A pharmacoeconomic comparison of misoprostol/diclofenac with diclofenac
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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
The misoprostol-diclofenac fixed combination preparation was compared with diclofenac and other prescribed nonsteroidal anti-inflammatory drugs (NSAIDs), to investigate the association between NSAIDs and admission to hospital for upper gastrointestinal (GI) haemorrhage and perforation and other upper GI events.

Type of intervention
Other: Secondary care.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients registered with a general practitioner (GP) in Scotland and held on a master file referred to as the Community Health Index. This was used to obtain information on patients registered with a GP in Tayside between 1 January 1989 and 31 December 1995. Details of the age, gender and health status of the patients were not provided.

Setting
The study was carried out using the Tayside Medicines Monitoring Unit (MEMO) database, which is a record-linking database that was not described in this paper. Therefore, details of the setting were not available. The economic study was carried out in Scotland, UK.

Dates to which data relate
The drug costs used related to 1998. The total costs for the use of each speciality for each hospital were obtained from 1997 data. The effectiveness outcomes were derived from records published between 1989 and 1995.

Source of effectiveness data
The estimate for the final outcomes was derived from a single study.

Link between effectiveness and cost data
The costing was not undertaken on the same patient sample as that used in the effectiveness study, instead, 1998 costs for the relevant drugs were used in the calculations. The costing was undertaken retrospectively.

Study sample
The sample size was not determined in the planning phase of the study. The study sample comprised all residents in Tayside who were registered with a Tayside GP between 1 January 1989 and 31 December 1995. The authors did not
fully justify their choice of the patient sample in relation to the characteristics of the treatment under investigation. No patients were excluded from the study. The number of patients included in the study was not reported.

**Study design**
This was a retrospective cohort study that was conducted in a single centre, and carried out using the MEMO database.

**Analysis of effectiveness**
The primary health outcomes were any periods of hospital care that were associated with an upper GI diagnosis and the risk of hospitalisation according to NSAID prescription. The numbers of endoscopic examinations performed in Tayside between 1989 and 1995 were also recorded. Other risk factors were also recorded:

the patients’ age;

whether it was the first period of NSAID exposure;

whether there had been a hospitalisation with a GI diagnosis; and

whether there had been a hospitalisation with a cardiovascular diagnosis.

The data from the Scottish Morbidity Record 1, which was used to obtain the association between dispensed prescriptions and admission to hospital, were evaluated. Other variables were obtained from the MEMO database. It was not stated whether the patients were analysed according to the intention to treat principle or on the basis of treatment completers only.

Patients were not excluded for incomplete data. All of the groups were comparable at analysis.

**Effectiveness results**
Among the GI patients with no prior history of GI events, there was a 30% higher risk of hospitalisation during exposure to diclofenac compared with misoprostol-diclofenac. In the NSAID group for GI patients with a history of GI events, there was an 83% higher hospitalisation for those on diclofenac compared with those on misoprostol-diclofenac. The hospitalisation rates were 8% lower with low doses and 29% higher with high doses.

For GI patients with no prior history of GI events, 89 days were spent in hospital by patients receiving misoprostol-diclofenac versus 1,348 days for those receiving diclofenac. The corresponding values for patients with a history of GI events were 3 days (misoprostol-diclofenac group) and 56 day (diclofenac), respectively.

**Clinical conclusions**
The clinical conclusion was that the use of diclofenac resulted in significantly greater hospitalisation rates.

**Measure of benefits used in the economic analysis**
The measure of health benefit used was the total number of days spent in hospital. This was derived directly from the effectiveness results. No discounting was carried out.

**Direct costs**
The direct costs of the hospital were included in the analysis. The Scottish Health Service Costs for the year ending 31 March 1997 provided all the daily total costs that were associated with the use of each specialty in each hospital. Further details of the direct costs were not provided. The unit costs and the quantity of each resource used were not provided. The costs were not discounted. The 1998 costs of the drugs were used to calculate the cost of treatment. The study reported incremental costs. The authors did not adjust the costs for inflation. In addition, they did not report whether any costs were excluded, whether adjustments were made to the observed costs to correct for new
technologies, or whether any budgetary impact was assessed.

**Statistical analysis of costs**
The resource use and costs were treated as point estimates. Therefore, the data were deterministic. The number of events (length of exposure, risk factors, number of endoscopies and number of hospitalisations) was modelled as Poisson variables. The distribution of the costs was treated as being normally distributed on a logarithmic scale. It was analysed using generalised linear models with log-normal error distribution. Power calculations were not undertaken.

**Indirect Costs**
No indirect costs were included in the study.

**Currency**
UK pounds sterling ( £ ).

**Sensitivity analysis**
Sensitivity analyses were carried out. One such analysis investigated the relative risks for misoprostol-diclofenac versus NSAID exposure for all patients who received NSAIDs at any time, within the study period. Another analysis was conducted on separately prescribed ulcer healing drugs (UHDs) in conjunction with misoprostol-diclofenac. Three scenarios, which reduced the co-prescribing of UHDs in conjunction with misoprostol-diclofenac by 100, 75 or 50%, were investigated.

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

**Cost results**
The total cost of diclofenac prescriptions was £47,000 for patients with a prior history of GI events. The incremental cost of replacing diclofenac with misoprostol-diclofenac was £12,000.

The total cost of diclofenac prescriptions was £2,290,000 for patients with no prior history of GI events. The incremental cost of replacing diclofenac with misoprostol-diclofenac was £560,000.

The sensitivity analysis showed that, with a 50% reduction in UHDs co-prescribed with diclofenac prior to any hospitalisation with a GI event, there would be cost-savings if diclofenac prescriptions for patients over 70 years and all GI patients with a prior history were switched to misoprostol-diclofenac. With a 75% reduction in UHD prescriptions, there would be cost-savings for all GI patients with a prior history and for GI patients with no prior history who were aged over 70.

**Synthesis of costs and benefits**
The costs and benefits were not combined.

**Authors' conclusions**
The misoprostol-diclofenac combination resulted in significantly less resource costs to the National Health Service (NHS) than diclofenac alone. The savings were largest in the elderly. For a 75% reduction in ulcer healing drugs (UHDs), the age at which savings could be realised was 20 years for those with a history of gastrointestinal (GI) hospitalisation and 60 to 70 years for those without a history.
CRD COMMENTARY - Selection of comparators
The aim of the study was to compare the misoprostol-diclofenac fixed combination versus diclofenac and other prescribed NSAIDs. You should decide if this comparator is appropriate for your setting.

Validity of estimate of measure of effectiveness
The basis of the analysis was a retrospective cohort study, which was appropriate for the study question. In addition, the study sample was representative of the study population. The methods of data extraction were reported in the study, suggesting that the internal validity of the study is likely to be good. No statistical analysis was undertaken to account for potential biases and confounding factors. Since no power calculations were reported, it is therefore not possible to ascertain whether the results obtained were due to the intervention or to chance.

Validity of estimate of measure of benefit
The measure of benefit was the number of days in hospital during exposure to misoprostol-diclofenac or diclofenac alone in all NSAID users. The estimation of benefits was obtained from the effectiveness analysis. The choice of estimate was not justified. Ideally, the quality-adjusted life year should be used as a summary measure of benefit, as this allows meaningful comparisons with other studies and technologies.

Validity of estimate of costs
The analysis of the costs was performed from the perspective of the NHS. It appears that all the relevant categories of costs, and relevant costs, have been included in the analysis. There does not appear to have been any omission of costs. The costs and the quantities were not reported separately. No statistical analysis of the quantities was conducted. A sensitivity analysis of the prices was not conducted. The prices were taken for one year even though the study period for the effectiveness data was 6 years.

Other issues
The authors did not make appropriate comparisons of their findings with those from other studies. They also did not address the issue of generalisability to other settings. The authors did not present their results selectively. The study was concerned with patients treated with a misoprostol-diclofenac fixed combination versus diclofenac and other prescribed NSAIDs, and this was reflected in the authors’ conclusions.

The authors reported several limitations of their study. First, they could not control for the confounding effects of smoking, alcohol consumption or the use of anticoagulants. Second, they did not know which patients had a history of upper GI disease that had been diagnosed in an outpatient environment. There were no data on symptoms of dyspepsia or abdominal pain, or other symptoms that might themselves have increased the risk of upper GI events. The study did not investigate the newer specific cyclooxygenase 2 inhibitors.

Implications of the study
There would be savings if patients on misoprostol-diclofenac needed less UHDs than patients on diclofenac. The authors noted that, for the NHS, it will be difficult to "recover the full average cost realised by preventing hospital admission". The cost-saving therefore rests on the cost-savings from the prescribing of misoprostol-diclofenac.

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Other publications of related interest

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