Effectiveness of pharmacist-participated warfarin therapy management: a systematic review and meta-analysis
Saokaew S, Permsuwan U, Chaiyakanaprak N, Nathisuwan S, Sukonthasarn A

CRD summary
This generally well-conducted review concluded that pharmacist participation in the management of warfarin therapy significantly reduced total bleeding and there was a non-significant trend towards decreases in other warfarin-related complications. Limitations of the evidence available mean that the conclusions should be treated with some caution.

Authors' objectives
To compare the effects of pharmacist-participated warfarin therapy management with usual care on bleeding and thromboembolic outcomes.

Searching
MEDLINE, SCOPUS, EMBASE, IPA, CINAHL, Cochrane Central Register of Controlled Trials (CENTRAL), Thai Index Medicus and Thai Medical Index were searched from inception to July 2009. There were no language restrictions. Search terms were reported. Reference lists of identified articles were scanned. Authors and experts in the field were contacted.

Study selection
Studies of warfarin in which a pharmacist was involved in warfarin management compared against a control where healthcare professionals other than pharmacists were used and that reported warfarin-associated bleeding, thromboembolic events or all-cause mortality were eligible for inclusion.

Most of the studies were conducted in outpatient units. Warfarin was prescribed for a wide range of indications. The most common pharmacist activities were warfarin dose adjustment, medication/drug interaction review and education. The average age of participants was 62.5 years (range 46 to 80.5 years) and 52.9% were male. Some studies were restricted to new warfarin users; others recruited warfarin-experienced patients.

Two reviewers independently selected studies for the review; disagreements were resolved by discussion.

Assessment of study quality
Two reviewers independently assessed study quality using the Downs and Black assessment tool. The Jadad scale was also used to assess randomised controlled trials (RCTs). Disagreements were resolved by discussion.

Data extraction
Two reviewers independently extracted data to calculate relative risks (RR) and 95% confidence intervals (CI); disagreements were resolved by discussion.

Methods of synthesis
Pooled relative risks and 95% CI were calculated using a DerSimonian and Laird random-effects model. Heterogeneity was assessed using Q and I² statistics. RCTs and non-RCTs were analysed separately. Sensitivity analyses were used to investigate the impact of analytical method, sample size, outlier studies, study quality, comparator used, patient age, patient population, setting, duration of follow-up and pharmacist activities. Publication bias was investigated using funnel plots and Egger's regression asymmetry test.

Results of the review
Twenty-four studies met the inclusion criteria (728,377 participants, range 51 to 717,396): five RCTs (862 participants), nine quasi-randomised studies and 10 cohort studies. Downs and Black scores ranged from 11 to 22 for observational studies and 21 to 29 for RCTs. The five RCTs all scored 3 on the Jadad scale.
Bleeding: Compared to usual care, pharmacist involvement significantly reduced the incidence of total bleeds (RR 0.51, 95% CI 0.28 to 0.94, I²=0%; four RCTs and RR 0.71, 95% CI 0.52 to 0.96, I²=77%; 19 non-RCTs). There was no difference in incidence of major bleeding in RCTs, but a significant reduction was observed in 11 non-RCTs (RR 0.49, 95% CI 0.26 to 0.93, I²=46.7%).

Thromboembolic events: Compared to usual care, pharmacist involvement showed no difference in the incidence of thromboembolic events in RCTs, but a significant reduction was observed in 15 non-RCTs (RR 0.37, 95% CI 0.26 to 0.53, I²=3.7%).

Mortality: There was no significant difference between usual care and pharmacist involvement in RCTs and non-RCTs.

Results of sensitivity analyses were reported; effects of pharmacist involvement were reported as consistent across all subgroups. There was no evidence of publication bias for any analysis.

Authors’ conclusions
Pharmacist participation in management of warfarin therapy significantly reduced total bleeding. There was a non-significant trend towards decreases in other warfarin-related complications.

CRD commentary
The authors addressed a clear review question supported by appropriate inclusion criteria. There was an extensive search without language restrictions for both published and unpublished studies. Each stage of the review was conducted in duplicate, which reduced risks of error and bias. Study quality was assessed with appropriate criteria, although only the composite score was reported.

The analyses combined studies that were clinically heterogeneous, which impacted on the generalisability of the pooled results. Heterogeneity was investigated. Ninety-nine per cent of the review population were derived from one USA observational study that scored 18 out of a possible 31 on the Downs and Black quality score. The only significant outcome based on RCTs was an analysis where one RCT was excluded as a potential source of heterogeneity; the result including this RCT was not presented.

This was generally a well-conducted review, but limitations of the evidence available mean that the conclusions should be treated with some caution.

Implications of the review for practice and research
Practice: The authors stated that the results of their review were consistent with current guidelines and supported implementation of anticoagulation monitoring services with pharmacists as an integral part. They authors stated that given the extent of the benefits of pharmacist involvement, policy makers and guideline developers may consider the inclusion of pharmacists as an effective measure in the optimal management of warfarin therapy in most hospital settings worldwide.

Research: The authors stated that cost-effectiveness and the impact of pharmacist involvement on the time within therapeutic range needed investigation.

Funding

Bibliographic details

PubMedID
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.