A meta-analysis of treatment outcome for panic disorder

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Authors' objectives
To compare the effectiveness of pharmacological, cognitive-behavioural and combined pharmacological and cognitive-behavioural treatments for panic disorder.

Searching
PsycLIT and MEDLINE were searched from 1974 to January 1994 using the following keywords: 'panic', 'agoraphobia', 'treatment outcome', 'long-term' and 'short-term'. Reference sections of identified articles were examined, and articles in press were identified from national conferences prior to January 1994.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs). Both single treatments and multiple treatments of combination treatments were included, as long as they included a control group (no-treatment, wait-list, drug or psychological placebo).

Specific interventions included in the review
Pharmacological interventions, cognitive-behavioural therapy and combined pharmacological and cognitive-behavioural treatments.

Pharmacological interventions included tricyclic antidepressants (clomipramine, imipramine, trazodone), monoamine oxidase inhibitors (phenelzine), serotonin-reuptake inhibitors (zimelidine), benzodiazepines (alprazolam, clonazepam, diazepam) and adrenergic agonists/antagonists (propranolol, clonidine)

Cognitive-behavioural therapies included: exposure (interoceptive exposure, situational exposure, flooding), psychotherapy cognitive-restructuring, paradoxical intention, guided coping, bibliotherapy, supportive therapy, behavioural therapy and relaxation techniques.

Participants included in the review
Patients with panic disorder, with or without agoraphobia, were included.

Outcomes assessed in the review
The outcome was panic frequency.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not state that they assessed quality.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
Two average standardised effect sizes were calculated, one across all outcome measures and the second using panic frequency alone.

Long-term outcome effect size was calculated within each group using post-treatment and follow-up measures, standardised by the post-treatment standard deviation. The minimum follow-up was 6 months.

**How were differences between studies investigated?**
The studies were classified by their treatment intervention as pharmacotherapy, cognitive-behavioural therapy, or a combination of the two. Pharmacological studies were broken down by drug type: antidepressants, benzodiazepines and others. Cognitive-behavioural studies were classified as: cognitive, cognitive-restructuring plus situational exposure, cognitive-restructuring plus interoceptive exposure, and other interventions.

Studies that did or did not use independent evaluators were compared.

**Results of the review**
Forty-three studies (4,133 patients) were included.

**Pharmacotherapy interventions.**
Sixteen studies (2,708 patients) yielded an average overall effect size of 0.47 (p<0.0001).

Nine separate study comparisons examined antidepressants versus control: the overall effect size was 0.55 (p<0.0001). Thirteen separate study comparisons examined benzodiazepines versus control: the overall effect size was 0.40 (p<0.0001). The difference in effect size between the two drug types was not significant (p=0.09).

The proportion of drop-outs for patients receiving pharmacological interventions alone was 19.8% (25.4% for antidepressants and 13.1% for benzodiazepines), compared to 32.5% for the drug placebo control groups.

**Cognitive-behavioural interventions (based on comparisons of the previous two groups).**
Nineteen studies (832 patients) yielded an average overall effect size of 0.63 (p<0.0001). The overall drop-out rate for these interventions was 5.6%, compared with 7.2% in the control groups.

**Pharmacotherapy versus cognitive-behavioural interventions.**
The overall effect size of cognitive-behavioural studies (0.63) was significantly higher than that of medication treatments using placebo control groups (0.47), p=0.05. Mean attrition rates were higher among patients receiving a medication intervention (20%) than those receiving a cognitive-behavioural intervention (6%). The control groups for cognitive-behavioural interventions (the majority of which were wait-lists) may perform worse than those for pharmacological interventions (the majority of which were pill placebos).

**Combined pharmacological and cognitive-behavioural interventions.**
Six of the 8 studies which examined this, looked at imipramine and cognitive-behavioural interventions versus imipramine alone. There was no significant difference between the effect sizes for combined treatment versus imipramine alone, 0.56 and 0.55, respectively. Attrition rates were 22% for both types of interventions.

**Long-term outcome.**
The overall within-group effect size was -0.17. The values for pharmacotherapy (3 studies, 363 patients), combined pharmacotherapy plus exposure (2 studies, 199 patients), and cognitive-behavioural interventions (8 studies, 358 patients) were -0.46, -0.07 and +0.06, respectively. None of the differences were statistically significant.

**Cost information**
The monthly costs for a typical course of treatments were estimated for both cognitive-behavioural and pharmacological treatments. The lowest cost interventions were imipramine treatment and group cognitive-behaviour therapy, with a yearly total of approximately US$600. Cognitive-behavioural therapy appears to be one of the most cost-effective and tolerable treatments currently available.

Authors' conclusions
Both pharmacological and cognitive-behavioural treatments offer significant advantages over control treatment. In general, cognitive-behavioural treatments yielded the largest effect sizes and the smallest attrition rates relative to pharmacotherapy and combined treatments, and are cost-effective. For patients with a primary diagnosis with panic disorder, the currently available evidence confers a number of advantages for cognitive-behavioural treatment, and encourages increased clinical utilisation of these interventions.

CRD commentary
It is unclear from the search strategy whether the search was restricted to English language articles, since no non-English language articles were included. In addition, there is the possibility of publication bias as there was no attempt to locate unpublished literature, except for articles in press. No quality assessment of the included studies is reported.

It would be useful to have more information about the primary studies, e.g. the outcome measures used, setting and follow-up. The authors have calculated an overall effect size for each study based on all of the outcome measures used in the study. However, details of what these outcomes measures are, are not given. The decision to amalgamate a number of potentially disparate outcomes measures into one overall effect size estimate may be questionable. It would be informative to have confidence intervals around the estimated effect sizes.

There are a few inconsistencies in the text and it is difficult to link the results given in the text with the tables.

As the authors explain, there are problems making comparisons across treatments with different control groups, due to the varying effect of different control treatments.

Bibliographic details

Indexing Status
Subject indexing assigned by CRD

MeSH
Antidepressive Agents /administration & dosage; Benzodiazepines /therapeutic use; Cognitive therapy; Panic Disorder /therapy

AccessionNumber
11996008034

Date bibliographic record published
30/11/1997

Date abstract record published
30/11/1997

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.