'Best practice' for Helicobacter pylori eradication in the primary care setting

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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
Nine proton-pump inhibitor-based (PPI-based) triple therapy regimens for the eradication of Helicobacter pylori (H. pylori) infection causing dyspepsia were studied. The regimens incorporated five branded PPIs (rabeprazole, esomeprazole, pantoprazole, lansoprazole and omeprazole) and four generic omeprazole preparations, in combination with the antibiotics amoxicillin and clarithromycin. Clarithromycin and metronidazole were used in second-line eradication therapies when applicable.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The patient population studied included Irish patients in receipt of triple therapy for H. pylori eradication, according to the General Medical Services (GMS) prescribing database.

Setting
The setting was primary care. The economic study was carried out in the Republic of Ireland.

Dates to which data relate
The effectiveness evidence and resource use data were drawn from patients in receipt of therapy during 2002, who were followed up for 12 months. The prices dated from 2003.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
It appears that the costing has been carried out retrospectively on the same sample of patients as that used in the effectiveness analysis.

Study sample
All 2,229 patients with a record of receiving triple therapy during 2002 were included in the study and were followed up for a 12-month period. The most frequently prescribed triple regimen included lansoprazole (679 or 30% of patients), while rabeprazole was least frequently used (110 or 5% of patients). A total of 573 patients received esomeprazole, 295 received pantoprazole and the remaining 572 patients received omeprazole (branded or generic).
Study design
This was a retrospective database study that relied on a prescribing database for its effectiveness estimation.

Analysis of effectiveness
The probability of each treatment outcome (further triple therapy, maintenance PPI/H2 receptor antagonist therapy, or no therapy) was determined from the GMS prescribing database. The proportion of patients requiring no further therapy was deemed asymptomatic and displayed successful eradication.

Effectiveness results
Of the 2,229 patients in the study, 966 (43%) patients did not require further anti-ulcer medications in the year following eradication treatment.

A small proportion of patients (48 patients) were re-treated with a combination of PPI-clarithromycin-metronidazole as a second-line therapy, with a success rate of 29%.

The majority of patients (54%) received maintenance PPI intermittently for an average duration of 5 months over the 12-month period.

Less than 3% of patients were prescribed maintenance H2 receptor antagonist therapy.

The effectiveness of the various PPIs was:
0.46 (95% confidence interval, CI: 0.37 to 0.55) for rabeprazole;
0.46 (95% CI: 0.42 to 0.5) for esomeprazole;
0.41 (95% CI: 0.37 to 0.45) for omeprazole (generics assumed to be identical to the branded drug);
0.43 (95% CI: 0.39 to 0.47) for lansoprazole; and
0.42 (95% CI: 0.37 to 0.48) for pantoprazole.

Clinical conclusions
The authors found that eradication rates in clinical practice (under 50%) were significantly lower than suggested in a clinical trial setting (approximately 90%). They stated that the efficacy rates of various PPIs have often appeared similar, but their study suggested a marginally greater effectiveness rate with rabeprazole.

Modelling
A decision analysis tree was designed, using TreeAge software, to compare the costs and effectiveness associated with the nine regimens.

Measure of benefits used in the economic analysis
The outcome measure used in the economic analysis was the proportion of patients with each treatment that was asymptomatic.

Direct costs
Discounting was not relevant. The quantities and the costs were analysed separately. Given the perspective of the Community Drugs Scheme, only the direct costs relating to the primary care setting were included (i.e. the ingredient cost of medications and the cost of general practitioner (GP) consultations). Costs relating to hospital consultations or
the treatment of ulcer-related complications were not included. It was assumed that patients visited their GP when treatment initially began and prior to any changes in treatment. Initial and second-line PPI-based eradication therapy was prescribed in accordance with published guidelines, with dosage levels taken from the GMS database. Resource use was measured during the follow-up of the effectiveness study in 2002 to 2003. An average cost of EUR 40 per GP consultation was applied. All medication costs were determined from the Monthly Index of Medical Specialities 2003 and remained unchanged at the time of publication.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not relevant.

Currency
Euro (EUR).

Sensitivity analysis
One- and two-way sensitivity analyses were carried out. The parameters and ranges used were not described.

Estimated benefits used in the economic analysis
The reader is referred to the effectiveness estimates reported (see 'Effectiveness Results' section). The incremental benefits were not calculated.

Cost results
The total costs associated with each strategy were:

- EUR 215 for rabeprazole;
- EUR 265 for esomeprazole;
- EUR 258 for omeprazole (Ulcid);
- EUR 274 for lansoprazole;
- EUR 259 for omeprazole (Lopraz);
- EUR 275 for pantoprazole;
- EUR 279 for omeprazole (Losepine);
- EUR 282 for omeprazole (Losamel); and
- EUR 310 for omeprazole (Losec).

The incremental costs were not calculated.

Synthesis of costs and benefits
The incremental cost-effectiveness was not analysed.
The authors presented average cost-effectiveness ratios only:

EUR 466 per asymptomatic patient for rabeprazole;
EUR 577 per asymptomatic patient for esomeprazole;
EUR 632 per asymptomatic patient for omeprazole (Ulcid);
EUR 634 per asymptomatic patient for lansoprazole;
EUR 635 per asymptomatic patient for omeprazole (Lopraz);
EUR 651 per asymptomatic patient for pantoprazole;
EUR 683 per asymptomatic patient for omeprazole (Losepine);
EUR 691 per asymptomatic patient for omeprazole (Losamel); and
EUR 759 per asymptomatic patient for omeprazole (Losec).

It was stated that the effectiveness rates for rabeprazole would have to fall below 27% before an alternative option would have the lowest average cost-effectiveness ratio.

The cost of initial rabeprazole therapy and the duration of the rabeprazole maintenance phase would simultaneously need to increase by 30% before rabeprazole would cease to have the lowest average cost-effectiveness ratio.

The authors noted that the average duration on maintenance rabeprazole was a major driver of the higher cost-effectiveness of this strategy.

Authors' conclusions
The triple therapy regimen containing rabeprazole, amoxicillin and clarithromycin was the most cost-effective therapeutic strategy.

CRD COMMENTARY - Selection of comparators
The comparators were justified on the basis of being recommended therapy for H. pylori eradication in Ireland, and hence current practice. All PPIs available at the time were included in the model. You should decide whether these represent current practice in your own setting.

Validity of estimate of measure of effectiveness
The study was based on a retrospective analysis of a prescribing database, which was convenient in light of the wish to estimate effectiveness in clinical practice (as opposed to in clinical trial settings). Prescribing information is not ideal for making effectiveness comparisons, not least because of limited data around patient compliance. A more appropriate study might have used primary care patient records to establish estimates of effectiveness based on clinical measurements, rather than purely prescribing patterns. The patient groups were not shown to be comparable at analysis; no demographic or clinical data were presented. The numbers of patients receiving each treatment varied widely, and the greater uncertainty (and hence, variation) in estimates from smaller sample sizes was not acknowledged. It was stated that the effectiveness results for the generic omeprazole preparations were assumed to be the same as for branded omeprazole, but it was unclear whether this was because only branded omeprazole was prescribed in the database, sample sizes for the generic preparations were too small, or the database did not denote the names of the omeprazole preparations. No statistical analyses or sensitivity analyses to account for potential biases and confounding factors were described.
Validity of estimate of measure of benefit
The estimation of benefit was obtained directly from the effectiveness analysis (proportion of patients requiring no further therapy). This choice of estimate was justified as a suitable proxy for the proportion of patients who were asymptomatic following eradication therapy.

Validity of estimate of costs
Although the costs were reported from the perspective of the Community Drugs Scheme, it was not clear whether all the relevant costs were included (e.g. prescribing system costs, pharmacy dispensing and overhead costs). These costs would be common among comparators at the initial treatment stage but may cause differences in costs later, depending on the level of second-line therapy required with each comparator. This perspective is particularly narrow as it does not require treatment consequences to be costed. The costs and the quantities were calculated separately but were not reported separately in the publication. The unit costs were adequately described and dated. Resource use was either taken from the effectiveness study or assumed by the authors. No statistical analysis of the quantities or prices was undertaken, and this limits the interpretation of the findings.

Other issues
The authors made comparisons with other studies that were not always appropriate as they appeared to favour rabeprazole. Other studies had shown similar efficacy rates for all PPIs, a result which was borne out by this study (all of the 95% CIs around the effectiveness estimates for the comparators overlapped). However, the authors used the nominally higher point estimate for rabeprazole to suggest that this drug was more effective, citing a published meta-analysis in support. This conclusion is misleading and was not supported by the study results. The issue of generalisability was not discussed. The authors did not present an incremental cost-effectiveness analysis but only an average cost-effectiveness analysis. Average cost-effectiveness ratios are misleading and should not be compared, although the authors did so and also conducted a sensitivity analysis around them. Although the authors did not present their sensitivity analysis in sufficient detail, they do not appear to have presented their results selectively. However, their interpretation of the results was not appropriate. The authors did not report any limitations to their study.

Implications of the study
The authors state that their study indicated that rabeprazole triple therapy represents best practice for H. pylori eradication in the community setting in Ireland.

Source of funding
None stated

Bibliographic details

PubMedID
16506682

Indexing Status
Subject indexing assigned by NLM

MeSH
2-Pyridinemethylsulfinylbenzimidazoles; Amoxicillin /therapeutic use; Anti-Bacterial Agents /therapeutic use; Anti-Ulcer Agents /therapeutic use; Benzimidazoles /therapeutic use; Clarithromycin /therapeutic use; Cost-Benefit Analysis; Decision Trees; Drug Therapy, Combination; Helicobacter Infections /drug therapy; Helicobacter pylori; Humans; Ireland; Omeprazole /analogs & derivatives /therapeutic use; Primary Health Care /standards; Rabeprazole