⁷; PADUA = The Padua Inventory ⁴³; PCL = PTSD Checklist ⁶²; PDS = Post-traumatic Stress Diagnostic Scale ⁷¹; PDSS = Panic Disorder Severity Scale

⁵⁰; PGE = Patient Global Evaluation ⁴⁷; PSWQ = Penn State Worry Questionnaire ³⁴; PTSD symptom scale = Post-traumatic Stress Disorder Symptom Scale⁶⁶; QOL = Quality of Life scale ⁷⁷; QOLI = Quality of Life Index ⁶⁹; SAD = Social Avoidance and Distress Scale ⁷⁶; SCL – 90-R-Depression = Symptom Checklist 90 Revised – Depression ⁸⁴; SCL – 90-R-IS = Symptom Checklist 90 Revised – Interpersonal Sensitivity ⁸⁴; SCL-90- PA = Symptom Checklist 90 Revised – Phobic Anxiety ⁸⁴; SDS = Sheehan Disability Scale ⁴⁷; SIAS = Social Interaction Anxiety Scale ⁷⁴; SISST = Social Interaction Self-Statement Test ⁷⁸; SPAI = Social Phobia Anxiety Inventory ⁸¹; SPDS-S = Social Phobic Disorder Severity and Change Form – Severity ⁸³; SPS = Social Phobia Scale ⁷⁴; SPWSS = Social Phobia Weekly Summary Scale ⁷³; SRT = Symptom Rating Test⁷²; STAI-T = State Trait Anxiety Inventory – Trait subscale ³²; WSAS = Work and Social Adjustment Scale ⁴²; YBOCS = Yale Brown Obsessive Compulsive Scale ⁴⁰; ZSRA = Zung Self-Rating of Anxiety Scale ³³.

Figure 1: Study selection and reasons for exclusions.

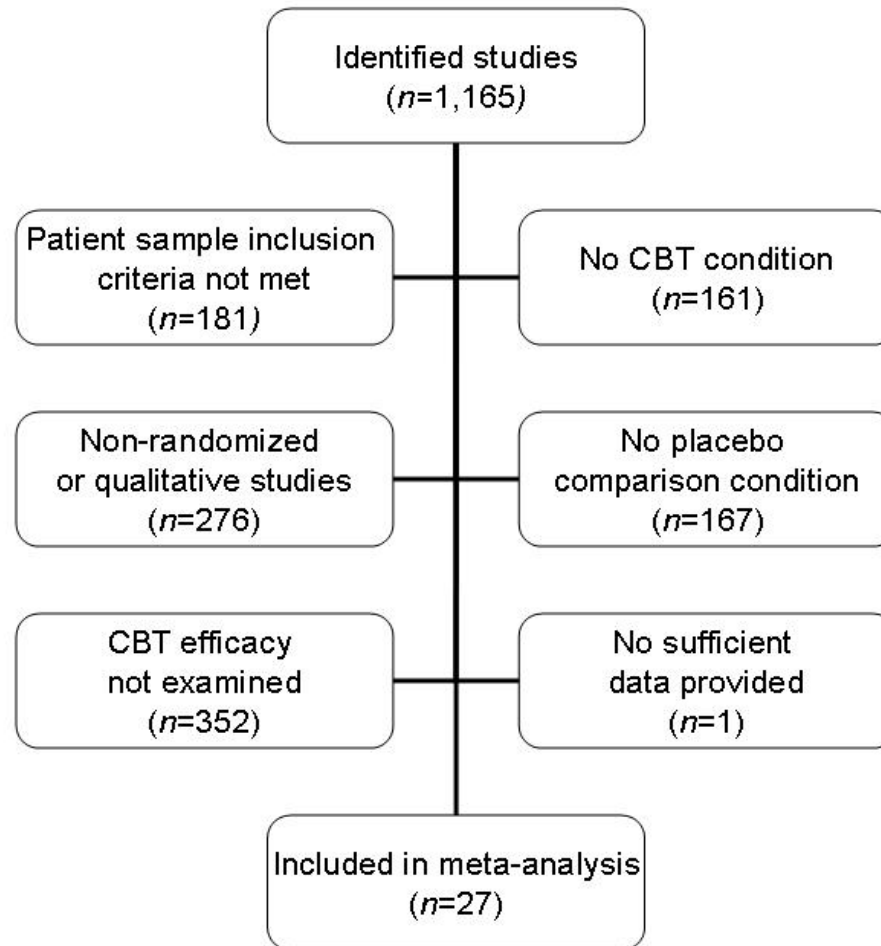
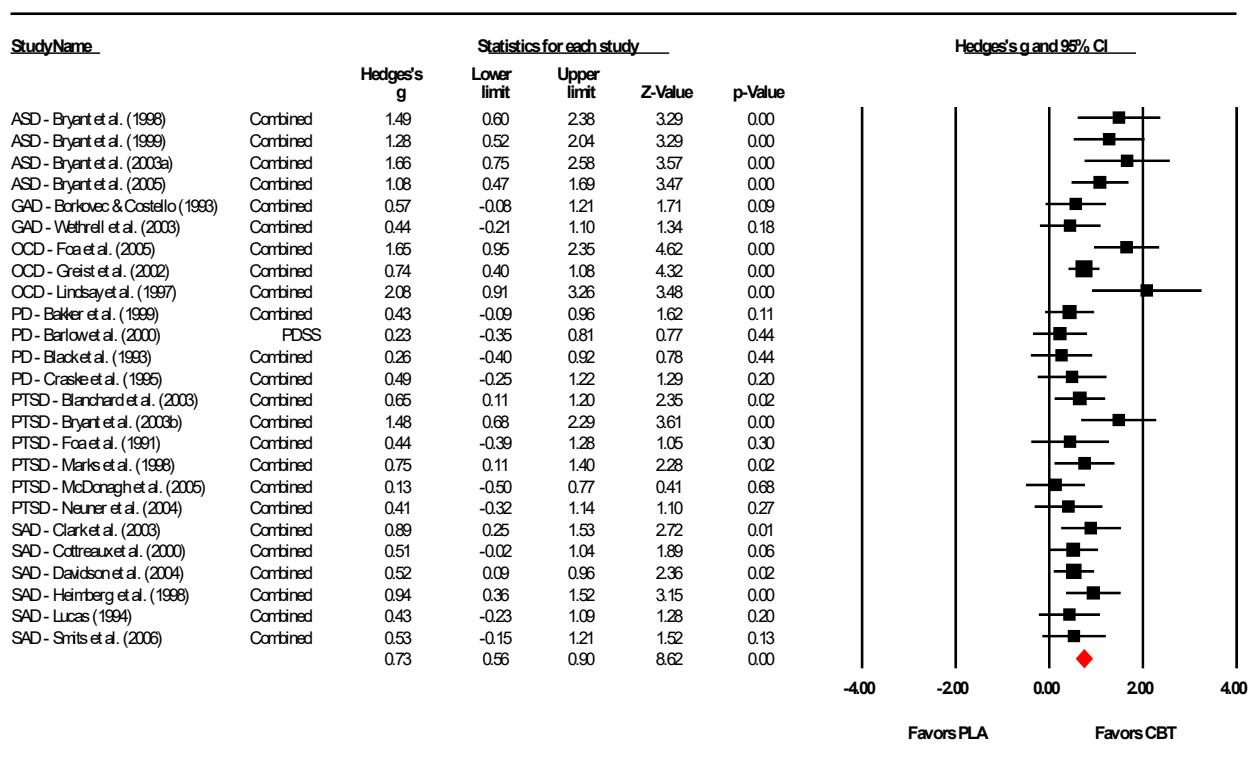
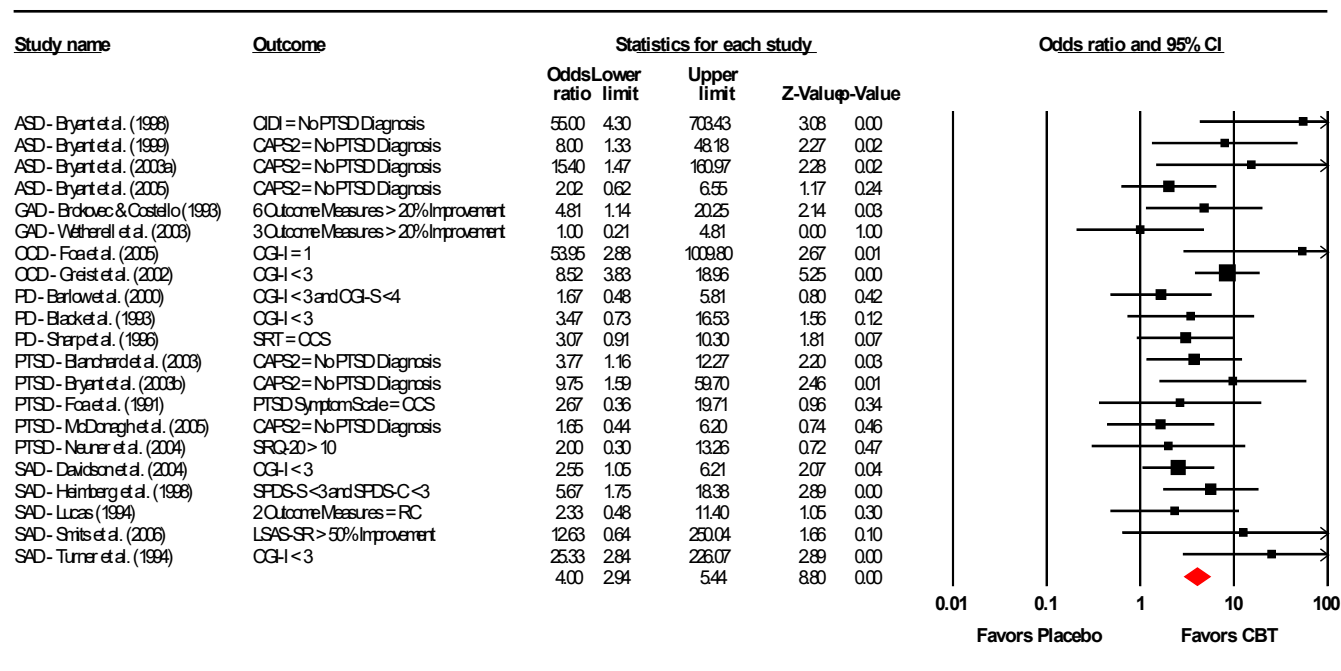


Figure 2: Effect size estimates (Hedges' g) and the statistical tests of the acute treatment efficacy of CBT compared to placebo on the primary continuous anxiety measures for the identified studies.



Note: ASD = Acute Stress Disorder; GAD = Generalized Anxiety Disorder; OCD = Obsessive-Compulsive Disorder; PD = Panic Disorder; PTSD = Post Traumatic Stress Disorder; SAD = Social Anxiety Disorder.

Figure 3: Odds ratios and statistical tests of the acute treatment response to CBT versus placebo for the identified studies.



Note: CIDI = Composite International Diagnostic Interview; CAPS-2 = Clinician Administered PTSD Scale, version 2⁵⁹; CGI - S = Clinical Global Impressions Scale – Improvement³⁹; SRT = Symptom Rating Test⁷²; PTSD symptom scale = Post-traumatic Stress Disorder Symptom Scale⁶⁶; SPDS-S = Social Phobic Disorder Severity and Change Form – Severity⁸³; LSAS-SR = Liebowitz Social Anxiety Scale – Self Report⁸⁷; CSS = Clinically Significant Change⁹⁷; RC = Reliable Change⁹⁷.

Figure 4: Average effect size estimates (Hedges' g) and corresponding 95% confidence intervals of the acute treatment efficacy of CBT as compared to placebo on the various anxiety disorders for the primary continuous anxiety measures (red bars) and depression measures (green bars).

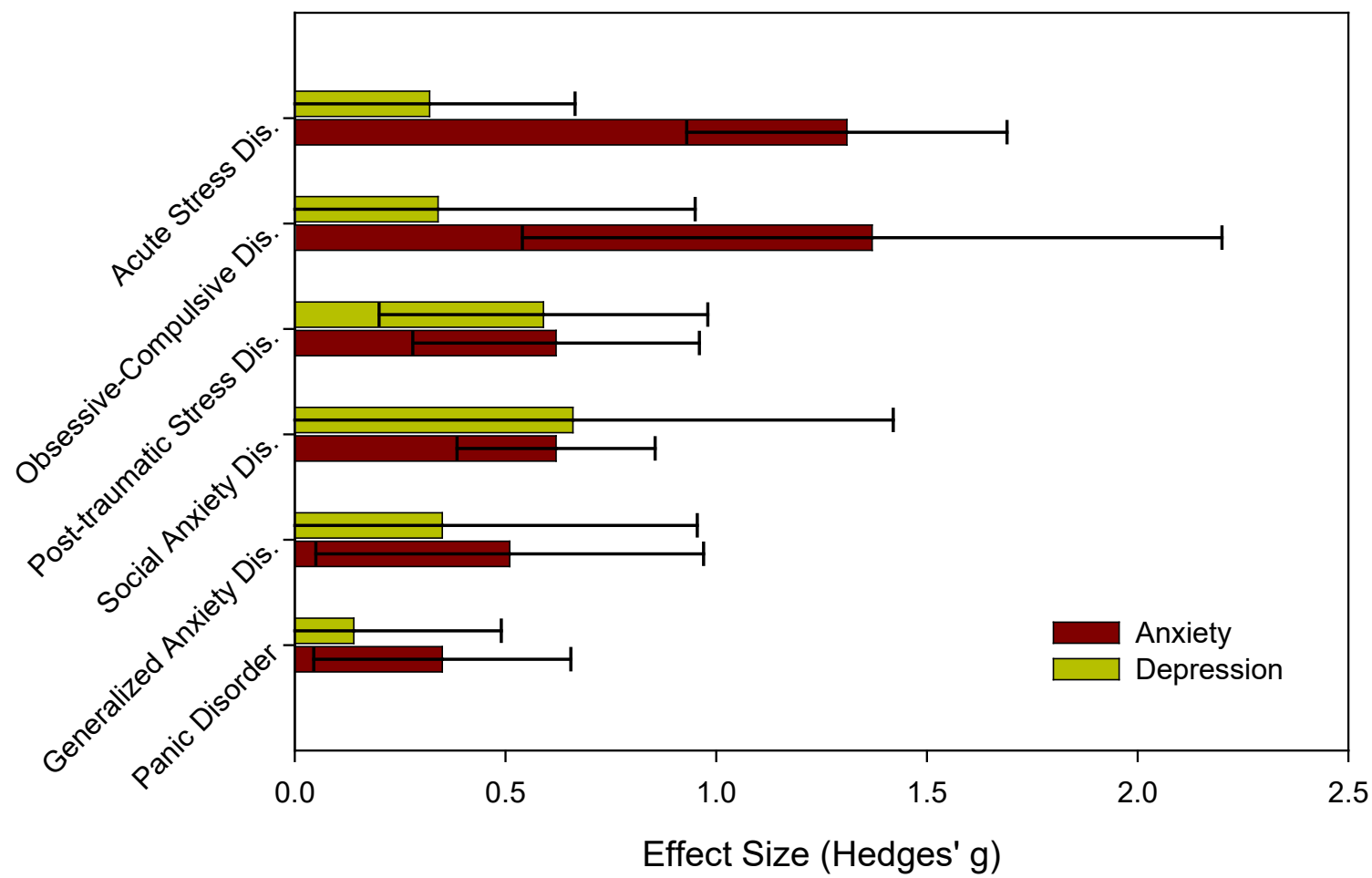


Figure 5: Average odds ratios of acute treatment response to CBT as compared to placebo and statistical tests for the various anxiety disorders. *: $P < .05$; **: $P < .001$

