Cost-effectiveness of Helicobacter pylori "test and treat" for patients with typical reflux symptoms in a population with a high prevalence of H. pylori infection: a Markov model analysis

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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
The study compared four initial management strategies for patients presenting with typical reflux symptoms in a population with high prevalence of Helicobacter pylori (HP) infection. The strategies were no therapy, empirical proton-pump inhibitor (PPI) therapy, HP "test-and-treat", and initial endoscopy.

Type of intervention
Treatment and secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The population comprised a hypothetical cohort of patients with typical reflux and high prevalence of HP infection who were presenting with weekly attacks of heart-burn or acid regurgitation. The exclusion criteria included a history of peptic ulcer or gastric surgery, the administration of non-steroidal anti-inflammatory drugs or PPIs during the previous 4 weeks, and dyspepsia as the predominant symptom. A further exclusion criterion was the presence of alarm symptoms such as weight loss, odynophagiam, dysphagiam, vomiting, gastrointestinal bleeding and gastric outlet obstruction.

Setting
The setting was secondary care. The economic study was carried out in Hong Kong, China.

Dates to which data relate
The studies providing the effectiveness evidence dated from 1994 to 2004. The cost data were derived from 2002 to 2003. The price year was not reported.

Source of effectiveness data
The evidence was derived from a review or synthesis of completed studies augmented, when necessary, with estimates based on authors' assumptions.

Modelling
A Markov (state transition) decision model was used to simulate the clinical outcomes and health care resource use for a cohort over a 12-month period. The cycle length was 1 month. The health states in the model included four exclusive underlying HP and PUD-related co-morbidities. Specifically, HP-related PUD, HP infection without PUD, PUD without HP infection, and the absence of both PUD and HP infection.
Outcomes assessed in the review
The parameters used in the model included:

- the prevalence of HP infection,
- the prevalence of PUD in HP-infected patients,
- the prevalence of PUD in non HP-infected patients,
- the sensitivity and specificity of the HP C-urea breath test,
- the eradication rate of triple therapy,
- the ulcer-healing rate of triple therapy,
- the risk of ulcer complications per year,
- the monthly transition probabilities for active and maintenance therapy for patients with gastroesophageal reflux disease (GERD), and
- odds ratios of symptomatic response and relapse to PPI in GERD patients with PUD.

Base-case values, ranges for the sensitivity analysis, and references were reported for all parameters.

Study designs and other criteria for inclusion in the review
No inclusion criteria for a review of any of the parameters were reported. However, the study designs used by the authors included systematic reviews, clinical trials, and primary studies of varying design.

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
The authors reported that approximately 34 primary studies provided the effectiveness evidence.

Methods of combining primary studies
The method of combining the studies was not clear.

Investigation of differences between primary studies
Not reported.

Results of the review
The following parameters were used in the model:

- 46% prevalence of HP infection,
- 37% prevalence of PUD in HP-infected patients,
- 1.6% prevalence of PUD in non HP-infected patients,
- 98% sensitivity and 97% specificity of the HP C-urea breath test,
- 91% eradication rate of triple therapy,
- 89% ulcer-healing rate of triple therapy, and
- 1.5% risk of ulcer complications per year.

The monthly transition probability for active therapy and response to standard dose was 0.49 in GERD patients, 0.46 in HP-negative GERD patients, and 0.50 in HP-positive GERD patients.

The monthly transition probability for active therapy and response to high dose was 0.55 in GERD patients.

The transition probability for maintenance therapy and symptomatic relapse on low-dose PPI was 0.032 in GERD patients, 0.079 in HP-negative GERD patients, and 0.014 in HP-positive GERD patients.

The transition probability for maintenance therapy and symptomatic relapse on standard-dose PPI was 0.045 in HP-negative GERD patients.

Probabilities of occurrence of reflux symptoms were 0.05 after eradication therapy and 0.04 without eradication therapy.

In GERD patients with PUD, the odds ratio was 0.8 for symptomatic response to PPI and 2.0 for symptomatic relapse to PPI.

**Methods used to derive estimates of effectiveness**

Some authors' assumptions were necessary to facilitate the simulation.

**Estimates of effectiveness and key assumptions**

Key model assumptions were reported in full detail in the paper. They included:

- in the no therapy arm, patients without PUD remained symptomatic throughout the whole study period and received no therapy;
- those patients with PUD only received treatment when ulcer complications occurred, or they remained symptomatic and received no therapy;
- after an ulcer complication was treated, the patient was assumed to be in remission for the rest of the study period;
- for the three management arms, the patient might have experienced reflux symptoms or have been in remission every month during the 12-month time horizon; and
- the occurrence of an ulcer complication was assumed to occur at the midpoint of the study period, and the treatment duration of an ulcer complication was assumed to be one month.

**Measure of benefits used in the economic analysis**
The primary clinical outcome for each study arm was the percentage of PUD patients treated. The total number of symptom-free patient-years gained was also estimated.

**Direct costs**
The cost of managing patients with GERD during symptomatic and symptom-free states and the cost of treating ulcer complications were retrieved from literature. The cost categories included were clinical visits, hospitalisations and diagnostic tests. The costs associated with selected resources, including labour costs, were approximated using charges for public hospitals listed in the Hong Kong Gazette. The drug cost was based on a local, specific acquisition cost. Discounting was appropriately not carried out since the costs were incurred during a 12-month period. The quantities and the costs were not analysed separately. The quantities and the costs were derived through modelling. The price year was not reported.

**Statistical analysis of costs**
No statistical analysis of the costs was reported.

**Indirect Costs**
In line with the perspective adopted, no indirect costs were included.

**Currency**
US dollars ($). No conversion rate was reported.

**Sensitivity analysis**
A one-way sensitivity analysis was carried out to examine the robustness of the model and to determine the impact of uncertainty in the base-case analysis. The sensitivity analysis was conducted with all the clinical probabilities and direct medical costs associated with the three study arms. Either the upper and lower limits of the variable (as derived from the literature) were used to provide the ranges for the analysis, or a range of +/- 20% of the base-case value was used.

**Estimated benefits used in the economic analysis**
Compared with no therapy, the incremental proportion of healed ulcers was 71.1% for the empirical PPI therapy strategy, 97.2% for the HP "test and treat" strategy, and 98.5% for the initial endoscopy strategy.

The symptom-free patient-years were 0.001 for the no therapy strategy, 0.714 for the empirical PPI therapy strategy, 0.637 for the HP "test and treat" strategy, and 0.685 for the initial endoscopy strategy.

**Cost results**
The cost per patient was $14 for the no therapy strategy, $1,548 for the empirical PPI therapy strategy, $1,742 for the HP "test and treat" strategy, and $1,784 for the initial endoscopy strategy.

Compared with no therapy, the incremental cost per patient was $1,534 for the empirical PPI therapy strategy, $1,728 for the HP "test and treat" strategy, and $1,770 for the initial endoscopy strategy.

**Synthesis of costs and benefits**
Comparing each strategy individually with the no therapy strategy, the incremental cost-effectiveness ratio (ICER) per ulcer healed was $1,778 for the HP "test and treat" strategy, $1,797 for the initial endoscopy strategy, and $2,158 for the empirical PPI therapy strategy.

The sensitivity analysis showed that the model was generally robust to variations in all variables. The exception was the
prevalence of HP infection among patients presenting with typical reflux symptoms, which was identified as impacting on the ICER of the HP "test and treat" strategy.

Authors’ conclusions
The analysis showed that the Helicobacter pylori (HP) "test and treat" strategy was associated with the lowest incremental cost-effectiveness ratio (ICER). This suggested that it was more cost-effective than the empirical proton-pump inhibitor (PPI) therapy and endoscopy for treating undiagnosed peptic ulcer disease (PUD) in Asian patients with a high prevalence of HP infection.

CRD COMMENTARY - Selection of comparators
The choice of the comparator was explicitly justified, mainly because the initial management approach for patients with typical reflux symptoms but no alarm symptoms is controversial and also because the early role of endoscopy in these cases is not known. The choice of these strategies was justified on the basis of published literature and standard clinical practice. You should judge whether these strategies are relevant in your own setting, or whether other comparators from other therapeutic strategies could have been relevant as well.

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature had been undertaken. Although this is common practice with models, it does not always ensure that the best data available are used. The authors appear to have used data from the available studies selectively. It was positive that clinical trials and systematic reviews were used to derive most input parameters and that the authors made few assumptions, but the selective use of studies can be problematic. The estimates were investigated in sensitivity analyses using ranges derived from the included literature. However, the lack of reporting on the methods used to identify and include the studies from which the model parameters were derived makes it difficult to ascertain the overall validity of the study findings.

Validity of estimate of measure of benefit
The authors used symptom-free patient-years and healed ulcers as the measures of benefit. These chosen measures are context specific and do not enable comparisons across health technologies as they can only be compared with similar studies.

Validity of estimate of costs
The perspective of the analysis was clearly reported. As such, it would appear that all the relevant costs were included. The costs were taken from published sources and, although no statistical analysis of the costs was undertaken, sensitivity analyses of the direct costs were conducted and were reported to have assessed the robustness of the estimates used. Discounting was appropriately not carried out since the time horizon was only 12 months. The price year was not reported, which will hamper any future reflation exercises.

Other issues
The authors made appropriate comparisons of their findings with those from other studies and found them to be similar. The authors' conclusions reflected the scope of the analysis. The authors discussed the issue of generalisability and stated that their model was designed to allow other countries or health systems to populate the model using their own data. They also highlighted limitations to their analysis. For example, the fact that some input parameters were derived from studies conducted on European and American populations and applied to an Asian population. In addition, the authors specifically stated that because Barrett's oesophagus is uncommon in the Asian population it was not included in the model. Another important limitation was stating that incremental cost-effectiveness ratios were reported, whereas the mean cost-effectiveness of each strategy was compared and no incremental comparisons were reported among them.
Implications of the study
In this particular setting, both test-and-treat or initial endoscopy appear to have been cost-effective. However, the limitations highlighted should be considered. The authors made no further recommendations for research.

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