Cost-effectiveness of adalimumab for the maintenance of remission in patients with Crohn's disease

Loftus EV, Johnson SJ, Yu AP, Wu EQ, Chao J, Mulani PM

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 investigated the cost-effectiveness of a new monoclonal antibody, adalimumab, compared with the usual non-biologic therapies, for the maintenance treatment of patients with severe or moderate-to-severe active Crohn's disease. The authors concluded that adalimumab was cost-effective. Despite some limitations, the methods appear to have been appropriate and comprehensive, and the conclusions reached by the authors reflected the scope of their analysis.

Type of economic evaluation
Cost-utility analysis

Study objective
The aim was to assess the cost-effectiveness of adalimumab, a fully human monoclonal antibody, for the treatment of severe or moderate-to-severe active Crohn's disease.

Interventions
Adalimumab was compared with non-biologic pharmacotherapies, which were azathioprine, 6-mercaptopurine, methotrexate, 5-aminosalicylates, sulfasalazine, mesalazine, and corticosteroids, for the maintenance treatment of Crohn's disease. Adalimumab was taken every other week and non-biologic therapies were taken at conventional baseline doses. Non-biologic therapies were considered as a class.

Location/setting
UK/out-patient care.

Methods
Analytical approach:
Regression methods were used on trial data that was then synthesised in a cost-utility framework. The efficacy was captured by mapping the Crohn's Disease Activity Index (CDAI) scores for individual patients over time. The base-case analysis lasted for one year and the authors stated that the perspective was that of the UK National Health Service.

Effectiveness data:
- The clinical efficacy of adalimumab was determined using the CDAI scores. Patient-level clinical data from two pivotal randomised controlled trials, with 1,153 patients, were analysed. These were the Clinical Assessment of Adalimumab Safety and Efficacy Studied as Induction Therapy in Crohn's Disease (CLASSIC) trial (Colombel, et al. 2007 see ‘Other Publications of Related Interest’ below for bibliographic details) and the Crohn's Trial of the Fully Human Antibody Adalimumab for Remission Maintenance (CHARM; Hanauer, et al. 2006, see ‘Other Publications of Related Interest’ below for bibliographic details). The data from CHARM (n=854) were used to derive the effectiveness for the adalimumab treatment cohort, whilst the data from the CLASSIC trial (n=299) were used to predict outcomes for the non-biologic cohort, which was not in the CHARM, with the characteristics of the CHARM population. This was achieved using an ordered probit regression model. The efficacy was mapped to four states for analysis and these were remission, or moderate, severe, or very severe Crohn's disease.

Monetary benefit and utility valuations:
The health-state values were based on primary data from a published study (Gregor, et al. 1997, see ‘Other Publications of Related Interest’ below for bibliographic details). This study used the standard gamble technique to elicit the utility...
estimates from 180 Canadian patients. The authors of that study reanalysed their individual patient data to create the utility scores for the four CDAI health states for this analysis: remission, or moderate, severe, or very severe Crohn’s disease.

Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs).

Cost data:
The direct medical costs included adalimumab therapy, hospitalisations, out-patient care, and other items. Hospitalisations related to Crohn's disease were directly from CHARM. Other cost estimates were derived from a published study (Bassi, et al. 2004, see ‘Other Publications of Related Interest’ below for bibliographic details), with a sample of 172 patients. This study used generalised linear regression models to assess the relationships between the costs and clinical or patient factors. These regression coefficients were used to estimate the costs for the health states. Productivity losses due to hospitalisation were reported separately from the base case. The costs were reported in 2006 UK pounds sterling (£). They were adjusted to 2006 using the annual UK health price index.

Analysis of uncertainty:
One-way sensitivity analyses were performed on the key parameters. Probabilistic sensitivity analysis was also undertaken by applying a beta distribution to the health utilities, a Poisson distribution to the hospitalisation rates, and gamma distributions to the cost data. One-thousand Monte Carlo simulations were run and 95% confidence intervals were generated. The results were presented as cost-effectiveness acceptability curves. A scenario analysis was performed to assess a lifetime horizon, with the costs and benefits discounted at 3.5% per annum.

Results
For patients with severe Crohn's disease, the mean cost per patient over 56 weeks was £10,882 for adalimumab and £8,992 for non-biologic therapies. For patients with moderate-to-severe Crohn's disease, the mean cost per patient was £9,696 for adalimumab and £6,649 for non-biologic therapies.

For patients with severe Crohn's disease, the mean QALYs were 0.8516 for adalimumab and 0.7339 for non-biologic therapies. For patients with moderate-to-severe Crohn's disease, the mean QALYs were 0.8647 for adalimumab and 0.7743 for non-biologic therapies.

The incremental cost per QALY gained for adalimumab over non-biologic therapies was £16,064 for severe patients, and £33,731 for moderate-to-severe patients. The probabilistic analysis suggested that the probability that the incremental cost per QALY gained would fall below £30,000 for patients with moderate-to-severe disease was 85.8% and for those with severe disease it was 88.9%.

The one-way sensitivity analyses found that the results were sensitive to variations in the key parameters. For example, having a lifetime horizon approximately halved the incremental cost-utility ratios and, when the hospitalisation costs were varied by ±40%, the results markedly increased or decreased.

Authors’ conclusions
The authors concluded that adalimumab, administered every other week, as maintenance therapy for Crohn’s disease, compared with conventional non-biologic therapies, was cost-effective.

CRD commentary
Interventions:
The authors chose a range of available conventional non-biologic therapies as a comparator to the newer drug adalimumab. Non-biologic therapies were considered as a class and there was no discussion of their dosages.

Effectiveness/benefits:
The modelling approach was unusual, with a regression analysis of trial data, which was then synthesised in an incremental analysis. The methods were fairly transparent and well reported. This method may prove more difficult for a non-expert to follow, but it appears to have circumnavigated some of the issues of a more traditional approach. It was
still not free from necessary assumptions about the data and choices for the regression model. The results suggested that the ordered probit model was a good fit and that the outcomes predicted the distribution of disease states well. Two randomised controlled trials were used, which suggests that no other trials were available, but this issue was not discussed.

Costs:
The direct medical costs were included and appear to have been appropriate for the perspective, but only limited detail of the resources used and how these were valued (i.e. the unit costs) were provided. Further details of the medical costs were available in the source publication (Bassi, et al. 2004). Statistical analysis of the costs, using generalised linear models, provided comprehensive cost estimates that took into account variation in the patient characteristics and health states.

Analysis and results:
The regression methods were reasonably well reported. The study methods were novel and, whilst overcoming some shortcomings of a traditional approach, they introduced some limitations of their own. The authors reported a number of these limitations including assumptions about the disease severity being constant over time with the non-biologic therapies, the extrapolation of short-term data to the long term, and the necessity for handling missing data. They evaluated the impact of data variability in thorough sensitivity analyses and presented the results fully.

Concluding remarks:
Despite some limitations, the methods appear to have been appropriate and comprehensive. The conclusions reached by the authors reflected the scope of their analysis.

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