Meta-analysis of trials of interventions to improve medication adherence

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CRD summary
This review assessed the effects of interventions intended to enhance medication adherence. Interventions to improve medication adherence were found to increase adherence by 4 to 11%. No single strategy appeared to be the best. The review has several methodological weaknesses and it's unclear whether the quality of the included studies and the synthesis of them, can be relied upon.

Authors' objectives
To identify tools and methods intended to enhance medication adherence that have been evaluated in randomised controlled trials (RCTs), and to determine, using meta-analysis the net and individual effects of these tools and methods.

Searching
MEDLINE, International Pharmaceutical Abstracts, PsycLIT, ERIC and EMBASE were searched from 1966 to December 2000. The search terms were given in paper. The search was limited to English language papers.

Study selection
Study designs of evaluations included in the review
Only RCTs with a minimum of 10 participants in each intervention group were sought. The duration of the studies ranged from 2 weeks to 12 months.

Specific interventions included in the review
The inclusion criteria stated that the intervention had to be aimed at the consumer (i.e. patient or caregiver), with the intention of increasing adherence to medication. In the included studies the interventions were behavioural or educational. Behavioural interventions were those designed to change skills or normal routines, i.e. dosage schedule or packaging changes, skill building, reward, pill counting, calendar, pillbox, mail, telephone or e-mail reminders. Educational interventions were those that provided information about the disease or medication, i.e. oral (by nurse pharmacist or physician), audiovisual, written, telephone, mailed or e-mailed material. Some studies evaluated combined (educational and behavioural) interventions.

The most common intervention was behavioural alone, with combined behavioural and educational being the next most common. The interventions were compared with placebo or alternative active treatment. The single most frequent intervention was dosage-schedule change. Treatment occurred in a variety of settings: 53% of all interventions took place in a physician's office, while other settings included managed care, long-term care, pharmacy, psychiatric hospital, community centre, worksite and home.

Participants included in the review
The inclusion criteria suggested that any studies of people on any medication were sought. The participants in the included studies were being treated for symptomatic and asymptomatic disease: asthma, depression, epilepsy, hyperlipidaemia, hypertension, schizophrenia, tuberculosis, otitis media, pain management and other unspecified diseases. The most common disease was hypertension (26% of all participants). The age of adults, where reported, ranged from 19 to 65 years. Some of the studies were also aimed at the carers of children or the elderly on medication. The studies included both male and female participants.

Outcomes assessed in the review
The outcome of interest was adherence to medication. In the included studies this was defined in various ways: the percentage of patients adhering to medication, the number of days adherence, the percentage achieving 70 to 90% adherence or an 'adherence score'. Adherence was measured by patient report, pill count or medication profile. Articles
that did not adequately describe the results were excluded.

**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.

**Data extraction**
Three reviewers extracted the data. No further information was given. The data extracted related to characteristics of the study, participants, intervention and outcome measures. The various outcome measures in the individual studies were converted to effect sizes.

**Methods of synthesis**
How were the studies combined?
All measures were converted into effect sizes. The overall effect sizes were combined using a random-effects meta-analysis and 95% confidence intervals (CIs) were calculated.

How were differences between studies investigated?
Heterogeneity was tested for using the Q statistic.

**Results of the review**
Sixty-six RCTs (18,922 participants) were included. Some studies had multiple treatment groups.

The studies were heterogeneous (Q=476, d.f.=94, P<0.001) so the results for the total number of studies were not combined.

For behavioural treatments alone, the studies were homogeneous (Q=42.48, d.f.=40, P=0.36). The overall effect size for behavioural interventions was 0.07 (95% CI: 0.04, 0.09).

For educational treatments alone, the studies were heterogeneous (Q=365.78, d.f.=20, P<0.001). The overall effect size for educational treatments was 0.11 (95% CI: 0.06, 0.15).

The combined behavioural and educational interventions were heterogeneous (Q=64.84, d.f.=31, P<0.01). The overall effect size for the combined interventions was 0.08 (95% CI: 0.04, 0.12).

A funnel plot to test for publication bias suggested that studies with a negative or small effect size may be missing.

**Authors' conclusions**
A meta-analysis of studies of interventions to improve medication adherence revealed an increase in adherence of 4 to 11%. No single strategy appeared to be the best.

**CRD commentary**
This was a wide-ranging review on a topic concerning a common and difficult problem related to medication prescribing. The aims were clearly stated and the sources searched were comprehensive. However, the search terms appear to have been somewhat limited in view of the difficulties related to definitions and language describing this intervention. In addition, only English language papers were sought. It is possible that studies were missed. The authors' tests for publication bias also suggested that studies were missing. Full details of the methods of the review (e.g. study selection, validity assessment) were not described. Information about the baseline characteristics of those in the included studies was limited, as were full descriptions of the interventions used.
The authors showed that the studies were statistically heterogeneous. There appears to have been some inconsistency in dealing with heterogeneity and the subsequent combination of studies. In addition, although details of the included studies were limited, they were conducted on participants with widely differing diseases and the interventions were varied. It may not have been appropriate to have combined the results using formal meta-analyses techniques. It was not altogether clear how the percentages in the authors' conclusions related to the 'Results' section.

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

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

**Research:** The authors implied that more research, using standardised research methods and definitions, is needed on this topic.

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