A community screening program for Helicobacter pylori saves money: 10-year follow-up of a randomized 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 study examined a community screening programme for Helicobacter pylori (H. pylori), with subsequent treatment using eradication therapy. Screening was based on a carbon-13-labelled urea breath test. Eradication therapy consisted of omeprazole 20 mg, clarithromycin 250 mg and tinidazole 500 mg, all twice daily for 7 days.

Type of intervention
Screening and treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised healthy individuals aged between 40 and 49 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 1994 to 2004. 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 retrospectively on the same sample of patients as that used in the effectiveness analysis.

Study sample
Power calculations were not reported for the clinical analysis. In the original trial, 8,407 participants were selected from their family practitioner lists. All these individuals were initially screened for H. pylori and the 2,324 patients testing positive were included in the further phase of the study. There were 1,161 patients allocated to the eradication treatment group and 1,163 assigned to placebo. Demographics of the patients included in the effectiveness analysis were not reported, but extensive details were provided for those patients who were available for the cost analysis.

Study design
This was a prospective, randomised clinical trial that was carried out in the Leeds and Bradford area of West Yorkshire in northern England. Two randomisations were carried out. First, the 8,407 patients undergoing initial screening were randomly selected from all patients included in family practitioner lists. Second, the 2,324 individuals testing positive were randomised, by a computer-generated block allocation schedule stratified by primary care centre, to eradication therapy or placebo. The length of follow-up of the original trial was 2 years. The current study followed patients for a further 8 years. Thus, the total follow-up was 10 years. The patients were contacted and were sent a postal questionnaire. The final study sample comprised 1,070 patients (46%) who gave fully analysable symptom data at 10 years. Blinding was maintained by a central trials unit that was not involved in patient evaluation.

Analysis of effectiveness
Only patients with complete follow-up data were taken into account in the analysis of effectiveness. The clinical end points used in the study were:

the presence of dyspepsia at 10 years;

the resolution of dyspepsia at 10 years in those who were symptomatic at original trial entry, and

the subsequent development of gastric cancer, peptic ulcer disease and gastroesophageal reflux disease (GERD) during 10-year follow-up.

The presence of dyspepsia was evaluated using the short-form Leeds dyspepsia questionnaire, which assesses both the frequency and severity of four symptoms (indigestion, heartburn, regurgitation and nausea), as well as asking the patient to identify the most troublesome upper gastrointestinal symptom. Dyspepsia symptom status at 10 years was dichotomised into symptomatic or asymptomatic. Sub-group analyses were also performed according to gender and excluding those individuals who, on being informed of their H. pylori status and treatment allocation, requested subsequent eradication therapy from their family practitioner between years 2 and 10.

At baseline, the study groups were well matched with respect to their clinical and demographic characteristics. A baseline comparison was also carried out between individuals who were successfully contacted and those who were not contacted or did not respond, as well as between individuals who agreed to the re-examination of primary care records and those who refused.

Effectiveness results
The overall prevalence of dyspepsia at 10 years was 40%. Of those with dyspepsia at baseline, 60% still had dyspepsia at the 10-year follow-up.

There was a trend toward a reduction in the risk of being symptomatic at 10 years in those assigned to eradication therapy (221 of 547 individuals symptomatic; 40%) in comparison with those assigned to placebo (228 of 523; 43.5%). This resulted in a 3.5% absolute risk reduction (ARR) which did not reach statistical significance. The relative risk (RR) of being symptomatic at 10 years was 0.93 (95% confidence interval, CI: 0.89 to 1.07).

When only those individuals who were symptomatic at original trial entry were considered, there was a non significant trend towards a reduction in the risk of remaining symptomatic at 10 years with eradication therapy (132 of 225 individuals remained symptomatic; 59%) in comparison with placebo (138 of 210; 66%). This gave an ARR of 7%, and the RR of remaining symptomatic at 10 years was 0.89 (95% CI: 0.77 to 1.03).

Similar results were observed in the sub-group analysis according to gender. However, the sub-group analysis that excluded patients who requested H. pylori eradication therapy from their family practitioner between years 2 and 10 increased the impact of H. pylori eradication therapy on dyspepsia symptoms, which was of borderline statistical significance. The RR of being symptomatic at 10 years was 0.76 (95% CI: 0.58 to 1.0; p=0.05).

Other clinical outcomes were comparable between the groups. For example, 75 of those assigned to placebo underwent a total of 92 endoscopies, compared with 75 of those allocated to eradication therapy who underwent 90 endoscopies. No patients were found to have an upper gastrointestinal malignancy. There were a total of 12 peptic ulcers in these
individuals (5 in the eradication therapy group and 7 in the placebo arm). An endoscopic diagnosis of GERD was made in 42 people (25 eradication therapy versus 17 placebo).

**Clinical conclusions**

The effectiveness analysis showed that there was a trend towards a reduction in risk of being symptomatic at 10 years in those assigned to eradication therapy in comparison with those assigned to placebo. However, differences between the groups did not achieve statistical significance.

**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. In effect, a cost-consequences analysis was carried out.

**Direct costs**

The study was carried out from the perspective of the NHS (health service payer). It assessed the total dyspepsia-related resource use per individual at 10 years. The costs were grouped in the following categories:

- primary care costs (family practitioner consultations),
- secondary care costs (outpatient consultations, accident and emergency attendances, and inpatient admissions as a consequence of dyspepsia),
- costs of prescribed drugs for dyspepsia (using total defined daily doses of acid suppression drugs and number of courses of eradication therapy), and
- costs of relevant investigations (barium meals, upper gastrointestinal endoscopy, and breath tests).

The unit costs were presented, but the quantities of resources used were not reported. Of the initial study sample of 2,324 patients, only 474 intervention patients and 440 placebo patients were available for the analysis of cost data. The remainder could not be traced, did not respond to the questionnaire, or did not agree to participate. The resource use data were obtained retrospectively by researchers blinded to treatment allocation. The costs came from the British National Formulary and UK national reference costs. The price year was 2002. Discounting might have been relevant, given the long timeframe of the analysis, but it was not applied.

**Statistical analysis of costs**

Power calculations were performed for the analysis of the costs. These suggested that a sample of 1,200 individuals in each group would have been able to detect a difference of $13.50 in health service dyspepsia costs between groups at a 90% power and 5% significance level. Cost-differences between groups were tested using the t-test with 95% CIs. Finally, the same sub-group analysis as that used in the effectiveness study was performed.

**Indirect Costs**

The indirect costs were not considered in the economic analysis.

**Currency**

The costs were estimated in UK pounds sterling () then converted into US dollars ($). The conversion rate was 1 = $1.8.

**Sensitivity analysis**

Sensitivity analyses were not performed.
Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
At 10 years, mean dyspepsia-related costs per patient were $303 (+/- 720) in the intervention group and $420 (+/- 887) in the placebo group. The cost-difference was $117 (95% CI: 11 to 220; p=0.03).

Among the sub-categories, only the difference in prescribing costs reached statistical significance. The prescribing costs were $117 (+/- 368) in the intervention group and $198 (+/- 556) in the placebo group (difference $81, 95% CI: 19 to 141; p=0.01).

When the costs were dichotomised, there were significantly fewer individuals in the eradication therapy group who incurred any dyspepsia-related cost (48.5%) than in the placebo group (72.5%). The RR of incurring any dyspepsia-related cost was 0.67 (95% CI: 0.60 to 0.75; p<0.001).

The sub-group analysis by gender revealed a trend towards greater reductions in dyspepsia-related costs in men allocated to eradication therapy than women, but the difference did not reach statistical significance.

The exclusion of patients who received H. pylori eradication therapy from their family practitioner between years 2 and 10 increased the difference in health service dyspepsia-related costs between the eradication and placebo groups. The mean difference in dyspepsia-related costs was $160 (95% CI: 48 to 272).

Synthesis of costs and benefits
A synthesis of costs and benefits was not relevant as a cost-consequences analysis was performed.

Authors’ conclusions
Helicobacter pylori (H. pylori) screening and treatment reduced dyspepsia-related costs in healthy individuals in the UK. The clinical outcomes were relatively comparable between patients undergoing screening and those receiving placebo, although this might have been due to the small of patients available at the last follow-up.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear as community screening was compared with the current standard of care. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The evidence came mainly from a published clinical trial, which was appropriate for the study question. The randomised, blinded and multi-centred design ensures a high internal validity. However, most of the details of sample selection and study design had been reported elsewhere. The long follow-up and the use of sub-group analyses represent further strengths of the study. The study groups were comparable at baseline. These issues tend to increase the robustness of the analysis. However, the authors noted that some confounding factors might have affected the results of the analysis. Further, a substantial proportion of patients were lost at the 10-year follow-up, which might reduce the validity of the clinical findings.

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 analysis of the costs was consistent with the NHS perspective, with only the direct medical costs being included. The source of the data was provided for each category of costs and the unit costs were reported. However, information on resource consumption was not provided, which limits the possibility of replicating the analysis in other settings. Statistical analyses were performed, but the impact of altering the cost estimates was not investigated in the sensitivity analysis. In effect, the cost estimates were specific to the study setting. The sample of patients included in the cost analysis was appropriate for the detection of statistically significant differences between groups in terms of the costs. The price year was reported, which will facilitate reflation exercises in other time periods. Despite the long timeframe of the analysis, discounting does not appear to have been carried out.

**Other issues**
The authors did not compare their findings with those from other studies, although they stated that other economic evaluations have suggested that H. pylori screening and treatment may be cost-effective. The issue of the generalisability of the study results to other settings was not addressed and sensitivity analyses were not performed, which limits the external validity of the study. The analysis referred to healthy individuals and this was reflected in the authors' conclusions.

**Implications of the study**
The study results suggested that an H. pylori "search and eradicate" strategy might be cost-saving.

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None stated.

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**Other publications of related interest**

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