Review of the long-term effectiveness of cognitive behavioral therapy compared to medications in panic disorder
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CRD summary
This review assessed the long-term effectiveness of cognitive-behavioural therapy (CBT) in patients with panic disorder. The authors concluded that more data are required before definitive conclusions can be drawn about the long-term effectiveness of CBT. These conclusions are likely to be reliable.

Authors' objectives
To assess the long-term effectiveness of cognitive-behavioural therapy (CBT) in patients with panic disorder.

Searching
MEDLINE, PsycINFO, SciSearch, SocSciSearch and the Cochrane Library were searched; the search terms were stated. References in reviews and primary studies were followed up.

Study selection
Study designs of evaluations included in the review
Controlled trials that presented sufficient data to permit an intention-to-treat analysis based on the original number randomised were eligible for inclusion. All of the included studies were randomised controlled trials (RCTs).

Specific interventions included in the review
Studies that directly compared CBT with control treatments were eligible for inclusion. Studies using only exposure or specific elements of CBT were excluded. The studies had to use a credible control treatment, defined as medication, waiting-list or placebo. The included studies used the following interventions: CBT alone; fluvoxamine with and without CBT; placebo plus CBT; moclobemide with CBT; moclobemide plus clinical management; CBT plus placebo; placebo plus clinical management; imipramine with and without CBT; CBT plus placebo; and placebo pills alone. Acute treatments lasted 10 to 12 weeks; one study included a 6-month maintenance treatment phase.

Participants included in the review
Studies of general samples of adults (18 years or more) with panic disorder were eligible for inclusion. Studies of special samples of patients (such as those who failed pharmacotherapy) were excluded.

Outcomes assessed in the review
The studies had to follow up patients for 6 months or more and present results using a clearly defined binary measure for patients who maintained remission. The studies also had to report relapses and use of treatment between follow-up interviews. In the review, these ‘survivors’ were defined as patients who were still present, were doing well using standardised criteria (as defined in the primary study), or did not require any additional treatment. The included studies measured remission using the Hamilton Anxiety Scale, Sheffield Symptom Rating Test, Fear Questionnaire-Agoraphobic subscale, Panic Disorder Severity Scale and the Clinical Global Impression Scale.

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

Assessment of study quality
The authors did not state that they assessed validity, but strict inclusion criteria were applied that took account of some aspects of validity.
Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Data on the sample size, study design, measures used to assess the outcomes, and results were extracted.

For each study, the percentage of survivors over the original number randomised was calculated for each treatment arm. The effect size was calculated, based on the difference in the proportion of survivors between treatments. In the two studies that did not report final data for patients who dropped out, all patients with missing data were classified as non-remitters. The scores for outcome measures were converted to binary measures using cut-off scores.

Methods of synthesis
How were the studies combined?
The characteristics of the included studies were summarised in the text of the review and accompanying tables. The studies were combined narratively in the 'Discussion' section of the review.

How were differences between studies investigated?
Differences between the studies were discussed in the text of the review.

Results of the review
Three RCTs (557 patients) were included.

One RCT (190 patients) compared CBT with fluvoxamine using five treatment arms. Using intention-to-treat analysis, the reviewers found no significant differences among treatments (P=0.65). The reviewers found small effect sizes for treatments (range: 0.14 to 0.28).

One RCT (55 patients) compared CBT with moclobemide using four treatment arms. Using intention-to-treat analysis, the reviewers found that CBT plus moclobemide maintained remission in a significantly greater proportion of patients than the other treatments (P<0.001), and that effect sizes for this combined treatment were moderate to moderately large (up to 0.7). The effect sizes for other treatments, including CBT alone, were small (from 0.14).

A last observation carried forward analysis was not possible in these two RCTs.

The third RCT (312 patients) was well conducted and compared CBT with imipramine using five treatment arms. It found that CBT remained effective at 6 months (P=0.001), but the effect sizes for all treatments were small.

Authors' conclusions
The authors concluded that more data are required before conclusions can be drawn about the long-term effectiveness of CBT.

CRD commentary
The review question was clear in terms of the study design, intervention, participants and outcomes. Several relevant sources were searched and the search terms were stated. It was unclear whether any language limitations had been applied, the dates searched were not specified, and no attempts were made to identify unpublished studies; the possibility of publication bias or language bias cannot, therefore, be excluded. The methods used to select the studies, assess validity and extract the data were not described, so it is not known whether any efforts were made to reduce errors and bias. Validity was not formally assessed, but some methodological limitations of the studies were discussed in the text.

The results were reported for intention-to-treat analysis. Given the small number of studies, a narrative synthesis was appropriate. The quality of the studies was taken into account in the synthesis. The authors' conclusions, that there is insufficient evidence available to draw conclusions about the long-term effectiveness of CBT, appear appropriate.
Implications of the review for practice and research

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

Research: The authors stated that studies should be designed with the aim of assessing long-term outcomes. They stated that studies should: follow up every patient; analyse data from all randomised patients, including drop-outs, on an intention-to-treat basis and using last observation carried forward analysis; classify patients who receive interval treatment as non-remitters; and define and use meaningful methods of measuring remission over longer and shorter intervals between assessments.

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