Cost-effectiveness of dabigatran for stroke prophylaxis in atrial fibrillation

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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.

CRD summary
This study assessed the cost-effectiveness of treatments to prevent stroke in patients with atrial fibrillation. The authors concluded that dabigatran 150mg twice daily was cost-effective for populations at high risk of haemorrhage or stroke, unless the control of the international normalised ratio with warfarin was excellent. The methods were good and reported adequately, with the results reported in full. Given the scope of the analysis, the authors' conclusions appear to be valid.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to assess the cost-effectiveness of treatments to prevent a stroke in patients with atrial fibrillation.

Interventions
The interventions were dabigatran 110mg twice daily, dabigatran 150mg twice daily, warfarin, dual therapy with aspirin and clopidogrel, aspirin alone, and no antithrombotic therapy.

Location/setting
USA/out-patient secondary care.

Methods
Analytical approach:
A decision model was used to combine published evidence for the costs and outcomes of the interventions. A hypothetical cohort of 70-year old patients, with atrial fibrillation, who had a moderate risk of stroke and no contraindication to anticoagulant therapy was used. The time horizon was 20 years. The authors reported that the perspective was that of an insurance company or Medicare.

Effectiveness data:
The effectiveness data were mainly from clinical trials, using an intent-to-treat analysis. The effectiveness of dabigatran, compared with warfarin, was from the Randomized Evaluation of Long-term Anticoagulant Therapy (RE-LY) trial. The effectiveness of the other interventions, in reducing stroke incidence, was from other published trials. The main clinical effectiveness estimate was the risk of ischaemic stroke.

Monetary benefit and utility valuations:
The utility estimates were from several published studies of the quality of life of patients with atrial fibrillation, incident stroke, recurrent stroke, and bleeds.

Measure of benefit:
The measure of benefit was quality-adjusted life years (QALYs) gained, and these were discounted at an annual rate of 3%.

Cost data:
The direct cost categories were adverse events and drugs. The costs of adverse events, including ischaemic neurological events, intracranial haemorrhage, bleeding, and myocardial infarction, were from published studies, the Healthcare Cost and Utilization Project, and Medicare. The costs of drugs, which included monitoring, were from prescriptions data and

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Medicare reimbursement rates. All costs were reported in 2010 US dollars ($) and were discounted at an annual rate of 3%.

Analysis of uncertainty:
One-way sensitivity analysis was undertaken, and the model parameters were varied over plausible ranges. The results of this analysis were presented in a bar graph. Two-way and three-way sensitivity analyses were undertaken.

Results
Compared with aspirin, the incremental cost-utility ratio was $50,000 for dabigatran 150mg, $66,000 for dabigatran 110mg, $12,500 for warfarin, and $99,000 for aspirin and clopidogrel.

Compared with warfarin, the incremental cost-utility ratio was $86,000 for dabigatran 150mg and $150,000 for dabigatran 110mg. Aspirin and clopidogrel was dominated by warfarin, as warfarin was more effective and less costly.

One-way sensitivity analysis showed that the most influential variables were the stroke and haemorrhage rates, the cost of dabigatran, and the time that a patient was within the international normalised ratio (INR) range. For patients with a moderate stroke rate, warfarin was cost-effective (its incremental cost-utility ratio was lower than $50,000 per QALY), unless the risk of haemorrhage was high or the control of the INR was poor.

The two-way sensitivity analysis of stroke and haemorrhage risk confirmed that low stroke rates favoured aspirin therapy and moderate rates favoured warfarin. For patients with a high risk of stroke, dabigatran 150mg was cost-effective, unless the control of the international normalised ratio was excellent.

Authors' conclusions
The authors concluded that dabigatran 150mg twice daily was cost-effective in atrial fibrillation populations at high risk of haemorrhage or stroke, unless control of the INR with warfarin was excellent. Warfarin was cost-effective for those at moderate risk of stroke, unless it provided poor control of the INR. Aspirin was cost-effective for populations at low risk of stroke.

CRD commentary
Interventions:
The interventions were reported clearly and appear to have been appropriate comparators.

Effectiveness/benefits:
The effectiveness data were mainly from clinical trials that used intention-to-treat analysis. Well-conducted randomised controlled trials are considered to be the gold standard when evaluating health interventions, and it is likely that the effectiveness parameters were internally valid. The relevant publications should be consulted to fully assess their quality. No systematic review was reported to identify these trials, making it impossible to determine if all the relevant data were analysed. The benefit measure appears to have been appropriate as it includes both morbidity and mortality. Little information was provided on how the benefit measure was derived and it is unclear if these methods were appropriate.

Costs:
The perspective was explicitly reported. It appears that all the major costs relevant to this health care insurance organisation (Medicare) perspective were included. The sources for the costs were reported, as were the time horizon, discount rate, and price year.

Analysis and results:
All the evidence was appropriately synthesised in a Markov decision analytic model. The model was described and a diagram was given. The uncertainty was tested in a series of one-, two-, and three-way sensitivity analyses. These types of analysis go some way towards evaluating the impact of uncertainty on the model results, but probabilistic sensitivity analysis is more thorough and evaluates the overall model uncertainty. The limitations of the study were clearly discussed, and the main one was that the effectiveness parameters for dabigatran were mainly from one trial that evaluated efficacy over two years.
Concluding remarks:
The methods were good. They were reported adequately and the results were given in full. Given the scope of the analysis, the authors’ conclusions appear to be valid.

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