Cognitive-behavioral therapy for adult anxiety disorders: a meta-analysis of randomized placebo-controlled trials

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CRD summary
The authors concluded that cognitive behavioural therapy was effective for adults with anxiety disorders, but that there was room for improvement. In view of the apparently limited quality of the heterogeneous studies and generally small sample sizes the authors’ conclusions should be interpreted with caution.

Authors’ objectives
To evaluate the efficacy of cognitive behavioural therapy (CBT) in adults with anxiety disorders.

Searching
MEDLINE via PubMed, PsycINFO, SCOPUS, ISI and Dissertation Abstracts International were searched from inception to March 2007. Search terms were reported. Colleagues in Germany, Japan, Korea, Netherlands, Portugal and Spain were contacted for additional studies published in any of their languages. Reference lists from studies, meta-analyses and reviews were screened.

Study selection
Randomised controlled trials (RCTs) that compared CBT with placebo in adults aged 18 to 65 years who met DSM-III-R (Psychiatry Diagnostic and Statistical Manual of Mental Disorders–3rd Edition Revised) or DSM-IV (Diagnostic and Statistical Manual of Mental Disorders 4th edition) criteria for an anxiety disorder assessed using a psychometrically sound and structured diagnostic tool were eligible for inclusion. Psychological control interventions had to control for non-specific factors. Placebo interventions were excluded if they included active treatment for the target condition. Studies had to assess the clinical severity of anxiety disorder using psychometrically sound clinician-reported or self-reported measures and report sufficient data to permit calculation of effect sizes. The review assessed anxiety severity, depression severity, treatment response and attrition.

The included studies were in patients with a variety of anxiety disorders, including social anxiety, post traumatic stress, panic, acute stress, obsessive compulsive and generalised anxiety disorder. The number of sessions ranged from three to 20. Control treatments included pills and various types of psychological interventions, including supportive counseling, relaxation and non-directive therapy. Studies used a variety of different instruments to measure anxiety; most studies used the Beck Depression Inventory to assess depression severity (details were reported).

Two reviewers independently selected studies.

Assessment of study quality
Studies were assessed using a modified version of the Jadad scale (study reported as randomised, adequate randomisation method, blinding, and reporting of withdrawals and drop-outs). The authors did not state how many reviewers assessed validity.

Data extraction
Two reviewers independently extracted valid and reliable interviewer-reported and self-reported outcome measures. Discrepancies were resolved by consensus. Two other reviewers independently extracted completer and if possible intention-to-treat data. If required, authors were contacted for intention-to-treat data, but without much success. The most conservative measures of treatment response were extracted. For each study, effect sizes (Hedge’s g) and odds ratios with their respective 95% confidence intervals (CI) were calculated for anxiety and depression severity. Average Hedge’s g effect sizes were calculated where studies provided multiple measures of outcomes of interest.

Methods of synthesis
Pooled odds ratios and effect sizes with 95% CIs were calculated using a random-effects model for both completer data.
and intention-to-treat data. Generalised linear regression was used to examine the influence of study characteristics (year and type of placebo) and clinical characteristics (type of anxiety disorder and number of sessions); completer data were used for these analyses. Significant differences between variables were further examined using pairwise comparisons with Bonferroni correction. Publication bias was assessed using the fail-safe N (number of additional studies required to reduce the overall effect size to a nonsignificant level).

**Results of the review**

Twenty-seven placebo-controlled RCTs were included (n=1,496). Eight studies scored 3 on the Jadad scale and the others scored 1 or 2. Few studies provided intention-to-treat data (six reported intention-to-treat continuous measures of anxiety disorders and eight reported intention-to-treat response rates).

There was no statistically significant difference in attrition rates between CBT and placebo (23% versus 22%, p=0.26).

**Completer analysis:** Compared to placebo, CBT was associated with a statistically significant medium to large effect on anxiety disorder severity compared to placebo (g=0.73, CI: 0.56 to 0.90, p<0.001), a significant increase in treatment response rate (odds ratio 4.06, CI: 2.78 to 5.92, p<0.001) and a small to medium statistically significant effect on depression symptom severity (g=0.45, CI: 0.25 to 0.65, p<0.001).

**Intention-to-treat analysis:** Similar results were obtained for anxiety severity and treatment response rates, but effect sizes were smaller.

There was no evidence of publication bias (fail-safe N ranged from 183 for depression severity to 829 for anxiety severity).

Pairwise comparisons showed that anxiety disorder severity effect sizes for acute stress disorder were significantly greater (p<0.05) than those for all other disorders apart from obsessive compulsive disorder. There were no significant differences in depression severity effect sizes between different types of disorders.

Anxiety disorder effect sizes were not influenced by any of the moderator factors examined.

**Authors’ conclusions**

CBT was efficacious for adults with anxiety disorders, but there was considerable room for improvement.

**CRD commentary**

The review question and inclusion criteria were clearly stated. Several relevant sources were searched and some attempts were made to minimise language bias. It was unclear if attempts were made to minimise publication bias. Appropriate methods were used to minimise reviewer error and bias during study selection and data extraction but it was not clear if similar methods were used to assess validity. Study quality was assessed, but only aggregate scores were presented, which made it difficult to assess the quality of the evidence. The authors did not take account of study quality when interpreting results of the meta-analysis. More than half of the studies had a sample size of less than 50, which cast some doubt on the strength of the evidence. Studies were pooled using meta-analysis and various subgroup analyses were conducted to examine the influence of some relevant factors. However, studies differed with respect to population, intensity/duration of interventions and length of follow up, which made it difficult to interpret results of the meta-analysis. In view of the apparently limited quality of the heterogeneous studies and generally small sample sizes, the authors’ conclusions should be interpreted with caution.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that future studies of CBT should include an intention-to-treat analysis.

**Funding**

One author has been a consultant for Organon and support from the National Institutes of Mental Health.

**Bibliographic details**

PubMedID
18363421

Original Paper URL

Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Anxiety Disorders /diagnosis /psychology /therapy; Cognitive Therapy /methods; Humans; Randomized Controlled Trials as Topic

AccessionNumber
12008107657

Date bibliographic record published
03/02/2009

Date abstract record published
09/09/2009

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.