Self monitoring of oral anticoagulation: systematic review and meta-analysis of individual patient data

Heneghan C, Ward A, Perera R

CRD summary
This high-quality IPD review found that self monitoring reduced thromboembolic events without increasing major haemorrhages and death. The review utilised appropriate methods to minimise potential biases and the conclusions are likely to be reliable.

Authors' objectives
To assess the effect of self-monitoring of oral anticoagulation on time to death, first major haemorrhage and first thromboembolic event, including the effect in important patient subgroups

Searching
EMBASE (1980 to 2009), MEDLINE (1966 to 2009), CINAHL (1982 to 2009), The Cochrane Library (issue 2, 2009) and Cochrane Central Register of Controlled Trials (CENTRAL) were searched for eligible trials. Search terms were reported. NRR and Trials Central were searched for ongoing or unpublished trials. Reference lists were checked.

Study selection
Randomised trials that compared self-monitoring or self-management of oral anticoagulation therapy against conventional care in adults on anticoagulant therapy were eligible for inclusion. Primary outcomes were time to death, first major haemorrhage and first thromboembolic events. Major haemorrhages included: bleeding that was fatal; symptomatic bleeding in a critical area or organ (such as intracranial, intraspinal, intraocular, retroperitoneal, intra-articular or pericardial, or intramuscular with compartment syndrome); and bleeding causing a fall in haemoglobin concentrations of 20g/L (1.24 mmol/L) or more or leading to transfusion of two units of packed red blood cells. Thromboembolic events were stroke, arterial embolism, symptomatic deep-vein thrombosis and pulmonary embolism.

Patients ranged in age from 17 to 94 years. More than half of the participants had atrial fibrillation. One third of the participants had a mechanical heart valve insertion.

Two reviewers independently assessed the articles for inclusion. Disagreements were resolved by discussion.

Assessment of study quality
Two researchers cross-checked trial details and summary measures. Major outcomes were cross-checked with prespecified outcome definitions against published articles. Any inconsistencies were discussed with the original trialist and corrections were made where appropriate. Methods of randomisation, allocation concealment and intention-to-treat analysis were verified for all trials.

Data extraction
IPD were collated on date of randomisation, age, indication for treatment, type of care, demographic and psychosocial characteristics at randomisation (including quality-of-life measures), treatment allocation, time to death, time to first major haemorrhage, time to first thromboembolic event and international normalised ratio measurements.

Methods of synthesis
Time to event data were summarised as (log) hazard ratios (HR). A two-step approach to meta-analysis was adopted with hazard ratios estimated for each trial and pooled with a random-effect for treatment. Heterogeneity was quantified using I^2. Interaction tests were used to explore differential treatment effects by age, sex, type of control-group care (anticoagulation clinic care versus primary care) and self-testing alone versus self-management. Numbers needed to treat were calculated. Publication bias was assessed using funnel plots alongside Begg and Egger tests of asymmetry.
Results of the review

Eleven trials were available in IPD format with data for 6,417 participants and 12,800 person-years of follow-up. IPD were unobtainable from a further 10 eligible trials.

There was a significant reduction in thromboembolic events in the self-monitoring group (HR 0.51, 95% CI 0.31 to 0.85), but not for major haemorrhagic events (HR 0.88, 95% CI 0.74 to 1.06) and death (HR 0.82, 95% CI 0.62 to 1.09). Participants younger than 55 years showed a large reduction in thrombotic events (HR 0.33, 95% CI 0.17 to 0.66, substantial heterogeneity $I^2=52\%$), as did participants with mechanical heart valves (HR 0.52, 95% CI 0.35 to 0.77, no substantial heterogeneity).

Statistically significant interactions between effectiveness in reducing thromboembolic events and IPD covariates were found for age, indication and self monitoring.

Authors’ conclusions

Self-monitoring was superior, halving the risk of thromboembolic events. Bleeding rates were similar in both groups. Self-monitoring had no major effect on mortality.

CRD commentary

This high-quality IPD review used appropriate methods to minimise bias in obtaining and synthesising data from 11 relevant trials. There was potential for publication and reporting biases as IPD were unavailable from 10 studies. Appropriate random-effects analyses were used to pool data and interaction tests were used to explore heterogeneity. These should be interpreted cautiously as there was potential for aggregation bias and statistical significance is not synonymous with clinical significance. Participants younger than 55 years were distinguishable from patients of other ages, but event rates were low in the former subpopulation and no trend was apparent. Differences in treatment effectiveness between indication and self-monitoring subgroups were less pronounced.

The overall conclusion that self monitoring reduces thromboembolic events without increasing major haemorrhages or death reflects the evidence and is likely to be reliable.

Implications of the review for practice and research

Practice: Patients with a mechanical heart valve who require long-term anticoagulation should be offered the option to self manage their disease with suitable back-up health care support. Self monitoring and self management are safe options for suitable patients.

The authors did not state any implications for further research.

Funding

National Institute for Health Research, UK.

Bibliographic details


PubMedID

22137798

DOI

10.1016/S0140-6736(11)61294-4

Original Paper URL

Indexing Status
Subject indexing assigned by NLM

MeSH
Administration, Oral; Anticoagulants /administration & dosage /adverse effects; Drug Monitoring; Hemorrhage /chemically induced; Humans; International Normalized Ratio; Self Care; Thromboembolism /prevention & control; Vitamin K /antagonists & inhibitors

AccessionNumber
12011007212

Date bibliographic record published
07/12/2011

Date abstract record published
21/12/2011

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.