Cost-effectiveness of alternative approaches in the management of dyspepsia
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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
Seven strategies for the management of uninvestigated dyspepsia were studied. The strategies were endoscopy, double-contrast barium meal, empirical eradication therapy, empirical antisecretory treatment, urea breath test (UBT), laboratory serology and sequential testing.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised adult patients with symptoms of dyspepsia. Patients presenting with symptoms suggestive of gastroesophageal reflux disease and alarm symptoms (e.g. weight loss, recurrent vomiting, dysphagia, bleeding, or anaemia) were excluded, as were those with biliary pain or irritable bowel syndrome. Patients taking nonsteroidal anti-inflammatory agents were also excluded. The population was divided into two age groups for the purpose of modelling. The cut-off age was 45 years.

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

Dates to which data relate
The effectiveness data were derived from studies published from 1966 to 1999. The dates during which the resource use data were collected were not reported. The price year appears to have been 1998.

Source of effectiveness data
The effectiveness data were derived from a review of published studies.

Modelling
A 6,666-node decision tree model was used in the economic analysis. The purpose of the model was to use data from the literature to undertake a decision analysis. The authors simulated possible choices that physicians have to confront in the investigation of dyspepsia. The time horizon of the model was 12 months.

Outcomes assessed in the review
The parameters of the model were the main outcomes assessed in the review, such as:
the sensitivity and specificity of the tests,

the prevalence of H. pylori,

the healing rates,

the recurrence rates,

treatment failure and

the cure rates.

Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
MEDLINE and Current Contents were searched for articles in English or French. The electronic searches were supplemented with handsearches.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
The initial search identified approximately 600 peer-reviewed articles and abstracts. A final group of approximately 50 studies provided the relevant data.

Methods of combining primary studies
The primary studies were combined by averaging the study results and/or using a published meta-analysis.

Investigation of differences between primary studies
Not reported.

Results of the review
The sensitivity and specificity of the diagnostic tests for H. pylori used in the model were:

UBT, sensitivity 96% (range: 90.2 - 100) and specificity 97% (range: 89 - 100);

rapid urease test, sensitivity 94.5% (range: 87.7 - 99) and specificity 97% (range: 92.6 - 100);

histology, sensitivity 94% (range: 91.1 - 96) and specificity 98% (range: 95 - 100); and

laboratory serology, sensitivity 85% (range: 79.9 - 100) and specificity 79% (range: 74 - 100).

The sensitivity of a barium meal was:
73% (range: 43 - 100) for the detection of duodenal ulcer;

74% (range: 43 - 92) for gastric ulcer;

89% (range: 73 - 100) for gastric cancer;

82% (range: 75.0 - 91.9) for oesophagitis; and

91% (range: 41 - 100) for non-ulcer dyspepsia (NUD).

Younger patients were separated from older adult patients on the basis of a cut-off age of 45.

The authors also reported the baseline parameters for the prevalence of H. pylori, healing rates, recurrence rates, treatment failure and cure rates.

Methods used to derive estimates of effectiveness
An expert panel of gastroenterologists made assumptions about effectiveness for which no data were available.

Estimates of effectiveness and key assumptions
The expert panel assumed that symptomatic failure rate in NUD patients who were H. pylori negative before and after treatment at 1 year was 70% (range: 50 - 100). They also assumed that the median length of time to treatment failure in NUD patients was 4 months (range: 2 - 6). Finally, the sensitivity and specificity of the 13C and 14C urea breath tests were assumed to be equivalent.

Measure of benefits used in the economic analysis
The proportion of patients remaining symptom-free over a 12-month time period after initial therapy was used as the measure of benefits (number of patients cured per 100 patients).

Direct costs
The direct costs to the health service were included in the analysis. These included pharmacological treatments, physician visits, diagnostic tests and complications. The cost of endoscopy was calculated using a micro-costing, time-motion study carried out at the Montreal General Hospital. Other unit costs were derived from the Quebec Drug Plan, Conseil Consultatif de Pharmacie, Capsules Pharmacotherapeutiques, Quebec Ministry of Health and Social Services and Quebec physician fee schedule. Complications and costs relating to possible development of oesophagitis after H. pylori eradication were not considered. The costs appear to have been expressed in 1998 prices. The costs were not discounted as the time horizon chosen was 12 months.

Statistical analysis of costs
The costs were treated as point estimates (i.e. the data were deterministic). The costs for each arm of the decision tree were calculated using the expected value approach.

Indirect Costs
The indirect costs were not included.

Currency
Canadian dollars (Can$).

Sensitivity analysis
Both one-way and multi-way sensitivity analyses were performed. Five key variables were varied using ranges obtained from the review of the literature. These variables were symptomatic recurrence rates, prevalence of duodenal ulcer in young patients, prevalence of H. pylori in duodenal ulcer patients, specificity of UBT and the symptomatic relapse rate in H. pylori-negative NUD patients. A threshold analysis was performed on three key parameters, that is, gastric cancer rate, cost attributable to UBT and laboratory serology costs.

**Estimated benefits used in the economic analysis**

For patients aged between 18 and 45 years, the numbers of patients cured with each strategy were as follows:

- 27.15 patients with empirical antisecretory treatment;
- 29.86 patients with the double-contrast barium meal,
- 30.58 patients with endoscopy,
- 32.00 patients with sequential testing,
- 32.07 patients with laboratory serology,
- 32.49 patients with empirical eradication therapy, and
- 32.84 patients with the UBT.

Compared with empirical antisecretory treatment, serology cures 4.96 additional patients per 100. Compared with empirical eradication treatment, UBT cures 0.35 additional patients per 100.

Detailed results for the numbers of patients cured in the over 45-year age group for the different alternatives were not presented. Compared with empirical eradication treatment, UBT cures 0.46 additional patients per 100. Evidence suggested that 2% of older patients had gastric cancer. All cases of gastric cancer were detected using a policy of early endoscopy.

**Cost results**

For patients aged between 18 and 45 years, the costs of the strategies were as follows:

- Can$62,904 for empirical antisecretory treatment,
- Can$74,871 for the double-contrast barium meal,
- Can$79,113 for endoscopy,
- Can$80,756 for sequential testing,
- Can$77,548 for laboratory serology,
- Can$80,241 for empirical eradication therapy, and
- Can$83,891 for the UBT.

The incremental costs were Can$14,644 for serology compared with empirical antisecretory treatment, Can$2,693 for empirical eradication compared with serology, and Can$3,650 for the UBT compared with empirical eradication.

Detailed costs for the different alternatives in the over 45-year age group were not presented.

**Synthesis of costs and benefits**
The costs and benefits were synthesised using the incremental cost-effectiveness ratio (ICER). Dominated and extended dominated alternatives were removed before applying the incremental analysis.

For patients aged between 18 and 45 years, endoscopy and sequential testing were dominated by laboratory serology. A combination of empirical antisecretory and laboratory serology approaches was more cost-effective than the barium strategy. The remaining four strategies were cost-effective in this patient group. The ICER of serology compared with empirical antisecretory treatment was Can$2,970 per additional patient cured. The ICER of empirical eradication therapy compared with serology was Can$6,412 per additional patient cured. Finally, the ICER of UBT compared with empirical eradication therapy was Can$10,429 per additional patient cured.

For patients aged over 45 years, empirical antisecretory treatment, barium examination, empirical eradication therapy and UBT were the cost-effective interventions. The ICER of UBT compared with empirical eradication therapy was Can$10,835 for each additional patient cured. The ICER of UBT compared with barium testing was Can$4,114 per additional patient cured.

Endoscopy became cost-effective when the difference in symptomatic recurrence rates dropped to less than 6.3%. When this difference dropped to 3% or lower, endoscopy and empirical antisecretory strategies were the only cost-effective alternatives in younger patients. The same result was achieved in the older group of patients, with a cut-off of 5.4%. When the cost of a UBT decreased to Can$44.28 and Can$36.60, laboratory serology and empirical eradication, respectively, were no longer cost-effectiveness strategies.

Authors' conclusions
The results suggested that a "test and treat" approach with a urea breath test (UBT) was the most effective, but most costly, initial test in both age groups. However, for patients over 45 years, endoscopy resulted in the early detection of most gastric cancers.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear. They appear to have represented current practice in the authors' setting. In additional, there was some uncertainty about the cost-effectiveness and trial data for current practice. You should decide if this is widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature had been undertaken. However, an extensive review of the literature was performed to collect the key parameters and ranges of the model. Given that only 50 of the 600 papers identified were included, it would have been useful if the inclusion criteria had been reported. In addition, it was not stated whether the authors considered the impact of differences between the primary studies when extracting the data. Therefore, the ranges used to conduct the sensitivity analysis may well have influenced the external validity of the model results.

Validity of estimate of measure of benefit
The estimation of benefits was obtained directly from the model. The choice of estimate was justified on clinically relevant grounds. The evidence presented by the authors in the introduction supported the use of symptoms as an outcome measure of benefits.

Validity of estimate of costs
All the categories of cost relevant to the perspective adopted were included in the analysis. The micro-costing approach used to calculate the cost of endoscopy supported the costing exercise. However, no data on resource use for the different categories were presented. This may limit the interpretation of the study findings since the model results were sensitive to some test costs. The authors did not report the sources from which the resource use data were derived. It was also unclear how the total cost of each alternative was calculated, thus raising doubts about the internal validity of
the model. The costs were taken from published sources. However, the price year was only reported in tables and it is not clear that all the costs were expressed using that year. The internal validity of the model is suspicious as threshold analysis suggested that the results were sensitivity to some test costs.

Other issues
The authors compared the results of their model with other published evidence and acknowledged the limitations of their study. The main limitation, as the authors acknowledged, was the lack of data necessary to complete some parameter information. Generalisability was addressed in the sensitivity analysis of the main parameters, which was performed well. The authors presented the results selectively in that they reported all results for 18- to 45-year-olds, but not for the over 45-year age group. This makes it difficult to determine how dominance and extended dominance were determined for this group.

Implications of the study
The authors favoured a "test and treat" approach in the primary care setting to manage patients with uninvestigated dyspepsia. The use of a UBT is recommended as the optimal detection method for the presence of H. pylori.

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