The contribution of active medication to combined treatments of psychotherapy and pharmacotherapy for adult depression: a meta-analysis

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CRD summary
The authors concluded active medication had a small but significant contribution to the overall efficacy of combined psychotherapy and pharmacotherapy treatments of adult depression. The conclusions reflect the evidence presented, but a lack of reporting of review methods, the small number of studies and variable quality of the included studies made the reliability of the conclusions uncertain.

Authors' objectives
To determine the contribution of active medication to combined psychotherapy and pharmacotherapy treatments for adult depression.

Searching
A database from a previous review was used to obtain studies for this review (see Other Publications of Related Interest). This database was compiled through searches of PubMed, PsycINFO, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) from 1966 to January 2009; search terms were reported.

Forty-two meta-analyses were examined for additional studies. For the present review, reference lists of five meta-analyses of comparisons between psychotherapy and pharmacotherapy and between each of the treatments alone and combined treatments were examined. Reference lists of included studies were scanned. No language restrictions were applied.

Study selection
Randomised controlled trials (RCTs) that compared the combination of psychotherapy and pharmacotherapy with the combination of psychotherapy and placebo for treatment of adults (aged 18 or over) with depression were eligible for inclusion. Studies aimed at relapse prevention or maintenance treatments were excluded.

Most participants were recruited from the community or by referral; other participants were clinical samples or recruited through systematic screening. The nature of comorbid conditions varied widely between studies. Half of the studies included participants with a major depressive disorder; the other studies included patients with diagnoses of other depressive disorders. Most studies used either selective serotonin reuptake inhibitors or tricyclic antidepressants; other studies used nefazodone.

Psychological treatments included cognitive-behavioural therapy, social skills training, interpersonal psychotherapy, marital therapy, supportive psychotherapy and relapse prevention counselling. Treatments were generally conducted using an individual format. The number of sessions ranged from six to 24. Where reported, baseline Beck Depression Inventory (BDI) ranged from 18.5 to 29.2 and baseline HAM-D ranged from 13.2 to 26.6. Studies were conducted in USA, Canada, Australia and UK.

The authors did not state how many reviewers selected studies for inclusion.

Assessment of study quality
Quality was assessed using criteria from the Cochrane Handbook for adequacy of random allocation concealment, blinding of outcome assessors and participants and withdrawals and drop-outs (maximum 4 points).

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

Data extraction
Data were extracted for each group for continuous variables to enable calculation of the effect size (Cohen's d) or standardised mean difference (SMD) and corresponding 95% confidence intervals (CI) at post-test of treatment effect. Where studies reported dichotomous outcomes (rates of recovery or remission) data were extracted to enable calculation of relative risk (RR) and corresponding 95% CIs. Numbers-needed-to-treat (NNT) were calculated.

The authors did not state how many reviewers conducted data extraction.

**Methods of synthesis**

Data were pooled using a random-effects model. A meta-regression analysis was used to assess the relationship between variables and effect size for continuous variables. Heterogeneity was assessed using the $I^2$ and $Q$ statistics. Subgroup analyses were conducted using a mixed-effect model and included recruitment method, target group, diagnostic category, comorbid substance-related disorder, type of psychotherapy, medication, type of analysis and quality of studies. Publication bias was assessed by visual inspection of funnel plot and by Duval and Tweedie’s trim-and-fill procedures.

**Results of the review**

Sixteen RCTs (n=852) were included in the review. Ten RCTs met three or more of the four quality criteria. Twelve RCTs reported blinding of assessors. Five RCTs reported that allocation to groups had been conducted independently. Fourteen RCTs reported blinding of participants. Ten RCTs reported using an ITT analysis.

Active medication combined with psychotherapy had a significant effect on the reduction of depressive symptoms compared to psychotherapy and placebo (SMD 0.25, 95% CI 0.03 to 0.46, NNT=7.14; 16 RCTs). Heterogeneity was moderate to high ($I^2=57.22\%$).

Active medication combined with psychotherapy also had a significantly greater effect for dichotomous outcomes (rates of recovery and remission) compared with psychotherapy and placebo (RR 1.38, 95% CI 1.05 to 1.83; 10 RCTs). Heterogeneity was moderate ($I^2=51.56\%$). There were no significant differences between groups for drop-out rates.

Subgroup analyses that removed two outlier RCTs did not significantly change the overall results; heterogeneity was no longer significant. Further analyses excluded the two outlier studies was conducted for studies that used HAM-D and BDI scales and found that differences between intervention and control groups for depressive symptoms were no longer statistically significant. Other subgroup analyses did not significantly alter the results.

There was no evidence of publication bias.

**Authors’ conclusions**

Active medication had a small but significant contribution to the overall efficacy of combined treatments of adult depression.

**CRD commentary**

The review question was clear with appropriate inclusion and exclusion criteria. Several relevant sources were searched without language restrictions, which reduced potential of language bias. No attempts were made to locate unpublished studies. Publication bias was formally assessed and no evidence of it was found. The authors did not report whether appropriate methods were used to minimise reviewer error and bias during study selection, quality assessment and data extraction. Validity was assessed using appropriate criteria and some results of the assessment were reported.

Studies were combined in a meta-analysis. Some sources of heterogeneity were explored. Some outcomes were unclear (for example, the result for dichotomous outcomes appeared to include multiple outcomes such as recovery and remission using different definitions).

The authors’ conclusions reflect the evidence presented, but a lack of reporting of review methods, the small number of studies and variable quality of the included studies made the reliability of the conclusions uncertain.
Implications of the review for practice and research

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

Research: The authors stated that further research was needed to examine the contributions of combined treatment to the overall effect. More research was needed to determine whether comparable interactions existed between pharmacotherapy and psychotherapy.

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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.