Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The authors compared oral anticoagulation therapy through self-management with oral anticoagulation therapy through physician management for patients with atrial fibrillation or with a mechanical heart valve.

Type of intervention
Primary and secondary prevention.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of patients with atrial fibrillation or with a mechanical heart valve.

Setting
The setting was primary care. The economic study was carried out in Canada.

Dates to which data relate
The effectiveness data were derived from studies published between 1993 and 2004. The price year was 2003.

Source of effectiveness data
The effectiveness data were derived from a review and synthesis of published studies.

Modelling
A Markov decision-analytic model was used to compare the costs and benefits accruing to patients in self-management or physician management strategies over a 5-year period. The model consisted of five main health states. These were no events, minor haemorrhagic event, major haemorrhagic event, major thrombotic event and death. The model was based on two assumptions. In one, all patients were assumed to be in the "no events" state at baseline. In the other, those who experienced a major haemorrhagic or thrombotic event were at risk of permanent disability and were switched to physician management if they were previously self-managing their therapy.

Outcomes assessed in the review
The outcomes assessed were:

the time spent below, in or above therapeutic range with each of the management strategies;
the event rate (i.e. thrombosis, major haemorrhage and minor haemorrhage) by the time spent below, in or above therapeutic range; and

the death rate following a major thrombotic or major haemorrhagic event.

**Study designs and other criteria for inclusion in the review**

Estimates for time in therapeutic range were taken from a randomised controlled trial conducted at Vancouver General Hospital (VGH). To determine the probability of an event given time in therapeutic range, the authors reviewed the literature for studies of directly monitored self-management or physician management with long-term vitamin K antagonists, therapeutic ranges similar to those in the VGH trial, and event rates related to all levels of anticoagulation ranges.

**Sources searched to identify primary studies**

To determine the probability of an event given time in therapeutic range, the authors searched MEDLINE between January 1990 and January 2005. However, no studies met the inclusion criteria for providing prior knowledge of time in therapeutic range. Therefore, estimates for event probabilities given time in therapeutic range were taken from a large prospective cohort study (ISCOAT) that followed 2,745 consecutive patients with heart valve prostheses, atrial fibrillation or venous thromboembolism. Finally, to provide prior information for event transition probabilities, a study involving patients with a mechanical heart valve was used.

**Criteria used to ensure the validity of primary studies**

Not reported.

**Methods used to judge relevance and validity, and for extracting data**

Not reported.

**Number of primary studies included**

Eleven primary studies were included in the review.

**Methods of combining primary studies**

Not reported.

**Investigation of differences between primary studies**

Not reported.

**Results of the review**

The time spent below, in and above therapeutic range was:

with self-management, 0.150 (95% confidence interval, CI: 0.144 to 0.156) below, 0.718 (95% CI: 0.710 to 0.725) in and 0.133 (95% CI: 0.127 to 0.137) above;

with physician management, 0.273 (95% CI: 0.266 to 0.280) below, 0.632 (95% CI: 0.624 to 0.639) in and 0.095 (95% CI: 0.090 to 0.100) above.

The thrombosis rate by time below, in and above therapeutic range was 0.120 (95% CI: 0.09 to 0.14) below, 0.012 (95% CI: 0.008 to 0.015) in and 0.006 (95% CI: 0.003 to 0.008) above.
The major haemorrhagic rate by time below, in and above therapeutic range was 0.004 (95% CI: 0.001 to 0.009) below, 0.005 (95% CI: 0.002 to 0.006) in, and 0.059 (95% CI: 0.05 to 0.07) above.

The minor haemorrhagic rate by time below, in and above therapeutic range was 0.00 below, 0.040 (95% CI: 0.034 to 0.045) in and 0.110 (95% CI: 0.096 to 0.117) above.

The death rate following major thrombotic events was 0.210 (95% CI: 0.140 to 0.300), and following major haemorrhagic events 0.140 (95% CI: 0.090 to 0.180).

Measure of benefits used in the economic analysis
The measure of benefits used was the quality-adjusted life-years (QALYs). Utility weightings associated with each health state in the model were derived from different studies that had administered the EQ-5D questionnaire. A utility weight of 0.70 was assigned to those patients after stroke with no disability. For those with permanent disability due to stroke, utility was 0.19 for the first year and 0.33 in subsequent years. Patients with non-disabling major haemorrhage were assigned a utility of 0.80, while those with disability were assigned a utility of 0.69. The health benefits were discounted at an annual rate of 3%.

Direct costs
The direct costs to the Canadian health care system were included in the analysis. Such costs covered self-management (including pharmacist training costs), physician management (including laboratory tests and telephone consultations), and the costs of major thrombotic and haemorrhagic events (i.e. diagnostic tests, emergency visits and treatment). The costs of self-management testing were obtained from the VGH trial, while the costs of physician management were obtained from the literature. The resource use and cost data for thrombotic events were obtained from the literature and the authors' own assumptions. Discounting was necessary, as the costs could be incurred over a 5-year period, and was performed appropriately at an annual rate of 3%. The authors reported the mean costs. The price year was 2003.

Statistical analysis of costs
The authors reported mean costs alongside the 95% CIs.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
Canadian dollars (CAD).

Sensitivity analysis
A probabilistic sensitivity analysis was undertaken. A Dirichlet distribution was specified to represent each transition probability. Standard deviations for costs were generated using a triangular distribution by assuming a 25% increase or decrease in cost. The authors also conducted one- and two-way sensitivity analyses in which the number of physician visits, the probability of disability after major thrombotic or haemorrhagic event, the discount rate, the utility weightings and the time horizon were varied.

Estimated benefits used in the economic analysis
Over 5 years, self-management resulted in 4.28 QALYs (95% CI: 4.24 to 4.30) and physician management in 4.21 QALYs (95% CI: 4.19 to 4.25).

Therefore, the incremental QALYs gained by using self-management over physician management were 0.07 (95% CI: 0.056 to 0.084).
Cost results
Over 5 years, the mean cost per patient was CAD 6,116 (95% CI: 5,426 to 6,830) in the self-management strategy and CAD 5,127 (95% CI: 4,390 to 5,894) in the physician management strategy.

Therefore, the average mean incremental cost of self-management in comparison with physician management was CAD 989 (95% CI: 310 to 1,655).

Synthesis of costs and benefits
The costs and benefits were combined using an incremental cost-utility ratio (i.e. the additional cost per QALY gained). Compared with physician management, the additional cost per QALY gained when using self-management was CAD 14,129. The results of the probabilistic sensitivity analysis showed that, at a willingness-to-pay of CAD 23,800, the probability that self-management was cost-effective was 95%.

The results of the one- and two-way sensitivity analyses showed that the results were robust to changes in parameter values. However, when the time horizon was reduced to one year, the additional cost per QALY gained when using self-management was CAD 236,667.

Authors’ conclusions
The model suggested that self-management was a cost-effective strategy for those receiving long-term oral anticoagulation therapy for atrial fibrillation or for a mechanical heart valve.

CRD COMMENTARY - Selection of comparators
An explicit justification was given for using physician management as the comparator. It was the current clinical standard of practice in Canada. You should decide if the comparator represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The authors did not report whether a systematic review of the literature had been undertaken to identify all relevant research and minimise biases. Despite this, they reported the methods used in their review of the literature and provided details of the studies included. They did not, however, report if it was necessary to combine the results from different studies and, if so, how differences between these studies were investigated. The authors undertook both probabilistic and deterministic sensitivity analyses to test the impact of uncertainty in the effectiveness parameters.

Validity of estimate of measure of benefit
The estimation of benefits was modelled using a Markov model, which was appropriate for the study question. As the health benefits could be gained over a 5-year period, all future benefits were appropriately discounted using the same rate as for the costs.

Validity of estimate of costs
All the categories of cost relevant to the health care perspective adopted were included in the analysis. No relevant major costs appear to have been omitted from the analysis. Further, the authors provide detailed results of their costing study in a separate appendix. The costs and the quantities were not reported separately, which will limit the generalisability of the authors' results. The costs and resources were derived from the literature and authors' assumptions. Appropriate sensitivity analyses of the total costs were conducted using both deterministic and probabilistic sensitivity analyses. Since the costs were incurred during a 5-year period, discounting was necessary and was appropriately performed. The price year was reported, which will aid any future inflation exercises.

Other issues
The authors made appropriate comparisons with other studies that had also found self-management to be cost-effective. The issue of generalisability to other settings was partly addressed in the sensitivity analysis. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of their analysis. The authors reported a number of other limitations to their study. For example, their model was not applicable to all clinical populations with an indication for chronic anticoagulation therapy, which was the result of the strict inclusion criteria in the VGH trial. Also, patient preferences for using the point-of-care device were not modelled.

Implications of the study
The authors recommended that further economic analysis should stratify cost-effectiveness by indication and by preference for using the point-of-care device, as this will assist in informing clinicians and decision-makers on which patients are most likely to benefit from self-management.

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Other publications of related interest
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