Effectiveness of interventions to improve antidepressant medication adherence: A systematic review.
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CRD summary
This review found that behavioural and multifaceted interventions can be successful in improving adherence to medication and clinical outcomes in patients with depression. Potential for missed studies means that the reliability of the authors' conclusions is unclear.

Authors' objectives
To assess the effectiveness of interventions to improve the adherence to medication of patients with unipolar depression on clinical outcomes.

Searching
MEDLINE, PsycINFO and EMBASE were searched for relevant articles in English published in peer-reviewed journals between January 1990 and December 2010; search terms were reported. The authors' personal files and reference lists of the retrieved studies and relevant reviews were checked for additional articles.

Study selection
Randomised controlled trials (RCTs) of at least six months duration in which at least one patient-focused intervention that aimed to improve adherence to prescribed antidepressants in patients aged 18 years or over with a primary diagnosis of unipolar depression was compared to usual care were eligible for inclusion. Additional inclusion criteria were that either primary or secondary outcomes of each RCT were anti-depression medication adherence and that the trials reported at least one clinical outcome. Studies that evaluated interventions that aimed to improve clinicians' adherence to treatment guidelines and whether they evaluated treatment other than antidepressant therapy were excluded from the review.

Most of the studies were conducted in the United States. All studies except one took place in primary care settings; the remaining trial was conducted in an outpatient psychiatric setting. The mean age of the patients ranged between 38 and 76 years. The proportion of female patients in the trials ranged from 7% to 88.9%. Most of the studies investigated multi-faceted interventions that utilised more than one single component strategy from educational, behavioural, affective and provider-targeted interventions. Care management or patient follow-up was the central component of these interventions. Education and behavioural interventions were the most common components of the multi-faceted interventions. Educational interventions involved provision of written and audiovisual material.Behavioural interventions involved patient follow-up by telephone or in clinics' pharmacy refill monitoring and development of relapse prevention plans. Follow-up ranged from one week to 12 months.

One reviewer performed the search and an initial screening of titles and abstracts and a second reviewer reviewed all included and excluded studies. Any differences were resolved by all the review authors.

Assessment of study quality
Methodological quality was assessed using components of the Jadad scale for randomisation, blinding of outcome assessment and losses to follow-up. The authors reported the use of power calculations.

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

Data extraction
Data were extracted as reported on adherence and clinical outcomes relating to depression. The interventions were grouped into educational, behavioural, affective and provider-targeted.

The authors did not state how many reviewers performed the data extraction.
Methods of synthesis
The results were summarised in a narrative synthesis.

Results of the review
Twenty-six RCTs (11,115 participants) were included in the review. Sample sizes ranged from 45 to 1,801 patients. Randomisation was adequately reported in 17 RCTs. Eighteen trials clearly reported blinding of outcome assessors. There was at least 80% follow-up in 19 RCTs. Seventeen studies reported sample size calculations.

None of the five studies of interventions with an educational focus reported improvements in educational adherence compliance or persistence. Two studies found improvements in treatment response and mental health status at six-months follow-up. One study used a behaviour-focused intervention that resulted in improvements in medication compliance and depressive symptoms.

Twenty studies evaluated 22 multifaceted interventions. Eleven interventions showed significantly positive effects on adherence outcomes and depression outcomes compared to usual care. Four interventions reported positive effects for medication adherence only and four interventions improved depression outcomes without improving adherence. There were no improvements in either adherence or depression outcomes reported for three interventions. All seven interventions that used pharmacy refill monitoring reported improvements in adherence to medication. Benefits in adherence and depression outcomes were observed in two trials of patients with major depression and in two further trials of patients with difficult-to-treat depression with interventions that consisted of collaborative care between primary care physicians and the mental health specialty sector. Intensive depression care programmes were found to improve adherence and clinical outcomes in two studies. Two of five trials that utilised telephone-based care management found benefits in adherence and clinical outcomes.

Authors’ conclusions
Improving adherence to antidepressant medication requires complex behavioural changes and there is some evidence that behavioural and multi-faceted interventions can be successful in improving adherence to medication and clinical outcomes in patients with depression. The most successful interventions were complex and multifaceted and utilised mental health specialists and proactive care management.

CRD commentary
The review addressed a clear question. Criteria for inclusion of studies were defined and replicable. Appropriate databases were searched for relevant studies. The review was restricted to studies in English so there was some risk of language bias. Only articles published in peer-reviewed journals were included, which risked publication bias. Some steps were taken to minimise errors and bias for study selection, but it was unclear whether data extraction and quality assessment were performed in duplicate. The authors assessed methodological quality using validated methods and the quality of the studies was generally good. The authors’ decision not to combine the results in a meta-analysis appeared justified given the clinical heterogeneity in the interventions administered.

The authors conclusions reflect the evidence presented, but the risk of publication and language biases with the potential for missed studies mean that the reliability of the findings is unclear.

Implications of the review for practice and research
Practice: The authors stated that it may be necessary to tailor interventions to specific phases of antidepressant treatment (acute compared to continuation and maintenance phases) as well as different treatment settings (primary care compared to psychiatric care).

Research: The authors stated that further research should explore the most appropriate ways to promote collaborative care among healthcare practitioners and integrate the skills into an effective model of treatment delivery for depression. More carefully designed and well-conducted studies were required to clarify the effect of interventions in different patient populations and in treatment settings.

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