Prevention of recurrences of erosive reflux esophagitis: a cost-effectiveness analysis of maintenance proton pump inhibition

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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
Prevention of recurrences of erosive reflux esophagitis with a proton pump inhibitor (lansoprazole) therapy.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
Patients with symptoms of erosive reflux esophagitis healed with a PPI or an H2-receptor antagonist. These patients had no recent evidence of peptic strictures, Zollinger-Ellison syndrome, chronic NSAID use, or alcohol or drug abuse at the start of maintenance therapy.

Setting
Secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from a study published in 1996. The date for the resource use data was not reported. Costs were reported in 1995 prices.

Source of effectiveness data
Effectiveness estimates were based on review of randomised trials and on expert opinion.

Modelling
A Markov decision analytic model was used to estimate expected number of outcome events and costs over a one year period.

Outcomes assessed in the review
The outcomes assessed were the monthly endoscopic recurrence probabilities for patients on PPI therapy, equivalent to 15 mg, 30 mg, and 45 mg once daily dose of lansoprazole. Probabilities of first and second endoscopic recurrence for patients on no preventive therapy were also assessed. In order to derive these probabilities, the authors also needed to know the proportion of recurrent events detected in the endoscopy which were also symptomatic.
Study designs and other criteria for inclusion in the review
Endoscopic recurrence probabilities were based on the results of one randomised controlled trial.

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
1 randomised controlled trial.

Methods of combining primary studies
Not applicable.

Investigation of differences between primary studies
Not applicable.

Results of the review
The annual probability of endoscopic recurrence was 21% for patients on PPI maintenance equivalent to 15 mg qd lansoprazole and 9% for 30 mg qd. The annual probability of first endoscopic recurrence with no maintenance was 75% and of second recurrence was more than 90%.

Methods used to derive estimates of effectiveness
The estimates of effectiveness were based on the authors’ assumptions and the conclusions of a panel of five gastroenterologists using a modified Delphi process.

Estimates of effectiveness and key assumptions
The authors assumed that all patients with erosive esophagitis are healed on 45 mg daily lansoprazole, and hence the probability of endoscopic recurrence is 0%. The expert panel's median estimated 81% of endoscopic recurrences would be symptomatic, that the time from onset of symptoms to initiation of treatment would be 3.3 weeks and that the time from initiation of treatment to resolution of symptoms would be 4 days.

Measure of benefits used in the economic analysis
The measures of benefit in the economic analysis were the number of symptomatic recurrences of erosive reflux esophagitis prevented and quality adjusted life years (QALYs) gained. A Markov model was used to estimate the expected number of recurrences per year under each of the treatment strategies. The utility values associated with a symptomatic state were subjected to a threshold analysis based on a utility valuation of “current health” obtained from a published study.

Direct costs
Estimates for resource use were obtained from an expert panel and unit costs were obtained from published US statistics. Quantities and costs were reported separately. Costs included cost of drugs, office visits, monitoring and tests. The cost boundary adopted was the national health care system. Costs were expressed in 1995 prices. Total costs were estimated using a model. Average wholesale and government procurement prices were used (separately) for unit drug costs. Medicare figures were used for laboratory and physician fees and mean hospital accounting costs were used for outpatient facility costs (from 6,000 US hospitals).

**Currency**
US dollars ($).

**Sensitivity analysis**
The sensitivity of the model was analysed by extending its time frame from 1 to 5 years (discounting by 3%) and by using costs and effectiveness data for an alternative drug (omeprazole). One-way simple sensitivity analysis was undertaken on monthly acquisition cost of lansoprazole and on the proportion of endoscopic recurrences which are also symptomatic. Hence, the analysis dealt with uncertainties related to the generalisability of the results and the variability in data. Best-worst case scenarios were also investigated based on the parameters thought to be associated with the greatest degree of uncertainty.

**Estimated benefits used in the economic analysis**
The mean number of symptomatic recurrences per year was 0.18 for "initial maintenance", 0.75 for "no maintenance until a first recurrence" and 1.33 for "no maintenance until a second recurrence" strategy. The economic analysis was based on incremental benefits of more intensive strategies using "no maintenance until a second recurrence" as a starting point.

**Cost results**
The annual cost was estimated to be $1,376 for "initial maintenance", $908 for "no maintenance until a first recurrence" and $865 for "no maintenance until a second recurrence" strategy.

**Synthesis of costs and benefits**
Incremental cost effectiveness was reported as cost per symptomatic recurrences prevented (1995 prices). The baseline incremental cost effectiveness ratio was $73 per prevented recurrence for the "no maintenance until a first recurrence" strategy (relative to "no maintenance until a second recurrence") and $819 per prevented recurrence for the "initial maintenance" strategy (relative to "no initial maintenance until a first recurrence"). The marginal cost effectiveness of the "initial maintenance" strategy was also estimated according to the severity of esophagitis prior to healing (grade 2, 3, or 4). In the most severe case (grade 4) the "initial maintenance" was both less costly ($1,400 versus $1,394) and more effective than "no maintenance until first recurrence". When the monthly acquisition cost of lansoprazole was less than $70 "no maintenance until a first recurrence" becomes cost saving (relative to "no maintenance until a second recurrence"). The authors also performed a threshold analysis in order to determine the minimum quality of life reduction from the symptoms of esophagitis, which would cause the maintenance strategies to show an incremental cost-utility ratio of $50,000 per QALY. The threshold reduction in quality of life was estimated to be 22% for "initial maintenance" (relative to "no maintenance until first recurrence") and 2% for "no maintenance until a first recurrence" (relative to "no maintenance until a second recurrence").

**Authors’ conclusions**
For grades 2 and 3 esophagitis, providing maintenance therapy after a patient experienced a further recurrence was a preferred option that appears cost-effective across a wide array of assumptions. Maintenance therapy from the outset appears cost-effective only for those patients who report a significant decline in quality of life associated with esophagitis or for those patients with baseline grade 4 esophagitis.
CRD COMMENTARY - Selection of comparators
A justification was given for the comparators used. The proton pump inhibitor therapy was considered as the most successful treatment in preventing recurrences of erosive reflux esophagitis. You, as a user of this database, should consider whether these are widely used health technologies in your setting.

Validity of estimate of measure of benefit
The main effectiveness estimates were derived from the results of one randomised controlled trial, and complemented with estimates provided by a panel of five experts. In the sensitivity analysis, the authors substituted omeprazole for lansoprazole effectiveness and cost data and found slight improvement in incremental cost effectiveness ratio. Given that the data were available, it would have been informative if a more comprehensive analysis of alternative drug(s) had also been included.

Validity of estimate of costs
Adequate details were given of the sources of unit cost estimates. The estimates of resource use provided by the panel of experts were reported separately from the costs.

Other issues
The conclusions reached by the authors were justified in terms of the sensitivity analysis. However the authors noted that the assumptions used in the analysis bias the analysis against maintenance from the outset. In particular, the exclusion from the analysis of recurrences other than those associated with endoscopic disease, for which all patients with symptoms eventually seek treatment, and the consequences associated with treating Barrett’s esophagus or peptic strictures, may make initial maintenance therapy look less attractive than might have been expected. There may be significant differences both in unit costs and treatment practices between countries, so that relevant costs may fall outside the range used in the sensitivity analysis.

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