Pharmacoeconomic evaluation of gastrointestinal tract events during treatment with risedronate or alendronate: a retrospective cohort study

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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 use of alendronate (5 or 10 mg/day, or 35 or 70 mg/week) and risedronate (5 mg/day), two commonly prescribed oral bisphosphonates used to treat postmenopausal and glucocorticoid-induced osteoporosis, was examined.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients aged 65 years or older who were taking alendronate or risedronate for the treatment of postmenopausal and glucocorticoid-induced osteoporosis.

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 June 2000 to June 2002. The price year was 2002.

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 clinical study.

Study sample
Power calculations were not reported. The patients were retrospectively identified from an integrated administrative, medical, and pharmaceutical claims database, covering more than 10 million lives. Selected patients were those with a new prescription for risedronate or alendronate, whose claims provided 6 months of observation before the first prescription and 4 months following the initiation of therapy. Patients with a prescription for a bisphosphonate and/or any GI event and/or GI-related medications during the 6 months pre-treatment period were excluded. Also excluded were patients who had at least one prescription for risedronate or alendronate, as well as a disease code of Paget's disease at any point during the study period. Patients who switched between the two treatments were also excluded. A final study sample of 4,259 patients was identified, of which 3,636 were in the alendronate group and 623 in the
risedronate group. The patients in the alendronate group had a mean age of 75.4 (+/- 6.6) years and 94% were women. The patients in the risedronate group had a mean age of 75.7 (+/- 6.4) years and 94% were women.

Study design
This was a retrospective cohort study that involved a large number of providers. The patients were followed for 4 months after the first bisphosphonate prescription. No patient was lost to the follow-up assessment since only patients with complete data were included in the analysis.

Analysis of effectiveness
All of the patients included in the initial study sample were accounted for in the analysis of effectiveness. The outcome measure used was the incidence of specific GI events during the 4-month follow-up period. GI events were defined using GI-related primary International Classification of Diseases, Ninth Revision, Clinical Modifications (ICD-9-CM) and/or primary Current Procedural Terminology (CPT-4) codes. GI events were grouped into the following categories:

- overall,
- GI bleeding,
- ulcer (gastric, peptic, duodenal, and oesophageal),
- GI symptoms (including dysphagia, vomiting, nausea, and heartburn),
- abdominal pain,
- oesophageal reflux, and
- other events (including gastritis, oesophagitis, and stomach function disorders).

The study groups were comparable at baseline in terms of age, gender, exposure to bisphosphonates, and the use of non-steroid anti-inflammatory drugs.

Effectiveness results
The overall incidence of GI events was 3.4% in the risedronate group and 5.4% in the alendronate group, (p=0.034).

The incidence of GI bleeding was 0.3% in the risedronate group and 1.1% in the alendronate group, (p=0.076).

The incidence of ulcers was 0.2% in the risedronate group and 0.4% in the alendronate group, (p=0.307).

The incidence of GI symptoms was 0.6% in the risedronate group and 1% in the alendronate group, (p=0.405).

The incidence of abdominal pain was 1.9% in the risedronate group and 5% in the alendronate group, (p<0.001).

The incidence of oesophageal reflux was 0% in the risedronate group and 0.4% in the alendronate group, (p=0.097).

The incidence of other GI events was 1.6% in the risedronate group and 1.4% in the alendronate group, (p=0.694).

Clinical conclusions
The effectiveness analysis showed that patients in the risedronate group experienced fewer GI events than those in the alendronate group.

Measure of benefits used in the economic analysis
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 since the costs were incurred during a short timeframe. The quantities of resources used were given, but the unit costs were not reported. The health services included in the economic evaluation were inpatient visits, outpatient visits and GI medication. Inpatient visits covered visits to surgical suites, extended care facilities, emergency rooms, and inpatient hospital stay. Outpatient visits covered outpatient hospital stay and physician office visits. GI medications including H2 antagonists, proton-pump inhibitors and cytoprotectives. Only GI-related resource use was considered.

The cost/resource boundary of the health service payer was adopted. Resource use was estimated using data derived from the sample of patients included in the effectiveness study. The two dose schedules for alendronate were considered equivalent and the data were combined in a single group. The costs came from the same administrative database and reimbursement rates were used. GI-related costs of less than $5 were excluded, while patients with total costs higher than $2,000 were further examined to determine whether a more severe condition affected the total expenses. If this was the case, the patients were excluded from the cost analysis. The price year was 2002.

**Statistical analysis of costs**
The costs were presented as mean values with 95% confidence intervals (CIs). A 2-sample, 2-sided t-test was used to examine the statistical significance of differences in the costs.

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

**Currency**
US dollars ($).

**Sensitivity analysis**
A sensitivity analysis was performed to examine the impact of keeping outliers in the cost analysis.

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

**Cost results**
The analysis showed that the number of inpatient and outpatient visits was lower for the risedronate group than for the alendronate group. No statistically significant differences in GI medication prescriptions were observed.

The total costs per 1,000 members per month were $2,164 (95% CI: 1,130 - 3,200) in the risedronate group and $5,639 (95% CI: 4,330 - 7,660) in the alendronate group, (p<0.001).

In particular, significantly lower inpatient and outpatient costs were observed in the risedronate group. The inpatient costs were $436 in the risedronate group versus $2,691 in the alendronate group, (p<0.001), while the outpatient costs were $860 versus $2,223, (p=0.009).

The differences in other categories of costs were not significant.

The inclusion of outliers increased the costs in both groups but did not alter the conclusions of the analysis.
Synthesis of costs and benefits
A synthesis of the costs and benefits was not relevant since a cost-consequences analysis was performed.

Authors’ conclusions
In a patient population aged 65 years or older who had initiated bisphosphonate therapy for osteoporosis, risedronate was associated with markedly lower gastrointestinal (GI)-related diagnoses, medical resource use, and direct medical costs in comparison with alendronate.

CRD COMMENTARY - Selection of comparators
The authors justified the choice of the comparators, which represented the two most commonly prescribed oral bisphosphonates in the USA. Dosages were clearly reported. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data came from a retrospective review of patients’ charts. An integrated database, which had been basically created for administrative purposes, was used. Thus, validation of the ICD-9-CM codes was not allowed. The retrospective nature of the study represents a limitation to the validity of the analysis. Moreover, no evidence of the appropriateness of the sample size was provided, and there were fewer patients in the risedronate group. The study groups were comparable at baseline. However, selection bias and confounding factors could have affected the results of the analysis, owing to the lack of random allocation and masking. The study sample was likely to have been representative of the patient population. The authors stated that the length of follow-up was appropriate.

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 stated explicitly which perspective was adopted in the study and only those costs relevant to the payer were included. However, the unit costs were not presented separately from the quantities of resources, because only the latter data were provided. This reduces the possibility of replicating the study. The source of the data was reported, as were the approaches used to deal with outliers. Statistical analyses of the costs were performed, but the costs were specific to the study setting. Further, the use of over-the-counter medications could not be captured using the administrative database, thus the burden of GI medications could have been underestimated. On the other hand, the database did not distinguish between inpatient costs that corresponded to primary or secondary diagnosis, thus the inpatient costs could have been slightly overestimated.

Other issues
The authors did not compare extensively their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. Alternative estimates were not used in the sensitivity analysis. The authors noted that the use of the administrative database, despite the limitations highlighted already, allowed the observation of treatment patterns occurring in real-world practice, also due to the large number of patients involved. The study referred to elderly patients taking bisphosphonates and this was reflected in the authors’ conclusions.

Implications of the study
The study results suggested that risedronate should be the treatment of choice for patients requiring bisphosphonate therapy. The authors stated that the use of risedronate could result in substantial savings, owing to the increasing prevalence of osteoporosis in the US population.
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Bibliographic details

Other publications of related interest


Indexing Status
Subject indexing assigned by CRD

MeSH
Abdominal Pain /prevention & control /complications; Alendronate /adverse effects /therapeutic use /economics; Clinical Trials as Topic; Cohort Studies; Costs and Cost Analysis; Drug Costs; Etidronic Acid /adverse effects /therapeutic use /economics; Gastroesophageal Reflux /prevention & control /complications; Gastrointestinal Diseases /prevention & control /complications; Gastrointestinal Hemorrhage /prevention & control /complications; Health Care Costs; Osteoporosis /drug therapy; Retrospective Studies

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