Costs and effects of various analgesic treatments for patients with rheumatoid arthritis and osteoarthritis in The Netherlands

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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 aim was to compare the costs and upper gastrointestinal side effects of six treatments for patients with rheumatoid arthritis and osteoarthritis. Arthrotec was the most cost-effective strategy for all and for medium-to-high risk patients, while celecoxib was preferred for high-risk patients. Overall the study was based on valid methodology. Some of the clinical data could have been reported in more detail, but the cost analysis and the results were well reported. The authors' conclusions appear to be appropriate.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The aim was to compare the costs and upper gastrointestinal side effects of six treatment strategies for patients with rheumatoid arthritis and osteoarthritis.

Interventions
The six treatment strategies were: non-steroidal anti-inflammatory drugs (NSAIDs) alone; NSAIDs plus proton-pump inhibitors (PPIs); NSAIDs plus histamine-2 receptor antagonists (H2RAs); NSAIDs plus misoprostol; Arthrotec, a fixed-dose combination of NSAID plus misoprostol; and celecoxib, a cyclooxygenase-2 inhibitor. The dosages were reported.

Location/setting
Netherlands/primary and secondary care.

Methods
Analytical approach:
A decision analytic model with a six-month time horizon was used. The authors reported that a societal perspective was adopted. The model characteristics were reported in detail in another publication (Burke, et al. 2001, see 'Other Publications of Related Interest' below for bibliographic details).

Effectiveness data:
The effectiveness data were derived from various sources including large randomised controlled trials and a meta-analysis. These were augmented with authors' assumptions, which were fully reported. The evidence highlighted several important risk factors associated with serious gastrointestinal events, so the authors devised a score system and applied this to patients to create risk groups. The results were presented for all risk groups. The main clinical outcomes were gastrointestinal events, which were gastrointestinal discomfort, symptomatic ulcers, serious gastrointestinal events necessitating hospitalisation (a bleeding ulcer, perforation, or obstruction), and misoprostol intolerance.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
Life-years gained (LYG) were extrapolated from the model and derived from the deaths averted with the six-month horizon. Each death due to gastrointestinal adverse events was assumed to be equivalent to 10 years of life lost.
Cost data:
The economic analysis considered the costs of the medications, gastrointestinal adverse events (including general practitioner visits), diagnostic tests, surgery, and hospitalisation. The resource use data for gastrointestinal adverse events were derived from a hospital database and augmented with expert opinion from a panel of four experts. The costs were obtained from official national sources and the methods used to derive the cost estimates were fully reported. The resource use data and unit costs were reported separately. All costs were in Euros (EUR) for the price year 2004.

Analysis of uncertainty:
The parameter uncertainty was investigated using one-way sensitivity analysis on all the model parameters. Probabilistic sensitivity analysis was also performed, and the methods used to derive the probability distributions were fully presented. Cost-effectiveness acceptability curves were generated.

Results
The results were reported separately for all patients, medium-to-high risk patients, and high-risk patients, assuming a cohort of 1,000 treated patients in each group.

For all patients, the number of deaths due to serious gastrointestinal adverse events ranged from 0.8 with NSAIDs alone to 0.31 with celecoxib. The expected costs ranged from EUR 166,000 with NSAIDs alone to EUR 284,000 with NSAIDs plus H2RAs, and EUR 285,000 with NSAIDs plus PPIs.

NSAIDs plus H2RAs and NSAIDs plus misoprostol were dominated by Arthrotec as it was more effective and cheaper. NSAIDs plus PPIs was dominated by celecoxib. These dominated treatments were excluded from the incremental analysis.

For all patients, NSAIDs alone resulted in an incremental cost-effectiveness ratio (ICER) of EUR 17 per LYG. Arthrotec had an ICER of EUR 5,676 per LYG compared with NSAIDs alone. Celecoxib had an ICER of EUR 56,667 compared with Arthrotec.

For medium-to-high risk patients excluding dominated treatments, NSAIDs alone resulted in an ICER of EUR 20 per LYG. Arthrotec compared with NSAIDs alone resulted in an ICER of EUR 526 per LYG and celecoxib compared with Arthrotec resulted in an ICER of EUR 33,684 per LYG.

For high risk patients, NSAIDs alone were also dominated, Arthrotec resulted in an ICER of EUR 23 and celecoxib compared with Arthrotec resulted in an ICER of EUR 15,429 per LYG.

The probabilistic sensitivity analysis showed that at a willingness-to-pay threshold of EUR 20,000 per LYG, for all patients, NSAIDs alone had a 44% probability of being the most cost-effective strategy, Arthrotec had a 38% probability and celecoxib 15%. Conversely, for high-risk patients, Arthrotec had a 41% probability of being the most cost-effective strategy and celecoxib 48%.

Authors' conclusions
The authors concluded that, at a willingness-to-pay threshold of EUR 20,000 per LYG, Arthrotec was the most cost-effective strategy for all and for medium-to-high risk patients with rheumatoid arthritis and osteoarthritis, while celecoxib was the preferred treatment for high-risk patients.

CRD commentary
Interventions:
The interventions were clearly reported. The study appears to have been thorough in its coverage of alternative treatments.

Effectiveness/benefits:
The effectiveness estimates were mainly derived from published RCTs and a meta-analysis, which potentially have the greatest level of internal validity. No details of how these studies were identified and selected for use were reported,
which makes it difficult to ascertain if the best available evidence was used. Only limited clinical study details were presented, but extensive sensitivity analyses were performed around the estimates used, which should make the results more robust. All assumptions made by the authors were explicitly reported. The use of LYG was appropriate and will allow comparisons to be made with other diseases.

Costs:
Although the authors stated that a societal perspective was adopted, the indirect costs such as carers’ productivity losses were not included. This exclusion was justified by the authors on the basis of the age of the population and the short time horizon. This does not, however, comply with the societal perspective. The resource use data were based on actual data from the authors’ setting. The sources of unit costs were reported and the resource quantities were given separately from the unit costs, increasing the transparency of the economic analysis. The price year was reported which will facilitate future reflation exercises. Overall, the economic analysis was well reported.

Analysis and results:
The synthesis of the costs and benefits was appropriately conducted using incremental analysis. The time horizon was short, but the authors stated that the lack of time dependent variables and the lack of one-off initial costs mean that the impact of the time horizon on the results was negligible. This seems to be reasonable. The issue of uncertainty was extensively investigated using a deterministic and a probabilistic approach. The results of the base case and the sensitivity analyses were reported appropriately. The limitations of the study were acknowledged and discussed by the authors.

Concluding remarks:
Overall the study was based on valid methodology. Some of the clinical data could have been reported in more detail, but the cost analysis and the results were well reported. The authors’ conclusions appear to be appropriate.

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