

Clinical effectiveness and cost-effectiveness of different models of managing long-term oral anticoagulation therapy: a systematic review and economic modelling

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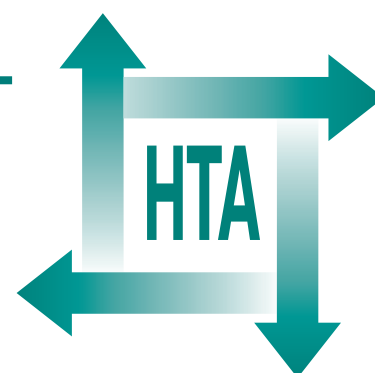
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Executive summary

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Executive summary

Background

Many disorders, including common cardiac conditions, are linked to increased risk from thrombosis and require anticoagulant therapy. Oral anticoagulation control (AC) is used to reduce the chance of unwanted thrombosis. AC therapy lengthens the time it takes for a sample of a patient's blood to clot. Such therapy, usually with warfarin, requires frequent monitoring to maintain a beneficial balance between decreased clotting and the tendency for increased bleeding that results from therapy. Conventional monitoring has involved patients attending clinic for measurement of clotting speed. A physician then adjusts the patient's anticoagulant dose to achieve the desired balance between reduced clotting and tendency to bleed. Two other anticoagulation management strategies have been developed that employ near-patient testing (NPT) devices. With these devices, patients can measure clotting speed themselves ('patient self-testing'); a physician uses the result to adjust the patient's anticoagulant dose or the patients adjust the dose of anticoagulant themselves in the light of their own measurements with the NPT device ['patient self-management' (PSM)]. These two strategies are collectively referred to as patient self-monitoring.

It is estimated that approximately 950,000 people (2% of the general practice population) in the UK are currently taking warfarin and the numbers continue to increase by about 10% each year, primarily driven by its use for patients with atrial fibrillation. The future impact of this expansion is indicated by estimates that currently more than half of those with atrial fibrillation may remain unidentified and less than half of those identified may be receiving treatment. These estimates considered together with an ageing population mean that future service load could increase substantially.

Objectives and methods

This report aims to examine the clinical effectiveness and cost-effectiveness of self-testing and self-management of oral anticoagulation treatment compared with clinic-based monitoring.

Methods

Comprehensive bibliographic searches were undertaken up to September 2005 to identify randomised and non-randomised controlled studies of patient self-monitoring for long-term oral anticoagulation therapy. Data about AC, adverse events, mortality, attrition and patient acceptability were extracted from the retrieved studies. Results about complication events and deaths were pooled in meta-analyses using risk difference (RD) as the outcome statistic (in order to include many studies that reported zero events). Heterogeneity across trials and possible publication bias were statistically measured. Subgroup analyses (*post hoc*) were conducted to compare results of self-testing versus self-management, low versus high trial quality, trials conducted in the UK versus trials in other countries and industry versus other sponsors.

Comprehensive bibliographic searches of major electronic databases were undertaken up to September 2005 to identify cost-effectiveness studies that evaluated the cost-effectiveness of patient self-monitoring of anticoagulation. We also developed a Markov-type, state-transition model for the evaluation of cost-effectiveness of patient self-monitoring of oral anticoagulation compared with the usual care currently provided in the UK. Input values for the model were mainly based on a review of relevant literature. Stochastic simulations using the model were conducted to investigate uncertainty in estimated model parameters.

Results

Evidence about effectiveness

Sixteen randomised trials were included. Patient self-monitoring of oral anticoagulation therapy is more effective than poor-quality usual care provided by family doctors. Poor quality of AC managed by family doctors is particularly associated with a greater proportion of time spent below the target therapeutic clotting range. This could be much reduced by patient self-monitoring. Patient self-monitoring is as effective as good-quality specialised anticoagulation clinics in maintaining the quality of anticoagulation therapy. ►

There was no significant RD of major bleeding events between patient self-monitoring and usual care controls [RD -0.0039, 95% confidence interval (CI) -0.0154 to 0.0077]. Pooled analyses found that compared with primary care or AC clinics, self-monitoring was statistically significantly associated with fewer thromboembolic events (RD -0.0224, 95% CI -0.0334 to -0.0115) and deaths (RD -0.017, 95% CI -0.0287 to -0.0053). However, the reduction in complication events and deaths was not consistently associated with the improvement of AC. The observed reduction in complications and deaths in some trials may be due to alternative explanations, including patient education and patient empowerment. In addition, random or systematic errors could not be ruled out from the included trials. More importantly, findings of meta-analyses by pooling results from all trials may not be applicable to the UK setting. The improved AC and the reduction of major complications and deaths by patient self-monitoring were mainly observed in trials conducted outside the UK.

Eight non-randomised controlled studies were included. The sample sizes of these studies were generally small, and the period of follow-up was similar to that in the randomised trials. The results from non-randomised studies were similar to those from the randomised trials. The impact of including data from the non-randomised studies in meta-analyses of major complications and death outcomes was negligible.

Patient selection and acceptability

Not all patients are capable of performing self-monitoring and some patients find it unnecessary because of high-quality care provided by existing anticoagulation clinics. Selected patients may consider self-monitoring of oral anticoagulation as an invaluable option. For example, self-monitoring may enhance the quality of life for some patients who are frequently away from home, who are in employment or education or who find it difficult to travel to clinics.

Pooling of available data from all trials suggested that, on average, 33% of eligible patients agreed to participate in the trials; 80% of patients randomised to patient self-monitoring were successfully trained and/or able to conduct self-monitoring, and 87% of those who started self-monitoring continued monitoring to the end of study. According to UK-specific data, for every 100 eligible patients, 24% would agree to conduct self-monitoring, 17 of the 24 patients (70%) could be successfully trained and able to carry out self-

monitoring and only 14 of these (80%) would conduct long-term self-monitoring.

Economic evaluation

Seven studies of evaluating the cost-effectiveness of patient self-monitoring of anticoagulation were identified. The applicability of six of these to the UK setting was limited. One UK study provided the most relevant data. This study found that patient self-management was more expensive than current routine care in the UK (£417 versus £122 per patient-year) and concluded that using a cost-effectiveness threshold of £30,000 per quality-adjusted life-year (QALY) gained, patient self-management does not appear to be cost-effective.

It was estimated that wide adoption of patient self-monitoring of anticoagulation therapy would cost the NHS an additional £8–14 million per year. The results of *de novo* modelling for this report found that the incremental cost per QALY gained by patient self-monitoring is £122,365 over 5 years and £63,655 over 10 years. The estimated probability that patient self-monitoring is cost-effective (up to £30,000/QALY) is 44% over a 10-year period. Therefore, self-monitoring by general patients of oral anticoagulation therapy is unlikely to be more cost-effective than current usual care in the UK.

Conclusions

For selected and successfully trained patients, self-monitoring is effective and safe for long-term oral anticoagulation therapy. Self-monitoring may enhance the quality of life for some patients who are frequently away from home, who are in employment or education, or those who find it difficult to travel to clinics. In general, patient self-monitoring is unlikely to be more cost-effective than the current high-quality care provided by specialised anticoagulation clinics in the UK.

Recommendations for further research

Published values of percentage of time or percentage of tests within the target range indicate that there is scope for further improvement of PSM beyond the performance currently achieved. Different dose algorithms and other procedures that could lead to alternative dosing regimes represent an element of PSM that might be profitably researched with the aim of improving performance. ►

Limited evidence indicated that patient education and training may improve clinical outcomes of anticoagulation therapy, even without performing PSM of AC. There is a lack of evidence about whether patient education alone is sufficient to reduce the risk of bleeding, thromboembolic complications and deaths in patients who receive long-term anticoagulation therapy. The clinical effectiveness and cost-effectiveness of patient education and training in long-term oral anticoagulation therapy need to be investigated.

Only one economic analysis of PSM of long-term anticoagulation therapy was identified that was directly relevant to the UK. Therefore, further cost-effectiveness research is required to build on the findings of this study, particularly taking into account the costs of PSM outside trial conditions. In addition, further consideration should be given to the measurement of the less tangible benefits of self-management, which the broad health measures used to calculate QALYs may not be able to capture.

Warfarin allows many children with heart disease to survive into healthy adulthood, but this brings families another set of problems. In addition to missing time off school to attend clinics, it makes timing of holidays difficult. For parents this may involve time away from work, with long clinic waits, often with other siblings. The PSM model, where children or carers have knowledge of changes in lifestyle and concurrent medication,

may also be effective in reducing risks of adverse events. Although a few studies have been conducted on PSM of anticoagulation therapy in children, there is a lack of RCTs and, as far as we are aware, no clinical trials are being undertaken in this area. Future research needs to evaluate the effectiveness of PSM in children.

PSM of anticoagulation therapy arose from development of NPT devices sufficiently user-friendly and compact that some patients satisfactorily control their anticoagulation. Further progress in the design, conception and ease of use of NPT devices may broaden the spectrum of patients able to undertake PSM and provide alternatives for this model of management. It is important that potential future developments are subjected to appropriate quality control and that effectiveness is investigated with well-designed RCTs with sufficient follow-up to capture key outcomes of complication events (thromboembolism, bleeds) and mortality.

Publication

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The research reported in this monograph was commissioned by the HTA Programme as project number 05/33/01. The contractual start date was in September 2005. The draft report began editorial review in May 2006 and was accepted for publication in April 2007. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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