Pharmacoeconomic comparison of treatments for the eradication of Helicobacter pylori

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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
Eight treatment strategies in the treatment of patients with duodenal ulcer (DU) were analysed:

1. Bismuth, metronidazole and tetracycline for 14 days at daily doses (4 times a day) of 4 (range: 3 - 8) tablets, 1200 (range: 750 - 1500) mg/d, and 2000 (range: 1000 - 2000) mg/day, respectively (BMT);

2. Clarithromycin, metronidazole, and omeprazole or lansoprazole (proton pump inhibitor (PPI)) for 7 days and at doses (twice a day) of 500 (500 - 1000) mg/day, 800 (800 - 1000) mg/day, and 40 or 60 (20-40 or 30-60) mg/day, respectively (CMPPPI);

3. Bismuth, metronidazole and tetracycline for 7 days at doses (4 times a day) of 4 (4-5) tablets, 1500 (1,000-1,600) mg/day, and 2,000 (1,250-2,000) mg/day, respectively, plus omeprazole or lansoprazole (PPI) for 10 days (4 times a day) at 40 or 60 (20-40 or 30-60) mg/day (BMTPPI);

4. Metronidazole, amoxicillin and omeprazole or lansoprazole (PPI) for seven days at doses (three times a day) of 1,200 (800-1,200) mg/day, 1,500 (1,500-2,000) mg/day, and 40 or 60 (20-40 or 30-60) mg/day (MAPPI);

5. Bismuth for 28 days at 4 (2-4) tablets per day, plus metronidazole and amoxicillin for seven days at doses (4 times a day) of 1,200 (750-1,200) mg/day and 1,500 mg/day, respectively (BMA);

6. Clarithromycin, amoxicillin, and omeprazole or lansoprazole (PPI) for 14 days at doses (twice a day) of 1,000 (500-1,500) mg/day, 2,000 mg/day, and 40 or 60 (20-40 or 30-60) mg/day, respectively (CAPPI);

7. Amoxicillin and omeprazole or lansoprazole (PPI) for fourteen days at doses (twice a day) of 2,000 (1,500-3,000) mg/day and 40 or 60 (20-40 or 30-60) mg/day, respectively (APPI);

8. Clarithromycin and omeprazole or lansoprazole for fourteen days at doses (three times a day) of 1500 (1000-1500) mg/day and 40 or 60 (20-40 or 30-60) mg/day, respectively (CPPI).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients aged 16 or older with a diagnosis of Helicobacter pylori infection and either, peptic ulcer, gastritis or nonulcerative dyspepsia.

Setting
Hospital. The economic evaluation was carried out by researchers from San Francisco, California, USA and from...
Farmington, Connecticut, USA based on studies carried out in different countries.

**Dates to which data relate**
The data for the effectiveness study were collected from studies published or reported between 1966 and January 1996. The resources used were based on experts’ opinions and data from 1993. The prices used in the final analysis were from 1995.

**Source of effectiveness data**
The effectiveness data were derived from a synthesis of previously completed studies and estimates based on a decision model and Monte Carlo simulations.

**Modelling**
A decision tree was used in order to estimate the costs and benefits associated with each strategy, for a 1-year time period after drug regimen termination. Five-hundred Monte Carlo simulations were used to deal with uncertainty in all parameters (probabilities of occurrence of health states) and cost values (simultaneously varied).

**Outcomes assessed in the review**
The outcomes assessed were: non-adjusted eradication rate, compliance-adjusted eradication rate, positive test result for Helicobacter pylori, true-positive result, true-negative result, test sensitivity and specificity, DU prevalence, H pylori-true-negative recurrence, H pylori-negative post-eradication recurrence, H pylori-positive post-eradication recurrence, recurrence with H2RA therapy, and ulcer complications.

**Study designs and other criteria for inclusion in the review**
Only prospective studies were included. Additional entry criteria included the following: patients had a "definitive" diagnosis of H. Pylori infection (by laboratory-based assays) with either peptic ulcer disease, gastritis or nonulcerative dyspepsia present; the eradication of H. Pylori was assessed at least 4 weeks after the end of the study treatment; the maximum duration of antibiotic treatment being 2 weeks; doses were restricted to the ranges reported above.

**Sources searched to identify primary studies**
MEDLINE and EMBASE were searched in addition to a manual review of selected bibliographies from papers, abstracts from Gastroenterology, the American Journal of Gastroenterology, and Gut, and "proceedings of H. Pylori-related conferences conducted world-wide through September 1995".

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

**Methods used to judge relevance and validity, and for extracting data**
Not reported. The data were extracted by means of summary statistics from each study.

**Number of primary studies included**
A total of 119 studies was included. There were from 4 to 35 studies included per strategy.

**Methods of combining primary studies**
Meta-analysis. The results were weighted according to sample sizes of the primary studies included.
Investigation of differences between primary studies
Not reported.

Results of the review
The non-adjusted and compliance-adjusted eradication rates (i.e. proportion of total number of patients without recurrences after 1-year) were as follows:

BMT 89% and 82%;
CMPPPI, 89 %, and 85%;
BMTPPPI, 93% and 86%;
MAPPI, 85% and 80%;
BMA, 76% and 70%;
CAPPI, 88% and 84%;
APPI, 71% and 68%;
CPPI, 77% and 72%;
H2RA, 72% for both rates.

Positive test result for Helicobacter pylori, true-positive result, and true-negative result were 90.30%, 99.90%, and 46.50%, respectively. Test sensitivity and specificity were 99% and 96%, respectively. DU prevalence, H pylori-true-negative recurrence, H pylori-negative post-eradication recurrence, H pylori-positive post-eradication recurrence, recurrence with H2RA therapy, and ulcer complications were 95%, 85%, 3%, 73%, 28%, and 2.7%, respectively.

Measure of benefits used in the economic analysis
The measure of benefit used in the economic analysis was ulcer recurrences avoided. A decision tree was used to deal with the uncertainty in the patient's clinical course associated with each strategy during one year of follow-up.

Direct costs
The resource quantities were reported separately from the prices. The cost items were not reported separately. The costs measured were operating costs (initial drug treatment, treatment of recurrences, testing) and complication costs. The national health care system perspective was adopted in the analysis. The resources used were derived mainly from experts' opinions. The (unit) costs were based on actual data. The sources of unit costs were Medicare Physician Fee Schedule (inpatient and outpatient physician services, testing and the "professional component" of the endoscopy), the California Office of Statewide Health Planning and Development (cost of hospitalisations). The former were obtained in 1995 values, whereas the latter were originally published in 1993 prices. The costs were inflated to 1995 figures (prices used in the final analysis) by means of the Prospective Payment System Medicare Hospital Input Price Index.

Indirect Costs
Not considered.

Currency
US dollars ($).
Sensitivity analysis
Costs components and probability values were varied according to reported variations in the sources, for the former, and according to 95% confidence intervals (CI), for the latter. The threshold analysis was performed to identify the cut-off values of costs and success rates at which the strategies adopted are cost saving relative to the comparator. The variability in data was investigated by means of a probabilistic sensitivity analysis and one-way sensitivity analysis.

Estimated benefits used in the economic analysis
For a hypothetical cohort of 100 patients, the expected number of patients without ulcer occurrence at 1 year corresponding to compliance adjusted data, for each strategy, were as follows: BMT, 82; CMPPI, 85; BMTPPI, 86; MAPPI, 80; BMA, 70; CAPPI, 84; APPI, 68; CPPI, 72; H2RA, 72.

Cost results
The expected annual costs per patient were as follows: BMT, $223; CMPPI, $235; BMTPPI, $236; MAPPI, $261; BMA, $297; CAPPI, $339; APPI, $345; CPPI, $410; H2 RA, $425.

Synthesis of costs and benefits
The authors synthesised the costs and benefits for only three strategies (BMT, CMPPI and BMTPPI). The costs were expressed at 1995 prices and represent the costs and benefits over a 1 year time span. The incremental cost per additional ulcer avoidance for CMPPI and BMTPPI with respect to BMT were $325 and $400, respectively. An additional figure could be calculated, corresponding to CAPPI relative to BMT: $5,800. The authors reported an increase in annual cost, for all regimens, of 62% when the complication rate was increased from 2.70% to 10% and a decrease of 23% when set at a 0% value. When the cost of complications was varied from $10,035 (unit cost) across the range of $2,500-$20,000, the costs moved up and down by 23% and 17%, respectively. Despite the variation in costs, the overall cost rank "was robust to the variation of all values". BMTPPI remained the most effective option when the probability of each event was varied across its range. The Monte Carlo simulations showed a consistent dominance of BMT, CMPPI and BMTPPI regimens over the other strategies analysed.

Authors' conclusions
Lower costs and better health outcomes obtain when patients with DU undergo testing for and treatment of H. pylori infection and are treated with all but one (CPPI) of the commonly used antibiotic therapies. Furthermore, the BMT, CMPPI and BMTPPI "may be the preferred regimens to maximise cost-effectiveness in patients who have not received metronidazole previously. If duration of treatment is a concern, the CMPPI and BMTPPI regimens offer the additional advantage of treatment for only one week. The CMPPI regimen has the added advantage of fewer drugs given less frequently than the BMTPPI regimen". For patients with metronidazole-resistance, "the CAPPI regimen is a clear choice over both the APPI and CPPI regimens".

CRD COMMENTARY - Selection of comparators
The reason for the choice of comparators is clear.

Validity of estimate of measure of benefit
The internal validity of the estimate of measure of benefit is likely to be weakened by the fact that the meta-analysis may have included studies other than randomised controlled trials. The differences between studies (international literature search) and how they can affect the final result of the study were not discussed. The authors pointed out that compliance values differing from those used in this study could change the conclusions reached.

Validity of estimate of costs
Resource quantities were reported separately from the prices. Adequate details of the methods of cost estimation were given. Given the perspective of the analysis (the US national health care system), no relevant costs were omitted.
Other issues
The authors' conclusions were justified, given the uncertainties in the data. The generalisability of the results was partially addressed, given the comprehensive sensitivity analysis performed, but it was not discussed in detail. Comparisons were made with other studies (two) supporting the results found by the authors.

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Other publications of related interest

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