Interventions to improve medication-adherence after transplantation: a systematic review
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CRD summary
This review concluded that a combination of interventions aimed at improved medication adherence in solid organ transplant patients may be effective long term. Significant methodological shortcomings in included studies, potential deficiencies in the review process and the high level of variation between type of studies, participants, interventions and outcomes, the authors’ conclusion appear overstated and may not be reliable.

Authors' objectives
To determine the effectiveness of interventions to improve adherence to medication regimens in patients undergoing solid organ transplantation.

Searching
CINAHL, MEDLINE, PsycINFO and The Cochrane Library were searched up to August 2008 with no limits applied for relevant studies. Search terms were reported. Abstracts were eligible for inclusion. Reference lists from identified studies were searched. It appeared that no searches were made for unpublished studies

Study selection
To be eligible for inclusion in the review, studies needed to include assessment of an intervention aimed at improving immunosuppressive medication-adherence in adults and children who underwent solid organ transplantation where medication-adherence was measured. It appeared that no limits were applied to types of study designs.

Types of transplant in the included studies included renal, heart/heart-lung and liver. Four of the 12 studies focused on children. Studies were undertaken in USA and Europe. Medications included cyclosporine, tacrolimus, prednisone and azathioprine. Interventions were implemented for varied time periods (five days to 12 months) and in various locations (clinic, home, hospital and internet). People who delivered the intervention included clinical pharmacists, clinical nurse specialists, a nurse practitioner and a whole transplant team.

Interventions were categorised as either having an educational/cognitive dimension, counselling/behavioural dimension or psychological/affective dimension; most studies used a mixed approach and focused on at least two of the dimensions. Educational/cognitive interventions conveyed information or knowledge individually or in groups delivered in various ways. Counselling/behavioural interventions focused on targeting, shaping and reinforcing patient behaviour to empower patients and make active changes in their skill levels. Psychologic/affective interventions worked on the feelings, emotions, social relationships and social supports of patients. Non-adherence was defined in different ways in the included studies.

[A: Two authors independently selected studies for the review. Disagreements were resolved by consensus.]

Assessment of study quality
All studies were assessed for quality and scored according to six methodological domains (clarity of the research question, sampling methods, description of non response, reported definitions, measurements, statistical analysis and presentation of results). Summary scores were defined as weak, moderate or strong (maximum score 23). Randomised controlled trials (RCTs) were also assessed by the CONSORT 22 criteria (maximum summary score of 22) that includes questions on title and abstract, introduction, methods, results and discussion.

[A: All review authors assessed studies for validity.] Consensus was reached on the final study scores.

Data extraction
For each included study, two authors extracted overall findings, direction of effect and (where relevant) statistical significance of any differences in effect. It was not reported how disagreements were resolved.
Methods of synthesis
Studies were summarised in narrative format according to either dimension(s) targeted or level of approach (patient, micro, meso or macro level).

Results of the review
Twelve studies (n=455) were included: five randomised controlled trials (RCTs); three were quasi-experimental studies; and four uncontrolled. Ten of the 12 studies used a mixed approach focusing on at least two of the three dimensions. One study was classed as weak quality, nine as moderate quality and two as strong quality. Quality scores of the RCTs ranged from 3 to 18 out of a maximum score of 22. Lack of allocation concealment, implementation and blinding were the most important shortcomings.

Five of the 12 studies reported a statistically significant improvement in at least one medication-adherence outcome with the intervention. Eight studies that intervened at the healthcare provider, healthcare setting or healthcare system level had inconsistent results with only some studies showing limited improvement in adherence. No single intervention showed an increase in medication adherence.

Authors' conclusions
A combination of interventions in a team approach may be effective in the long term for increasing medication adherence in people who had organ transplantation.

CRD commentary
The review had broad criteria for study design, type of participants, interventions and outcomes. The authors searched four databases and efforts were made to find further information by reviewing reference lists. [A: No language restrictions were applied.] It appeared that no attempts were made to find unpublished studies, so publication bias could not be ruled out. [A: Appropriate methods for study selection, data extraction were reported.]

All studies were assessed using relevant criteria. RCTs were further assessed by an additional comprehensive checklist. There were methodological shortcomings in most of the included studies and they were underpowered. Details of included studies were reported in tables. There were clinical and methodological differences between studies. A variety of study designs were included: RCTs, quasi experimental designs and four without a control group. Interventions were heterogeneous, but were classified broadly as educational/cognitive, counselling/behavioural or psychologic/affective and these dimensions informed the interpretation of the results. There were variations in how the interventions were administered and for how long.

Types of comparator varied from usual care and routine clinic services, monitoring without feedback and no interactions with pharmacist. There was also wide variation in how the primary outcome of non-adherence was defined. Given the heterogeneity of the studies, the presentation of the results in a narrative format was appropriate. Due to significant methodological shortcomings of the included studies and the high level of variation between type of studies, participants, interventions and outcomes, the authors' conclusions appear overstated and may not be reliable.

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

Research: The authors stated that further RCTs of adequate power that adhered to CONSORT guidelines to ensure quality were needed. Studies should make baseline assessments of adherence prior to use of interventions and develop clear and consistent definitions of non adherence. Studies should be based on a specific theoretical framework and assess multidimensional and multilevel patient-tailored interventions that focus on micro, meso and macro levels.

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