Proton pump inhibitors or histamine-2 receptor antagonists for the prevention of recurrences of erosive reflux esophagitis: a cost-effectiveness analysis

Harris R A, Kuppermann M, Richter J E

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
Proton pump inhibitors and Histamine-2 receptor antagonists in the prevention of recurrences of erosive reflux esophagitis.

Type of intervention
Secondary prevention.

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

Study population
Hypothetical patients with symptomatic erosive reflux esophagitis who have healed with a PPI and have no recent peptic strictures, gastric or duodenal ulcers, or histories of alcohol or drug abuse.

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

Dates to which data relate
The effectiveness data were derived from studies previously published between 1994 and 1996. The date for the resource use data was not reported. The price year was 1995.

Source of effectiveness data
Effectiveness estimates were based on a review of randomised controlled trials, on case series 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 monthly recurrence probabilities and the probability of symptomatic recurrences. Due to the lack of evidence in the literature with respect to this probability, the authors created a parameter to translate the probability of endoscopic recurrences (published in the literature) into the probability of symptomatic recurrences.

Study designs and other criteria for inclusion in the review
Recurrence probabilities were based on the results of three randomised controlled trials.

**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**
3 randomised controlled trials.

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

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

**Results of the review**
The annual probability of an endoscopic recurrence was 21% for patients on PPI maintenance equivalent to lansoprazole 15 mg qd and 14% for those on PPI maintenance equivalent to 30 mg qd. The annual probability of an endoscopic recurrence was 51% and 61% for patients on H2RA maintenance equivalent to ranitidine 300 mg bid, and 150 mg bid, respectively.

**Methods used to derive estimates of effectiveness**
The effectiveness estimates were also 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 a daily dose of 45mg lansoprazole. Hence, the probability of endoscopic recurrence is 0%. The physician panel estimated that 81% of endoscopic recurrences would be symptomatic, and that the time from recurrence of symptoms to treatment initiation and then symptom resolution would be 3.9 weeks.

**Measure of benefits used in the economic analysis**
The measures of benefit were the number of symptomatic recurrences of erosive reflux esophagitis prevented and quality-adjusted life years (QALYs) gained. The Markov model was used to estimate the expected number of recurrences per year under each of the maintenance strategies. In the cost-utility analysis, the authors determined the extent to which patients must be bothered by symptoms of esophagitis for the PPI strategy to be cost-effective, using $50,000 per QALY gained as a cost-effectiveness threshold.

**Direct costs**
Costs were not discounted given the short time period of the study (less than 1 year). Quantities and costs were not reported separately. Direct costs included treatment costs and drug costs. The quantity/cost boundary adopted was that of the health service. Total costs were estimated using a model. Average wholesale prices and managed care prices were separately used for unit drug costs, Medicare figures were used for laboratory costs and mean hospital accounting costs were used for outpatients facility costs. Estimates for resource use were obtained from the physician panel and unit costs were obtained from published US statistics. The price year was 1995.

Statistical analysis of costs
Not reported.

Indirect Costs
Not included.

Currency
US dollars ($).

Sensitivity analysis
One-way sensitivity analysis was undertaken on recurrence probabilities, the time from symptom recurrence to treatment initiation and costs. A two-way sensitivity analysis was conducted to examine how both the difference in drug acquisition costs between PPIs and H2RAs and the quality of life impact of recurrences affect cost-effectiveness.

Estimated benefits used in the economic analysis
The provision of maintenance PPI leads to 0.151 recurrences over the course of a year. The provision of high-dose and standard dose H2RA leads to 0.469 and 0.549 recurrences over the course of a year.

Cost results
The annual cost was estimated to be $1,360 for PPI, $2,047 for high-dose H2RA, and $1,337 for standard dose H2RA.

Synthesis of costs and benefits
Since high-dose H2RA is less effective and more costly than PPI for most drug cost scenarios, only PPI and standard dose H2RA were compared in the economic analysis. Using average wholesale prices and managed care costs for PPI and standard dose H2RA (ranitidine), the marginal cost-effectiveness of PPI versus H2RA was $59 and $52 per recurrence prevented, respectively. Using average wholesale prices and government procurement prices for PPI and H2RA (cimetidine), the marginal cost-effectiveness was $412 and $677 per recurrence prevented, respectively. Using market-weighted average managed care costs for PPI and H2RA, the marginal cost-effectiveness was $335 per recurrence prevented. The decrement in quality of life due to esophagitis for PPI to be cost-effective relative to the standard-dose H2RA at a cost-effectiveness threshold of $50,000 per QALY gained varied between 1.4 and 18.2 for the various drug cost scenarios. The PPI strategy is cost-effective when the drugs are similar in price for PPI and standard-dose H2RA and/or recurrences of esophagitis significantly bother patients.

Authors' conclusions
The high-dose H2RA is not preferred in terms of either costs or benefits. The PPI strategy appears cost-effective relative to the standard-dose H2RA strategy in the following situations: when patients are significantly bothered by esophagitis and in institutional settings where the difference in drug costs between PPIs and H2RAs is small.
The rationale for the choice of the comparator was clear.

**Validity of estimate of measure of benefit**
The effectiveness data were derived from published studies and expert opinion. Panel information may not reflect the nuances of clinical practice. Therefore, they were subjected to an extensive sensitivity analysis. In the sensitivity analysis omeprazole was substituted for lansoprazole and a slightly improved cost-effectiveness ratio was found. Given that the data were available, it would have been informative if a more comprehensive analysis of alternative drugs had also been undertaken. The authors did not elicit actual utility values from patients who seek treatment for erosive esophagitis. It would have been informative to extend the time frame to, for instance, five years in the sensitivity analysis.

**Validity of estimate of costs**
Adequate details were given of the sources of unit cost estimates and estimates of resource use. Since cost data are specific to the setting, a sensitivity analysis was conducted.

**Other issues**
The two most important variables that determine the cost-effectiveness of PPI relative to standard dose H2RA are quality of life and drug acquisition costs. These variables are likely to vary among patients and across institutional settings, respectively. The assumptions used in the study are likely to bias the analysis against PPI.

**Implications of the study**
The results of the cost-utility analysis should be confirmed by eliciting utility values from patients who seek treatment for erosive esophagitis.

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**
9399748

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
2-Pyridinylmethylsulfinylbenzimidazoles; Anti-Ulcer Agents /economics /therapeutic use; Case-Control Studies; Cost-Benefit Analysis; Decision Support Techniques; Delphi Technique; Drug Costs; Enzyme Inhibitors /economics /therapeutic use; Esophagitis, Peptic /economics /prevention & control; Follow-Up Studies; Gastroenterology; Histamine H2 Antagonists /administration & dosage /economics /therapeutic use; Humans; Lansoprazole; Medicare /economics; Omeprazole /analogs & derivatives /economics /therapeutic use; Probability; Proton Pump Inhibitors; Quality of Life; Randomized Controlled Trials as Topic; Ranitidine /economics /therapeutic use; Recurrence; Relative Value Scales; Sensitivity and Specificity; United States; Value of Life