Cost-utility analysis of infliximab and adalimumab for refractory 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.

CRD summary
This study evaluated the cost and health effects of strategies for the treatment of hypothetical 40-year-old patients with moderate-to-severe active refractory ulcerative colitis. The authors concluded that infliximab was not cost-effective, in the short-term (five years), at the accepted willingness-to-pay threshold. The methods were good and they and the results were adequately reported. The conclusions reached by the authors appear to be appropriate.

Type of economic evaluation
Cost-utility analysis

Study objective
The aim was to assess the cost and health effects of strategies, involving recombinant monoclonal antibodies, for the treatment of moderate-to-severe ulcerative colitis. A hypothetical cohort of patients who were aged 40 years, weighed 80kg, and had moderate-to-severe active refractory ulcerative colitis was studied.

Interventions
The three strategies were usual care, infliximab 5mg per kg with a switch to adalimumab if there was no response or if the response was lost during maintenance therapy, and infliximab 5mg per kg with a switch to 10mg per kg if there was no response and a switch to adalimumab if the response was lost during maintenance therapy. Both the infliximab and adalimumab strategies consisted of initial treatment at weeks zero, two, and six, followed by maintenance treatment every eight weeks. The usual care was conventional medical management with 5-aminosalicylic acid, corticosteroids, and immunosuppressants. Adalimumab was started at 160mg, with 80mg two weeks later, and 40mg every week from the fourth week.

Location/setting
Canada/out-patient care.

Methods
Analytical approach:
A Markov model was constructed to synthesise the published data from sources that included key randomised controlled trials (RCTs) and epidemiological and national reports. The authors stated that the perspective was that of the publicly funded health care system and the analysis had a five-year time horizon.

Effectiveness data:
The effectiveness data were mostly from two pivotal RCTs, reported in one article (Rutgeerts, et al. 2005, see 'Other Publications of Related Interest' below for bibliographic details). A fixed-effect meta-analysis of the findings of these two trials was performed for the remission rates. Other published studies provided data for the rates of surgery after therapy, complications from surgery, and remission on adalimumab. The remission rates in responders and non-responders, the probabilities of early and late one-stage ileal-pouch anal anastomoses, and the probabilities of complications were the main clinical effectiveness estimates.

Monetary benefit and utility valuations:
The health state values were from a study of patients with ulcerative colitis (Arseneau, et al. 2006, see 'Other Publications of Related Interest' below for bibliographic details).

Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs), and they were discounted at an annual rate of 5%.

Cost data:
The direct medical costs included drugs, medical examinations, one-stage ileal-pouch anal anastomosis, and surgical complications. The drug costs were marked up by 8%. The resource use for usual care was based on clinical opinion. The remaining values were estimated from public sources, such as the Ontario Schedule of Benefits and the Alberta Health and Wellness, Interactive Drug Benefit List. All costs were discounted at 5% and reported in 2008 Canadian dollars (CAD).

Analysis of uncertainty:
One-way sensitivity analyses assessed the uncertainty in the key parameters and results. Probabilistic sensitivity analysis was undertaken, with Monte Carlo simulations, and 95% confidence intervals were generated. The results were illustrated on cost-effectiveness acceptability curves.

Results
The discounted mean cost per patient over five years was CAD 24,268 with usual care, CAD 82,756 with infliximab then adalimumab, and CAD 101,272 with increased dose then adalimumab. The QALYs were 2.015 with usual care, 2.178 with infliximab then adalimumab, and 2.149 with increased dose.

The incremental cost per QALY gained was CAD 358,088 with infliximab then adalimumab and CAD 575,540 with increased dose, compared with usual care. Infliximab then adalimumab was less costly and more effective than increased dose.

One-way sensitivity analyses showed that the incremental cost per QALY gained was sensitive to the remission rates, early ileal-pouch anal anastomosis rate, and the utility values. The probabilistic sensitivity analysis indicated that it was 100% likely that usual care was cost-effective below a willingness-to-pay threshold of CAD 150,000. With a willingness-to-pay threshold of CAD 400,000, there was a 50% probability that infliximab then adalimumab was cost-effective. The commonly accepted willingness-to-pay threshold was CAD 50,000.

Authors' conclusions
The authors concluded that infliximab was not cost-effective for the short-term treatment of patients with active ulcerative colitis, at the accepted willingness-to-pay threshold.

CRD commentary
Interventions:
The authors provided clear descriptions of the treatment options and a diagram of the treatment switching pathways. The interventions appear to have been appropriate comparators and the usual care was included. These options might be available in other settings.

Effectiveness/benefits:
The model structure was clearly illustrated and all the inputs and data sources were given. The measurement and valuations of the efficacy and utilities were from published studies, which should be consulted to assess their quality. No description was given for the two RCTs that provided the main effectiveness data and the trial publication should be read to assess their quality and if all the best available evidence was used. The benefits were appropriately discounted.

Costs:
The direct medical costs were included and they seem to have been appropriate for the perspective. The resource types, how they were measured and valued, and their unit costs were clearly provided. Clinical opinion was used to derive the resource consumption for usual care. The costs were appropriately discounted and adjusted for inflation.

Analysis and results:
The analysis appears to have been comprehensive and the incremental results were appropriately presented. The authors' interpretation of the incremental cost-utility results was reasonable as they found virtually no scenario in which infliximab was likely to be cost-effective. They reported a number of study limitations, including the omission of
serious infections (e.g. lupus-like reactions and neurologic diseases) that might arise from infliximab, and the omission of treatment strategies after surgery. Comparisons were made with a UK economic evaluation of infliximab and the differences in strategies, model structure, and assumptions were discussed.

Concluding remarks:
The methods were good and they and the results were adequately reported. The conclusions reached by the authors appear to be appropriate.

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