Randomised controlled trial of omeprazole or endoscopy in patients with persistent
dyspepsia: a cost-effectiveness analysis

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
Empirical treatment with omeprazole in patients with persistent dyspeptic symptoms, and, in the case of symptom relapse, serological screening for Helicobacter pylori (H. pylori) infection followed by eradication therapy in seropositive patients.

Type of intervention
Diagnosis and treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with persistent dyspeptic symptoms. Eligible patients were those aged 18 years or older, with persistent dyspeptic symptoms of sufficient severity, as judged by the general practitioner, to justify diagnostic upper gastrointestinal endoscopy. The excluded patients were those using proton pump inhibitors before recruitment, signs or suspicion of malignancy (food transit complaints, weight loss, anaemia, vomiting of blood), treatment with NSAIDs, previous gastrointestinal surgery, pregnancy or lactation, chronic alcoholism or drug abuse, or lack of motivation.

Setting
Hospital. The economic analysis was carried out in the Netherlands.

Dates to which data relate
Effectiveness and resource use data corresponded to patients enrolled in the study between January 1995 and July 1997. The price year was 1995.

Source of effectiveness data
The evidence for the final outcomes was based on a single study.

Link between effectiveness and cost data
Costing was conducted prospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were used to determine the sample size (the calculations were based on the data from the authors’ decision analysis according to which, 23 patients had to be included in each group with a power of 90% to detect a true difference between the strategies of 38 symptom-free days). A total of 84 patients were randomly assigned to either the
empirical group (n=42) with a mean age of 43 (range: 39-47) years, or to the conventional group (n=42). Four patients from the conventional group were excluded from the analysis because of protocol violations, and the remainder (n=38) had a mean age of 44 (range: 40-48) years.

Study design
This was a randomised, controlled trial, carried out in a single centre. The mean duration of the follow-up was 266 (95% CI: 226-307) days in the empirical group versus 255 (95% CI: 209-302) days in the conventional group. The empirical group had no loss to follow-up versus 4 patients in the conventional group. A computer-generated randomisation list was used to assign patients to the study groups. Patients were selected by 48 general practitioners in the south-eastern part of the Netherlands from about 110,000 people. In order to keep the workload low it was agreed to include only two patients per general practitioner.

Analysis of effectiveness
The principle used in the analysis of effectiveness appears to have been treatment completers only. The health outcomes were proportion of patients who underwent endoscopy, days without dyspeptic symptoms (symptom-free days), the number of malignancies found, and quality of life (as assessed at the beginning of the study period, at 10 weeks, and at 12 months using the Dartmouth COOP Functional Health Assessment Charts/WONCA). The patients were asked to record daily absenteeism from work and symptoms, i.e. epigastric pain or discomfort, heartburn, postprandial fullness, regurgitation or other relevant symptoms for 1 year. A special calender was developed to record these items. The calender sheets for the previous month were collected at the beginning of every new month to avoid any retrospective data entry. The study groups were comparable in terms of clinical and demographic characteristics.

Effectiveness results
The effectiveness results were as follows:

The proportion of patients who underwent endoscopy was 31% in the empirical group versus 100% in the conventional group.

The mean symptom-free days were 166 (95% CI: 128-204) in the empirical group and 159 (95% CI: 119-198) in the conventional group.

The malignancies found were 2 cases in the empirical group versus 1 case in the conventional group.

The mean quality of life at 10 weeks was 16 (95% CI: 14-17) in the empirical group versus 18 (95% CI: 16-20) in the conventional group.

The corresponding values at 1 year were 15 (95% CI: 13-17) in the empirical group versus 16 (95% CI: 14-17) in the conventional group.

Clinical conclusions
The study demonstrated that an empirical treatment strategy with the proton pump inhibitor omeprazole resulted in equal clinical effects with a conventional treatment strategy.

Measure of benefits used in the economic analysis
The benefit measure was days without dyspeptic symptoms (symptom-free days).

Direct costs
Only cost due to depreciation of the endoscopy equipment was discounted. Some quantities were reported separately from the costs. Cost items were reported separately. Cost analysis covered the costs of consultations, diagnostics,
medication, and non-medical costs including transportation, and out-of-pocket costs. The perspective adopted in the cost analysis was that of society. The patients were asked to record daily out-of-pocket costs. Costs of gastrointestinal endoscopy were based on the real costs from the study institution. Overhead costs and personnel costs were included in the cost analysis. Charges for laboratory tests were used as estimates for the costs of histological assessment of the biopsies and H. pylori serology. Retail prices were used for calculating the cost of medication per day. The price year was 1995.

Statistical analysis of costs
95% confidence intervals were reported for cost items.

Indirect Costs
Indirect costs were not discounted due to the short time frame of the cost analysis. The patients were asked to record daily absenteeism from work. Quantities related to days off work were reported separately. The average cost per lost work day was used to calculate the monetary value of days off work. The price year was 1995.

Currency
Dutch guilders (Dfl). The conversion rate using the 1995 mean exchange rate was Dfl 1 = US$0.62.

Sensitivity analysis
A sensitivity analysis was performed to assess the impact of varying the cost figure of upper gastrointestinal endoscopy on the mean cost of the two strategies.

Estimated benefits used in the economic analysis
The mean days without dyspeptic symptoms (symptom-free days) were 166 (95% CI: 128-204) in the empirical group and 159 (95% CI: 119-198) in the conventional group.

Cost results
The average medical cost was $284 in the empirical group versus $491 in the conventional group. Non-medical cost items were reported individually.

Synthesis of costs and benefits
The incremental and average costs for a symptom-free day per patient were calculated as the measures of cost-effectiveness. Cost-effectiveness ratios were stratified in terms of time interval and age. The average cost for a symptom-free day per patient was $1.7 in the empirical group versus $3.1 in the conventional group. The corresponding values in terms of time intervals were $1.6 in the empirical group versus $2.8 in the conventional group for greater than 60 days; $1.5 in the empirical group versus $2.6 in the conventional group for greater than 180 days with an incremental cost-effectiveness ratio of $2.5 for the conventional strategy as compared to the empirical therapy; $1.5 in the empirical group versus $2.6 in the conventional group for greater than 300 days; $1.7 in the empirical group versus $4.7 in the conventional group for age less than 45 years; and $1.8 in the empirical group versus $2.2 in the conventional group for age greater than 45 years, leading to an incremental cost-effectiveness value of $4.1 for the conventional strategy as compared to the empirical therapy. The empirical strategy was the dominant strategy in cases where incremental cost-effectiveness ratios were not reported.

Authors' conclusions
The empirical drug treatment strategy in patients with persistent dyspeptic symptoms resulted in 69% fewer diagnostic endoscopies with lower medical costs and equal effectiveness in the first year, compared to prompt endoscopy followed by directed medical treatment.
CRD COMMENTARY - Selection of comparators
A justification was given for the choice of the comparator (prompt endoscopy followed by directed medical treatment as the conventional treatment strategy). You, as a database user, should consider whether this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness results are likely to be internally valid given the randomised nature of the study design, and the power calculations performed. However, the analysis of effectiveness appears to have been based on the principle of treatment completers only rather than intention-to-treat. The study groups were comparable in terms of baseline characteristics. The study sample appears to have been representative of the study population.

Validity of estimate of measure of benefit
The estimate of benefits was obtained directly from the effectiveness analysis. The choice of estimate appears to be justified.

Validity of estimate of costs
Some quantities were reported separately from the costs and adequate details of methods of cost estimation were given. The authors adopted a societal perspective in the study, which was reflected in the cost analysis. In cost calculations, some cost items were based on true costs while others represented charge data. The effects of alternative procedures on indirect costs were addressed. The price year was specified. Statistical analyses were performed on some resource use data and cost data. However, statistical tests comparing costs were not performed. Costs might not be generalisable outside the Dutch setting.

Other issues
The authors' did not fully account for the uncertainties in the data, as it appears that only limited sensitivity analyses were performed on the cost of upper gastrointestinal endoscopy. Some comparisons were made with other studies. The study sample was representative of patients with persistent dyspeptic symptoms and this was acknowledged in the authors' comments. The authors acknowledged the following potential problems with empirical treatment: delay in diagnosis; and the chance of missing pre-malignant conditions such as Barrett's mucosa.

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MeSH
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