**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**
The study assessed the cost-effectiveness of dabigatran etexilate compared with warfarin, aspirin, or no therapy for the prevention of stroke and systemic embolism in patients with heart atrial fibrillation. The authors concluded that their economic evaluation supported the use of dabigatran etexilate as a cost-effective first-line treatment in eligible UK patients. The study used a conventional cost-effectiveness framework that considered various areas of uncertainty and used appropriate methods. The authors’ conclusions appear robust.

**Type of economic evaluation**
Cost-utility analysis

**Study objective**
The study assessed the cost-effectiveness of dabigatran etexilate compared with warfarin, aspirin, or no therapy for the prevention of stroke and systemic embolism in patients with atrial fibrillation.

**Interventions**
Dabigatran etexilate (150mg twice daily for patients up to 80 years old, then 110mg twice daily afterwards) was compared against conventional warfarin, aspirin, or no treatment.

**Location/setting**
UK/secondary care.

**Methods**
Analytical approach:
The analysis was based on a Markov model that simulated the clinical and economic impact of dabigatran etexilate in two patient populations (up to 80 years and 80 years or older) over their lifetime. The perspective adopted in the study was not explicitly stated.

Effectiveness data:
Most clinical inputs were derived from the Randomised Evaluation of Long-Term Anticoagulation Therapy (RE-LY) published clinical trial (Connolly, et al. 2009, see ‘Other Publications of Related Interest’ below for bibliographic details). The RE-LY trial directly compared dabigatran etexilate with warfarin with a six month follow-up. Patients’ characteristics were taken from the RE-LY trial. Other inputs were based on data from a network meta-analysis. The efficacy of treatments in preventing stroke and systemic embolism was a key input of the model and was obtained from RE-LY and other clinical trials. Assumptions were made on the long-term efficacy of treatment.

Monetary benefit and utility valuations:
Utility valuations were from published studies including an economic evaluation.

Measure of benefit:
Quality-adjusted life-years (QALYs) were used as the summary benefit measure. They were discounted at an annual rate of 3.5%. Other clinical inputs such as reduction in stroke or intracranial haemorrhage were reported.

Cost data:
The economic analysis included the three main cost categories of drugs (acquisition and monitoring), events (stroke, systemic embolism, transient ischaemic attack, haemorrhage, minor bleeding, and acute myocardial infarction), and follow-up (depending on the severity of disability). Costs were estimated from official UK sources such as NHS reference costs, National Institute for Health and Clinical Excellence (NICE) guidelines, official drug prices, and a recent study of atrial fibrillation patients’ data from a UK stroke registry. Costs were in UK £. An annual discount rate of 3.5% was applied. The price year was 2010.

Analysis of uncertainty:
Deterministic one-way sensitivity analyses were carried out on model inputs to identify key determinants of model outcomes. A probabilistic sensitivity analysis was carried out by performing 5,000 simulations for each comparison in which inputs were varied simultaneously and randomly within conventional statistical distributions, based on their means and confidence intervals or assumed standard errors.

Results
The use of dabigatran etexilate generally reduced strokes and other events compared with warfarin. For dabigatran etexilate, lifetime QALYs were 8.06 and costs were £19,645 with dabigatran etexilate. For warfarin, lifetime QALYs were 7.82 and costs were £18,474. The incremental cost per QALY gained with dabigatran etexilate over warfarin was £4,831 in the population younger than 80 years and £7,090 in those of 80 years or older.

When aspirin and no treatment were compared with dabigatran etexilate without a second-line treatment, the expected QALYs for dabigatran etexilate were 7.99, for aspirin were 7.59 and for no treatment were 7.12. The lifetime costs with dabigatran etexilate were £19,96, with aspirin were £18,561, and with no treatment were £20,475. In the population initiating treatment before age 80, the incremental cost per QALY gained with dabigatran etexilate over aspirin was £3,457. Dabigatran etexilate dominated no treatment, which was simultaneously more expensive and less effective.

The deterministic analysis showed the robustness of the base case findings. The most influential inputs were the degree of international normalised ratio (INR) control attained by patients on warfarin, the relative risk and overall rates of fatal/non-fatal events for dabigatran etexilate versus warfarin, the cost of long-term follow-up for patients with disability, and the time horizon. However, the incremental cost per QALY for dabigatran etexilate compared with warfarin always remained lower than standard thresholds for cost-effective strategies.

The probability of dabigatran etexilate being cost-effective at a threshold of £20,000 per QALY was 98% against warfarin and 100% against either aspirin or no treatment in patients that started treatment below the age of 80 years. The probability fell to 63% in patients that started treatment at 80 or older with dabigatran etexilate against warfarin.

Authors’ conclusions
The authors concluded that their economic evaluation supported the use of dabigatran etexilate as a cost-effective first-line treatment for the prevention of stroke and systemic embolism in eligible UK patients.

CRD commentary
Interventions:
Appropriate comparators were used in that the available preventive strategies were considered. In particular, the authors noted that most patients received warfarin but some of them were under-treated, treated with aspirin, or untreated because of the complexity of warfarin administration due to the requirement for continuous monitoring and dose adjustments. The authors stated that, in this scenario, dabigatran etexilate represented a new and less complex stroke-prevention therapy for this patient population. Doses of dabigatran etexilate were based on the approved European label.

Effectiveness/benefits:
Most clinical inputs on treatment effect, toxicity and patients’ characteristics were taken from a head-to-head clinical trial. The results were based on intention-to-treat analysis and data were stratified by patients’ age. These points tend to enhance the robustness of the clinical analysis. Other data were taken from a meta-analysis of trials, which was a valid source. The authors stated that the international normalised ratio for warfarin obtained from the RE-LY study might have overestimated the benefits of this drug, so the results might be conservative against dabigatran etexilate. Patient-
level data were available from the trial and extensive sensitivity analyses were conducted. QALYs were a valid benefit
measure, which captured the impact of the disease on patients’ health and allowed cross-disease comparisons to be
made. Little information on the sources of utility weights was provided.

Costs:
The perspective of the cost analysis was not explicitly stated but was clearly that of the public payer. The types of costs
included in the economic analysis and the sources used suggested the viewpoint of the UK NHS. Details of some unit
costs and resource quantities were provided and a breakdown of cost items was presented. This increased the
transparency of the economic analysis. Typical UK sources were used and estimates were representative of the authors’
setting. Costs were varied in the sensitivity analysis using appropriate statistical distributions. Other details such as the
price year and the discount rate were given.

Analysis and results:
An incremental analysis was carried out to synthesise the costs and benefits of the various approaches. Both
deterministic and probabilistic sensitivity analyses were conducted and the results were clearly presented. The Markov
model was presented both narratively and as a diagram. The results were reported extensively for all comparators. The
authors compared their results with those from other published studies that had generally demonstrated the cost-
effectiveness of dabigatran etexilate. It was likely that the study findings could be transferred to other settings with
similar patients’ characteristics, clinical practices and prices. Limitations and strengths of the analysis were reported.

Concluding remarks:
The study used a conventional cost-effectiveness framework that considered various areas of uncertainty and used
appropriate methods. The authors’ conclusions appear robust.

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Bibliographic details
Kansal AR, Sorensen SV, Gani R, Robinson P, Pan F, Plumb JM, Cowie MR. Cost-effectiveness of dabigatran etexilate
for the prevention of stroke and systemic embolism in UK patients with atrial fibrillation. Heart 2012; 98(7): 573-578

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22422743

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http://heart.bmj.com/content/98/7/573.abstract

Other publications of related interest
Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, Parekh A, Pogue J, Reilly PA, Themeles E, Varrone J,
Committee and Investigators. Dabigatran versus warfarin in patients with atrial fibrillation. New England Journal of

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