Assessing the cost-effectiveness of COX-2 specific inhibitors for arthritis in the Veterans Health Administration


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 rofecoxib and celecoxib, two cyclo-oxygenase-2 specific inhibitors, in comparison with non-selective non-steroidal anti-inflammatory drugs in patients with arthritis who were at high risk of developing clinically significant upper gastrointestinal events. The two populations studied were patients of any age with a previous medical history of perforation, ulcer or bleed (PUB), and patients aged 65 years and older. Celecoxib was a potentially cost-effective strategy, especially in arthritis patients with a PUB history, while rofecoxib was considered not cost-effective. The quality of the study methodology was generally good and the authors’ conclusions are robust.

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

Study objective
The objective was to examine the cost-effectiveness of two cyclo-oxygenase-2 specific (COX-2) inhibitors, rofecoxib and celecoxib, in comparison with non-selective non-steroidal anti-inflammatory drugs (NSAIDs) in two populations of patients with arthritis, who were at high risk of developing clinically significant upper gastrointestinal events (CSUGIEs). The two populations were patients of any age with previous medical history of perforation, ulcer or bleed (PUB), and patients aged 65 years and older (regardless of history of PUB).

Interventions
The three strategies under examination were celecoxib 200 mg once daily, rofecoxib 25 mg once daily and NSAIDs (ibuprofen 800 mg three times daily and naproxen 500 mg twice daily).

Location/setting
USA/primary care.

Methods
Analytical approach:
This economic evaluation was based on a decision analytic model, which simulated patient management under the three treatment strategies. The model focused on the incidence of adverse events (AEs) since the effectiveness of the three treatments was considered to be similar for arthritic pain. The time horizon was 1 year in the cost-effectiveness analysis and lifelong in the cost-utility analysis. The authors stated that the perspective of the Veterans Health Administration (VA) was adopted in the study.

Effectiveness data:
The clinical estimates were derived from an extensive literature review of commonly used databases. Clinical data on the impact of the three treatment strategies on CSUGIE were obtained from two randomised clinical trials (RCTs), the Celecoxib Long-term Arthritis Safety Study and the Vioxx GI Outcomes Research study. Some details of these studies were reported. Baseline risk of AEs was taken from population-based studies with patients similar to those of the VA, when available. The key clinical outcome was the incidence of AEs and CSUGIEs with the treatment strategies under analysis.

Monetary benefit and utility valuations:
Utility valuations were derived from published sources, details of which were not given. Utility weights were associated
with each AE, including myocardial infarction, dyspepsia, anaemia, renal toxicity, hypertension and congestive heart failure.

Measure of benefit:
The two summary benefit measures used were quality-adjusted life-years (QALYs) in the cost-utility analysis and the number of CSUGIEs in the cost-effectiveness analysis.

Cost data:
The economic analysis considered the costs of medications and treatment of AEs. Resource use was based on published evidence supplemented with expert opinion. The costs reflected, in general, VA rates. Medication costs were derived from the Federal Supply Schedule pricing. The costs were in US dollars ($). The price year was 2001.

Analysis of uncertainty:
One- and multi-way sensitivity analyses were carried out on key model inputs. Specifically, the influence on the results of the incidence of cardiovascular AEs attributed to COX-2 inhibitors was investigated in depth in specific scenarios. Published ranges of clinical values appear to have been used. Economic data were arbitrarily varied (± 15% of the base-case value). A Monte Carlo simulation was conducted by attributing probabilistic distributions to the model inputs.

Results
In the PUB population, the expected 1-year (lifetime) costs were $38,184 ($46,468) with NSAIDs, $66,967 ($79,383) with celecoxib and $79,951 ($110,992) with rofecoxib. The expected number of CSUGIEs was 6.65 with NSAIDs, 2.80 with celecoxib and 4.10 with rofecoxib. The expected QALYs lost were -5.27 with NSAIDs, -4.10 with celecoxib and -8.92 with rofecoxib.

The incremental cost per CSUGIE avoided over NSAIDs was $7,476 with celecoxib and $16,379 with rofecoxib. The incremental cost per QALY gained with celecoxib was $28,214, while rofecoxib was dominated (simultaneously less effective and more expensive than NSAIDs).

In the elderly population, similar findings were achieved. The incremental cost per CSUGIE avoided over NSAIDs was $14,294 with celecoxib and $18,376 with rofecoxib. The incremental cost per QALY gained with celecoxib was $42,036, while rofecoxib was again dominated by NSAIDs.

The sensitivity analysis demonstrated that the most influential parameters were the rates and costs of myocardial infarction, CSUGIE and coronary heart disease, and acquisition cost of COX-2 inhibitors. In particular, when no cardiovascular effect was considered, the cost-effectiveness of rofecoxib improved substantially. In general, celecoxib remained a cost-effective strategy, while rofecoxib remained dominated, except in very favourable scenarios. The cost-effectiveness acceptability curves showed that, at a threshold of $50,000 per QALY, there was an 88% and 94% probability that celecoxib would be cost-effective in the elderly and PUB populations, respectively.

Authors’ conclusions
The authors concluded that celecoxib was a potentially cost-effective alternative to NSAIDs from the perspective of the VA, especially in arthritis patients with a PUB history. Rofecoxib was considered not cost-effective, owing to the increase in the risk of cardiovascular complications.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear since the standard of care (i.e. NSAIDs) was compared against two new treatments available for chronic pain. Furthermore, celecoxib and rofecoxib are two of the most commonly prescribed COX-2 inhibitors, although the authors pointed out that rofecoxib was recently withdrawn from the market because of an increased risk of cardiovascular events.

Effectiveness/benefits:
The use of a systematic review to identify the clinical data was appropriate since the most relevant literature was selected. The authors provided some information on the two key primary studies, especially with respect to the types of
patients included and the comparability (homogeneity) of the specific patient populations. They also stated that these were the only 2 RCTs comparing COX-2 with NSAIDs. There was little information on the other sources of data, which might limit the possibility of judging the quality of the clinical estimates. The authors did not describe the sources of the utility weights used to calculate QALYs.

Costs:
The cost categories included in the analysis were consistent with the viewpoint of the study. The costs were presented as macro-categories, which were not broken down into individual items. Sources of economic data were cited but not described. Nevertheless, they represented the costs relevant to the payer. The price year was reported, which enhances the possibility of performing reflation exercises. The sensitivity analyses investigated the issue of uncertainty surrounding the cost estimates.

Analysis and results:
The synthesis of the costs and benefits was carried out appropriately. The issue of uncertainty was extensively addressed and appropriately discussed. The results of both the base-case and the sensitivity analyses were presented clearly. The sub-group analyses further enhanced the validity of the study. The authors compared their findings with those from previous studies. Some limitations of the analysis were pointed out. First, the authors acknowledged that mixed sources of data were used. Second, the study population might not reflect the typical patient considered in the current model. Finally, the analysis did not consider the impact of multiple risk factors of gastrointestinal complications on the treatment cost-effectiveness.

Concluding remarks:
The quality of the study methodology was generally good. The extensive use of sensitivity analyses enhanced the robustness of the authors' conclusions.

Funding
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Bibliographic details

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Aged; Anti-Inflammatory Agents, Non-Steroidal /adverse effects /economics /therapeutic use; Arthritis /drug therapy /economics; Cost-Benefit Analysis; Cyclooxygenase Inhibitors /adverse effects /economics /therapeutic use; Gastrointestinal Diseases /chemically induced; Humans; Lactones /economics /therapeutic use; Pyrazoles /economics /therapeutic use; Quality-Adjusted Life Years; Risk Factors; Sulfonamides /economics /therapeutic use; Sulfones /economics /therapeutic use; United States; United States Department of Veterans Affairs

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