Economic evaluation of Helicobacter pylori eradication in the CADET-Hp randomized controlled trial of H-pylori-positive primary care patients with uninvestigated dyspepsia


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
Two treatments for Helicobacter pylori (H. pylori)-positive patients with uninvestigated dyspepsia were examined. The study compared eradication therapy with omeprazole (20 mg), metronidazole (500 mg) and clarithromycin (250 mg) (OMC), versus no eradication therapy with omeprazole (20 mg), placebo metronidazole (500 mg) and placebo clarithromycin (250 mg) (OPP). Both treatments were administered twice daily for one week.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised adult patients with uninvestigated dyspepsia of at least moderate severity and without alarm symptoms. The patients had not undergone an initial upper endoscopy. H. pylori infection was confirmed by a 13C-urea breath test. Dyspepsia was defined as a symptom complex of epigastric pain or discomfort thought to originate in the upper gastrointestinal tract. It could include additional symptoms such as heartburn, acid regurgitation, excessive burping or belching, increased abdominal bloating, nausea, a feeling of abnormal or slow digestion, or early satiety. Patients with heartburn and/or regurgitation alone were excluded.

Setting
The setting was primary care. The economic study was carried out in Canada.

Dates to which data relate
The period during which the effectiveness and resource use data were gathered was not reported. The price year was 1999.

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

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the effectiveness study.

Study sample
There was limited information on the sample size since details of the clinical trial had been reported elsewhere. Initially,
294 patients were enrolled, but efficacy data were not available for 6 patients. Thus, an overall sample of 288 patients was considered. Of these, 142 were included in the OMC group and 146 in the OPP group.

**Study design**
This was a prospective, randomised, double-blinded, placebo-controlled, parallel-group, multi-centre trial. The patients were followed for one year. The loss to follow-up was not reported.

**Analysis of effectiveness**
The analysis of the clinical study was conducted on an intention to treat basis. The main outcome measure used was treatment success. This was defined as a score of either 1 (none) or 2 (minimal) on the global overall severity scales at the final visit (7-point Likert scale). The baseline comparability of the study groups was not discussed.

**Effectiveness results**
Treatment success was 50% (95% confidence interval, CI: 42 - 58) in the OMC group and 36% (95% CI: 28 - 44) in the OPP group.

The absolute benefit increase of 14% was statistically significant, (p=0.02). The relative benefit increase was 37% (95% CI: 5 - 80).

The number-needed-to-treat to achieve one treatment success with OMC with respect to OPP was 7 (95% CI: 4 - 63).

Patients who received successful H. pylori eradication had a treatment success rate of 54% (95% CI: 45 - 63), compared with 39% (95% CI: 31 - 48) in those who remained H. pylori positive.

**Clinical conclusions**
The effectiveness analysis showed that eradication therapy (OMC) was more successful than OPP in the treatment of H. pylori-positive patients with uninvestigated dyspepsia.

**Measure of benefits used in the economic analysis**
The summary benefit measure used was treatment success. This was derived directly from the effectiveness study.

**Direct costs**
Discounting was not relevant, as the costs were incurred during less than two years, and was not carried out. The unit costs were presented separately from the quantities of resources used. The health services included in the economic evaluation were drugs (omeprazole, clarithromycin and metronidazole), hospitalisation, doctor visits (family practitioner, gastroenterologist and surgeon), nurse visits, endoscopy, upper gastrointestinal barium enema, 13C-urea breath test, and laboratory tests (including complete blood count, creatinine, blood sugar and helical rapid whole blood test).

The perspective adopted in the analysis of the direct costs was that of the third-party payer (i.e. the Ontario MOH). Resources use was based on the usual treatment pattern since the trial was near-pragmatic. The quantities of resources used were derived from patient-level data for the sample of patients included in the effectiveness study. The cost data were collected prospectively every 4 weeks using a Health Resource Utilization Questionnaire over the 1-year period. The costs associated with study protocol visits were not included because they were incurred equally in both arms. The costs were derived from typical MOH sources, such as the Ontario Drug Benefit Formulary/Comparative Drug Index, the Canadian Coordinating Office for Health Technology Assessment, and Ontario Health Insurance Plan Schedule of Benefits. The price year was 1999.
Statistical analysis of costs
The 95% CI of the mean costs per patient were calculated using a bootstrap method because the cost data were highly skewed.

Indirect Costs
The indirect costs (i.e. productivity losses) were included in the economic analysis so as to reflect the societal perspective. The costs associated with days of missed work were calculated according to the human capital approach. Unemployed and senior patients reported days lost from usual activities. The unit costs were presented separately from the quantities of resources used. Resource use was derived from the same sample of patients as that used in the clinical trial. The costs were derived from Canadian statistics on labour force and unpaid work. As in the analysis of the direct costs, the indirect costs were not discounted and the price year was 1999.

Currency
Canadian dollars (Can$). The conversion rates from Canadian dollars into US dollars ($) and UK pounds sterling () were Can$1 = $0.60 = 0.43.

Sensitivity analysis
Sensitivity analyses were not performed.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
From the MOH perspective, the mean yearly total costs were Can$136 (range: 0 - 1,066) in the OMC group and Can$181 (range: 0 - 1,860) in the OPP group. The difference in costs was Can$45 (95% CI: -20 - 114).

From the societal perspective, the mean yearly total costs were Can$477 (range: 27 - 3,069) in the OMC group and Can$530 (range: 31 - 3,315) in the OPP group. The difference in costs was Can$53 (95% CI: -86 - 180).

Synthesis of costs and benefits
The costs and benefits were combined using two different approaches, the incremental cost-effectiveness ratio (ICER) and the incremental net benefit (INB).

The ICER is the ratio between the change in costs and the change in effectiveness. The INB is the difference between the product of the change in effectiveness and the willingness-to-pay (WTP) and the change in cost. The WTP corresponds to the amount of money that a health service provider would be willing to pay for the value of the benefit of achieving one extra treatment success with eradication therapy.

The value of the ICER was negative, suggesting that eradication therapy dominated OPP, which was both less effective and more costly.

When the INB was used and the 95% CI considered, OMC was significantly cost-effective over OPP from a societal perspective for a WTP estimate of over Can$607 (INB above zero). From the MOH perspective, OMC was significantly cost-effective over OPP for a WTP estimate of over Can$100. In fact, the cost-effectiveness acceptability curve showed that there was a 95% chance that OMC was cost-effective if the WTP was Can$100 from the MHO perspective. Similarly, there was a 95% chance that OMC was cost-effective if the WTP was Can$607 from the societal perspective.
Authors' conclusions
Compared with a strategy of not eradicating Helicobacter pylori (H. pylori) in Canadian H. pylori-positive patients with uninvestigated dyspepsia, the strategy comprising a 13C-urea breath test and H. pylori eradication therapy was cost-effective from the perspectives of society and the service providers.

CRD COMMENTARY - Selection of comparators
The selection of the comparators appears to have been appropriate as they represented two recommended strategies for the treatment of H. pylori patients with uninvestigated dyspepsia. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a well-conducted clinical trial, which was appropriate for the study question. The trial was randomised, double-blinded and multi-centred, which enhances the validity of the evidence. However, limited information on the design of the study was reported, because the effectiveness trial had already been published.

Validity of estimate of measure of benefit
The summary benefit measure was specific to the disease considered in the study. It appears hardly comparable with the benefits of other health care interventions.

Validity of estimate of costs
The authors adopted two different perspectives in the economic analysis. As such, it appears that all the relevant categories of costs have been included. The unit costs were presented separately from the quantities of resources used, which enhances the possibility of replicating the results of the analysis. In addition, the source of the data was provided and the price year was reported. Thus, it is possible to perform reflation exercises in other settings. Statistical tests of the costs were performed, but the cost estimates were specific to the study setting since sensitivity analyses were not carried out. The authors noted that the trial was as pragmatic as possible, in order to reflect the true resource consumption. Accordingly, study protocol visits were not considered in the cost calculation.

Other issues
The authors made few comparisons of their findings with those from other studies, stating that results consistent with those reported in their analysis were observed. The issue of the generalisability of the study results to other settings was not addressed and sensitivity analyses were not performed. This reduces the external validity of the analysis. The study referred to H. pylori-positive patients with uninvestigated dyspepsia and this was reflected in the authors’ conclusions.

Implications of the study
The study results suggested that the "test and treat" strategy should be used for the treatment of H. pylori-positive patients with uninvestigated dyspepsia. The authors suggested that future studies should compare the "test and treat" strategy with an alternative strategy of giving all patients empirical acid suppressive therapy.

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