Helicobacter pylori eradication in clinical practice: retreatment rates and costs of competing regimens

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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
Eradication regimens for Helicobacter pylori infection.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of patients who were aged 16 years or older, who were continuously eligible for healthcare benefits from 1 April 1995 to 31 December 1996 and had filled prescriptions for two or more drugs included in H. pylori regimens on the same date (regimen date) during a one year period (1 June 1995 - 31 May 1996) and during the 60 days (plus or minus) around the regimen date had at least one claim that met one or more of several clinical criteria. Clinical criteria included: the International Classification of Disease, 9th revision (ICD-9) code for ulcer disease, gastritis/duodenitis, stomach function disorder, or H. pylori infection, or the current procedural terminology code for endoscopy or H. pylori assay.

Setting
Primary care and secondary care.

Dates to which data relate
The dates of the effectiveness and resource use data spanned the period 1 April 1995 to 31 December 1996.

Source of effectiveness data
The evidence for final outcomes was derived from a single study.

Link between effectiveness and cost data
The costing was undertaken on the same patient sample as that used in the effectiveness study.

Study sample
Of 50,639 continuously eligible enrolees aged 16 years old or older, 615 patients met study criteria for method 1 (treatment assumed to be without acid-reducing agent) and 509 met criteria for method 2 (treatment assumed to be with acid-reducing agent). Classification under methods 1 or 2 was necessary in 29% of cases where it was not possible to infer whether or not the acid-reducing agent (H2RA or PPI) had been discontinued with treatment. The sample (method
1) yielded 99% power to detect a difference of 15% for PPI-dual versus 5% for triple therapies (PPI-based and bismuth-based regimens combined, 1-tailed, 0.05 significance level). The sample's power to detect a 5-15% difference between bismuth-based and PPI-based triple therapies was 73% (2-tailed, 0.05 significance). Classifying patients under method 1 gave 98 patients in the bismuth based regimen, 337 in the PPI-based dual and 180 in the PPI-based triple regimen. Method 2, gave 76 patients in the bismuth-based regimen, 262 in the PPI-based dual and 171 in the PPI-based triple regimen. There were 12 different regimens: 2 x bismuth; 4 x PPI-dual and 6 x PPI-triple.

Study design
The study design was a retrospective cohort study based on patients' claims from an integrated medical and pharmacy claims database. Patients were located throughout the USA. The duration of follow-up ranged from a minimum of 7 months to a maximum of 19 months.

Analysis of effectiveness
The primary health outcome used in the analysis was the rate of retreatment, defined as filling prescriptions for any eradication regimen after the regimen date and prior to the end of the study. At analysis groups were stated to have been comparable in age and gender. The proportion of patients with a gastrointestinal (GI) specialist claim from 30 days before to seven days following the regimen date was higher for bismuth-based (39%) and PPI-based triple (42%) than for PPI-based dual therapy (28%). Similarly, more stringent diagnostic criteria were met by higher percentages of bismuth based (64%) and PPI-based triple (68%) therapy than PPI-based dual therapy (54%). These differences were controlled for by subgroup analyses and Cox regression analysis was used to control for age, gender, GI specialist utilisation and stringency of clinical criteria with regimens with bismuth-based triple as the reference category.

Effectiveness results
Using method 1 classification, 6.1% of patients initially treated with a bismuth-based regimen were retreated with a second regimen. 15.4% in the PPI-based dual regimen were retreated and 10% of patients in the PPI-based triple regimen were retreated. Retreatment rates were significantly higher in PPI-based dual versus the two other regimens combined, (p=0.011). There was no significant difference in retreatment rates between bismuth-based and PPI-based triple therapy, (p=0.271).

Using method 2 classification 5.3% of patients initially treated with a bismuth-based regimen were retreated with a second regimen. 15.3% in the PPI-based dual regimen were retreated and 7.6% of patients in the PPI-based triple regimen were retreated. Retreatment rates were significantly higher in PPI-based dual versus the two other regimens combined, (p=0.003). There was no significant difference in retreatment rates between bismuth based and PPI-based triple therapy, (p=0.503).

For subgroup analysis generally the results were generally the same for dual and triple except for an increase in p values, all of which remained less than or equal to 0.05, except for patients who saw a GI specialist (p<0.1) and excluding PPI-amoxicillin (p<0.1). With the Cox regression, the increase in risk of retreatment for dual versus triple was 162%, (p=0.026) and for PPI-triple versus bismuth triple the result was not stated but was said to be "not significant".

Clinical conclusions
Retreatment rates were higher for PPI-based dual treatment regimens than for triple regimens, while rates for bismuth-based and PPI-based triple therapies did not significantly differ.

Measure of benefits used in the economic analysis
The measure of benefit used in the economic analysis was the number of successfully treated patients. Although no definition was given, one could infer that success equated to not having retreatment.
Direct costs
Costs were not discounted, although some patients were followed for more than one year. Some quantities (drug dosages) were reported separately from costs. The costs measured were the billed mean charges per month. Two analyses were conducted. The first was for follow-up costs, excluding the first two weeks of treatment (including the regimen date). The second analysis measured costs for the entire post-regimen period, including the costs of the treatment regimen drugs. Costs included all services, office visits, laboratory, drug, medical/surgical procedures, hospital and GI services. The perspective adopted was that of the third party payer. The estimation of quantities and costs was based on patients' claims. The price year was not specified.

Statistical analysis of costs
A multivariate general factorial analysis (ANCOVA) was used to adjust costs for age, gender, stringency of clinical criteria, speciality physician utilisation and monthly preregimen costs specific to service category, for example office visits. Costs were log transformed to account for skewness and the geometric mean used.

Indirect Costs
Indirect costs were not included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were not conducted.

Estimated benefits used in the economic analysis
No results were given.

Cost results
Mean unadjusted costs for the follow up period (from 14 days after regimen date to end of study) were $455 for PPI dual and $440 for combined bismuth and PPI triple regimens. Mean adjusted costs were $192 and $163 respectively. Mean unadjusted total costs (from regimen date to end of study) were $529 for PPI dual and $473 for the combined bismuth based and PPI triple. Mean total adjusted costs were $278 and $217 respectively.

Synthesis of costs and benefits
Drug costs per successfully treated patient were $30 for bismuth-based triple therapy, $172 for PPI-based triple therapy and $208 for PPI based dual therapy.

Authors' conclusions
PPI-based dual-therapy regimens are not cost-effective in H. pylori treatment.

CRD COMMENTARY - Selection of comparators
The choice of comparator was explicitly justified as the treatment regimens were representative of widespread clinical practice. You, as a user of the database, should decide if this is a widely used health technology in your own setting.

Validity of estimate of measure of benefit
The analysis was based on a retrospective cohort study, which was appropriate for the study design, although the claims
on which the analysis was based were not sufficiently detailed to allow for clear cut classification of patients into regimen groups and made two methods of classification necessary. The study sample was representative of the study population. Patient groups were shown to be comparable at analysis and analyses were conducted to adjust for confounding factors. The estimation of benefits was obtained directly from the effectiveness analysis.

Validity of estimate of costs
Positive aspects of the cost analysis were that some quantities were reported separately from costs, and statistical analyses were conducted to adjust for confounding factors. Negative aspects were that too little detail was given about the categories that were included in the cost analysis, charges were used to estimate prices which reduces generalisability, and the price year was not reported. Also costs were not given by regimen category for triple therapies and average cost-effectiveness only accounted for drug costs.

Other issues
An incremental analysis of costs and benefits was not performed, which hinders the validity of any claims regarding cost-effectiveness. The authors made appropriate comparisons of their findings with those from other studies and the issue of generalisability to other settings was addressed. The authors reported some limitations to the study, namely the limitations inherent in the use of claims databases. It was possible that some patients were asymptomatic and did not present for retesting during the 7 to 19 month time period. Although the hypothesis that retreated patients would experience higher medical costs was supported by the results, the authors reported that the statistical power of the study was insufficient to assess the effect of retreatment on services that are less often used, including medical procedures and hospitalisations.

Implications of the study
The study does show some appropriate accounting for confounding, thus improving the validity of the effectiveness results. However, the flaws in the presentation of the cost results, the lack of reporting of separate quantities and unit prices and the lack of appropriate analysis to show cost-effectiveness, reduce the usefulness of the study in decision making. Additional research is required to clarify the relationship between adverse effects, dosing schedules, compliance and retreatment. More research is required to compare bismuth-based and PPI-based triple therapies.

Source of funding
None stated

Bibliographic details

PubMedID
10860132

Indexing Status
Subject indexing assigned by NLM

MeSH
Adolescent; Adult; Aged; Antacids /economics /therapeutic use; Anti-Bacterial Agents; Bismuth /economics /therapeutic use; Drug Therapy, Combination /economics /therapeutic use; Female; Helicobacter Infections /drug therapy; Helicobacter pylori; Humans; Male; Middle Aged; Multivariate Analysis; Proton Pump Inhibitors; Retrospective Studies

AccessionNumber
2200001042