Decision analysis of histamine H2-receptor antagonist maintenance therapy versus Helicobacter pylori eradication therapy: a randomised controlled trial in patients with continuing pain after duodenal ulcer

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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
Use of Helicobacter pylori (H. pylori) eradication therapy (for 14 days) comprising omeprazole 20 mg twice daily plus amoxicillin 500mg 4 times daily plus metronidazole 400mg 3 times daily (OAM) or omeprazole 20 mg twice daily plus clarithromycin 500mg 3 times daily (OC) if allergic to penicillin, in managing/controlling symptoms in patients with chronic ulcer.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with chronic duodenal ulcer confirmed as H. pylori-positive, free from active ulceration and who were receiving maintenance H2-receptor antagonist therapy.

Setting
General practice and hospital clinic. The economic study was carried out in the UK (Scotland).

Dates to which data relate
Effectiveness and resource use data were collected between November 1994 and May 1996. The ranges of values for some clinical measures were obtained from studies published in 1993 and 1997. The price year was 1996.

Source of effectiveness data
Effectiveness data were derived from a single study and from a review of the literature.

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

Study sample
Power calculations were not used to determine the sample size. The study sample consisted of 119 patients randomly allocated to either the eradication group (n=61) with a mean age of 56.6 (95% CI: 53.3-59.8) years or to the maintenance group (n=58) with a mean age of 53.8 (95% CI: 50.9-56.6) years.
Study design
The study was a randomized, non-blind, controlled trial, carried out in general practices (number not given) and a hospital clinic. The duration of the follow up was 1 year. The number of patients lost to follow-up or dead at 1-year follow-up was 5 in the eradication group and 6 in the maintenance group. Blinding was not used because of anticipated difficulties expected to lead to a high loss to follow-up rate.

Analysis of effectiveness
The principle used in the analysis of effectiveness was both intention to treat and treatment completers only (per protocol). The clinical outcome measures were:

(1) successful per protocol H. pylori eradication,

(2) percentage of patients treated with OAM who were free of symptoms on per protocol basis,

(3) percentage of patients treated with eradication therapy who were not receiving acid-suppressing therapy at the end of 1 year on intention-to-treat basis, and

(4) percentage of patients treated with the maintenance therapy needing no further investigation on per protocol basis.

Effectiveness results
The results were as follows:

(1) successful per protocol H. pylori eradication, 100%;

(2) the percentage of patients treated with OAM who were free of symptoms on per protocol basis, 87% (46/53);

(3) percentage of patients treated with eradication therapy who were not receiving acid-suppressing therapy at the end of 1 year on intention-to-treat basis, 80.3% (49/61); and

(4) percentage of patients treated with the maintenance therapy needing no further investigation on per protocol basis, 98% (51/52).

1 patient with active ulcer at endoscopy required pump inhibitor and maintenance therapy. Probability of being treated with omeprazole/clarithromycin was 5% (3/56). Probability of being treated with OC and eradicated at first attempt and free from symptoms was 100% (3/3). These data were used as the principal variables to populate the decision tree with probabilities for each outcome.

Clinical conclusions
(This) study showed that about 13% of patients treated per protocol with eradication therapy still remained symptomatic and were still dependent on acid-suppressing therapy.

Modelling
A decision tree was developed employing the software package Decision Analysis, by TreeAge (DATA) version 3, to assess the costs and effects associated with each strategy in controlling the ulcer symptoms based on 1-year and 5-year follow-up.

Outcomes assessed in the review
The range of values for the following measures were used as inputs in the sensitivity analysis: percentage of patients treated with eradication therapy who were free of symptoms, and percentage of patients treated with the maintenance therapy needing no further investigation.
Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
A total of 4 studies were included in the review.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The ranges of values were as follows: percentage of patients treated with OAM who were free of symptoms, 60%-90%; and percentage of patients treated with the maintenance therapy needing no further investigation, 70%-98%.

Measure of benefits used in the economic analysis
No summary benefit measure was identified in the economic analysis, and only separate clinical outcomes were reported. It seems that the authors proceeded with the implicit assumption of equal effectiveness for the two health strategies involved, thus turning the study into a cost-minimisation analysis.

Direct costs
Costs of maintenance therapy were discounted. Some quantities were reported separately from the costs. Cost items were reported separately. Cost analysis covered the costs of drugs, urea breath test (UBT), endoscopy, and the physician's time. The follow-up considered for the study was 1 and 5 years. The perspective adopted in the cost analysis was that of the health authorities. The resource utilisation was based on protocol-defined procedures and trial experience. The sources of cost data were the study hospital and the British National Formulary (for drug costs). The ranges of values (used in sensitivity analysis) for some cost components were obtained from the literature published between 1995 and 1997. The date of the price data was 1996.

Indirect Costs
Not considered.

Currency
UK pounds sterling (\).
Sensitivity analysis
A series of one-way sensitivity analyses was performed on most parameters of the model based on a 1-year and 5-year follow-up time frame. Threshold values were identified for the sensitive parameters.

Estimated benefits used in the economic analysis
Not applicable. See effectiveness results above.

Cost results
The discount rate was 5%. The expected cost of the eradication therapy over 1-year follow-up was 168 versus 210 for the maintenance therapy. Without the cost of UBT, the eradication therapy was associated with expected costs of 103 for 1 year, 140 for 2 years, and 239 for 5 years. The corresponding values for the maintenance therapy were 210 for 1 year, 214 for 2 years, and 224 for 5 years.

Synthesis of costs and benefits
Costs and benefits were not combined. The threshold value (in terms of the percentage of patients treated with eradication therapy who were free of symptoms) for the eradication therapy to cease to be the least costly strategy in the framework of 1-year and 5-year model was 60%.

Authors’ conclusions
If dyspepsia persists long term, H. pylori eradication treatment may not be the least-cost option for patients with duodenal ulcer.

CRD COMMENTARY - Selection of comparators
A justification was given for the choice of the comparator (maintenance therapy). It represented the conventional therapy in the context in question. 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 benefit
The internal validity of the estimates of effectiveness is likely to be high due to the randomized design of the study used as the main source of the effectiveness data. It seems that the authors proceeded on the implicit assumption of equal effectiveness for the two health strategies involved and, thus, turned the study into a cost-minimisation analysis. The effectiveness ranges obtained from the literature were not based on a systematic literature review and quality assessment of the studies included in the review.

Validity of estimate of costs
Quantities were not fully reported separately from the costs. Adequate details of methods of cost estimation were given.

Other issues
Given the randomized design of the study and the sensitivity analyses performed, the authors’ conclusion appear to be justified. The issue of generalisability to other settings or countries was not fully addressed despite discussing the limitation of the study with respect to not following a blinded design, and the study population not being at first diagnosis of duodenal ulcer. Appropriate comparisons were made with other studies.

Implications of the study
It was reported that some health authorities are already experiencing this scenario (increasing drug costs (and
eradication therapy not being the least costly option) due to adoption of eradication therapy as a management strategy in chronic duodenal ulcer). The authors speculated that this will become even more evident with time.

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