Diagnosis of Helicobacter pylori after triple therapy in uncomplicated duodenal ulcers: a cost-effectiveness 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 health technologies in the study were two different strategies for the diagnosis of Helicobacter pylori (H. pylori) in patients with uncomplicated duodenal ulcer who had already had H. pylori eradication treatment:

systematic performance of post-treatment urea breath test and new treatment if positive; and
clinical follow-up and then 13C-urea breath-test if dyspeptic symptoms recurred and eradication treatment if the test was positive.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised uncomplicated duodenal ulcer patients who had received 7-day triple therapy, already tested positive for H. pylori infection and treated with eradication therapy (such as omeprazole, clarithromycin, and amoxycillin, (OCA)) for 7-14 days.

Setting
The setting was hospital. The economic study was carried out in Spain.

Dates to which data relate
Effectiveness evidence and resource used data were gathered between 1992 and 1999. The price year was 1997.

Source of effectiveness data
The effectiveness data were derived from published studies.

Modelling
A decision tree was devised in order to estimate expected clinical outcomes and costs of a hypothetical cohort of 100 patients in a time horizon of 2 years. The major choice to be made in the decision tree was between 13C-urea breath test systematically performed post-treatment (if positive, the test was followed by a second antibiotic course; after a negative test, patients were clinically followed) and clinical follow-up, followed first by 13C-urea breath test performed only in symptomatic patients and then second line therapy only on positive patients.
Outcomes assessed in the review
The probability values assessed from the literature were OCA cure rate, quadruple (omeprazole, metronidazole, oxytetracycline, and bismuth subcitrate) therapy cure rate, specificity and sensitivity of 13C-urea breath test, persistence of non-ulcer dyspepsia (NUD)/gastro-oesophageal reflux disease (GERD) symptoms after H. pylori cure, duodenal ulcer relapse in H. pylori eradicated, H. pylori re-infection after 2 years, symptoms relapse after failed H. pylori treatment, complication rate after 2 years in non-eradicated patients, cure rate of third line treatment, and relapse rate of GERD and NUD after proton pump inhibitor (PPI) treatment.

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
Fifteen primary studies were used as sources of the probability values used as input parameters in the model. Several other references were taken into account to formulate assumptions necessary to build the decision tree.

Methods of combining primary studies
The method of combination of primary studies was not reported. However, many estimates were derived from a single study and not combined.

Investigation of differences between primary studies
Not reported.

Results of the review
The results of the review were as follows:

The OCA cure rate was 86%.

The quadruple therapy cure rate was 87%.

The specificity and sensitivity of 13C-urea breath test were 88% (specificity) and 94% (sensitivity).

The persistence of non-ulcer dyspepsia (NUD)/GERD symptoms after H. pylori cure was 20%.

The duodenal ulcer relapse in H. pylori eradicated was 6%.

The rate of H. pylori re-infection at 2 years was 4%.

The symptoms relapse rate after failed H. pylori treatment was 90%.
The complication rate after 2 years in non-eradicated patients was 4.5%.

The cure rate of third line treatment was 70%.

The relapse rate of GERD and NUD after proton pump inhibitor (PPI) treatment was 30%.

**Measure of benefits used in the economic analysis**
The global cure rate of H. pylori infection was used as benefit measure obtained from the decision model.

**Direct costs**
Discounting was not relevant because costs occurred over a period of 2 years. Quantities and costs were not reported separately. The cost/resource boundary adopted was that of the hospital. The analysis included costs of quadruple therapy, PPI, 13C-urea breath test, endoscopy and histology, endoscopy and culture, complications, office visits, H2-blocker, third-line treatment, and cost of PPI maintenance. Costs were estimated for two different settings: low-cost area (Spain) and high-cost area (US). The estimation of costs was based on actual data from the Catalan Public Health Service for the low-cost setting and on data from two published study for the high-cost setting. Resource use data were derived from studies published between 1992 and 1999. The price year was 1997.

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

**Indirect Costs**
Indirect costs were not directly accounted for in the analysis, due to the difficulty of estimation. However, it was assumed that indirect costs increased in parallel with the number of clinical visits and procedures, therefore, costs of clinical visits were increased in the sensitivity analysis.

**Currency**
Euros (EUR) and US dollars ($).

**Sensitivity analysis**
Sensitivity analyses were carried out to investigate the robustness of the model results. A very wide range of values of both probability assumptions and cost estimates were used in one-way, two-way, and three-way sensitivity analyses. A worst-case scenario for baseline assumptions was also considered. The ranges used for sensitivity analyses were derived from the published literature.

**Estimated benefits used in the economic analysis**
The global cure rate of H. pylori infection was 99.2% in the 13C-urea breath test branch and 98% in the clinical follow-up branch.

**Cost results**
The cost results were as follows:

In the low-cost area, the cost was EUR 63 (range used in the sensitivity analysis: 87 - 39) for quadruple therapy, EUR 33 (range: 58 - 10) for 4-week PPI, EUR 40 (range: 126 - 20) for 13C-urea breath test, EUR 42 (range: 150 - 30) for endoscopy and histology, EUR 80 (range: 160 - 30) for endoscopy and culture, EUR 902 (range: 1,800 - 400) for complications, EUR 30 (range: 60 - 19) for office visits, EUR 20 (range: 40 - 10) for 4-week H2-blocker, EUR 65 (range: 125 - 30) for third-line treatment, and EUR 400 (range: 696 - 120) for PPI maintenance.
In the high-cost area, the cost was $70 (range used in the sensitivity analysis: 87 - 40) for quadruple therapy, $77 (range: 91 - 30) for 4-week PPI, $231 (range: 300 - 50) for 13C-urea breath test, $595 (range: 1,000 - 250) for endoscopy and histology, $647 (range: 800 - 300) for endoscopy and culture, $10,035 (range: 20,000 - 2,500) for complications, $44.7 (range: 65 - 20) for office visits, $25 (range: 38 - 19) for 4-week H2-blocker, $100 (range: 200 - 50) for third-line treatment, and EUR 924 (range: 1,092 - 360) for PPI maintenance.

In the low-cost setting, the expected total costs per patient amounted to EUR 197 in the 13C-urea breath test branch and EUR 132 in the clinical follow-up branch.

In the high-cost setting, the expected total costs per patient amounted to $614 in the 13C-urea breath test branch and $340 in the clinical follow-up branch.

Synthesis of costs and benefits
Costs and benefits were not combined. The authors stated that 13C-urea breath test was substantially more expensive than clinical follow-up in both the cost settings. Thus, 13C-urea breath test was not cost-effective compared to clinical follow-up. These results remained unchanged in the sensitivity analyses. The variables that had most influence on the results were efficacy of OCA, sensitivity and cost of 13C-urea breath test, and rate of patients with symptom relapse after failed eradication. Even in the worst possible scenario (50% reduction of cost of 13C-urea breath test and 100% sensitivity and specificity of 13C-urea breath test), clinical follow-up remained cost-effective.

Authors’ conclusions
The authors concluded that 13C-urea breath test after H. pylori eradication therapy was considerably more expensive than re-assessment if symptoms recur, and not necessarily more useful in low-risk patients (with uncomplicated duodenal ulcer). However, it was important to mention that with the clinical follow-up strategy, between 2% and 5% of patients would probably remain not cured and at a limited risk of further complications.

CRD COMMENTARY - Selection of comparators
The rationale for the selection of comparators was clear. The strategies were chosen because they represented different diagnostic and therapeutic approaches to uncomplicated duodenal ulcer. You should consider whether they are widely used technologies in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness measures (model parameters) were not derived from a systematic review of the literature, but from estimations obtained from primary studies which were often not combined. Search methods and criteria that help to ensure the validity of primary studies were not reported. Furthermore, the problems concerning the impact of differences between the primary studies were not addressed or considered in the analysis.

Validity of estimate of measure of benefit
The estimation of benefit (global cure rate) was modelled through a decision tree, which appeared appropriate to simulate the current diagnostic approach to the disease.

Validity of estimate of costs
All the costs relevant to the perspective adopted were included in the analysis. Indirect costs were not calculated directly, but as a proportion of costs of visits. These were then accounted for not in the base case but in the sensitivity analyses. However, the authors stated that indirect costs were likely to be underestimated and their inclusion in the main analysis would have increased the advantage of clinical follow-up over 13C-urea breath test. Furthermore, only limited details relative to the resources used were reported. Greater transparency in the reporting of resource use data may have increased the generalisability of the results obtained.
Other issues
The robustness of the study results was tested by performing a wide variety of sensitivity analyses. The generalisability of the results to other settings was specifically addressed considering two different settings (high- and low-cost areas). The authors made limited but worthwhile comparisons of their findings with those of other studies.

Implications of the study
The analysis suggested that systematic diagnostic strategies for the detection of H. pylori after eradication therapy in uncomplicated duodenal ulcer patients should not be performed routinely. However, the authors highlighted that "the conclusion of this study should be limited to the group of low risk patients defined initially". Indeed, there are several specific situations in which systematic testing is necessary.

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