Optimal duration of combined psychotherapy and pharmacotherapy for patients with moderate and severe depression: a meta-analysis

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CRD summary
This review concluded that combined psychotherapy and pharmacotherapy was more effective than pharmacotherapy alone in attaining remission and preventing relapse in patients with major depressive disorder. Given the lack of clarity on the review processes and the variety between the included trials, these conclusions should be regarded as informative rather than definitive.

Authors' objectives
To investigate the efficacy and optimal duration of combined psychotherapy and pharmacotherapy for patients with depression.

Searching
The following databases were searched to February 2010: PubMed, EMBASE, Web of Science, The Cochrane Library and PsycINFO. Search terms were reported and reference lists were checked. Only articles published in English were considered for inclusion.

Study selection
Parallel-group randomised controlled trials (RCTs) comparing combined psychotherapy and pharmacotherapy versus pharmacotherapy alone were eligible for inclusion if they had at least 10 participants with major depressive disorder. Drop-out rates had to be less than 50%, and the outcomes had to include response, remission or relapse rates. Trials focusing on patients with major depressive disorder that was co-morbid with other conditions, or where the depression was a consequence of other conditions, such as cancer, pain, postpartum depression, dysthymia or seasonal depression, were excluded.

The included trials had a range of populations, with some trials including only adolescents or only geriatric patients. The type of depression included chronic, recurrent, non-responding and remittent. A range of styles of psychotherapy were evaluated including group-based, family-based and individual. Most trials used cognitive or cognitive-behavioural therapy. The number of sessions varied from five to over 30, with session duration ranging from 30 minutes to two hours; one trial evaluated therapy delivered entirely by telephone. Trials provided psychotherapy in the acute, acute and continuation, or the maintenance phase of treatment.

Two reviewers independently screened studies for inclusion and disagreements were resolved by discussion.

Assessment of study quality
Included trials were assessed for validity, using the Cochrane Risk of Bias tool, which has items on the generation of the allocation sequence, allocation concealment, blinding and incomplete outcome data.

It was not clear how many reviewers assessed trial quality.

Data extraction
For each treatment arm the number of patients and the following clinical outcomes were extracted: the number of patients with a full response or remission; the number with a partial or no response or remission; the number with a relapse; and the number with sustained remission. Where the response or remission rate were measured on several scales, data from the Hamilton Rating Scale for Depression (HRSD) were extracted. If the event rates were reported as percentages, back calculations were performed.

A series of 2x2 tables was constructed to facilitate the calculation of odds ratios and 95% confidence intervals for each trial and each outcome. Trials were grouped according to the reported outcome and the phase when psychotherapy was provided (acute, acute and continuation, or maintenance).
It was not clear how many reviewers extracted these data.

**Methods of synthesis**

Where three or more trials were similar in their provision phase, type of outcome reported and time of assessment, they were pooled using the DerSimonian and Laird method to produce a random-effects estimate. $X^2$ and $I^2$ were used to test for heterogeneity. Subgroup analyses were planned to explore variations between the acute phase (up to 12 weeks) versus longer psychotherapy when assessing remission. Trials were removed individually to explore their impact on the pooled estimates.

**Results of the review**

Thirty-one trials were included in the review, and 22 were included in the meta-analysis; the other nine trials reported unmatched time-point outcomes or a different schedule of psychotherapy. Fourteen trials reported adequate sequence generation and one had a high risk of bias; 14 trials reported adequate allocation concealment; assessors were blinded in 23 trials; and intention-to-treat analysis was carried out in 18 trials. Eight trials met all of the quality criteria. Samples sizes ranged from 20 to 491.

**Remission**

Patients receiving combined psychotherapy and pharmacotherapy had a significantly higher chance of reaching remission compared with those on pharmacotherapy alone, at all time-points assessed (two, three, four, six and 12 months). Substantial heterogeneity was noted for the six-month analysis. The effect was largest at four months after starting treatment (OR 2.36, 95% CI 1.58 to 3.55; $I^2=0$; four trials). When duration of treatment was considered, the effect of combination therapy was more pronounced in trials in which psychotherapy was provided for longer than 12 weeks, but substantial heterogeneity was found in both analyses.

**Relapse**

Patients receiving pharmacotherapy alone were at significantly higher risk of relapse than those receiving combined psychotherapy and pharmacotherapy at nine and 12 months. The strongest effect was noted at 12 months where psychotherapy was provided only during the acute phase (OR 4.56, 95% CI 0.79 to 26.30; $I^2=59.6$%; three trials). Where combined treatment was provided in both the acute and maintenance phases, the risk of relapse for patients receiving pharmacotherapy alone was an odds ratio of 3.28 (95% CI 1.76 to 6.09; $I^2=0$; four trials).

Sensitivity analyses based on the removal of individual trials did not significantly alter the results.

**Authors' conclusions**

Combined psychotherapy and pharmacotherapy was more effective than pharmacotherapy alone in attaining remission and preventing relapse in patients with major depressive disorder. Psychotherapy provided in both the acute and continuation phases was most effective.

**CRD commentary**

This review addressed a clear clinical question, with reasonable searches and detailed inclusion criteria. Language bias cannot be ruled out as only reports in English were considered. The use of two reviewers to minimise error and bias was reported for study selection, but this was not reported for quality assessment and data extraction. The included trials were appropriately quality assessed, but the results do not appear to have been used in the synthesis. The meta-analysis appears to have been appropriate but where substantial heterogeneity was found it was not explored. The authors acknowledged some of the limitations of their review, such as small samples and low trial quality.

Given the lack of clarity on the review processes and the variety between the included trials, the conclusions should be regarded as informative rather than definitive.

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

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

**Research:** The authors recommended that research should explore the effectiveness of combined treatment in different target populations, and compare combined treatment with each individual antidepressant.

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