Effect of medication dosing frequency on adherence in chronic diseases
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CRD summary
This review concluded that patients with chronic diseases were more compliant with once-daily regimens compared with twice or thrice daily when assessed using the medication event monitoring scheme. The small size and short follow-up of the studies, potential for missed studies and lack of quality assessment mean that the conclusions and recommendations for practice should be interpreted with some caution.

Authors' objectives
To investigate the impact of dosing regimens on adherence to medication for chronic diseases as assessed by the Medication Event Monitoring Scheme (MEMS).

Searching
MEDLINE, EMBASE and The Cochrane Library were searched for English-language full paper publications from 1986 to August 2007; search terms were reported. Bibliographies of reviews were scanned. The full search strategy was available in an online appendix.

Study selection
Prospective controlled trials of adults with chronic diseases characterised by remission or asymptomatic periods were eligible for inclusion. Eligible studies needed to: be of patients who were prescribed oral medication to be taken up to four times a day; have at least six weeks follow-up; and report adherence using MEMS.

Studies were excluded if: patients took complex multiple treatment regimens, such as with HIV (human immunodeficiency virus) or cancer; patients had comorbid psychiatric illnesses; or the studies assessed interventions designed to improve adherence.

Most studies recruited patients with cardiovascular disorders; other conditions included type 2 diabetes, epilepsy, migraines, and various disorders. Drugs evaluated included antihypertensives and other cardiovascular drugs, antidiabetic agents, antiepileptic drugs and migraine prophylaxis. Where reported, mean age of participants ranged from 50 to 69 years, the proportion of males was from 24% to 100% and the duration of follow-up was from 42 to 214 days.

Two independent reviewers screened articles for inclusion; disagreements were resolved by consensus.

Assessment of study quality
The authors did not state that they formally assessed study quality; some aspects of study quality were presented, such as randomisation, patient blinding and dropouts.

Data extraction
The proportion of days with the correct number of bottle openings and/or the proportion of correct bottle openings over the course of the study were extracted by two independent reviewers; disagreements were resolved by consensus.

Methods of synthesis
Studies were combined in a narrative synthesis. Differences between studies were discussed in the text. Study details and results were presented in tables.

Results of the review
Twenty studies met the inclusion criteria (n=2,000, range 19 to 250): 11 were randomised (n=1,366); eight were cohort studies (n=615); and in one the study design was unclear (n=19). Only three studies reported blinding of patients to MEMS, one of these in only 68% of patients.
The range of adherence rates were consistently lower with increased number of doses, for patients with hypertension (49% to 94% for 1/day and 5% to 82% for 2/day; six studies), angina (84% to 97% for 1/day and 59% to 88% for 2/day; four studies), type 2 diabetes (79% to 94% for 1/day and 38% to 67% for 3/day; six studies) and for other chronic diseases (77% to 90% for 1/day; four studies), (60% to 86% for 2/day; five studies), (50% to 80% for 3/day; 54 studies) and 39% for 4/day; 14 studies).

Within-study differences ranged from 5% to 44% for hypertension (four studies), 9% to 26% for angina (six studies), 13% to 41% for type 2 diabetes (four studies) and 2% to 20% for 1/day versus 2/day and 10% to 38% for 1/day versus 3/day for other chronic conditions (four studies).

Authors' conclusions
Patients were more compliant with once daily compared with twice or thrice daily treatment regimens.

CRD commentary
The authors addressed a clear review question with appropriate inclusion criteria. Relevant sources were searched, but the restriction to published studies in English meant that studies could have been missed. Study selection and data extraction were conducted in duplicate, which reduced the risk of error and bias. The authors did not appear to undertake a systematic assessment of the quality of the included studies and insufficient study details were provided to allow the reader to do so. The use of a narrative synthesis seemed appropriate. Many of the included studies were small with relatively short follow-up durations (up to approximately seven months). Although the overall ranges of adherence were lower with regimens that required less frequent dosing, there was substantial overlap in the ranges across studies; within-study differences were as low as 2%. Given the limitations of both the included studies and the review, the conclusions and recommendations for practice should be interpreted with some caution.

Implications of the review for practice and research
Practice: The authors stated that physicians who treated patients with chronic diseases should consider prescribing medications that required less frequent dosing.

Research: The authors stated that future studies should be sufficiently powered randomised trials that used a standardised outcome measure for adherence. Studies were required in chronic conditions that had acute flares.

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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.