Assessment of decisions in the treatment of Helicobacter pylori-related duodenal ulcer: a cost-effectiveness study

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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
Two treatments for Helicobacter Pylori (H. pylori) are studied: amoxycillin + metronidazole + tagamet (AMT) and omeprazole + amoxycillin (AO). The doses were, for the AMT group: 1g of amoxycillin bid for two weeks, 200mg of metronidazole tid for two weeks, and 800mg of tagamet each night for six weeks. For the AO group, the doses were 20mg of omeprazole bid for two weeks followed by 20mg per night for the next weeks, and 1g of amoxycillin bid for two weeks.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
 Patients aged over 18 years, with duodenal ulcers confirmed by endoscopy, and H. pylori confirmed by histology urease test. Exclusion criteria included additional gastric or pyloric ulcers, treatment with omeprazole, bismuth salts, or antibiotics during the four weeks prior to endoscopy, history of ulcer surgery, renal insufficiency, congestive heart failure, severe liver disease, clotting disorders, known penicillin hypersensitivity, continuation of potentially ulcerogenic drugs, and suspected lack of compliance.

Setting
Hospital. The economic study was carried out in Zhong Shan, Shanghai, China.

Dates to which data relate
The effectiveness data relate to endoscopic examinations made between January 1995 and June 1995. Resource use and costs were reported in US dollars, and no price year was stated.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costs reported were those of the patients' bills. These were the same patients from which the effectiveness data were reported.

Study sample
All patients entering Zhong Shan hospital with active duodenal ulcer were considered. After applying exclusion criteria, 96 patients remained. There was no statistical evidence of any difference between those included and those excluded, for gender, age, smokers or history. Each treatment group contained 48 patients. No power calculations relating to sample size were reported. Note: correspondence with the authors subsequent to this abstract being written has indicated that power calculations were, in fact used in determining the sample size which was calculated based on P1 = 80%, P2 = 50%, alpha = 0.05 and beta = 0.20 (power = 0.8) resulting in n=44 for each group.

**Study design**
A single centre, randomised controlled trial was used. Patients were randomised using block randomisation (four patients in each block). No blinding method was reported. The follow up period was six months. Seven patients dropped out (7.3%): 5 patients refused an endoscopic examination at 7th and 8th week and 2 patients did not finish the trial because they experienced side effects.

**Analysis of effectiveness**
Effectiveness results were based upon treatment completers only. Effectiveness measures were rates of healing of the duodenal ulcer or eradication of H. pylori, confirmed by an endoscopic examination after seven weeks of treatment, and recurrence rate during the 6 month follow-up period. Other measures included days to pain relief; days to pain disappearance; days absent from work due to sickness; and days lost due to caring for patient, as well as a summary of undesirable side-effects (mouth burning, diarrhoea, constipation, dizziness and rashes). The patients recorded the measures and side-effects in a diary. There was no statistical difference in demographic or clinical characteristics between the two treatment groups. Results were presented by patient characteristics (e.g. smokers, gender, ulcer history).

**Effectiveness results**
The effectiveness results were as follows:

- Ulcer healing rates were 93.5% for OA group and 83.7% for AMT (p=0.27).
- Eradication of H. pylori rates were 69.6% for OA and 65.1% for AMT (p=0.60).
- Eradication of H. pylori was significantly lower in both groups for large ulcers (larger than 1cm in diameter) than smaller ulcers (less than or equal to 1 cm): 50% versus 77%.

There was no statistically significant difference in recurrence rate between the two groups, (p>0.05). Helicobacter pylori was detected in all patients who suffered ulcer recurrence.

- Mean days until pain relief, 1.2 for OA and 1.5 for AMT;
- days until pain disappearance, 2.0 for OA and 3.0 for AMT;
- days absent due to sickness, 4.4 for OA and 4.9 for AMT;
- and days lost due to care, 0.5 for OA and 0.4 for AMT.

In the OA group, 21 patients experienced slight side-effects, compared to 18 in the AMT group;

- 3 OA patients suffered moderate side-effects compared to 2 AMT patients;

no OA patients experienced severe side-effects, whilst 2 AMT patients did. These differences were not statistically significant.

**Clinical conclusions**
After accounting for any differences in characteristics between groups, there was no statistically significant difference between the ulcer healing rates or H. pylori eradication rates between the two groups.

**Measure of benefits used in the economic analysis**
The major outcomes measured in the study were: ulcers healed in six weeks, H. pylori eradicated in six weeks, and ulcers non-recurrent after six months. No discounting was necessary on benefits, as the study duration was less than one year.

**Direct costs**
No discounting was performed on direct costs, as the study duration was six months. Quantities/costs were not reported separately. Direct medical costs included the cost of the medicine, the cost of registration, the cost of monitoring and treating side effects and the cost of further treatment and examination. Transportation costs were also included. The estimation of costs and quantities was based on actual data. The price year was not given. The mean cost of each treatment was then used in the cost-effectiveness analysis.

**Statistical analysis of costs**
Not carried out.

**Indirect Costs**
No discounting was performed on the indirect costs, since the study period was six months. Quantities were reported separately, while item costs were not reported. Indirect costs included: the time lost from work (patients and families); absence from work for endoscopy examinations, visiting a doctor, hospitalisation and recovery time. The average daily salary was used in order to estimate these costs. No price year was given.

**Currency**
US dollars ($). A conversion rate of $1.0 = RMB 8.4 yuan was given.

**Sensitivity analysis**
A one way sensitivity analysis was performed on costs, including costs of treatment at recurrence.

**Estimated benefits used in the economic analysis**
For the OA group, 43 of 46 ulcers were healed after six weeks, 32 of 46 cases of H. pylori were eradicated after six weeks, and 41 of 46 showed no recurrence of ulcers after six months.

For the AMT group, these figures were 36 of 43 ulcers were healed after six weeks, 28 of 43 cases of H. pylori were eradicated after six weeks, and 38 of 43 showed no recurrence of ulcers after six months. No side effects are considered in the economic analysis.

**Cost results**
Total costs over the six week period were $6,718 for OA group (n=46) and $2,369 for AMT (n=43). Over six months, total costs were $7,037 for OA group and $2,932 for AMT.

**Synthesis of costs and benefits**
Results were provided for: cost per healed ulcer ($156.24 for OA, $65.81 for AMT); cost per H. pylori eradicated ($209.94 for OA and $84.62 for AMT); and cost per ulcer non-recurrent ($171.63 for OA and $77.16 for AMT). Cost-effectiveness ratios were presented in the form of the cost-per ulcer cleared by AMT divided by the cost per ulcer.
cleared for OA. No incremental analysis was performed. AMT appeared to have an even lower cost-effectiveness ratio than OA when patients' ulcers were less than 1cm in size. These results were not sensitive to variations in parameters.

Authors’ conclusions
The authors concluded that, whilst OA had a higher ulcer healing rate and a higher H. pylori eradication rate than AMT, it was more costly. Since no incremental analysis was performed, no policy conclusions could be drawn from this. However, the paper's abstract states that "the AMT therapy was more effective and less costly than the OA therapy", a statement, which was not entirely supported by the paper's findings.

CRD COMMENTARY - Selection of comparators
The two treatments considered (AMT and OA), were measured against each other, as both were commonly used in the authors' setting. You, as a database user, should consider whether this applies to your own setting.

Validity of estimate of measure of effectiveness
Effectiveness was measured in a simple 'yes' or 'no' response to the questions "have the ulcers healed?" and "has the H. pylori been eradicated?" following an endoscopic examination. The sample sizes of 46 and 43 for the OA and AMT groups respectively can be considered large enough to give statistically significant results based on the power calculations reported by the authors. However, the analysis was based on treatment completers only, which might have introduced biases in the study. In addition, the follow-up period might have been too short for the purpose of establishing the ulcer recurrence rates.

Validity of estimate of costs
Costs were estimated based on actual data. The indirect costs of time off work due to illness and recovery were based on the average daily salary. It is not clear, however, how the average daily salary was calculated. As acknowledged by the authors, the cost of treatment in China might be considerably lower than costs in developed countries, therefore they should only be applicable in the South of China and possibly in other developing countries. (For example, the average wage in China, where the study was performed, is significantly lower than that in Western European countries). This would still be limited by the fact that only few quantities and no item costs were reported in the paper.

Other issues
The authors reported the ratios of the cost-effectiveness of each treatment as well as the ratio of the cost-effectiveness of the two treatments. However, according to the study findings the two treatments demonstrated similar effectiveness and, therefore, the economic evaluation was reduced to a cost-minimisation analysis. This would have required comparison of costs only.

Implications of the study
The study is unlikely to have any international consequences, since it was performed under local conditions.

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Bibliographic details

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Other publications of related interest


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