Prevention of complicated ulcer disease among chronic users of nonsteroidal anti-inflammatory drugs: the use of a nomogram in cost-effectiveness 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
Eight strategies for the prevention of complicated ulcer disease in patients taking nonsteroidal anti-inflammatory drugs (NSAIDs) were examined. The strategies were:

- conventional NSAID therapy, consisting of 800 mg ibuprofen three times daily (strategy 1);
- conventional therapy plus a single dose of regular-strength proton-pump inhibitor (PPI), such as 30 mg lansoprazole daily (strategy 2);
- conventional therapy plus 200 microg misoprostol three times daily (strategy 3);
- coxib (100 mg celecoxib twice daily) (strategy 4); and

Helicobacter pylori treatment (bismuth subsalicylate-metrodinazole-tetracycline combination and PPI treatment twice daily for 2 weeks), followed by each of the first four strategies (respectively, strategy 5 through strategy 8).

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of patients requiring NSAID therapy.

Setting
The setting was primary care. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1991 and 2001. The dates relating to resource use were not reported. The price year was 1999.

Source of effectiveness data
The effectiveness evidence was derived from a review of published studies and authors' assumptions.

Modelling
A decision tree model was used to assess the costs and clinical benefits of the alternative treatment strategies in a...
A hypothetical 55-year-old patient with osteoarthritis who required NSAID therapy for one year. The structure of the model was not reported.

**Outcomes assessed in the review**
The outcomes assessed from the literature were:

- the baseline annual risk of clinical UGI event with conventional NSAID therapy;
- the fold increase in the annual risk of clinical UGI events due to factors such as age over 65 years, use of anticoagulants, use of steroids, history of peptic ulcer disease, high dose of NSAID, presence of Helicobacter pylori; and
- the percentage reduction in risk due to PPI co-therapy, coxib, Helicobacter pylori treatment in an infected person, and 200 microg of misoprostol co-therapy.

**Study designs and other criteria for inclusion in the review**
Not stated.

**Sources searched to identify primary studies**
Not stated.

**Criteria used to ensure the validity of primary studies**
Not stated.

**Methods used to judge relevance and validity, and for extracting data**
Not stated.

**Number of primary studies included**
The effectiveness evidence was obtained from 16 primary studies.

**Methods of combining primary studies**
Not stated.

**Investigation of differences between primary studies**
Not stated.

**Results of the review**
The baseline annual risk of a clinical UGI event with conventional NSAID therapy was 2.5% (range: 1.5 - 4.5).

The fold increase in the annual risk of a clinical UGI event was:

- 2.5 (range: 1.5 - 5.5) for age over 65 years,
- 2.5 (range: 2 - 5) for the use of anticoagulants,
- 2 (range: 1 - 3) for the use of steroids,
5 (range: 2 - 12) for a history of peptic ulcer disease,

2 (range: 1.5 - 3) for a high dose of NSAID, and

1.5 (range: 1 - 3) for the presence of Helicobacter pylori.

The reduction in risk was 50% for PPI co-therapy, 50% for coxib, 50% for Helicobacter pylori treatment in an infected person, and 40% for 200 microg misoprostol co-therapy.

**Methods used to derive estimates of effectiveness**
The authors made a key assumption about the efficacy of the treatment strategies.

**Estimates of effectiveness and key assumptions**
It was assumed that all treatment strategies had comparable anti-inflammatory efficacy and pain relief. The authors also stated that the opinion of one of the authors was used to assess the most reliable values derived from the literature when there were significant differences in the primary estimates.

**Measure of benefits used in the economic analysis**
The summary benefit measure was the rate of clinical UGI events per year. This was obtained from the decision model. It was calculated both for the baseline scenario, which assumed a 2.5% risk of UGI events with conventional NSAIDs, and for the alternative scenario in which the risk of UGI events with conventional NSAIDs was 6.5% (high-risk patients).

**Direct costs**
Discounting was not relevant since the costs were incurred during a 1-year timeframe. The unit costs were given, but the details on resource use were unclear. The health services included in the economic evaluation were drugs and treatment of UGI events. The cost of the Helicobacter pylori serologic analysis was also considered. The cost/resource boundary of the third-party payer was adopted. The costs were estimated from the Red Book for drugs and from a published study for the cost of a clinical UGI event. The source of the resource use data was not reported, but the data were likely to have been based on standard drug dosages and probabilities derived from the literature. The costs were presumably presented in 1999 values.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
The indirect costs were not included in the economic evaluation.

**Currency**
US dollars ($).

**Sensitivity analysis**
A three-way sensitivity analysis was presented as a nomogram. This was constructed to support the management decisions of physicians, and was based on the patient's risk of developing UGI events. The nomogram consisted of three vertical lines representing, respectively, the difference in the annual cost of the drugs, the difference in the annual risk of clinical UGI events, and the incremental cost-effectiveness ratio (ICER).
Estimated benefits used in the economic analysis
In the base-case, the annual risk for clinical UGI events was 2.50 for strategy 1, 1.25 for strategy 2, 1.50 for strategy 3, 2.25 for strategy 4, 2.25 for strategy 5, 1.13 for strategy 6, 1.35 for strategy 7, and 1.13 for strategy 8.

In the high-risk patient scenario, the corresponding values were 6.50 for strategy 1, 3.25 for strategy 2, 3.90 for strategy 3, 3.25 for strategy 4, 5.85 for strategy 5, 2.93 for strategy 6, 3.51 for strategy 7, and 2.93 for strategy 8.

Cost results
When only drug costs were considered, in the base-case, the annual costs were $239 for strategy 1, $1,632 for strategy 2, $1,209 for strategy 3, $1,029 for strategy 4, $423 for strategy 5, $1,816 for strategy 6, $1,393 for strategy 7, and $1,213 for strategy 8.

When the costs of treating clinical UGI events were considered, the corresponding figures were:

for the average-risk patient scenario, $939 for strategy 2, $1,982 for strategy 2, $1,629 for strategy 3, $1,379 for strategy 4, $1,053 for strategy 5, $2,131 for strategy 6, $1,771 for strategy 7, and $1,528 for strategy 8; and

for the high-risk patient scenario, $2,059 for strategy 1, $2,445 for strategy 2, $2,301 for strategy 3, $1,939 for strategy 4, $2,061 for strategy 5, $2,538 for strategy 6, $2,375 for strategy 7, and $2,032 for strategy 8.

Synthesis of costs and benefits
An ICER was calculated to combine the costs and benefits of the strategies under evaluation, compared with conventional NSAID therapy.

The ICERs (cost per clinical UGI event prevented) relative to strategy 1 were:

for the base-case analysis, $111,440 with strategy 2, $97,000 with strategy 3, $63,200 with strategy 4, $73,600 with strategy 5, $114,691 with strategy 6, $100,348 with strategy 7, and $70,836 with strategy 8; and

for the high-risk scenario when only drug costs were considered, $42,862 with strategy 2, $37,308l with strategy 3, $24,308 with strategy 4, $28,308 with strategy 5, $44,112 with strategy 6, $38,595 with strategy 7, and $27,245 with strategy 8.

After including the costs of treating clinical UGI events, the ICERs relative to strategy 1 were:

for the base-case analysis, $83,440 with strategy 2, $69,600 with strategy 3, $35,200 with strategy 4, $45,600 with strategy 5, $86,691 with strategy 6, $72,348 with strategy 7, and $42,836 with strategy 8; and

for the high-risk scenario, $11,877 with strategy 2, $9,308 with strategy 3, dominant (more effective and less costly) with strategy 4, $308 with strategy 5, $16,112 with strategy 6, $10,595 with strategy 7, and dominant with strategy 8.

The use of the nomogram permitted the cost-effectiveness of each strategy to be assessed under alternative scenarios.

Authors' conclusions
The most cost-effective strategy was to use relatively expensive medications such as coxib, or to add a proton-pump inhibitor (PPI) to the standard therapy for patients with a high-risk for clinical upper gastrointestinal (UGI) events. However, when the risk for clinical UGI events was moderately high, all strategies were well above the conventional threshold for the cost-effectiveness of health care interventions.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear. Ibuprofen was appropriately selected to represent conventional therapy and the choice of the other therapies was made to cover all possible interventions for reducing the
development of clinical UGI events. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness estimates were derived from published studies, but a review of the literature was not conducted. Therefore, it appears that primary studies have been identified selectively from the literature. The authors stated that the estimates used in the model were based on their own interpretation of the published literature. Further, no information on how the primary estimates were extracted and then combined was provided. The analysis relied on a strong assumption about the equal efficacy of all the strategies, which was neither justified nor investigated in the sensitivity analysis.

Validity of estimate of measure of benefit
The summary benefit measure was specific to the strategies considered in the study. Therefore, it would be difficult to compare it with the benefits of other health care interventions. The benefits were derived from the decision model, which was not described. The discussion on quality of life issues would have been useful, as this is a relevant issue for patients requiring NSAID therapy.

Validity of estimate of costs
The authors stated explicitly which perspective was adopted in the study. Only drug costs and the costs associated with treating clinical UGI events were considered in the analysis, which was consistent with the perspective adopted. The unit costs were provided, but a detailed breakdown of items included in the resource defined as 'management of clinical UGI events' was not reported since this cost was derived from a published study. The price year was implicitly reported given that the costs were mainly reported in 1999 values. The costs were treated deterministically, but wide variations of all estimates were conducted in the sensitivity analysis. This enhanced both the robustness of the analysis and the transferability of the results to other settings.

Other issues
The authors did not make extensive comparisons of their findings with those from other studies. The issue of the generalisability of the study results was implicitly addressed using a nomogram. This permitted the cost-effectiveness of the strategies under evaluation to be assessed in different scenarios, where both the costs and risk of developing clinical UGI events could be varied. The study referred to the general population of patients taking NSAIDs and this was reflected in the conclusions of the analysis. The authors presented the advantages of their model, but also stated that it could be applied only to models with two predicting variables.

Implications of the study
The study results suggested that the use of coxib or PPI added to conventional NSAID therapy represent the most cost-effective strategies.

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None stated.

Bibliographic details

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Other publications of related interest


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