Is it beneficial to add pharmacotherapy to cognitive-behavioral therapy when treating anxiety disorders? A meta-analytic review

Hofmann SG, Sawyer AT, Korte KJ, Smits JA

CRD summary
The authors concluded that cognitive-behavioural therapy combined with pharmacotherapy was effective in the short term for some anxiety disorders. The review process was generally well conducted, but the lack of good quality trials, the small population sizes, and the substantial clinical variability across trials, suggest that the pooled results and conclusions should be treated with caution.

Authors' objectives
To determine the benefit of adding pharmacotherapy to cognitive-behavioural therapy (CBT) in the treatment of anxiety disorders.

Searching
PubMed, PsycINFO, and the Cochrane Library were searched to July 2008. The bibliographies of retrieved articles, review papers, and chapters were examined for further reports. There were no attempts to retrieve unpublished data. Search terms were reported.

Study selection
Randomised controlled trials (RCTs) were eligible for inclusion if they evaluated CBT combined with pharmacotherapy for the treatment of adults (18 to 65 years), who met the Diagnostic and Statistical Manual of mental disorders (DSM)-III-R or DSM-IV criteria for anxiety disorders. Diagnosis had to be made using a psychometrically sound structured instrument and clinical severity had to be measured by similarly sound clinician-administered or self-report questionnaires. Trials had to report sufficient data to calculate an effect size.

The included trials recruited patients, with a variety of disorders, who were treated with a range of medications, and measured outcomes in terms of ritual rates, free of panic attacks, or a variety of scales. It appears that the comparator in all studies was CBT plus placebo. No two studies evaluated the same combination of patient spectrum, medication, and outcome. The number of treatment sessions ranged from five to 48.

Two reviewers independently selected trials and disagreements were resolved by discussion.

Assessment of study quality
Trial quality was assessed using the Jadad scale, which is based on randomisation, blinding, and withdrawal or drop-out criteria, and the maximum score was five.

Two reviewers independently performed the quality assessment.

Data extraction
Data were extracted to calculate Hedges' g for continuous data or an odds ratio (OR) for dichotomous data, with a 95% confidence interval (CI).

Two reviewers independently extracted the data and disagreements were resolved by consensus.

Methods of synthesis
Data were pooled using a random-effects model. The impact of assessment procedure, study year, number of treatment sessions, and clinical and study characteristics were investigated using meta-regression. Fail-safe N tests were used to assess publication bias.
Results of the review
Eleven RCTs (n=547 patients; range 15 to 92) were included in the meta-analysis. Two trials received a Jadad score of two, eight scored three, and one scored four.

CBT plus pharmacotherapy significantly improved measures of anxiety disorder severity (Hedges' g 0.59, 95% CI 0.29 to 0.90) and treatment response (OR 1.95, 95% CI 1.25 to 3.03), in comparison with CBT plus placebo.

The significant results in the meta-regression were: CBT plus pharmacotherapy improved panic disorder (Hedges' g 0.99, 95% CI 0.26 to 1.71) and generalised anxiety disorder (Hedges' g 0.81, 95% CI 0.18 to 1.44); only benzodiazepines plus CBT were more effective than placebo (Hedges' g 1.28, 95% CI 0.90 to 1.66); and the size of effect of CBT plus pharmacotherapy decreased with increasing publication year (p=0.003). Publication bias was not found for measures of anxiety disorder severity, but could not be discounted for response rates.

Authors' conclusions
Pharmacotherapy might be useful for enhancing short-term CBT outcomes, especially for panic disorder and generalised anxiety.

CRD commentary
The review question was clearly stated and supported by clear (though broad) inclusion criteria. Relevant sources were searched for published data. There appeared to be no search for publications not in English nor unpublished data, which may result in the omission of relevant trials. A recognised assessment tool was used to evaluate trial quality. The authors reported that the average trial quality was good, but some only scored two. The quality was reported as a composite score and it was unclear which criteria were failed.

Adequate steps were taken throughout the review process to minimise error and bias. The authors calculated standardised effect sizes for some outcomes, and used random-effects analyses, but the substantial clinical heterogeneity across trials meant that the appropriateness of pooling and the reliability of the pooled estimates was uncertain. Heterogeneity was not formally assessed, but meta-regression was used to explore potential effect modifiers. Of the four drug groups investigated in the meta-regression, only benzodiazepines plus CBT achieved statistical significance, but the number of trials for each drug was small, making the reliability of these results uncertain.

The review process was generally well conducted, but the lack of good quality trials, the small population sizes, and the substantial clinical heterogeneity across trials, suggest that the pooled results and conclusions should be treated with caution.

Implications of the review for practice and research
Practice: The authors stated that there was no support for the use of combination therapy for maximising long-term CBT outcomes.

Research: The authors stated the need for high quality trials with intention-to-treat data. These trials should assess the efficacy of combination therapies across different anxiety disorders, and evaluate novel combination strategies targeting the mechanisms underlying CBT.

Funding
Dr Hoffman was paid by Organon and supported by NIMH grant 1R01MH078308; Dr Smits was supported by NIMH grant 1R01MH075889.

Bibliographic details
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.