A two-stage decision analysis to assess the cost of 5-aminosalicylic acid failure and the economics of balsalazide versus mesalamine in the treatment of ulcerative colitis

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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
The use of two oral 5-aminosalicylic acid (5-ASA) agents, balsalazide (6.75 g/day) and mesalamine (2.4 and 4.8 g/day), in the treatment of ulcerative colitis (UC).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The modelled population comprised a specific type of UC patient commonly seen in the USA, with the following characteristics:

chronic symptoms;
newly diagnosed (first referral to a gastroenterologist);
patient-stated preference to avoid rectal (topical) therapy;
patient presents primarily with left-sided UC; and
physician hesitant to prescribe sulfasalazine because of the perceived potential for adverse events.

Setting
The setting was specialist care. The economic study was conducted in the USA.

Dates to which data relate
The clinical justification for the 6-step algorithm, with over 200 references, was presented in Kornbluth and Sachar 2004 (see 'Other Publications of Related Interest' below for bibliographic details). The effectiveness data were drawn from 13 studies published between 1982 and 2005. The cost data were stated to have been taken from published sources, but no references were given. The price year was not reported.

Source of effectiveness data
The treatment algorithm was derived from the ACG guidelines. The proportions of patients receiving each of the two doses of mesalamine were taken from current US prescribing data. The model used incremental remission rates after 4 weeks for each step of the ACG guidelines.
Modelling
A two-stage decision analysis model was constructed using TreeAge Pro 2000 software. The first stage was used to estimate the average cost of treatment failure, incorporating treatment decisions according to the evidence-based ACG guidelines, clinical trial results and published costs. The second stage was used to estimate the clinical and cost outcomes associated with the comparators for a specific patient type, and also incorporated published trial outcomes and costs. The second stage covered a time horizon of 178 days (6 months), reported as the minimum time for all patients to progress through all 6 steps of the ACG treatment algorithm.

Sources searched to identify primary studies
For most of the ACG guideline steps, no studies evaluated the remission rates for those treatments in precisely the same population and sequence under consideration. Where studies were found, they were mainly observational rather than randomised controlled trials. Randomised clinical trials were available to supply the efficacy data for the two 5-ASA agents (step 1).

Methods used to judge relevance and validity, and for extracting data
It was unclear whether a systematic review was conducted. The author presented the results of the search and the values used in the model, as supported by the published data available. It appears that the data have been taken from published sources where possible, although some linear extrapolation to 4-week time points and some assumptions had been necessary.

Measure of benefits used in the economic analysis
The clinical measure "days without symptoms or steroids" (DWSS) was used in the economic analysis. This signified time spent in remission.

Direct costs
Stage 1 of the model estimated the average cost of 5-ASA treatment failure, excluding the cost of 5-ASA therapy before and/or after therapy. Resource use was based on the ACG guidelines and author assumptions. The costs of other drug therapies, physician visits, laboratory tests, procedures (e.g. flexible sigmoidoscopy and biopsy), surgery and non-surgical hospital admissions were included. A graphical representation of the model and its inputs was presented. Stage 2 of the model included the costs of 5-ASA therapy. References and sources of resource use and cost data were not provided.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
Productivity costs were not relevant to the perspective chosen. The author provided data from other published studies that had investigated the indirect costs (Hay and Hay 1992, see 'Other Publications of Related Interest' below for bibliographic details).

Currency
US dollars ($).

Sensitivity analysis
The author performed some threshold analysis but did not clarify whether all of the parameters were investigated in a sensitivity analysis. Remission data for the 5-ASA agents from different studies were tested in the model.
Estimated benefits used in the economic analysis
Patients treated with balsalazide experienced 104 of 178 (58%) DWSS, while patients treated with mesalamine experienced 78 of 178 (44%) DWSS.

Cost results
The average cost of 5-ASA failure was $11,501, excluding the cost of 5-ASA therapy before and/or after failure.

Daily drug costs of $11.16 for balsalazide, $6.60 for 2.4 g/day mesalamine and $13.20 for 4.8 g/day mesalamine were reported.

Total drug and medical costs over 6 months of $9,319 for balsalazide and $11,066 for mesalamine (weighted average of the two doses) were reported.

The costs of complications were not addressed in the model, which had a time horizon of only 6 months.

Synthesis of costs and benefits
The average cost-effectiveness ratios were calculated.

The cost per DWSS was $89.61 for balsalazide and $141.87 for mesalamine.

The authors stated that the remission rate in the balsalazide arm would have to be reduced from 38% to 22% before the two treatments had equal health care costs.

The hypothetical remission rate reduction would have to be reduced from 35% to 14% before the two treatments were associated with similar average cost-effectiveness.

Authors’ conclusions
Balsalazide was considerably more cost-effective than mesalamine. The results were robust.

CRD COMMENTARY - Selection of comparators
The comparison incorporated the most commonly prescribed branded 5-ASA products in the USA. These drugs were recommended as first-line therapy for UC in the ACG guidelines. The modelled population was defined in such a way as to exclude patients willing to receive rectal therapy or whose physicians would consider an alternative drug (sulfasalazine). You should decide if the chosen comparators reflect relevant practice in your own setting.

Validity of estimate of measure of effectiveness
The clinical parameters were derived from published sources and explained assumptions. The author did not report any search methods, although he did justify the chosen estimates. Complications and adverse events were not considered. Full remission was assumed to occur on the last day of a 4-week period, even though data describing time to remission had been reported for the 5-ASA agents. The author noted that treatments with a faster onset did not achieve the full benefit of their earlier onset in the analysis. The exclusion of a randomised controlled trial comparing the two 5-ASA agents was excluded on the basis of the population studied and the data available from that study; this seemed reasonable. Maintaining separate effectiveness estimates for the two mesalamine doses would have been more informative as current prescribing patterns may not be optimal.

Validity of estimate of measure of benefit
The author justified the choice of benefit measure, noting that "days without symptoms" was used as a measure of benefit in other disease areas and that the use of steroids was expected to lead to significant side effects. However, this measure did not capture the full benefits of the interventions and was inaccurate in that the adverse events of treatment or complications of disease were ignored in its calculation.
Validity of estimate of costs
The inclusion of the direct medical costs was appropriate for the payer perspective. The direct medical costs in the analysis did not include the pharmacists’ dispensing fees, the costs of treating complications related to UC, or the costs of steroid use. These omissions may well have affected the findings of the study. It was impossible to judge the quality of the cost estimates since total event costs were used and no references or sources were given. It was not stated whether the cost estimates were taken from a single price year, but no inflation of the costs was reported. The author listed several types of indirect cost associated with UC, none of which were included. Maintaining separate cost estimates for the two mesalamine doses would have been more informative as current prescribing patterns may not be optimal.

Other issues
The authors made appropriate comparisons with other studies. When comparing the results of the stage 1 model with a published natural history study, the author noted that it appears to have underestimated the proportion of patients going on to receive surgery (the underestimate was substantial: estimate of 18% of patients who had received steroids compared with 29% in the published study). However, no sensitivity analysis was performed to investigate the impact of this discrepancy on the effectiveness or costs. Generalisability was not addressed. The author did not present the results selectively and the conclusions reflected the scope of the study, although combining the two mesalamine doses reduced the information available. The average cost-effectiveness, which is not informative for decision-makers, rather than incremental cost-effectiveness (best practice in economic evaluation), was presented. However, it was clear that balsalazide, having improved clinical outcomes and lower cost, would dominate mesalamine in the incremental cost-effectiveness analysis. The author noted that, as with all models, a true validation of the entire algorithm within a single trial would be required to determine if the findings are accurate.

Implications of the study
The author concluded that using the most effective 5-ASA and achieving good patient adherence is necessary to reduce the number of patients who do not achieve remission and go on to incur high health care costs because of increased morbidity. The study shows that patients treated with balsalazide have improved costs and outcomes compared with those treated with mesalamine.

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Bibliographic details
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Other publications of related interest

