A randomized controlled trial of test-and-treat strategy for Helicobacter pylori: clinical outcomes and health care costs in a managed care population receiving long-term acid suppression therapy for physician-diagnosed peptic ulcer disease


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 Helicobacter pylori (HP) test-and-treat (T&T) strategy. Patients testing positive for HP received 20 mg of omeprazole, 500 mg of clarithromycin, and 1 g of amoxicillin twice daily for 10 days. For those allergic to penicillin, 500 mg of metronidazole was substituted for amoxicillin.

Type of intervention
Diagnosis and treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with physician diagnosed PUD.

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

Dates to which data relate
The effectiveness data were collated between September 1996 and August 1998. Resource use was measured 15 months after randomisation. A price year was not reported.

Source of effectiveness data
The effectiveness data were 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 in the effectiveness study.

Study sample
The study sample comprised patients listed on the Kaiser Permanente (KP) database, who were aged between 18 and 80 years and were receiving histamine, receptor antagonists or proton-pump inhibitors for at least three 30-day periods within a 12-month timeframe. Patients with an outpatient diagnosis of duodenal ulcer, gastric ulcer, gastritis, or unspecified PUD were invited to participate. The authors defined strict rules for inclusion and exclusion. The sample size was chosen to ensure 90% power to detect a statistically significant difference in self-reported symptom rates of 15%, assuming a dropout rate as high as 20%. A total of 650 patients (mean age 57 years; 48% males) were
randomised. There were 321 into the intervention group (T&T) and 329 in the usual care control group (UCC).

**Study design**
The analysis was based on a randomised controlled trial that was conducted in a single managed care setting. The patients were randomised in blocks of 8 by the recruitment coordinator, using a computerised random assignment algorithm. Follow-up occurred at 6 and 12 months. There was no report of physicians or analysts being blinded to the care protocol. The participants were not blinded as this would have required the introduction of placebo drugs.

**Analysis of effectiveness**
The patients were analysed on an intention to treat basis. The demographic variables and disease-specific variables of the patient groups were compared, and no statistically significant differences were observed. The primary health outcomes were:

- the effectiveness of treatment in eliminating HP;
- the percentage reporting dyspepsia symptoms at baseline and 6 and 12 months;
- the Gastrointestinal Symptom Rating Scale (GSRS) score (abdominal pain and all responses) at baseline and 6 and 12 months; and
- the percentage using acid-reducing medications at baseline and 6 and 12 months.

**Effectiveness results**
The effectiveness of treatment in eliminating HP was 78% when analysed by intention to treat and 84% when analysed by per protocol.

The results are presented here for baseline, and 6 and 12 months. Readers are referred to the original paper for the complete results.

The percentage reporting dyspepsia symptoms at baseline was 84.7% for the control group and 83.3% for the intervention group, (p=0.63). At 6 months it was 81.9% for the control group and 71.5% for the intervention group, (p=0.01), and at 12 months it was 80.2% (control) and 69.4% (intervention), (p=0.01).

The GSRS score for abdominal pain at baseline was 2.1 for the control group and 2.2 for the intervention group, (p=0.78). At 6 months it was 2.1 for the control group and 1.8 for the intervention group, (p<0.001), and at 12 months it was 2.0 (control) and 1.9 (intervention), (p=0.02).

The GSRS score for all responses at baseline was 2.1 for the control group and 2.1 for the intervention group, (p=0.92). At 6 months it was 2.0 for the control group and 1.8 for the intervention group, (p=0.04), and at 12 months it was 2.0 (control) and 1.9 (intervention), (p=0.14).

The percentage using acid-reducing medications at baseline was 96.4% for the control group and 97.5% for the intervention group, (p=0.39). At 6 months it was 77.8% for the control group and 66.0% for the intervention group, (p=0.001), and at 12 months it was 70.2% (control) and 57.9% (intervention), (p=0.001).

The percentage with any usage during 6 to 12 months was 82.7% for the control group and 75.1% for the intervention group, (p=0.02).

**Clinical conclusions**
The authors concluded that symptoms of PUD in the T&T group decreased from baseline compared with the UCC group. The use of acid-reducing medication was significantly lower in the T&T group than the UCC group at 6 months and 12 months.
Measure of benefits used in the economic analysis
The authors did not derive a summary measure of benefits. The study was, in effect, a cost-consequences analysis.

Direct costs
The economic analysis was carried out from the perspective of the health care payer. The unit costs were taken from KP Northern California Cost Information Management System database. They included facility overheads and the costs of the study's T&T intervention. Resource use was measured from the medical records of consenting participants, at 15 months after randomisation, to compare usage over the preceding 12- and 15-month periods. The costs were also compared for the 12 months post randomisation. The analysis covered services such as acid-reducing medications, outpatient visits and diagnoses, notes relating to PUD, hospitalisations, gastrointestinal procedures, and any evidence of HP testing and/or eradication. Discounting was not carried out and the price year was not reported.

Statistical analysis of costs
Comparisons were made across time within a study group using the Wilcoxon rank sum test, and between groups using the Wilcoxon signed rank test.

Indirect Costs
The indirect costs were not reported.

Currency
US dollars ($).

Sensitivity analysis
The authors did not report any sensitivity analysis being carried out.

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

Cost results
The mean-outpatient related acid-peptic-related costs in the 12 months prior to randomisations were $205 (standard error, SE=21) for the control group and $182 (SE=17) for the intervention group, (p=0.41).

In the 12 months after randomisation these costs were $145 (SE=15) for the control group and $227 (SE=15) for the intervention group, (p<0.001).

The mean pharmacy-related acid-peptic-related costs in the 12 months prior to randomisations were $191 (SE=13) for the control group and $187 (SE=13) for the intervention group, (p=0.85).

In the 12 months after randomisation these costs were $174 (SE=15) for the control group and $201 (SE=12) for the intervention group, (p<0.001).

The mean inpatient-related acid-peptic-related costs in the 12 months prior to randomisation were $179 (SE=74) for the control group and $78 (SE=38) for the intervention group, (p=0.41).

In the 12 months after randomisation these costs were $60 (SE=30) for the control group and $68 (SE=43) for the intervention group, (p=0.79).
The mean total acid-peptic-related costs in the 12 months prior to randomisation were $574 (SE=83) for the control group and $447 (SE=51) for the intervention group, (p=0.55).

In the 12 months after randomisation these costs were $380 (SE=40) for the control group and $496 (SE=53) for the intervention group, (p<0.001).

Synthesis of costs and benefits
The costs and benefits were not combined as the study was, in effect, a cost-consequences analysis.

Authors' conclusions
The pharmacy, outpatient and total acid-peptic-related costs after randomisation were significantly higher in the test-and-treat (T&T) group than in the usual care control (UCC) group, whereas at baseline there had been no significant difference. Overall, T&T provided only minor symptom relief and no cost-savings in the authors' population after 12 months of follow-up.

CRD COMMENTARY - Selection of comparators
The authors compared T&T with usual care in their own setting. T&T was assessed on account of the high number of patients in the setting who were reported to be treated without confirmation of the physician's diagnosis by radiography or endoscopy. The choice of the comparator, usual care, was justified by it being the common practice in the absence of testing and treatment for HP infection. You should decide if it is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a randomised controlled trial. This design minimises systematic differences between the groups, reducing the possibility that confounding variables have influenced the results. The sample was representative of the study population, including patients with an outpatient diagnosis of duodenal ulcer, gastric ulcer, gastritis or unspecified PUD, and whose initial diagnosis might be confirmed before treatment is commenced. The patient groups were shown to be comparable, with no statistical differences between them being observed in the parameters compared. Appropriate statistical analyses were carried out and the authors discussed potential reasons for the unexpected minimal response including a relatively small sample of patients having documented PUD.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of health benefit. The study was, in effect, a cost-consequences analysis.

Validity of estimate of costs
The costing was carried out from the perspective of the third-party payer and all relevant costs relating to this perspective were included in the analysis. These included inpatient, outpatient and pharmacy-related costs. The indirect costs were not considered in the study. Discounting was not necessary since all of the costs were incurred during less than two years. The unit costs were not reported separately from the quantities and sensitivity analyses were not carried out. These factors will limit the readers' ability to form opinions concerning which are the key cost-drivers. The price year was not reported, which will present difficulties in terms of any future reflation exercise.

Other issues
The authors were able to draw comparisons with other randomised controlled trials and a recent meta-analysis in which only minor symptom relief was also reported. Although the authors did not explicitly consider the issue of generalisability, they did suggest that, in specific settings where the proportion of patients with documented PUD is greater and the HP prevalence is higher, T&T may prove more beneficial than was demonstrated in the present study. The authors carried out statistical analyses for both clinical and cost elements, to demonstrate the differences between the two treatment strategies, and used these analyses to justify their conclusions. Limitations such as the short length of
follow-up were highlighted.

**Implications of the study**
The authors reported that PUD "must be documented by radiography or endoscopy before adopting a strategy of routine testing for and treating of HP infection in patients". There were no suggestions for further work.

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**Other publications of related interest**


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