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## **Dabigatran versus rivaroxaban for the prevention of stroke and systemic embolism in atrial fibrillation in Canada: comparative efficacy and cost-effectiveness**

*Kansal AR, Sharma M, Bradley-Kennedy C, Clemens A, Monz BU, Peng S, Roskell N, Sorensen SV*

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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 examined the cost-effectiveness of dabigatran versus rivaroxaban as anticoagulation therapies for prevention of stroke and systemic embolism in patients with atrial fibrillation. The authors concluded that dabigatran was an economically and clinically superior strategy from the perspective of the Canadian payer. This analysis was based on an indirect treatment comparison approach, which considered the differences between studies using valid statistical approaches. The authors' conclusions appear robust.

### **Type of economic evaluation**

Cost-utility analysis

### **Study objective**

The study examined the cost-effectiveness of anticoagulants dabigatran etexilate (dabigatran) versus rivaroxaban as anticoagulation therapies for the prevention of stroke and systemic embolism in patients with atrial fibrillation.

### **Interventions**

Dabigatran (150mg twice daily up to 80 years, then 110mg for older patients) was compared with rivaroxaban. In a secondary analysis, both anticoagulant drugs were compared with warfarin.

### **Location/setting**

Canada/secondary care.

### **Methods**

#### **Analytical approach:**

The analysis was based on a previously published Markov model with a lifetime horizon. The authors stated that the perspective of the study was that of the Canadian payer.

#### **Effectiveness data:**

Selective sources of data were taken to derive clinical inputs. Two pivotal clinical trials were considered as main sources of data, including the RE-LY trial (Connolly 2009, see Other Publications of Related Interest) that focused on dabigatran and the ROCKET-AF trial for rivaroxaban (Patel 2011, see Other Publications of Related Interest). Given the differences in the baseline populations, a specific indirect treatment comparison methodology was applied, using baseline features of the simulated population from the ROCKET-AF trial. Warfarin was used as common comparator as included in both trials. Event rates (such as all strokes, systemic embolism, intracranial haemorrhage, acute myocardial infarction and mortality) were key inputs of the clinical analysis.

#### **Monetary benefit and utility valuations:**

Utility valuations were taken from a previous publication of dabigatran in the Canadian atrial fibrillation population, supplemented with data from other published sources.

#### **Measure of benefit:**

Quality-adjusted life-years (QALYs) were used as the summary benefit measure and were discounted at annual discount rate of 5%.

#### Cost data:

The costs included the drugs under examination and all direct medical costs associated with event and disability management costs. Resource use was presumably taken from the studies used for clinical events. Costs were in Canadian dollars (CAD). A 4% annual discount rate was applied.

#### Analysis of uncertainty:

Several deterministic analyses were carried out in a one-way sensitivity analysis to test the robustness of model results to variations in selected parameters. Subgroup analyses were also carried out considering variations in dabigatran dosages or severity of disease. A probabilistic sensitivity analysis was conducted by varying all clinical, cost, and utility parameters. Cost-effectiveness acceptability curves were generated.

#### Results

The expected QALYs were 6.167 with dabigatran and 6.015 with rivaroxaban. Total lifetime costs per patient were CAD 59,613 with dabigatran and CAD 59,766 with rivaroxaban. Dabigatran was the dominant strategy because it was associated with lower costs and greater benefits than rivaroxaban. The net monetary benefit of dabigatran was CAD 4,717 per patient, which suggested that dabigatran was preferred to rivaroxaban.

In the secondary analysis, compared with warfarin, the incremental QALYs were 0.233 with dabigatran and 0.066 with rivaroxaban. The incremental costs per patient were CAD 1,579 with dabigatran and CAD 1,732 with rivaroxaban. The incremental cost per QALY gained over warfarin was CAD 6,889 with dabigatran and CAD 22,475 with rivaroxaban. At a cost-effectiveness threshold of CAD 30,000 per QALY, the net monetary benefit was CAD 5,297 with dabigatran and CAD 580 with rivaroxaban.

The probability of dabigatran being the most cost-effective strategy was 93% at a threshold of CAD 20,000/QALY and 98% at a threshold of CAD 30,000/QALY. For lower thresholds, such as below CAD 8,000 per QALY, warfarin was likely to be the most cost-effective strategy.

The most important drivers of the model were the risk of ischaemic stroke and the relative risk of intracranial haemorrhage, but dabigatran remained the preferred strategy in most scenarios.

#### Authors' conclusions

The authors concluded that dabigatran was an economically and clinically superior strategy from the perspective of the Canadian payer.

#### CRD commentary

##### Interventions:

The rationale for the selection of the comparators was clear as the available strategies were considered. Two dosages were appropriately considered for dabigatran.

##### Effectiveness/benefits:

Clinical data came from two different clinical trials, one for dabigatran and one for rivaroxaban. Given the lack of head-to-head comparisons, an indirect treatment comparison was made, using warfarin as common comparator. Methods to deal with differences in patient population and other characteristics of the trials were reported and appeared appropriate. Both an intent-to-treat analysis and safety-on-treatment analysis were made. Extensive sensitivity analyses on clinical inputs were also conducted. The use of QALYs as main benefit measure appeared appropriate given the impact of disease on mortality and morbidity. Few details on source of utility values were provided.

##### Costs:

The analysis was not fully reported as most data had been already incorporated in a previous decision model. Most details were provided in an online appendix to the study, so details on the costs and quantities of resources used, as well as the types of sources used, were not reported in the paper. In addition, the price year was not reported. Variations in economic inputs were taken into account in the sensitivity analysis.

##### Analysis and results:

An incremental approach was appropriately used to synthesise costs and benefits of the alternative strategies using

conventional cost-effectiveness thresholds and the net monetary benefit approach. Deterministic and probabilistic sensitivity analyses were used to investigate uncertainty. The methods and results of these approaches were clearly illustrated. The study results were clearly reported. The authors stated that a limitation of the study was the lack of head-to-head comparisons between the two drugs considered, but it appeared that this was overcome by the sophisticated statistical analysis. Study results were specific to the Canadian setting but might be relevant for country with similar costs.

#### **Concluding remarks:**

This analysis was based on an indirect treatment comparison approach, which considered the differences between studies using valid statistical approaches. The authors' conclusions appear robust.

#### **Funding**

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#### **Bibliographic details**

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#### **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, Wang S, Alings M, Xavier D, Zhu J, Diaz R, Lewis BS, Darius H, Diener HC, Joyner CD, Wallentin L; RE-LY Steering Committee and Investigators. Dabigatran versus warfarin in patients with atrial fibrillation. *New England Journal of Medicine* 2009; 361(12): 1139-1151.

Patel MR, Hellkamp AS, Lokhnygina Y, Piccini JP, Zhang Z, Mohanty S, Singer DE, Hacke W, Breithardt G, Halperin JL, Hankey GJ, Becker RC, Nessel CC, Berkowitz SD, Califf RM, Fox KA, Mahaffey KW. Outcomes of discontinuing rivaroxaban compared with warfarin in patients with nonvalvular atrial fibrillation: analysis from the ROCKET AF trial (Rivaroxaban Once-Daily, Oral, Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation). *Journal American College of Cardiology*. 2013; 61(6): 651-658.

#### **Indexing Status**

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