Cost effectiveness of rivaroxaban versus enoxaparin for prevention of post-surgical venous thromboembolism from a US payer's perspective

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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 rivaroxaban versus enoxaparin for prevention of venous thromboembolism in patients who underwent major orthopaedic surgery such as total hip or total knee replacement. The authors concluded that rivaroxaban provided greater health benefits and was cost-saving compared to enoxaparin in both orthopaedic populations from the perspective of the USA payer. The authors used valid and transparent methodology that enhanced the robustness of their conclusions.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The study examined the cost-effectiveness of rivaroxaban versus enoxaparin for the prevention of venous thromboembolism (VTE) in patients who underwent major orthopaedic surgery such as total hip replacement or total knee replacement.

Interventions
In the total hip replacement population, 35 days of rivaroxaban was compared to either 35 days or 10 to 14 days of enoxaparin. In the total knee replacement population, 10 to 14 days of rivaroxaban was compared to 10 to 14 days of enoxaparin.

Location/setting
USA/outpatient.

Methods
Analytical approach:
The analysis was based on a decision-analytic model with one- and five-year time horizons. The model consisted of three modules: prophylaxis period, post-prophylaxis period and long-term complications. The first two stages were analysed using a decision tree model. The third stage was represented by a Markov model. The authors stated that the perspective was that of the health care payer.

Effectiveness data:
Clinical inputs were taken from a selection of known relevant studies. Most data for the short-term model were derived from three of the four RECORD studies (REgulation of Coagulation in ORthopaedic surgery to prevent Deep vein thrombosis and pulmonary embolism), which were randomised controlled double-blind phase III trials that compared rivaroxaban with enoxaparin. RECORD1 compared 35 days of rivaroxaban to 35 days of enoxaparin in total hip replacement patients, RECORD2 compared 35 days of rivaroxaban to 10 to 14 days of enoxaparin in total hip replacement patients and RECORD3 compared 10 to 14 days of rivaroxaban to 10 to 14 days of enoxaparin in total knee replacement patients. RECORD1 and RECORD2 were pooled as they enrolled a comparable patient population. Rates of deep vein thrombosis (DVT) and pulmonary embolism were key inputs of the model. Additional data were taken from other studies using an indirect comparison methodology when required.

Monetary benefit and utility valuations:
Venous thromboembolism-related utility valuations were taken from published sources.
Measure of benefit:
The primary summary benefit measure was the number of symptomatic venous thromboembolism events avoided. Quality-adjusted life-years (QALYs) were used in an alternative analysis.

Cost data:
The economic analysis included the costs of drugs, administration, monitoring, diagnosis and treatment of venous thromboembolism as well as treatment of post-thrombotic syndrome and recurrent venous thromboembolism. Key unit costs were reported as well as data on quantities of resources used. Costs were derived mainly by using Medicare reimbursement rates supplemented with data from USA studies. Resource quantities were based on large USA databases for patients undergoing orthopaedic surgery. Costs were in US dollars ($). The price year was 2010. A 3% annual discount rate was used in the long-term analysis.

Analysis of uncertainty:
Alternative scenarios were considered in deterministic sensitivity analyses using confidence intervals derived from RECORD trials for specific events and clinical assumptions. A probabilistic sensitivity analysis investigated the issue of uncertainty using a multivariate approach and conventional probability distributions for groups of inputs based on published sources or authors’ assumptions. An alternative analysis was conducted using data from a fourth RECORD trial.

Results
In the total hip replacement population, total costs per patient and symptomatic event rates were $378.90 and 0.55 with rivaroxaban and $890.84 and 2.00 with enoxaparin. Rivaroxaban was the dominant strategy as it was both more effective and less expensive.

For total knee replacement, total costs per patients and symptomatic event rates were $335.00 and 1.18 with rivaroxaban and $800.74 and 3.11 with enoxaparin. Rivaroxaban was dominant over enoxaparin.

In the cost-utility framework, rivaroxaban led to a gain of 0.0019 QALYs and saved $511.93 per total hip replacement patient. Corresponding figures for total knee replacement were 0.0024 QALYs and $465.74.

The sensitivity analysis confirmed the dominance of rivaroxaban in all deterministic and probabilistic simulations.

Authors’ conclusions
The authors concluded that rivaroxaban provided greater health benefits and was cost-saving compared with enoxaparin in both orthopaedic populations from the perspective of the USA payer.

CRD commentary
Interventions:
The rationale for selection of the comparators was clear. The authors stated that enoxaparin was one of the most commonly prescribed medications for thromboprophylaxis and rivaroxaban was a new once-daily orally administered agent that had been approved for prevention of venous thromboembolism in patients with total hip or total knee replacements. The two drugs were examined in the RECORD1 to RECORD4 trials.

Effectiveness/benefits:
Short-term treatment effect data were taken from head-to-head and large randomised clinical trials that were partly described and were likely to provide high internal validity. Appropriate statistical approaches were used to extrapolate short-term data to a longer-term. Other data were taken from published studies that were not fully described, but parameters and assumptions were tested in the sensitivity analysis. A disease-specific outcome measure was used in the base case, but QALYs were considered in an alternative scenario that provided the same conclusions. Utility weights were taken from published studies that were not described.

Costs:
The economic analysis was performed satisfactorily. The cost categories included in the analysis and the sources used to derive them were consistent with the perspective of the USA payer. Unit costs and resource quantities were presented separately and this enhanced the transparency of the economic analysis. The assumptions made by the authors were
explicitly reported. Typical USA sources were used and justified. Other details such as the price year and use of
discounting were clearly stated. Variations in economic inputs were considered in the sensitivity analyses.

Analysis and results:
The study results were presented clearly. In particular, total and incremental findings were reported for each patient
population. Cost-effectiveness ratios were not calculated because of the dominance of rivaroxaban over enoxaparin. An
extensive description of the decision model and the underlying assumptions was provided. The issue of uncertainty was
addressed satisfactorily with both deterministic and stochastic analyses and alternative scenarios were considered. The
authors acknowledged some limitations of the analysis, based mostly on assumptions that were generally against
rivaroxaban. The study results might be transferable to settings with similar relative prices.

Concluding remarks:
The authors used valid and transparent methodology that enhanced the robustness of their conclusions.

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