Clinical interventions for treatment non-adherence in psychosis: meta-analysis

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CRD summary
This review assessed interventions used by community psychiatric services to reduce nonadherence with medication and appointments in patients with psychosis or schizophrenia. The authors concluded that community psychiatric services can provide effective clinical interventions to reduce patient non-adherence. The lack of a validity assessment and the poor reporting of the review process make it difficult to comment on the strength of the evidence or the authors’ conclusions.

Authors’ objectives
To assess the effectiveness of clinical interventions that can be used by community psychiatric services to reduce nonadherence with medication and appointments in patients with psychosis.

Searching
MEDLINE and PsycINFO were searched from January 1980 onwards for reports published in English; the search terms were stated. The bibliographies of relevant reports and systematic reviews were checked for references to published and unpublished studies.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) and non-randomised controlled clinical trials (CCTs) were eligible for inclusion.

Specific interventions included in the review
Studies of clinical interventions to reduce nonadherence compared with standard care were eligible for inclusion. Studies of after-care programmes were included. Studies of compulsory treatment were excluded, as were studies that assessed adherence to first appointments. In the review, the interventions were grouped into five categories: educational strategies, psychotherapy, prompts, specific service policies, and family interventions. Approximately half of the included studies used educational strategies. Details of specific interventions in the included studies were presented.

Participants included in the review
Studies of patients with schizophrenia and related disorders, or psychosis were eligible for inclusion. The studies had to recruit patients from a psychiatric setting. The participants in the included studies were out-patients, hospital-discharged patients and in-patients.

Outcomes assessed in the review
Studies in which one of the primary outcomes was adherence were eligible for inclusion. The review assessed nonadherence to medication (not taking psychotropic drugs as prescribed) and appointments (not keeping scheduled appointments). The length of follow-up (excluding studies of after-care adherence) ranged from 2 to 72 weeks (median 24 weeks).

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
Two reviewers independently extracted the data using a data extraction form. The extracted data included study setting, study design, the number of patients in each treatment group, the length of follow-up, characteristics of the patients and interventions, the number of patients analysed, definition of nonadherence, and results.

Results reported as percentages were converted to absolute numbers. For each study, the odds ratio (OR) and 95% confidence interval (CI) were calculated for dichotomous data and the standardised mean difference (SMD) was calculated for continuous data. The review classified methods used to assess the outcomes into four categories: patient interview, case-note evaluation, rating scale, and urine test.

**Methods of synthesis**

How were the studies combined?
Studies with adequate outcome data were combined using a random-effects model for the meta-analysis. Pooled weighted ORs (with 95% CIs) and pooled SMDs (with 95% CIs) were calculated. A funnel plot was used to assess publication bias.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared statistic. A subgroup analysis was used to assess the influence on the results of: study design (RCT or CCT); the length of follow-up (shorter or longer than 6 months); diagnosis (schizophrenia or severe mental disorders); type of intervention; outcome (nonadherence to medication or appointments); and study setting (in-patients, out-patients, or hospital discharge). Meta-regression was also used to explore the influence of these study characteristics on the results.

**Results of the review**

Forty-seven studies met the inclusion criteria, but only 24 studies were included in the meta-analysis. These 24 studies comprised 14 RCTs (n=1,548) and 10 CCTs (n=2,030). The number of patients per study ranged from 21 to 660.

Overall studies: the interventions significantly reduced nonadherence compared with control. The pooled OR (19 studies) was 2.59 (95% CI: 2.21, 3.03); statistically significant heterogeneity was found (P<0.001). The pooled SMD (5 studies) was 0.36 (95% CI: 0.06, 0.66); no statistically significant heterogeneity was found (P=0.274).

The funnel plot was asymmetrical, suggesting the possibility of publication bias.

The meta-regression showed a greater effect with a shorter length of treatment and an increased effect in patients with schizophrenia. Other factors were not significantly associated with treatment effect. The results were reported.

**Authors' conclusions**

Community psychiatric services can provide effective clinical interventions to reduce patient nonadherence.

**CRD commentary**

The review question was clear in terms of the study design, intervention, participants and outcomes. Two databases and relevant bibliographies were searched and the search terms were stated. The attempts to locate unpublished studies were limited, but the authors did assess the potential for publication bias. It was not reported whether any language restrictions were applied, thus the potential for language bias could not be assessed. The methods used to select the studies, assess validity and extract the data were not described; hence, it is not known whether any efforts were made to reduce errors and bias. Validity was neither assessed nor discussed, thus the strength of the evidence could not be evaluated.

The studies were combined in a meta-analysis, but the finding of significant heterogeneity for the meta-analysis of dichotomous data suggests that a meta-analysis may not have been appropriate. The authors explored the influence of various study characteristics (including study design) on the results using subgroup analyses and meta-regression. Overall, it is difficult to comment on the strength of the evidence underpinning the authors' conclusions, as the quality of the included studies and the methods used to conduct the review were not reported.
Implications of the review for practice and research
Practice: The authors stated that until long-term results are available, clinical interventions should be implemented as short-term measures. They recommended that pre-discharge contracts between patients and the out-patient team, or pre-discharge psychotherapeutic programmes, should become part of routinely delivered service policy and be offered each time patients are scheduled for discharge.

Research: The authors stated that large, well-conducted experimental studies are required to assess the long-term effectiveness of educational strategies, psychotherapeutic programmes and specific service policies in patients recruited from a wide variety of settings. They stated that patients with schizophrenia should be studied separately. Trials should be well reported; in particular, reports should detail exclusion rates, reasons for exclusion, the proportion of patients not adhering to treatment at the end of the acute phase and the proportion remaining adherent at follow-up, and results reported as absolute numbers and outcomes reported for intention-to-treat and completer samples.

Bibliographic details

PubMedID
12948991

Original Paper URL
http://bjp.rcpsych.org/cgi/content/full/183/3/197

Indexing Status
Subject indexing assigned by NLM

MeSH
Community Mental Health Services /methods; Controlled Clinical Trials as Topic; Humans; Patient Compliance /psychology; Patient Education as Topic /methods; Psychotherapy /methods; Psychotic Disorders /drug therapy /therapy; Randomized Controlled Trials as Topic; Telephone; Treatment Outcome

AccessionNumber
12003008606

Date bibliographic record published
30/04/2005

Date abstract record published
30/04/2005

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.