A critical review of interventions to increase compliance with medication-taking, obtaining medication refills, and appointment-keeping in the treatment of cardiovascular disease

Newell S A, Bowman J A, Cockburn J D

Authors' objectives
The authors' stated objectives were to critically review the literature regarding the interventions to improve cardiovascular patients' compliance with medication taking, obtaining medication refills, or appointment keeping. What the authors appeared to study were these interventions in relation to the primary and secondary prevention of cardiovascular disease.

Searching
MEDLINE, HealthPLAN and PsycLIT databases were searched from 1985 to 1996 for English language papers, using the following search terms and MeSH: 'cardiovascular', 'heart', 'hypertens' and 'interven' or 'study', 'trial' and 'patient compliance'. Additional published and unpublished literature was obtained by examining bibliographies of all relevant papers, and by contacting health-related government and non-government bodies, experts in the field, and other organisations.

Study selection

Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were included.

Specific interventions included in the review
Any single or multiple interventions aimed at increasing patients' compliance with medication taking, obtaining medication refills, or appointment keeping, with or without 'no treatment' control groups. Interventions included: patient-focused strategies (e.g. counselling), structural strategies (e.g. reducing dose frequency) and physician-focused strategies (e.g. sending prompt devices).

Participants included in the review
Patients with cardiovascular disease, e.g. angina or myocardial infarction, or people referred to a cardiac rehabilitation programme; patients with elevated levels of cardiovascular risk factors including those with high blood-pressure or elevated cholesterol levels, or those overweight. Patients of all ages, men and women, were included in the review.

Outcomes assessed in the review
The outcomes assessed were: compliance with medication taking, obtaining medication refills or appointment keeping. Direct measures for measurement of compliance included appointment records, biochemical markers and drug metabolites; indirect measures included pill counts.

The subjective measures included patient self-reporting.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection. [A: One author did the initial selection, based on the title and the abstract (where available)]

Assessment of study quality
The methodological quality of the studies was assessed according to the following 8 criteria, based on Haynes et al. (see Other Publications of Related Interest): selection and description of the sample, specification of the illness or condition, type of compliance measures, description of the regimen, definition of compliance, description of the intervention, consent, and loss to follow-up rates. 20% (8 papers) of the papers eligible for inclusion were coded by 2 reviewers. The process is not reported for the remaining papers. [A: Remaining papers were coded by one reviewer, ambiguities on initial review were discussed by the three authors]
Assessing quality percentages to the studies: studies could obtain scores of up to a total of 35 points, which were then divided by 35 and multiplied by 100 to give quality percentages. These classified each study as follows: good-quality studies with 66.7% or greater; fair-quality studies between 50 and 66.6%; poor-quality studies, with less than 50%, were excluded from the review.

Data extraction
Data were extracted from only good- and fair-quality studies with respect to the patient group targeted, sample size, and the nature and effectiveness of the strategies in the trials. Where control groups received some intervention, the effectiveness of only additional strategies received by the intervention group were assessed. The authors do not state how many of the reviewers performed the data extraction. [A: The data were extracted by one reviewer]

Methods of synthesis
How were the studies combined?
The results were summarised narratively across studies, exploring each intervention strategy and within each target behaviour. Strong recommendations were only made where at least 3 studies, including at least one of good quality, had investigated the strategy; consistent evidence from numerous fair-quality studies resulted in tentative recommendations, and inconsistent evidence resulted in no recommendation about the strategy.

How were differences between studies investigated?
A meta-analysis (for combining studies) was not conducted due to wide variations in the nature of interventions, outcome measures, length of follow-ups and the presentation of results.

Results of the review
A total of 20 studies with 4,976 participants were included in the review. Another 13 studies met relevance criteria but were excluded due to poor quality.

Two independent reviewers assigned identical quality classification codes for 7 of the 8 papers double-coded, giving a kappa score of 0.82.

Of the 33 studies reviewed, the best performances were seen in the definition of compliance and description of intervention criteria, but performance on the remaining criteria were suboptimal.

Intervention effectiveness: 6 papers discussed 4 fair-quality studies exploring interventions aimed at increasing compliance with medication taking. The only interventions that improved patients' medication taking were reducing dose frequency, and one of the multiple strategy interventions (involving home visits, counselling, written medical schedules, education tools for the patients and compliance-enhancing packaging).

Interventions targeting obtaining medication refills: 2 papers discussed 3 fair-quality studies exploring interventions aimed at increasing compliance with obtaining medication refills. All the trialed interventions (sending reminder letters to patients, supplying medications in compliance-enhancing packaging, and combinations of these interventions and others) increased patients' compliance with obtaining medication refills.

Interventions targeting appointment keeping: 10 papers discussed 10 fair-quality studies and 1 good-quality study exploring interventions aimed at increasing compliance with appointment keeping. Most interventions were found to increase compliance, although interventions aimed solely at physicians were consistently ineffective.

Authors’ conclusions
The methodological quality of many of the identified trials was less than optimal, prohibiting strong recommendations. Thus, further good-quality, randomised trials are necessary to clarify the effectiveness of those strategies identified as potentially useful in the review.
The selection criteria were limited; therefore, some relevant studies may not have been included in the review, and the results may not be generalisable to people without cardiovascular disease. The search was restricted to English language papers published between 1985 and 1996. EMBASE and Cochrane databases were not searched. An effort was made to identify unpublished literature and the reference list was verified by experts. The review authors assessed validity of reviewed studies but used an outdated scale, which did not include adequacy of randomisation and masking of outcome assessment. The researchers used the validity assessment criteria to exclude a lot of studies when a sensitivity analysis would have been more appropriate.

Substantial study details were provided but details of outcomes were limited to qualitative assessment of whether intervention was better than control and p-values. The quality, intensity and duration of interventions were not considered in the analysis of the data.

Major sources of clinical heterogeneity (clinical setting, patients included) are not discussed. Narrative synthesis was appropriate in an attempt to review a range of complex interventions.

The criteria for making recommendations is based on the number of positive to negative trials, which takes no account of the size of the studies and the strength of effect.

The authors’ conclusions seem appropriate in view of the limitations stated above, although not all aspects of methodological quality were assessed.

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

**Practice:** The authors state that it is not possible to make strong recommendations due to the relatively poor methodological quality of many of the studies identified.

**Research:** The authors state that any future trials should be randomised controlled trials, with the randomisation protocol detailed in publications; have follow-up periods of at least 6 months, where appropriate; involve no-intervention control groups; employ adequate sample sizes to detect feasible and meaningful significant increases in compliance; employ direct, objective measures, wherever possible; and, if direct measures are unavailable or not feasible, employ multiple-outcome measures or assess the used measure’s validity in a subgroup of patients.

Reviewer’s statement: It is also important to consider interventions that may be effective in the short term.

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**Other publications of related interest**

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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.