Utilization of nonsteroidal anti-inflammatory drugs and antisecretory agents: a managed care claims analysis

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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.

Health technology
Two types of nonsteroidal anti-inflammatory drugs (NSAIDs) were examined. These were traditional NSAIDs and cyclooxygenase-2 (COX-2) selective inhibitors.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised adult patients requiring NSAIDs for the treatment of inflammatory, arthritic and musculoskeletal conditions. Patients with a diagnosis of gastroesophageal reflux disease were excluded.

Setting
The setting was primary and secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness and resource use data were gathered from 1998 to 2001. The price year was not explicitly reported.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was carried out retrospectively on the same sample of patients as that used in the effectiveness study.

Study sample
Power calculations were not reported. The study sample was identified from all eligible patients who had continuous enrolment in the calendar years 1998 to 2001 and drug coverage for the entire enrolment period. Data were retrieved from a large administrative database. Patients were classified as users and were only included in the study if they were continuously enrolled in the pre-period (one year), did not have evidence of a similar prescription in the pre-period, and were continuously enrolled during the follow-up period (one year). Patients dying during the enrolment period were excluded. A sample of 106,564 patients was identified. Of these, 37,100 (59% female) were in the traditional group, 36,472 (67% female) were in the COX-2 inhibitor group without prior NSAID use, and 32,992 (67% female) were in the COX-2 inhibitor group with prior NSAID use. Therefore, 65.2% were COX-2 users, while 34.8% were traditional...
NSAID users. The mean ages of the patients in the three groups were 54.3 (+/- 13.7) years; (NSAID), 63.3 (+/- 13.3) years (COX-2, without prior NSAIDs) and 61 (+/- 12.8) years (COX-2, with prior NSAIDs), respectively.

Study design
This was a retrospective case-control study that was carried out at several centres. The patients were followed for one year after the first prescription, and outcomes in the year before the first prescription were also examined. Therefore, a two-year follow-up period was considered. No patient was lost to the follow-up assessment as only patients with complete data were included in the study.

Analysis of effectiveness
All of the patients included in the initial study sample were accounted for in the effectiveness study. The outcome measures used were:

- the use of NSAIDs or COX-2 inhibitors in patients with different GI or cardiovascular risk factors;
- the use of antisecretory agents, primarily proton-pump inhibitors but also histamine H2-receptor antagonists and misoprostol); and
- the incidence of GI and cardiac events.

The baseline comparability of the study groups was not explicitly reported. Regression analyses were performed to examine the impact of baseline factors, such as age, gender, and GI or cardiovascular risk factors, on the outcomes associated with the different types of NSAIDs.

Effectiveness results
The descriptive analysis showed that, in comparison with traditional NSAID users, COX-2 inhibitor users were older and more likely to have osteoarthritis, rheumatoid arthritis, or musculoskeletal pain, with a higher prevalence of gastroesophageal reflux disease.

The use of COX-2 inhibitors versus traditional NSAIDs was more common among those with GI risk factors (odds ratio, OR=2.86, 95% confidence interval, CI: 2.79 - 2.95) or cardiovascular risk factors (OR 1.64, 95% CI: 1.59 - 1.69).

Traditional NSAIDs were used in 65% of patients without risk factors, 12% of patients with GI risk factors only, 12% of patients with cardiovascular risk factors only, and 11% of patients with both risk factors.

COX-2 inhibitors without prior NSAIDs were used in 40% of patients without risk factors, 26% of patients with GI risk factors only, 11% of patients with cardiovascular risk factors only, and 24% of patients with both risk factors.

COX-2 inhibitors with prior NSAIDs were used in 45% of patients without risk factors, 23% of patients with GI risk factors only, 13% of patients with cardiovascular risk factors only, and 20% of patients with both risk factors.

These differences were all statistically significant.

The analysis also revealed that the use of antisecretory agents was significantly more common in COX-2 inhibitor patients than in NSAID patients, for all categories of risk factors.

The incidence of GI and cardiac events was uncommon and was comparable between the groups. The results were unchanged in the adjusted analysis.

Clinical conclusions
The effectiveness analysis showed that COX-2 inhibitors were prescribed not only to patients at high-risk of GI and
cardiovascular events, but also to patients without a risk of such events. Further, antisecretory therapy was more commonly used in patients taking COX-2 inhibitors than in those prescribed traditional NSAIDs. The increased use of COX-2 inhibitors did not result in a reduction in clinical adverse events.

**Measure of benefits used in the economic analysis**
The health outcomes were left disaggregated and no summary benefit measure was used in the economic evaluation. In effect, a cost-consequences analysis was carried out.

**Direct costs**
Discounting was not relevant because the costs were incurred during two years. The unit costs were not presented separately from the quantities of resources used and a detailed breakdown of the cost items was not reported. The economic evaluation considered all inpatient, outpatient and prescriptions claims. The cost/resource boundary of the payer was adopted. The estimation of both costs and resource use was based on the same research database as that used for clinical data. The price year was not reported.

**Statistical analysis of costs**
Standard analyses of the costs were carried out to test the statistical significance of differences between the groups. A multiple linear regression model was also used to assess the association between the type of NSAID used and total health care expenditures, including age, gender and pre-period of health care use as covariates. A log transformation was required because of the skewed nature of financial data.

**Indirect Costs**
The indirect costs were not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analyses were not performed.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
The estimated adjusted health care expenditures per patient were:

$7,120 (95% CI: 7,005 - 7,235) with traditional NSAIDs,

$8,879 (95% CI: 8,736 - 9,022) with COX-2 inhibitors with prior NSAID use, and

$8,119 (95% CI: 7,966 - 8,272) with COX-2 inhibitors without prior NSAID use.

The differences between COX-2 inhibitors and traditional NSAIDs reached statistical significance.

**Synthesis of costs and benefits**
A synthesis of costs and benefits was not relevant since a cost-consequences analysis was carried out.
**Authors' conclusions**

Cyclooxygenase-2 (COX-2) selective inhibitors were widely used, regardless of the level of risk for gastrointestinal (GI) and/or cardiovascular events. However, such a prescribing pattern did not lead to a reduction in clinical adverse events, use of antisecretory therapy, or the costs of care from the payer perspective.

**CRD COMMENTARY - Selection of comparators**

The selection of the comparator was appropriate as NSAIDs represented the traditional pattern of prescription for patients requiring treatment of inflammatory, arthritic, and musculoskeletal conditions. You should decide whether this is a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**

The effectiveness data came from a case-control study, which has a number of limitations, mainly in relation to the retrospective design and the definition of study groups by outcome. Under such a design, selection and assessment bias cannot be excluded. Similarly, confounding factors could have affected the study results. The authors carried out some statistical analyses to investigate the impact of baseline characteristics on the results of the analysis. These issues tend to limit the internal validity of the study. Further, the authors noted that the use of a specific database could limit how representative the study sample was. Finally, the definition of risk profiles was uncertain for some patients, owing to the limited information retrieved from claims data.

**Validity of estimate of measure of benefit**

No summary benefit measure was used in the analysis because a cost-consequences analysis was conducted. Please refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

**Validity of estimate of costs**

The authors reported explicitly the perspective adopted in the study. However, no information on resource consumption and the unit costs was provided because only the total costs were reported. Further, a detailed breakdown of the cost items was not given. This limits the possibility of replicating the study. Statistical analyses of the costs were undertaken because of the skewed distribution of financial data. Regression analyses were also carried out to examine the impact of baseline factors on the total costs. The price year was not reported, which makes reflation exercises in other settings difficult. The authors noted that the use of over-the-counter medications could not be estimated. The source of the cost data was reported.

**Other issues**

The authors made few comparisons of their findings with those from published studies. The issue of the generalisability of the study results to other settings was not addressed and sensitivity analyses were not performed. This reduced the external validity of the study. The study referred to patients requiring NSAIDs for the treatment of inflammatory, arthritic, and musculoskeletal conditions.

**Implications of the study**

The study results suggested that the widespread use of COX-2 inhibitors and antisecretory therapy could impose an unnecessary financial burden to the health care payer, without any evidence of benefit in most patients. The authors stated that future studies should investigate the clinical and economic impact of COX-2 inhibitors in aspirin users.

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