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 assessed the cost-effectiveness of the two biological agents, infliximab and adalimumab, for the treatment of moderate-to-severely active Crohn’s disease, in comparison with standard care. The authors concluded that both infliximab and adalimumab could be cost-effective, when used for limited durations (up to four years) in initial responders. Longer treatment periods reduced their cost-effectiveness. The study was well carried out and satisfactorily presented. The authors’ conclusions appear to be valid.

Type of economic evaluation
Cost-utility analysis

Study objective
This study assessed the cost-effectiveness of two biological agents, namely infliximab and adalimumab, for the treatment of adults with moderate-to-severely active Crohn’s disease, in comparison with standard care.

Interventions
The two anti-tumour necrosis factor alpha drugs were: infliximab 5mg per kg in intravenous infusions at weeks zero, two, and six, for the induction of remission, then eight-weekly for the maintenance of remission; and adalimumab 80mg subcutaneously at week zero and 40mg at week two, for the induction of remission, then 40mg on alternate weeks for the maintenance of remission. Each treatment was added to the standard care, for one or two years.

Standard care consisted of surgery and medical management, using 5-aminosalicylic acid derivatives, immunosuppressive agents (azathioprine or mercaptopurine), corticosteroids, antibiotics, symptomatic therapies, and topical therapy.

Location/setting
UK/secondary care.

Methods
Analytical approach:
The analysis was based on a Markov model with a lifetime horizon. The authors stated that the study was carried out from the perspective of the UK National Health Service (NHS).

Effectiveness data:
The clinical data were derived from a systematic review of the literature in commonly used electronic databases, supplemented by manual searches of reference lists. The inclusion criteria were reported and only randomised controlled trials (RCTs) were considered. Two relevant trials (one for each drug) were identified; the ACCENT I trial for infliximab and the CHARM trial for adalimumab. The details of adjustment procedures used to fit the trial data into the model were clearly presented. The natural progression of disease with standard care was based on a cohort study. The treatment efficacy, which was the reduction in disease progression, was the key clinical input.

Monetary benefit and utility valuations:
The utility values were based on pooled European Quality of life (EQ-5D) questionnaire scores from three trials. These
scores were mapped from Crohn’s Disease Activity Index scores using a published algorithm.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and were discounted at an annual rate of 3.5%.

Cost data:
The analysis included those costs associated with in-patient and out-patient services, investigations, medications, and surgery. Except for the two drugs, the medical costs were derived from a published economic evaluation. They were recalculated to match the health states of the simulation model. The unit costs of the two drugs were taken from the British National Formulary, using doses reflecting the management of patients in a UK study. Administration costs were included. All costs were in UK pounds sterling (£) for the fiscal year 2006 to 2007 and a 3.5% annual discount rate was applied.

Analysis of uncertainty:
A probabilistic sensitivity analysis was undertaken by running 1,000 Monte Carlo simulations. The key sources of uncertainty were the costs of treatment, the cost of managing patients with Crohn’s disease, and the utility values. Other model inputs were also varied in a deterministic one-way and threshold sensitivity analysis.

Results
The mean cost of treatment was £43,490 with standard care, £50,330 with infliximab for one year, £58,230 with infliximab for two years, £46,730 with adalimumab for one year, and £53,090 with adalimumab for two years. The mean QALYs were 14.209 with standard care, 14.568 with infliximab for one year, 14.901 with infliximab for two years, 14.682 with adalimumab for one year, and 15.156 with adalimumab for two years.

In comparison with standard care, the incremental cost per QALY gained was £19,050 with infliximab for one year, £21,300 with infliximab for two years, £7,190 with adalimumab for one year, and £10,310 with adalimumab for two years.

The sensitivity analysis showed that the model was highly sensitive to the duration of treatment and to the time horizon. The threshold analyses showed that, after four years, infliximab was no longer cost-effective at a threshold of £30,000 per QALY gained, while adalimumab had the potential to remain cost-effective over longer time frames, but the need for extrapolation of data made this uncertain. When the time horizon was as short as the duration of treatment, neither drug was cost-effective at £30,000 per QALY.

Authors’ conclusions
The authors concluded that both infliximab and adalimumab could be cost-effective, when used for limited durations (up to four years) in initial responders. Longer treatment periods reduced their cost-effectiveness.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear. The authors compared the licensed regimens recommended in the UK for both biological agents.

Effectiveness/benefits:
A systematic review of the literature was appropriate for identifying the relevant sources of data. The authors provided the main inclusion criteria, which should ensure the validity and suitability of the clinical inputs. The use of data exclusively from RCTs was a strength of the analysis given the methodological rigour of their design. Patient-level data were available, which is another strength of the analysis. The details of the adjustment procedures to fit the trial data into the model were clearly presented. In general, the clinical analysis was well carried out. The benefit measure (QALYs) was appropriate for capturing the impact of the disease on both quality of life and survival in patients with Crohn’s disease. An appropriate tool was used to elicit the patient preferences. The authors described the method used to convert disease-specific scores into utility valuations.

Costs:
The categories of costs were consistent with the study perspective. Most of the economic data were derived from a published study, the details of which were not extensively presented. The authors noted that one strength of this study was the use of detailed patient-level data for the economic analysis. Other details of the current analysis, such as the price year, source of data for drugs, assumptions made in the determination of dosages, and the use of discount rates, were clearly presented.

Analysis and results:
The incremental approach was an appropriate framework for the analysis. The model outputs (costs, benefits, and cost-utility ratios) were reported. The issue of uncertainty was appropriately investigated, and the key results were clearly presented. A clear description of the model (transition patterns, assumptions, and general features) was provided. The authors did not use a mixed-treatment comparison to synthesise the data from the two clinical trials as there was too much heterogeneity between them.

Concluding remarks:
The study was well carried out and satisfactorily presented. The authors’ conclusions appear to be valid.

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