Using multiple pharmacoeconomic methods to conduct a cost-effectiveness analysis of histamine H-2-receptor antagonists

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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
A formulary decision to designate cimetidine as the primary histamine H2-receptor antagonist (H2RA) and to restrict the use of famotidine in patients receiving stress ulcer prophylaxis.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients receiving stress ulcer prophylaxis. Patients were excluded if they were receiving concomitant therapy with a proton-pump inhibitor or sucralfate, had a history of peptic ulcer disease, were receiving oral H2RA therapy, were receiving iv therapy for less than 72 hours, or were younger than 18. In addition, patients had to be admitted to the surgical intensive care unit, medical intensive care unit, GI surgery/GI diseases unit, or neurosurgical floor.

Setting
Hospital. The economic analysis was carried out in Iowa City, USA.

Dates to which data relate
Effectiveness and resource use data were gathered in the period between October and November 1997. The price year appears to have been 1997.

Source of effectiveness data
The evidence for the final outcomes was based on a single study.

Link between effectiveness and cost data
Costing was retrospectively conducted on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were not used to determine the sample size. The study sample consisted of 62 patients with an average age of 52 years. There were 43 patients in the cimetidine group and 19 in the famotidine group.

Study design
This was a case series, carried out in a single centre. The duration of the follow-up was until discharge from the hospital. The number of patients who were lost to follow-up was not reported. The formulary change was successfully implemented in the study institution in November 1995 and H2RA use was, at the time of the study, 90% cimetidine and 10% famotidine. This study was conducted to assess the clinical and financial impact of this change.

**Analysis of effectiveness**
The principle (intention to treat or treatment completers only) used in the analysis of effectiveness was not explicitly specified. The primary outcome measure of the study was success rate. Success was defined as a patient either not developing acute upper-GI bleeding while receiving therapy with iv cimetidine or famotidine for stress ulcer prevention, or not having adverse reactions to cimetidine or famotidine requiring the discontinuation of the primary agent or the addition of alternative therapies. Treatment failure was defined as a patient requiring alternative or additional medications because of ineffective cimetidine or famotidine therapy, or having intolerable adverse effects and requiring alternative therapy. No comparisons were made of the baseline characteristics of the two study groups.

**Effectiveness results**
The probability of success for the cimetidine group was 90% (39 of 43 patients) and 89% (17 of 19) for the famotidine group.

**Clinical conclusions**
Efficacy was equal between cimetidine and famotidine.

**Modelling**
A decision tree was used to estimate the costs and effects associated with each treatment modality. Multi-attribute utility theory (MAUT) was used to incorporate a humanistic evaluation of the treatments (i.e. the tool took into account the number of doses administered per day and the number of times dosages changed during the course of therapy as the convenience factors) in addition to the economic and clinical evaluations.

**Measure of benefits used in the economic analysis**
As the efficacy was equal between the two treatment modalities, the decision analysis was reduced to a cost-minimisation study. However, MAUT was used to incorporate a humanistic evaluation of the treatments in addition to the economic and clinical evaluations.

**Direct costs**
Costs were not discounted due to the short time frame of the cost analysis. Resource use quantities were not reported separately from the costs and cost items were not reported separately. The cost analysis covered the costs of adverse reactions, monitoring for potential drug interactions, treatment of therapeutic failure, the addition of other medications, and a complete change in therapy. The perspective adopted in the cost analysis was that of the pharmacy and therapeutic committee. The price year appears to have been 1997.

**Indirect Costs**
Indirect costs were not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analyses were performed by changing the probabilities of success in the decision analytic model and by changing attribute weights related to efficacy, costs, and convenience factors.

**Estimated benefits used in the economic analysis**
The convenience factors used in the MAUT analysis were as follows:

- Number of doses per day: 1.87 (cimetidine) versus 1.4 (famotidine);

- Dosages were changed on average: 1.32 times (cimetidine) and 0.84 times (famotidine).

**Cost results**
The decision tree revealed that the average cost of receiving cimetidine for stress ulcer prophylaxis in this study was $82.01 and the average cost of famotidine therapy was $92.45.

**Synthesis of costs and benefits**
MAUT was used to incorporate a humanistic evaluation of the treatments in addition to the economic and clinical evaluations. The authors arbitrarily decided that efficacy would contribute 60% to the final decision, cost would contribute 20%, and the number of doses and number of dosage changes would each contribute 10%. To determine the most favourable alternative, the agent with the highest total was selected. It was found that by incorporating convenience factors at a weight of 20% in the MAUT analysis, famotidine had a slightly higher value than cimetidine (512 versus 488) and appeared to be the preferred agent. In the decision analysis, sensitivity analysis showed that as long as cimetidine is 80% effective and famotidine is equal to or less effective than cimetidine, cimetidine is the more cost-effective agent. In the MAUT analysis, it was shown that cimetidine was the preferred agent as long as cost was weighted at greater than 60% of the decision-making process and drug efficacy remained equal.

**Authors' conclusions**
The decision analysis showed that as long as cimetidine is 80% effective and famotidine is equal to or less effective than cimetidine, cimetidine is the more cost-effective agent. When MAUT analysis was performed famotidine was the preferred agent.

**CRD COMMENTARY - Selection of comparators**
No explicit justification was provided for the choice of the comparator. You, as a database user, should consider whether this is a widely used health technology in your own setting.

**Validity of estimate of measure of effectiveness**
The internal validity of the effectiveness results cannot be assured given the observational nature of the study design, which is prone to biases. The sample size in the study was not justified and may not have been sufficiently powered. Furthermore, it was not explicitly specified whether the effectiveness analysis was based on intention to treat or on treatment completers only and no comparisons regarding the baseline characteristics were made between the two study groups. It would have been helpful if findings from previous studies had been provided for comparison with the inputs to the decision tree.

**Validity of estimate of measure of benefit**
In the decision analysis, the analysis of benefit was based upon therapeutic equivalence of treatment alternatives and the economic analysis therefore included only costs. In the MAUT analysis, the estimate of benefit measures (the convenience factors) was directly obtained from the effectiveness analysis. Its use was justified based on the need to incorporate the humanistic evaluation in the analysis.
Validity of estimate of costs
Positive aspects of the cost analysis, likely to have enhanced its validity, were as follows. The price year and perspective adopted in the cost analysis were reported, and details of the model and the method of combining benefits and costs to estimate the cost-effectiveness of the two options were provided. However, it is not clear whether the cost data were based on true costs or charges, statistical analyses were not performed on resource use and cost data and the effects of the treatment modalities on indirect costs were not addressed. Cost results may not be generalisable outside the study setting.

Other issues
Given the inherent limitations of the study design, the study results may need to be treated with some degree of caution. Limited sensitivity analyses were performed varying only clinical success and failure and not costs or resource use. The issue of generalisability to other settings or countries was not addressed nor were any comparisons made with other studies. The degree to which the study sample was representative of the study population was not discussed in the authors’ comments. The appropriateness of the MAUT analysis should be analysed with regard to the arbitrariness of the attribute weights adopted in the study.

Implications of the study
This study has a methodological value as it illustrates the use of two pharmacoeconomic methods used to support a formulary decision at a health care institution. The results of the analyses however should be carefully interpreted taking into consideration their limitations and the characteristics of one’s own setting.

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