Effectiveness of pharmacist care in the improvement of adherence to antidepressants: a systematic review and meta-analysis

CRD summary
This review of six trials concluded that use of a pharmacist interventions improved adherence of depressed out-patients to antidepressants. The small number of trials, low sample sizes and variation between trials results in uncertainty about what types of intervention are appropriate for what types of patient, but the authors’ recommendation for further research seems appropriate.

Authors’ objectives
To assess the effectiveness of pharmacist care in improving adherence of depressed out-patients to antidepressants.

Searching
MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), Web of knowledge and The Spanish National Research Council were searched (from inception to April 2010) using specified search terms with no language restrictions. References were checked and experts were contacted to identify additional material.

Study selection
Eligible randomised controlled trials evaluated the impact of pharmacist interventions on improving adherence to antidepressants in depressed patients in an out-patient setting. Patients had to be ambulatory and diagnosed using a validated psychiatric interview or clinical diagnosis for a mood disorder and initiating or maintaining treatment with any form of antidepressant. Any measure of adherence was accepted as an outcome (such as pharmacy records, electronic pill containers or self-reporting adherence).

Interventions were educational messages and counselling, monitoring and medication dosage adjustment and management of adverse effects. Most patients (74%) were initiating pharmacological treatment for moderate or severe depression (measured on a range of scales). Follow-up period ranged from two to 12 months. Studies were conducted between 1998 and 2005 and were mainly undertaken in the USA, with one from the Netherlands and one from Australia. Mean age of patients ranged from 38 to 54 years, 57 to 85% were female.

Two reviewers assessed study eligibility with reference to a third to resolve discrepancies.

Assessment of study quality
Trial quality was assessed using the Jadad scale (a five point scale that which examined potential biases in the conduct of randomised controlled trials).

Two reviewers independently assessed study quality.

Data extraction
Two reviewers independently extracted data using a prespecified tool with a third consulted to resolve any disagreements. Adherence was extracted as a binary outcome based on percentage of adherent patients at six months (where possible) to allow calculation of odds ratios (OR) and associated 95% confidence intervals (CIs). The authors stated that continuous outcome metrics were also extracted.

Methods of synthesis
An unspecified random-effects model was used to pool odds ratio's and 95% confidence intervals. Heterogeneity was measured using $I^2$ and tested for statistical significance using a Cochran Q test. Subgroup analyses (pharmacist setting, main adherence measure, clinical diagnosis or validated diagnostic instrument) were used to explore heterogeneity. Egger tests and funnel plots were used to assess the potential impact of publication biases and leave-one-out analysis was performed to assess sensitivity to individual trials.
Results of the review
Six trials (887 patients with reported data) were eligible. Trial quality was variable with unclear allocation concealment and non-adherence to intention-to-treat problematic in some trials. Studies scored between 2 and 5 on the Jadad scale.

There was a statistically significant increase in adherance with pharmacist intervention compared with control (OR 1.64, 95% CI 1.24 to 2.17) with no heterogeneity ($I^2<0.001$) which reflected consistent effect direction and high imprecision as indicated by large confidence intervals. There was no evidence of interaction between subgroups and results were insensitive to leave-one-out analysis. No continuous outcomes were presented. There was no evidence of publication bias.

Authors’ conclusions
Pharmacist intervention was effective in improving adherance of depressed out-patients to antidepressants but data were limited and further work was required.

CRD commentary
This review used appropriate methods to search for and identify relevant studies whilst minimising potential bias. Trial quality was assessed and introduced some uncertainty as the evidence-base was not exclusively high quality. Methods of data extraction and synthesis appeared appropriate but no results were presented for continuous outcomes mentioned in the methods. Pharmaceutical intervention, nature of control and number of adverse events were unreported but inclusion criteria, method of assessing depression and pharmacist intervention were all variable. There was considerable clinical heterogeneity and methodological variation between trials, but the small sample sizes and low number of trials inhibited the authors’ attempts to explore variation (including the potential impact of publication biases).

The conclusion that further work was required reflected the evidence and was clearly reliable given the deficiencies in the evidence base. The conclusion that pharmacist intervention was effective was less certain particularly given the variation in pharmacist intervention, short follow-up and the absence of information regarding the comparator and number of adverse events resulting from pharmaceutical intervention. The authors’ conclusions reflected the evidence, but the limitations of the data should be considered. The authors’ recommendation for further research seems appropriate.

Implications of the review for practice and research
hawks: The authors do not state any implications for practice.

Research: Further work was required particularly outside the United States.

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