Meta-analysis of randomized controlled comparisons of psychopharmacological and psychological treatments for anxiety disorders

Bandelow B, Seidler-Brandler U, Becker A, Wedekind D, Ruther E

CRD summary
The authors appeared to conclude that no differences were found between drug and cognitive behavioural treatments and, for patients with panic disorder, combined treatment was superior to either treatment alone. This review had several methodological flaws regarding unclear study quality, chosen methods of synthesis, and absence of detail in describing the review process. The conclusions are unlikely to be reliable.

Authors' objectives
To compare pharmacological and psychological treatments in patients with anxiety disorders.

Searching
MEDLINE, PsycINFO, and EMBASE were searched from 1980 to identify published studies for inclusion in the review. Search terms were reported.

Study selection
Randomised studies of patients with panic disorder and agoraphobia, social phobia, and generalised anxiety disorder were eligible for inclusion. Patients had to meet the Diagnostic and Statistical Manual of mental disorders (DSM)-III, DSM-III-R, or DSM-IV criteria for each disorder. Included studies had to compare cognitive-behavioural therapy (CBT) and pharmacological treatments (alone or in combination). Outcomes had to be measured by self-report questionnaires or clinician-based ratings.

Included studies contained pharmacological and psychological placebos within the comparisons. Included pharmacological treatments were tricyclic antidepressants, selective serotonin reuptake inhibitors, benzodiazepines, irreversible monoamine oxidase inhibitors and reversible inhibitors of monoamine oxidase A. Included cognitive-behavioural therapies were cognitive techniques, exposure and anxiety-management. The average treatment duration was 12 weeks (range eight to 16 weeks). Longer term follow-up was reported in some studies. Outcome measures included the Clinical Global Impression Scale, Hamilton Anxiety Scale, Anxiety Disorders Interview Schedule and a variety of questionnaires.

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Study quality was assessed on the adequacy of randomisation and blinding, sample size, use of suitable rating scales, and accuracy of statistical calculations.

The authors did not state how many reviewers performed the validity assessment.

Data extraction
Data were extracted to calculate comparison effect sizes (ES) (post-treatment differences were compared in one study) and pre-post-treatment effect sizes (measuring the difference in scores before and after each treatment), along with 95% confidence intervals (CI). Separate data were collected for self report and clinician based ratings, using according-to-protocol data.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Effect sizes were pooled in meta-analyses, weighted by the inverse variance method. Drug classes and psychotherapy modalities were grouped together, and the analysis was reported as drug, CBT, drug plus CBT, and CBT plus placebo.

Results of the review
Twenty-four studies were included in the review. Sample sizes ranged from 15 to 189. Study quality results were not presented.

Panic disorder (sixteen studies): Combination of cognitive-behavioural therapy (CBT) and drug treatment was statistically superior to drug treatment alone on clinician rating (ES 0.39, 95% CI 0.09 to 0.69) and self-reporting (ES 0.61, 95% CI 0.22 to 0.99). This combination was also superior to CBT plus placebo using clinician rating (ES 0.23, 95% CI 0.05 to 0.41) and self-reporting (ES 0.43, 95% CI 0.21 to 0.66). All treatment modalities showed large pre-post effect sizes, with clinician-rated combined drug and cognitive-behavioural therapy showing the largest pre-post treatment difference (ES 2.07, 95% CI 1.77 to 2.38).

Social anxiety disorder (six studies): A statistically significant difference was found for the comparison between CBT plus drug treatment versus CBT plus placebo on clinician rating (ES 0.42, 95% CI 0.18 to 0.68). All treatment modalities showed large pre-post treatment effect sizes, with the largest for clinician ratings of drug treatments (ES 2.18, 95% CI 1.75 to 2.62).

Generalised anxiety disorder (two studies): There were insufficient data available to perform meta-analysis for this outcome. In general, CBT, or CBT in combination with drug treatment, was superior to drug treatment alone.

No statistically significant differences were found between drug and CBT in direct comparisons. The analysis of available follow-up studies did not show a clear long term effect of CBT. Mixed results were reported for other comparisons.

Authors' conclusions
No differences were found between drug and CBT in direct comparisons. Combined pharmacological and psychological treatment was found to be superior to drug or CBT treatment alone for patients with panic disorder.

CRD commentary
The review question was clear and supported by inclusion criteria which would seem reproducible for all aspects except for outcomes. The restriction to published studies in three databases had potential limitations in terms of missed studies and publication bias. Although study quality assessment was reported to have been carried out, the absence of results made it difficult to judge the reliability of findings. Added to this difficulty was the absence of detail on how studies were selected, and how validity assessment and data extraction were carried out. Adequate study details were presented, but (as the authors acknowledged) evidence from a small numbers of studies, together with the grouping of drugs and psychotherapies in this analysis, may be of limited value to the evidence base. Given the apparent and untested heterogeneity amongst the included studies, it was not clear whether meta-analysis was an appropriate method of synthesis. The authors' conclusions appear to be contradictory in parts of the paper, and some potential conflicts of interest were noted in terms of author connections with the drug industry. This was a poorly-reported review and the conclusions are unlikely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that the use of combination therapy (drug and CBT) is supported for patients with panic disorder, but not for social phobia.

Research: The authors stated that combination treatment should be investigated in a trial where patients have an insufficient response to monotherapy.

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