Self-monitoring of oral anticoagulation: a systematic review and meta-analysis


CRD summary
This review assessed the effectiveness of self-monitoring by patients on oral anticoagulation treatment. It concluded that self-monitoring showed statistically significant reductions in thromboembolic events, all-cause mortality and major haemorrhage, compared with usual care. The review methods were appropriate, although it is difficult to reliably assess the conclusions given that details of quality and differences between studies were not reported.

Authors' objectives
To assess current evidence for the effectiveness of self-monitoring and self-adjustment by patients on oral anticoagulation treatment.

Searching
EMBASE, MEDLINE, and CINAHL were searched from inception to 2005. Additional searches of the Cochrane CENTRAL Register, the Cochrane Library (Issue 2, 2005), the UK National Research Register and Trials Central were also conducted. Reference lists were checked and manufacturers and experts in the field were contacted. Details of the search terms were reported and no language restrictions were applied.

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

Specific interventions included in the review
Studies comparing self-monitoring (with or without self-adjustment of dose) of anticoagulation with control and dosage by personal physician, or of anticoagulant management clinics or managed services, were eligible for inclusion. Self-monitoring patients in the included studies were provided with educational or training sessions of varying frequency, with some providing additional telephone support. The control groups received standard medical care from either their family doctor or a specialist anticoagulation clinic.

Participants included in the review
Studies of adults and children on anticoagulant therapy, irrespective of the indication for treatment, were eligible for inclusion. The average age of the patients in the included studies ranged from 42 to 75 years. Most of the studies included patients on long-term anticoagulation treatment.

Outcomes assessed in the review
Studies reporting thromboembolic events and major bleeding episodes were eligible for inclusion. The primary outcomes were thromboembolic events, major bleeding episodes, all-cause mortality and the proportion of measurements within the therapeutic range. The secondary outcomes were frequency of testing, minor bleeding episodes and drop-out rates. The duration of the included studies ranged from 2 to 24 months.

How were decisions on the relevance of primary studies made?
Three reviewers independently assessed articles for inclusion. Any disagreements were resolved by contacting the study authors, or by discussion.

Assessment of study quality
Study validity was assessed using the following criteria: method of randomisation, allocation concealment, use of masked outcome assessments, intention-to-treat analysis and follow-up rates.
The authors did not state how many reviewers performed the validity assessment.

**Data extraction**
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. The numbers of patients experiencing the event of interest were extracted, and the odds ratio (OR) and 95% confidence interval (CI) were calculated for each study.

**Methods of synthesis**
*How were the studies combined?*
The studies were combined using the Mantel-Haenszel fixed-effect model. Peto's method was used to confirm these results for outcomes where there were few events. If statistically significant heterogeneity was observed then the studies were combined using the random-effects model of DerSimonian and Laird. Publication bias was assessed using funnel plots, Begg's rank correlation and Egger's regression test.

*How were differences between studies investigated?*
Heterogeneity was examined using the chi-squared and I-squared statistics. A sensitivity analysis was performed by excluding studies of the lowest quality. A meta-regression was used to perform pre-specified subgroup analyses of clinical indication (mechanical valve replacement or atrial fibrillation) and type of therapy (self-monitoring only or self-monitoring plus self-adjustment). A post hoc subgroup analysis of the type of control group care (specialist anticoagulation clinic or family physician) was also performed.

**Results of the review**
Fourteen RCTs (n=3,049) were included.

Four trials were judged to be of poor quality with unclear allocation concealment and no intention-to-treat analysis or masking.

Thromboembolic events.
There was a statistically significant reduction in thromboembolic events for self-monitoring patients compared with control patients (10 studies; OR 0.45, 95% CI: 0.30, 0.68). This result was not affected by the removal of the 4 low-quality studies (OR 0.41, 95% CI: 0.25, 0.70). Statistically significant reductions were also seen in the subgroups of studies with and without self-adjusted treatment.

Major haemorrhage.
There was a statistically significant reduction in major haemorrhage for self-monitoring patients compared with control patients (10 trials; OR 0.65, 95% CI: 0.42, 0.99). This result was no longer statistically significant when the 4 low-quality studies were excluded (OR 0.66, 95% CI: 0.37, 1.16). A statistically significant reduction was also seen in the subgroup of studies of self-monitoring only, but not for studies of self-monitoring with self-adjustment.

All-cause mortality.
There was a statistically significant reduction in the number of deaths from any cause for self-monitoring patients compared with control patients (6 studies; OR 0.61, 95% CI: 0.38, 0.98). This result was not affected by the removal of the 4 low-quality studies (OR 0.58, 95% CI: 0.36, 0.95). A statistically significant reduction was also seen in the subgroup of studies of self-monitoring with self-adjusted treatment, but not for the subgroup of studies of self-monitoring only.

Other outcomes.
Eleven studies reported improvements in the self-monitoring group in terms of the mean proportion of international normalisation ratios in range, with 6 studies reporting statistically significant improvements. Four studies reported an
improvement in the proportion of time within ranges, of which two were statistically significant. Nine trials reported on minor haemorrhage, but these were not pooled because of statistically significant heterogeneity (P=0.01). The ratio of tests performed in the self-monitoring group compared with the control group ranged from 1.69 to 4.98, and this tended to increase with the duration of the study.

Authors' conclusions
Although no individual trial showed statistically significant results, the combined trials suggest that self-monitoring of oral anticoagulation leads to a significant one-third reduction in death from all causes. Both benefits and harms of anticoagulation seemed to be improved by self-monitoring: thromboembolism decreased by 55% and major haemorrhage was also decreased. In patients who also self-adjusted therapy, there seemed to be a greater reduction in thromboembolic events and mortality than self-monitoring alone, but there was less reduction in haemorrhage.

CRD commentary
This review had a clearly stated research question and inclusion criteria. The search was comprehensive and there were no language restrictions. Efforts were made to locate unpublished data by searching trial registers and contacting manufacturers and experts in this area. Three reviewers independently screened studies for inclusion, which minimises the risk of bias. However, the authors did not state how the data were extracted, so it is not possible to judge if steps were taken to prevent errors in this process. Study quality was assessed using appropriate criteria. Sensitivity analyses were conducted to assess the impact of the poor-quality studies upon the pooled results, though the precise cut-off point for poor quality and whether it was defined a priori was unclear.

The methods of statistical analysis appeared appropriate although, with the exception of one outcome, the authors did not report the results of tests for heterogeneity. This was a well-conducted review and the authors' conclusions are likely to be reliable, although it is not possible to draw a firm conclusion about this as there was insufficient information on study quality and heterogeneity.

Implications of the review for practice and research
Practice: The authors stated that self-monitoring is not feasible for all patients and requires the identification and education of suitable candidates. Guidelines exist for institutions considering the implementation of self-monitoring of anticoagulation.

Research: The authors stated that an individual patient data meta-analysis is needed to further understand the effect of self-monitoring on both the time in range and tests in range.

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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.