An economic model of adverse events and costs for oral anticoagulants used for atrial fibrillation
Leigh J P, White R H

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 clinical and economic impact of warfarin versus a second anticoagulant in hypothetical cohort of 70-year-old patients with atrial fibrillation. There was substantial variation in rates and costs of adverse events when considering all possible scenarios, but the difference in costs between the two drugs was modest. Overall, the analysis focused more on the costs of adverse events than on the relative cost-effectiveness of the drugs. Thus, some caution will be required when interpreting the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to examine the clinical and economic impact of warfarin versus a second anticoagulant in a hypothetical cohort of 70-year-old patients with atrial fibrillation, focusing on the costs associated with adverse events.

Interventions
Warfarin and a second anticoagulant (ximelagatran) were compared.

Location/setting
USA/secondary care.

Methods
Analytical approach:
A Markov model was developed to determine the clinical and economic impact of the adverse events of treatment. It considered 20 potential events (four possibilities for ischemic strokes and 16 for haemorrhages) and four levels of international normalised ratio (INR) of the prothrombin time. The two time horizons considered were one and five years. The authors stated that the analysis was carried out from the perspective of the third-party payer.

Effectiveness data:
The clinical data were derived from a selection of known, relevant studies, supplemented by authors’ opinions. The characteristics of the patient cohort were mainly derived from two observational studies and a randomised controlled trial (RCT). The rates of adverse events associated with each level of INR were obtained from the two observational studies. The other sources were not described. The key clinical input was the risk of adverse events associated with warfarin or ximelagatran.

Monetary benefit and utility valuations:
None.

Measure of benefit:
A summary benefit measure was not used because a cost-consequences analysis was carried out. The key clinical endpoints were number of adverse events (such as strokes or haemorrhages) and deaths.

Cost data:
The authors did not provide a breakdown of cost categories, but reported the costs associated with each health state.
(adverse event). Presumably, the main cost categories were drugs, hospital stay, physician visits, and post-hospital care. The cost and resource use data were derived from national Medicare or Medicaid sources and authors’ assumptions. All costs were in US dollars ($) and the price year was 2003. Discounting was not performed.

Analysis of uncertainty:
A deterministic univariate sensitivity analysis investigated how robust the model results were to variations in time in nursing home, time (or probability) outside INR therapeutic range, probability of stroke, and haemorrhage rate. Reasonable ranges of values were used.

Results
The analysis showed that, for both drugs, the most expensive events over one year were severe stroke, moderate stroke, and severe gastrointestinal (GI) haemorrhage, while the least costly events were mild intracranial or intracerebral haemorrhage, and fatal upper GI haemorrhage.

Over the five-year time horizon in the whole cohort of 10,000 hypothetical patients, the overall number of adverse events was 1,618.67 with warfarin and 1,390.29 with ximelagatran. The costs of these events were $18,330,662 and $17,102,847, respectively, for a difference of $1,261,991 (or $126 per patient, see ‘CRD commentary’)

For both drugs, the number of deaths and the costs of these fatalities were greater for haemorrhages than for the ischemic strokes.

Overall, there were 123 fatalities for warfarin and 101 fatalities for ximelagatran. Thus, warfarin was more costly and less effective (more adverse events and more deaths) compared with ximelagatran.

The sensitivity analysis suggested that assumptions regarding the length of stay in a nursing home had the greatest impact on the cost results.

Authors’ conclusions
The authors concluded that there was a substantial variation in rates and costs of adverse events when considering all possible scenarios. Nevertheless, the difference in costs between the two drugs was modest.

CRD commentary
Interventions:
The two drugs were appropriately selected. Warfarin was commonly used for the management of atrial fibrillation. The second drug was selected because of the similarities between warfarin and ximelagatran, as shown in the literature.

Effectiveness/benefits:
The methodology used to derive the clinical data was not described. Little information was provided on the approach used to select the sources of estimates or the characteristics of these sources (design, characteristics of the patient population, follow-up, etc), except for one RCT and two observational studies used to derive the baseline clinical features of the hypothetical patient cohort. Thus, it is difficult to judge the validity of the clinical inputs to the model. These clinical values were not varied in the sensitivity analysis.

Costs:
The analysis of costs reflected the viewpoint of the third-party payer, which was consistent with the types of sources used. However, the cost categories were not reported explicitly as most were grouped into macro-categories related to the adverse events reported in the clinical analysis. Moreover, the unit costs and quantities of resources used were not presented separately. These issues reduce the transparency of the economic analysis. The price year was reported, but the use of discounting was not mentioned although it may have been relevant given the five-year time horizon.

Analysis and results:
A synthesis of costs and benefits was not performed, which was appropriate given the cost-consequences framework of the analysis. The number of clinical events was used to calculate the costs of the two strategies. The issue of uncertainty was only partially addressed since the sensitivity analysis focused on individual model inputs which were varied in a
univariate analysis. The results of both the base-case and the sensitivity analyses were clearly presented, although there was some discrepancy in the data in Table 4. The authors acknowledged some limitations to their analysis such as the lack of published evidence for some inputs and the selection of a third-party payer perspective, which prevented the inclusion of non-medical costs. Finally, variations across practice settings were not explicitly considered, thus limiting the external validity of the study.

Concluding remarks:
Overall, the analysis focused more on the costs of adverse events than on the relative cost-effectiveness of the two drugs. Thus, some caution will be required when interpreting the authors’ conclusions.

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