A cost-effectiveness analysis of diagnostic strategies for symptomatic patients with healed pouch-anal anastomosis


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 compared six strategies for diagnosing and treating patients with suspected pouchitis. There were four treat-first strategies (i.e. diagnosis of pouchitis based on symptoms alone and empirically treat patients with antibiotics) and two test-first strategies. The treat-first strategies evaluated were:

- metronidazole (MTZ);
- ciprofloxacin (CIP);
- treatment with MTZ and, in case the patient did not respond, administration of CIP (i.e. MTZ then CIP); and
- treatment with CIP followed by MTZ if the patient did not respond (i.e. CIP then MTZ).

All MTZ regimens consisted of 500 mg taken orally, three times daily, for 14 days. All CIP regimens consisted of 500 mg taken orally, twice daily, for 14 days.

The test-first strategies included pouch endoscopy with and without biopsy, combined with an assessment of symptoms using a diagnostic instrument (the Pouchitis Disease Activity Index, PDAI). Patients who met the diagnostic criteria for pouchitis were treated with MTZ followed by CIP if necessary.

Type of intervention
Diagnosis and treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The target population comprised adult patients suffering from ulcerative colitis with symptoms suggestive of pouchitis. Patients with Crohn's disease, or chronic refractory pouchitis receiving chronic maintenance therapy, were excluded from the study.

Setting
A setting was not explicitly stated, but it may have been secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1989 and 2003. Medication costs were derived from a source published in 2001, while dates relating to the rest of the costs and the price year were not reported.
Source of effectiveness data
The effectiveness data were derived from a non-systematic review that synthesised published studies, and from expert opinion and authors' assumptions.

Modelling
The authors constructed a decision analytic model to estimate the cost-effectiveness of the different strategies. The time horizon considered at analysis was not stated clearly, but it appears to have been 30 days.

Outcomes assessed in the review
The input parameters used in the decision analytic model that were assessed in the review were:

- the probability of pouchitis in symptomatic patients,
- the probability of response to CIP and MTZ, and
- the diagnostic sensitivity of pouch endoscopy without biopsy.

Study designs and other criteria for inclusion in the review
The authors did not report the inclusion or exclusion criteria used to identify the studies that were included. However, they did state that they reviewed randomised controlled trials, placebo-controlled trials, non-controlled trials and other published literature.

Sources searched to identify primary studies
Not reported.

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
Overall, at least 11 studies were included in the review.

Methods of combining primary studies
The authors did not report any specific method used to combine the primary studies, although a narrative method appears to have been used.

Investigation of differences between primary studies
The authors reported some of the effectiveness estimators independently for each individual study, identifying the design, duration and doses administered in some of the studies reviewed, although they did not state whether any statistical test of homogeneity was performed.

Results of the review
The probability of pouchitis in symptomatic patients was 0.52 (range: 0.37 - 0.80),
the probability of response to CIP was 0.85 (range: 0.60 - 0.99),

the probability of response to MTZ was 0.75 (range: 0.50 - 0.90), and

the diagnostic sensitivity of pouch endoscopy without biopsy was 0.97 (range: 0.90 - 100).

**Methods used to derive estimates of effectiveness**

Some estimates of effectiveness were based on experts' opinion and authors' assumptions.

**Estimates of effectiveness and key assumptions**

The authors mentioned that, owing to the small number of cases reported in the literature, the efficacy of CIP was conservatively assumed to be 85% (smaller than the estimates derived from the literature). It was assumed that symptoms in patients without inflammation on endoscopy and histology were due to irritable pouch syndrome.

The probability of endoscopy with biopsy for patients who failed empiric regimens was 1.00 (range: 0.25 - 1.00).

Diagnostic delay with biopsy and histology was 3 days (range: 1 - 5).

The rate of adverse effects on drug therapy that required a return clinic visit was 0% (range: 10 - 90).

The rate of placebo response to empiric antibiotics in symptomatic patients without pouchitis was 20% (range: 0 - 30).

In the baseline analysis it was assumed that pouch endoscopy and histology combined with symptom assessment were sufficient to accurately diagnose all patients with pouchitis on a single clinic visit.

**Measure of benefits used in the economic analysis**

The measure of benefit used was the length of time the patient spent correctly diagnosed and appropriately treated. This measure of benefit appears to have been derived from the model. The time horizon considered for the estimation of health benefits might have been 30 days, although it was not clearly identified.

**Direct costs**

The direct costs included in the study would appear to be those of the health service. These covered the costs of medication, pouch endoscopy (with and without biopsy) and histological evaluation. Some but not all of the unit costs and resource quantities were reported independently. The costs were derived from published sources and were based on actual data. Discounting was not carried out, although this was appropriate as the time horizon of the model was shorter than 2 years. The dates relating to costs derived from Medicare were not reported. The price year was also not reported for all costs included. The cost results were given as the average cost per correct diagnosis and initiation of appropriate treatment.

**Statistical analysis of costs**

No statistical analyses of the costs were reported.

**Indirect Costs**

The indirect costs were not included in the analysis.

**Currency**

US dollars ($).
Sensitivity analysis
One-way sensitivity analyses were carried out on all parameters in the model to investigate variability in the data. The ranges used were based on published data and on expert opinion (see ‘Results of the Review’ and ‘Estimates of Effectiveness and Key assumptions’ sections), while all costs estimates ranged by +/- 50%.

A second sensitivity analysis was performed by simultaneously increasing and decreasing the duration of treatment with MTZ and CIP. A further sensitivity analysis was performed in which the effectiveness of treat-first regimens was based on the beginning of regimens to which patients responded. Finally, sensitivity analyses were used to investigate the impact of second clinic visits in patients who did not respond to empiric antibiotic therapy and in patients who experienced adverse effects from the drug therapy.

Estimated benefits used in the economic analysis
The time that the patient spent correctly diagnosed and appropriately treated in a specific period of time (that appeared to be 30 days) was 12.2 days with MTZ, 27.6 days with test-no biopsy, 6.7 days with MTZ then CIP, 7.4 days with CIP then MTZ, 12.9 days with CIP, and 25.0 days with test-biopsy.

The incremental effectiveness (in terms of the additional number of days the patient spent correctly diagnosed and appropriately treated) was:

for pouch endoscopy without biopsy compared with the MTZ treatment strategy, 15.4 days;
for the MTZ then CIP strategy compared with the MTZ treatment strategy, -5.5 days;
for the CIP then MTZ strategy compared with pouch endoscopy without biopsy, -20.1 days;
for the CIP treatment strategy compared with pouch endoscopy without biopsy, -14.6 days; and
for pouch endoscopy with biopsy compared with pouch endoscopy without biopsy, -2.6 days.

Cost results
The cost per correctly diagnosed and appropriately treated patient was:

for the MTZ treatment strategy, $193.7;
for the MTZ then CIP strategy, $208.1;
for pouch endoscopy without biopsy, $243.4;
for the CIP then MTZ treatment strategy, $261.4;
for the CIP treatment strategy, $278.8; and
for pouch endoscopy with biopsy, $352.3.

Synthesis of costs and benefits
The estimated health benefits and costs were combined using cost-effectiveness ratios, which measured the cost per day of being correctly diagnosed and appropriately treated. An incremental cost-effectiveness analysis was also performed, in which the incremental cost-effectiveness ratio (ICER) was calculated as the cost per additional day of being accurately diagnosed and appropriately treated when one of the strategies was compared with another. The CIP, the MTZ then CIP, and the CIP then MTZ treatment strategies and pouch endoscopy with biopsy were associated with higher costs and lower effectiveness, and were therefore dominated. Pouch endoscopy without biopsy resulted in a cost of $3.24 per additional day of being diagnosed and initiated for correct treatment when compared with the MTZ treatment strategy.
In the sensitivity analysis, when the cost of pouch endoscopy without biopsy was raised from $210 to $375, pouch endoscopy with biopsy was no longer dominated, but it still remained less effective than pouch endoscopy without biopsy. When assuming that 10% of patients under drug therapy would experience adverse effects and would return for a second clinic visit, the ICER for pouch endoscopy without biopsy decreased to $2.76. When this rate was raised to 90%, the ICER would further decrease to $1.72.

Authors’ conclusions
Pouch endoscopy without biopsy strategy was the most cost-effective approach to diagnosing and treating patients with symptoms suggestive of pouchitis, avoiding diagnostic delay and unnecessary antibiotic use.

CRD COMMENTARY - Selection of comparators
A justification was provided for the comparators used. The treat-first strategies seem to represent common practice in the authors’ setting. On the other hand, published studies have demonstrated that test-first strategies are more reliable in providing an accurate diagnosis of pouchitis than the symptom assessment alone. You should decide whether any of these strategies represents a widely used technology in your own setting.

Validity of estimate of measure of effectiveness
The authors did not explicitly state that a systematic review of the literature had been undertaken. The sources searched, inclusion criteria and data extraction methodology were not reported. It is therefore possible that there may be some bias due to the potential exclusion of some relevant studies. The data from the available studies appears to have been used selectively. The authors did not perform any statistical analysis of homogeneity for the included studies, nor did they report on the methods used to combine the estimates, if in fact they did combine them. Given the level of reporting, it is difficult to judge the quality of the effectiveness parameters used as model inputs. However, the authors carried out a number of sensitivity analyses and these improve both the internal validity and the generalisability of the study results, by demonstrating the robustness of the results to changes in the base-case estimates.

Validity of estimate of measure of benefit
The summary measure of benefit used in the economic analysis (i.e. difference in length of time being correctly diagnosed and adequately treated) appears to have been derived from the model.

Validity of estimate of costs
The perspective of the economic analysis was not reported clearly, although it might have been that of the health service. Since the perspective was unclear, it cannot be assessed whether all the relevant costs were included in the analysis. The unit costs and the resource quantities were derived from published sources and were based on actual data. Sensitivity analyses were conducted on ranges of all unit cost inputs. The price year and any possible inflation adjustments performed were not reported, thus limiting reflation exercises in other settings.

Other issues
The authors did not make appropriate comparisons of their findings with those from other studies. However, as the authors highlighted, this may have been due to a lack of published economic evaluations in this specific area. The sensitivity analyses undertaken improve the generalisability of the study findings to other settings. Regarding this issue, the authors recommended that pouch endoscopy without biopsy could be appropriate for patients having Crohn's disease of the pouch, chronic pouchitis, or cytomegalovirus-related pouchitis.

The authors highlighted some of the limitations of their study. For example, the lack of an analysis of indirect costs such as loss of productivity or leisure time due to delayed diagnosis, and adverse effects from inappropriate therapy. Also, the majority of the studies included in the decision model had limited sample sizes. Thus, it was unclear whether the study samples were representative of the study population and whether changes in the sample size would have affected the results. However, the sensitivity analyses demonstrated the robustness of the results of the base-case
Implications of the study
In terms of changes in practice, the authors recommended pouch endoscopy without biopsy as the most cost-effective strategy in order to avoid delayed diagnosis and unnecessary antibiotic use. No further research was proposed, but the discussion highlighted areas where further research would be valuable.

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