Impact of helicobacter pylori eradication on dyspepsia, health resource use, and quality of life in the Bristol helicobacter project: randomised controlled trial

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 use of a community programme for screening and subsequent eradication of Helicobacter pylori. The Bristol Helicobacter project invited (by letter) patients aged 20 to 59 years who were registered at general practices to attend Helicobacter pylori (H. pylori) screening. The 13C urea breath test was used to screen attendees for H. pylori. Those testing positive could receive H. pylori eradication therapy, which consisted of ranitidine bismuth citrate (400 mg) and clarithromycin (500 mg) twice daily for 14 days.

Type of intervention
Screening and treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised individuals aged 20 to 59 years.

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

Dates to which data relate
The effectiveness and resource use data were gathered from 1996 to 2001. The price year was 2002.

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 analysis.

Study sample
Power calculations were performed in the preliminary phase of the study. These suggested that a sample of 1,550 individuals would be required to detect a reduction in the consultation rate from 8.5% to 4.25% in the eradication group, with 90% power at a two-sided significance level of 5%. Eligible patients were recruited from all patients registered at seven general practices between 1996 and 1999. Of the 27,536 individuals registered at the practices, 507 were ineligible by general practitioner (GP) screening, 826 had an incorrect address, and 15,489 did not attend. The authors stated that non-responders were more likely to be male, younger and from the lower socioeconomic groups than
would responders.

Of the 10,714 who attended screening, 127 did not meet the inclusion criteria and 50 refused to participate. Therefore, 10,537 were enrolled, of which 8,901 were H. pylori negative. However, a further 78 were excluded because they either declined to participate (76 patients) or ineligible (2 patients: one a 61-year-old patient and the other allergic to the study drug). Thus, the actual study sample comprised 1,558 patients, of which 787 (49% men) were in the treatment group and 771 (49% men) in the placebo group. The mean age of the patients was 48.4 (+/-8.0) in the treatment group and 48.6 (+/- 7.9) in the placebo group.

**Study design**

This was a prospective, double-blind, randomised clinical trial that was carried out at seven general practices in southwest England. Staff independent of the study prepared the randomisation sequence with a block size of 10. Randomisation was stratified by gender and age into four 10-year age bands (20 - 29, 30 - 39, 40 - 49 and 50 - 59). Pharmacists, who had no contact with the participants, prepared drug packs, while research nurses who were blind to the treatment allocation dispensed them. Eradication was assessed by a 13C urea breath test 6 months later. Both the participants and outcome evaluators were blind to the result of the test. The length of follow-up was 2 years. Follow-up was 99% (1,539 patients) for the primary outcome and 92% (1,438 patients) for the secondary outcomes.

**Analysis of effectiveness**

The analysis of the clinical study was by intention to treat since all patients initially included in the clinical trial were considered in the analysis of effectiveness. A secondary analysis was based on treatment completers only, and only patients with completed follow-up questionnaires were considered. The primary outcome measure was the consultation rate for dyspepsia (epigastric pain) in primary care over 2 years, estimated on the basis of primary care records. Also considered were:

- all consultations related to dyspepsia (epigastric pain) or to heartburn, reflux, or dysmotility-type symptoms;
- prescribed dyspepsia treatments; and
- referrals to secondary care for dyspepsia.

The secondary outcome measures were the frequency and type of symptoms and their impact on quality of life. Symptom frequency was assessed within a 3-month period using 5-point Likert-type scales. Participants rated the frequency of dyspepsia (epigastric pain) symptoms, as well as heartburn and reflux, belching (wind), nausea and bloating, from 1 (none) to 5 (daily). The SF-36 questionnaire was used to assess generic health status (quality of life), where 0 indicated poor health and 100 indicated good health. The baseline comparability of the study groups was not explicitly reported, but it is likely that there were no statistically significant differences between the two groups, given the method of randomisation.

**Effectiveness results**

The number of people consulting for dyspepsia in primary care was reduced by 35% (55 of 787 versus 78 of 771) over 2 years in the treatment group compared with the placebo group (odds ratio 0.65, 95% confidence interval, CI: 0.46 to 0.94; p=0.021). Therefore, 30 people with H. pylori would have to be treated to prevent one person consulting their doctor for dyspepsia. There was no difference in the numbers consulting for dyspepsia according to gender.

Regular symptoms of dyspepsia (epigastric pain) were reported by 29% fewer participants 2 years after H. pylori eradication treatment than after placebo (odds ratio 0.71, 95% CI: 0.56 to 0.90).

No differences existed between the two groups in any of the quality of life dimensions at 2 years.

**Clinical conclusions**

The effectiveness analysis showed that H. pylori eradication was effective in reducing symptoms of dyspepsia and
primary care consultations.

**Measure of benefits used in the economic analysis**
The health outcomes were left disaggregated and no summary benefit measure was used in the economic analysis. The authors stated that a cost-consequences analysis was carried out.

**Direct costs**
The cost analysis took the perspective of the NHS. It included the costs of dyspepsia (epigastric pain)-related GP consultations, secondary care referrals, endoscopies and drugs (both eradication and prescription drugs). The unit costs and the quantities of resources used were presented separately. Resource use was derived from the note reviews of the same patients as those included in the clinical trial. The costs came from the British National Formulary, the Personal Social Services Research Unit and the North Bristol NHS Trust. Costs incurred in the second year were discounted at an annual rate of 3.5%. The price year was 2002.

**Statistical analysis of costs**
The t-test was used to assess cost-differences between the groups.

**Indirect Costs**
The indirect costs were not considered.

**Currency**
UK pounds sterling ( ).

**Sensitivity analysis**
Sensitivity analyses were not carried out.

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

**Cost results**
The mean health care costs per study participant were 108.72 (+/- 94.14) in the treatment group and 21.13 (+/- 101.39) in the placebo group (difference 84.70, 95% CI: 74.90 to 93.91).

The extra costs associated with the intervention were almost totally due to the cost of the eradication drugs (difference 83.4).

**Synthesis of costs and benefits**
A synthesis of the costs and benefits was not relevant since a cost-consequences analysis was carried out.

**Authors' conclusions**
The test-and-treat strategy for Helicobacter pylori (H. pylori) in the general practice population was found to significantly reduce the number of people who consulted for dyspepsia (epigastric pain) and who had symptoms. However, this benefit was achieved at increased cost because of the costs of eradication treatment.
CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator (i.e. no treatment) was appropriate. The dosage of the eradication therapy was reported. You should decide whether they are valid comparators in your setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence was derived from a clinical trial, which was appropriate for the study question. The randomised, double-blinded multi-centre design, as well as the use of intention to treat, should ensure the internal validity of the analysis. However, since the clinical trial had been published in a separate study, few details of the design and other features of the study were reported. Nevertheless, power calculations and extensive information on the method of sample selection were reported. The authors stated that the sample of patients enrolled was highly representative of the patient population, as a large sample of individuals was enrolled and few patients were excluded. These issues enhance the robustness of the clinical estimates. Demographic and clinical characteristics of non-participants could not be accessed, but the authors stated that patients declining participation were more likely to be male, younger and from lower socioeconomic groups than responders.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis because a cost-consequences analysis was conducted. Please refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
The cost analysis was conducted in accordance with the perspective adopted in the study. Typical NHS sources were used to derive the costs. Extensive details on the unit costs and quantities of resources used were provided. This enhances the possibility of replicating the analysis in other settings. Statistical analyses of the costs were performed, but the cost estimates were specific to the study setting and the impact of using alternative economic estimates was not investigated. The price year was reported, which enables reflation exercises in different time periods.

Other issues
The authors stated that the clinical results were comparable to those observed in other population-based clinical trials. However, few comparisons were made for the economic analysis. The authors noticed that the cost of eradication drugs in the UK is likely to be lower than that used in this analysis. The issue of the transferability of the cost results to other settings was not explicitly addressed and sensitivity analyses were not performed. In effect, the external validity of the cost analysis was low. The study referred to patients with H. pylori and this was reflected in the authors’ conclusions.

Implications of the study
The study results appear to support a strategy of community screening and eradication of H. pylori in the general population, although the benefits of the programme have to be balanced against the cost of eradication therapy.

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