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 study examined the use of gabexate for standard routine prophylaxis of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis. The comparator was no gabexate prophylaxis. For the study group, the total dose of gabexate was 1 g. The dose was halved in patients younger than 18 years who had a body weight of less than 50 kg.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a series of consecutive patients undergoing ERCP procedures in a single tertiary referral centre over 6 years.

Setting
The setting was tertiary care. The economic study was performed in Italy.

Dates to which data relate
The effectiveness data and costs before the introduction of gabexate prophylaxis were reported in the first 3 years from June 1996, while those after the introduction of gabexate prophylaxis were reported in the following 3 years. The price year appears to have been 2002.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The cost data appear to have been calculated retrospectively for the same sample of patients as that included in the effectiveness analysis.

Study sample
Of the 2,461 patients undergoing ERCP procedures, there were 1,312 without gabexate prophylaxis for post-ERCP pancreatitis over a 3-year period and 1,149 with gabexate prophylaxis in the subsequent 3-year period. The sub-groups were formed based on patient- and technique-related risk factors, which the authors clearly defined. Overall, the male-
to-female ratio was 1,155:1,306. The participants were aged from 5 to 94 years. The use of power calculations to determine the sample size was not reported.

**Study design**

This was a retrospective comparative study with a historical control, which was carried out at a single tertiary referral centre. Four endoscopists in a 24-hour hospital stay regimen conducted all of the endoscopic procedures during the 6-year study period. The study groups comprised patients treated before and after the introduction of gabexate prophylaxis. All samples were monitored according to a standard post-ERCP monitoring protocol. The length of follow-up was to the point of discharge. No patients were lost to follow-up.

**Analysis of effectiveness**

All patients entered in the study were included in the analysis. The groups were comparable in terms of their age and gender. The health outcomes were the frequency of pancreatitis and the cases with serum amylase values higher than five times the upper normal limit at 4 - 6 hours and 24 hours after the ERCP procedures.

**Effectiveness results**

Of the 1,312 versus 1,149 overall patients in the pre-gabexate versus gabexate periods, the frequency of post-ERCP pancreatitis was 51 (3.9%) versus 25 (2.2%), (p=0.019), and the severity of post-ERCP pancreatitis was 11 (0.8%) versus 3 (0.3%).

Of the 805 versus 672 standard-risk patients during the pre-gabexate versus gabexate periods, the frequency of post-ERCP pancreatitis was 14 (1.7%) versus 7 (1.0%), (p=0.36), and the severity of post-ERCP pancreatitis was 4 (0.5%) versus 1 (0.1%), (p=0.25).

Of the 507 versus 477 high-risk patients during the pre-gabexate versus gabexate periods, the frequency of post-ERCP pancreatitis was 37 (7.3%) versus 18 (3.8%), (p=0.02), and the severity of post-ERCP pancreatitis was 7 (1.4%) versus 2 (0.4%), (p=0.10).

The frequency of severe hyperamylasaemia at 4 - 6 hours after the procedure during the pre-gabexate versus gabexate periods was:

- 109 (8.3%) versus 55 (4.8%) for overall patients, (p=0.001);
- 30 (3.7%) versus 16 (2.4%) for standard-risk patients, (p=0.183); and
- 79 (15.6%) versus 39 (8.2%) for high-risk patients, (p=0.001).

The frequency of severe hyperamylasaemia at 24 hours after the procedure during the pre-gabexate versus gabexate periods was:

- 70 (5.3%) versus 35 (3.1%) for overall patients, (p=0.007);
- 19 (2.4%) versus 10 (1.5%) for standard-risk patients, (p=0.3); and
- 51 (10.1%) versus 25 (5.2%) for high-risk patients, (p=0.001).

**Clinical conclusions**

Routine gabexate prophylaxis significantly reduced the frequency of post-ERCP pancreatitis and severe hyperamylasaemia. However, gabexate appears to have been unable to reduce the incidence of severe pancreatitis.

**Measure of benefits used in the economic analysis**

NHS Economic Evaluation Database (NHS EED)
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The summary benefit measure used was the number of patients without complications in each group.

**Direct costs**
The direct costs included in the analysis were the overall post-ERCP pancreatitis costs and gabexate-related costs. The overall post-ERCP pancreatitis costs were determined through the use of code-related Diagnosis-Related Group (DRG) reimbursement referring to acute pancreatitis (code: 204, 475 and 191), in accordance with Italian DRG tariffs. It would appear that the gabexate-related costs were from Italian Ministry of Health Hospital Discharge Data. The costs and the quantities were not reported separately. The quantity/cost boundary was not reported. Discounting was not carried out, but it was not relevant to the economic analysis. The price year appears to have been 2002.

**Statistical analysis of costs**
The cost data were treated deterministically, only point estimates being provided.

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

**Currency**
Euros (EUR).

**Sensitivity analysis**
No sensitivity analysis was undertaken.

**Estimated benefits used in the economic analysis**
The authors decided to report the measure of benefit results per patient. This is strange as it is interpreted as "the number of patients without complications per patient".

The measure of benefit was 0.961 for the group without gabexate prophylaxis and 0.978 for the group with gabexate prophylaxis. This gave an incremental benefit of 0.017 for gabexate prophylaxis.

**Cost results**
The costs per patient during the pre-gabexate versus gabexate periods were EUR 2,732 versus EUR 2,759, with incremental costs of EUR 27 for overall patients.

**Synthesis of costs and benefits**
The incremental cost-effectiveness ratio was EUR 1.540 per patient for overall patients, EUR 7.758 per patient for low-risk patients, and -EUR 182 per patient for high-risk patients. Gabexate was dominant in high-risk patients.

**Authors’ conclusions**
Routine gabexate prophylaxis was cost-effective for high-risk patients. For low-risk patients, the incidence of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis and severe hyperamylasaemia did not really differ with or without gabexate prophylaxis, and prophylaxis was not cost-effective.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparators was clear. ‘No pharmacological prophylaxis’ was used as a comparator to the routine gabexate prophylaxis as it was the common practice in the authors’ setting. You should decide whether
these two comparators are also relevant in your own setting and whether there are other relevant alternatives to gabexate.

Validity of estimate of measure of effectiveness
The source of the effectiveness data was a retrospective comparative study with a historical control. The lack of randomisation and the different time periods means that there is a possibility of a confounding factor biasing the results, although the two patient groups were shown to be comparable in terms of the baseline criteria recorded. The study sample appears to have been representative of the study population. An appropriate statistical analysis was undertaken to evaluate the statistical significance of differences between the two groups.

Validity of estimate of measure of benefit
The benefit measure used in the economic analysis was disease specific and you should consider whether it provided an adequate measurement of all the significant health benefits from the treatment. The costs and benefits do require the same units, but reporting the benefit “the number of patients without complications per patient” is a little awkward. The total benefits and costs for each group could have been reported.

Validity of estimate of costs
The study perspective was not stated. The cost data were clearly presented. The source and price year were also given. The unit costs and the resource quantities were not reported separately, which may hinder the reproducibility of the results. No statistical or sensitivity analyses were performed, although this is to be expected when using reimbursement cost data.

Other issues
The authors did not compare their findings with those from other studies. In addition, the generalisability to other settings does not appear to have been addressed. The authors did not present their results selectively. The authors noted that there were potential biases resulting from the study design (i.e. retrospective cohort study) that, in theory, could influence the results. However, the authors provided an analysis of the reasons why it was unlikely that such biases would, in fact, have influenced their results.

Implications of the study
The findings of this study support the use of routine gabexate prophylaxis only for high-risk patients undergoing ERCP procedures.

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None stated.

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Other publications of related interest
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**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Adolescent; Adult; Aged; Aged, 80 and over; Amylases /blood /drug effects; Child; Child, Preschool; Cholangiopancreatography, Endoscopic Retrograde /adverse effects /economics; Cost-Benefit Analysis; Data Collection; Female; Follow-Up Studies; Gabexate /economics /therapeutic use; Humans; Hyperamylasemia /epidemiology /etiology /prevention & control; Incidence; Italy /epidemiology; Male; Middle Aged; Pancreatitis /epidemiology /etiology /prevention & control; Referral and Consultation; Retrospective Studies; Risk Factors; Serine Proteinase Inhibitors /economics /therapeutic use; Treatment Outcome

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