Cost-effectiveness of dabigatran for stroke prevention in non-valvular atrial fibrillation in Spain
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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
The study examined the cost-effectiveness of dabigatran compared with warfarin and other prescribing patterns for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation in Spain. The authors concluded that dabigatran cost effective and provided value for money for stroke prevention from the perspectives of the Spanish NHS and the society. The analysis used a valid and transparent methodology that considered key areas of uncertainty. The authors’ conclusions appear robust.

Type of economic evaluation
Cost-utility analysis

Study objective
The study examined the cost-effectiveness of dabigatran for the prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more thromboembolic risk factors.

Interventions
The three preventive regimens compared were dabigatran etexilate (150mg twice daily up to 80 years of age and 110mg thereafter), warfarin (a vitamin K antagonist), and the prescribing pattern observed in the authors’ setting (60% of patients receiving vitamin K antagonists, 30% taking aspirin, and 10% receiving no treatment).

Location/setting
Spain/secondary care.

Methods
Analytical approach:
The analysis was based on a previously published Markov model that assessed the cost-effectiveness of dabigatran in other economic evaluations. A lifetime horizon was considered. The authors stated that the study took the perspective of the Spanish NHS.

Effectiveness data:
Data sources appear to have been selectively identified. Most inputs had already been included in the model. Selected data on the patient population and key inputs on treatment efficacy (rates of reduction of stroke and systemic embolism) were taken from the Randomized Evaluation of Long-term anticoagulation therapy (RE-LY) trial that included 18,113 patients and compared two blinded doses of dabigatran with warfarin (Connolly 2009 see Other Publications of Related Interest). Other trials or a meta-analysis of indirect comparisons were used for treatment effect of aspirin and no treatment. Demographical and mortality rates were taken from Spanish life tables. Some assumptions were also made and were clearly reported.

Monetary benefit and utility valuations:
Utility valuations had already been incorporated in the simulation model and were based on EQ-5D scores taken from UK studies.

Measure of benefit:
Quality-adjusted life-years (QALYs) were used as the summary benefit measure and were discounted at a yearly rate of
3%.

Cost data:
The costs included drugs, the costs of treating clinical events, and the cost of monitoring of the international normalized ratio (INR), which was an additional cost with vitamin K antagonist therapy and whose amount depended on the setting in which it was performed (hospital, primary care, or home). Drug costs were based on retail price, considering the 7.5% discount in medications within the Spanish NHS. Other costs were estimated using official NHS price lists and a Spanish study. Unit costs were reported. Costs were in Euros (EUR). A 3% annual discount rate was applied. The price year was 2010.

Analysis of uncertainty:
One-way sensitivity analyses were carried out on selected assumptions of the model, including discount rate, time horizon, subpopulation of patients of 80 years or older, and different percentage of time within the therapeutic range in INR monitoring. Subgroup analyses were also performed to observe the efficacy in four patient groups to examine the societal perspective, which included non-health care costs and informal care received by stroke survivors. A probabilistic sensitivity analysis was based on 10,000 Monte Carlo simulations and considered probability distributions for sets of inputs (beta for baseline risks and utilities, log normal for relative risks, and gamma for costs).

Results
With dabigatran, the expected cost was EUR 15,193 and the QALYs were 8.73.

With warfarin, the expected cost was EUR 10,343 and the QALYs were 8.45.

With the Spanish prescribing pattern, the expected cost was EUR 9,426 and the QALYs were 8.32.

The incremental cost per QALY gained with dabigatran was EUR 17,581 compared with warfarin and EUR 14,118 compared with the Spanish prescribing pattern.

In the deterministic sensitivity analysis, the incremental cost per QALY ranged from EUR 14,651 to EUR 57,719 for dabigatran versus warfarin and from EUR 11,519 to EUR 52,160 for dabigatran versus the Spanish prescribing pattern. In particular, the worst cost-effectiveness ratios for dabigatran were observed with shorter time horizons (five years).

When a broad societal perspective was adopted, dabigatran was a dominant strategy as it was simultaneously more effective and less expensive than either comparator.

At a willingness to pay threshold of EUR 30,000 per QALY, the probability of dabigatran being cost-effective was 96.4% versus warfarin and 99.9% versus the Spanish prescribing pattern. Similar figures were observed in the subgroup analyses.

Authors’ conclusions
The authors concluded that dabigatran used for the prevention of stroke was an efficient strategy and provided value for money from the perspectives of the Spanish NHS and the society.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear. Dabigatran was the proposed intervention and was compared to the conventional preventive strategies used for the Spanish patient population.

Effectiveness/benefits:
Clinical data generally came from appropriate sources. Treatment effect for dabigatran and warfarin was taken from a large head-to-head blinded clinical trial that should have ensured high internal validity. A comparison was made also with current clinical practice in Spain to increase the external validity of the study. An extensive sensitivity analysis was conducted on all model inputs. QALYs were an appropriate benefit measure because the disease affected both survival and quality of life. A validated instrument was used to elicit patient preferences for health conditions. The authors stated that UK tariffs were used given the lack of Spanish values. Life-years were also reported although they were not
combined with costs.

Costs:
The economic analysis was satisfactorily carried out. The costs included in the model were appropriate for both the Spanish NHS and the societal perspectives. Key unit costs were reported, although some costs were presented as totals because of the accounting system of the Spanish NHS. Limited information on quantities of resources used was given, but data sources were reported for most data. Reflation exercises were possible as the reference year was clearly stated. Alternative cost assumptions were considered in the sensitivity analyses.

Analysis and results:
An incremental approach was appropriately used to identify the optimal strategy using conventional cost-effectiveness thresholds. The model was taken from previous publications and a multidisciplinary panel of Spanish experts adapted it to the country-specific setting. The expected costs and benefits of the three strategies were clearly presented. Both deterministic and probabilistic sensitivity analyses were used to investigate uncertainty; these methods and findings were clearly presented and discussed. The authors stated that previously published cost-effectiveness analyses of dabigatran conducted in other countries had showed similar findings, so these results could also be valid also for other jurisdictions.

Concluding remarks:
The analysis used a valid and transparent methodology that considered key areas of uncertainty. The authors’ conclusions appear robust.

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MeSH
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