Modelling the cost effectiveness of TNF-alpha antagonists in the management of rheumatoid arthritis: results from the British Society for Rheumatology Biologics Registry

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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
The study examined the cost-effectiveness of tumour necrosis factor alpha (TNF-α) antagonist therapies in comparison with traditional disease-modifying anti-rheumatic drugs (DMARDs) for the treatment of rheumatoid arthritis in the UK, using data from the British Society for Rheumatology Biologics Registry. The authors concluded that the current policy of prescribing TNF-α antagonists to rheumatoid arthritis patients who have failed at least two DMARDs is cost-effective from the perspective of the UK National Health Service. The study methodology was robust and clear, thus the authors’ conclusions appear valid.

Type of economic evaluation
Cost-utility analysis

Study objective
The primary objective of the study was to examine the cost-effectiveness of tumour necrosis factor alpha (TNF-α) antagonist therapies in comparison with traditional disease-modifying anti-rheumatic drugs (DMARDs) for the treatment of rheumatoid arthritis (RA) in the UK in patients who had failed at least two DMARDs, using data from the British Society for Rheumatology Biologics Registry (BSRBR).

Interventions
The TNF-α antagonist therapies under examination were infliximab, etanercept and adalimumab. These three therapies were considered as a class. The conventional DMARDs included hydroxychloroquine, methotrexate, intramuscular gold, sulphasalazine and leflunomide.

Location/setting
UK/secondary care.

Methods
Analytical approach:
A decision model was developed in order to assess the clinical and economic impact of the new therapy versus the traditional approach using data mainly derived from the BSRBR. The time horizon of the analysis was the patients’ lifetime. The authors stated that the perspective of the National Health Service, the policy maker for formulary decisions (i.e. the National Institute for Clinical Excellence), was adopted.

Effectiveness data:
The clinical data were derived from the BSRBR database, which followed 7,083 RA patients (8,284 patient-years: 2,971 etanercept, 4,474 infliximab and 839 adalimumab) with active disease treated with TNF-α antagonists and 870 RA patients treated with conventional DMARDs over 3 years. Since the BSRBR only followed patients up to 18 months, observational data from a Swedish cohort were used to extrapolate these estimates to a longer time horizon. Mortality data were obtained from UK life tables. Some assumptions also had to be made. The key clinical end point was response to treatment, which was estimated on the basis of the EULAR criteria (mild, moderate, severe).

Monetary benefit and utility valuations:
Utility valuations were elicited using two methods. In one the SF-36 data collected in the BSRBR database were translated to a societal health utility through the SF-6D algorithm, in the other EQ-5D values were indirectly calculated.
through the values obtained in the Health Assessment Questionnaire.

Measure of benefit:
The summary benefit measure was the quality-adjusted life-years (QALYs). These were estimated using the modelling framework and were discounted at an annual rate of 1.5% in the base-case.

Cost data:
The three main cost categories considered were drugs, monitoring and hospitalisations. The unit cost of drugs came from the British National Formulary, while the costs of monitoring and hospitalisations came from a published study. The resource use data were derived from the BSRBR database using a multivariate regression model. The costs were in UK pounds sterling (£). The price year was 2004. An annual discount rate of 6% was applied to future costs in the base-case.

Analysis of uncertainty:
The issue of uncertainty was addressed by means of a probabilistic sensitivity analysis. One hundred Monte Carlo simulations were run. In addition, the analysis considered alternative scenarios related to different ages, gender, baseline disability, disease duration, withdrawal policies and number of previous DMARDs. The authors also considered scenarios of combination therapy and sequential anti TNF-α therapy in which response to a second TNF-α antagonist was independent of response to the first.

Results
The expected lifetime costs per patient were £57,919 with TNF-α antagonists as a class and £20,706 with DMARDs.

The expected QALYs were 5.1514 with TNF-α antagonists and 3.5931 with DMARDs.

Therefore, under baseline conditions, the incremental cost per QALY gained with TNF-α antagonists over DMARDs was £23,882.

The probabilistic sensitivity analysis showed that there was an 84% probability that the incremental cost per QALY was below the threshold of £30,000.

The sensitivity analyses generally confirmed the base-case findings. Nevertheless, the incremental cost per QALY for the TNF-α antagonists was higher than £30,000 in the following scenarios: costs and benefits discounted at a 3.5% annual rate; use of the SF-6D to elicit utility valuations; starting age higher than 70 years. Sequential therapy resulted in a very similar cost-effective ratio to that for monotherapy.

Authors' conclusions
The authors concluded that the current policy of prescribing TNF-α antagonists to RA patients who had failed at least two DMARDs was cost-effective from the perspective of the UK National Health Service.

CRD commentary
Interventions:
The rationale for the selection of the comparators was appropriate. The analysis of the TNF-α antagonists as a class represented a new approach to evaluating biologicals, which are usually compared amongst themselves. They are likely to be the relevant treatment options in many health care settings.

Effectiveness/benefits:
Most of the clinical data were taken from a UK database in order to reflect current practice in the authors' setting. The large sample size represents a strength of the analysis. The authors stated that the groups differed at baseline in terms of age and level of RA severity. Treatment effect was taken from patient-level data and modelled through individual simulations. An extensive sensitivity analysis was conducted in order to reflect the variability among patients and uncertainly in model parameters. QALYs were appropriately used as the measure of benefit and utility weights were estimated using two different approaches. In general, the analysis of the clinical data was conducted satisfactorily.
Costs:
The costs were presented as macro-categories, which appear to have been relevant from the viewpoint adopted in the study. However, a more detailed breakdown of the cost items would have been helpful. The authors explicitly excluded some categories of costs and these exclusions were justified. The sources of resource use were appropriate and a price year was given. Different discount rates were also assessed and costs were varied in the sensitivity analysis, thus enhancing the external validity of the results.

Analysis and results:
The conduct and presentation of the analysis was clear. The authors highlighted the assumptions made in the model and justified the selection of model inputs. The use of statistical tests and probabilistic sensitivity analysis was appropriately described. The issue of uncertainty was extensively addressed. In general, the main strength of the study was the use of the BSRBR. Most of the previous cost-effective analyses on biologicals for RA were based on pivotal trials, which have a strong internal validity but which may not reflect real practice.

Concluding remarks:
Overall, the study methodology was appropriate and reported clearly. The authors' conclusions appear appropriate.

Funding
British Society of Rheumatology.

Bibliographic details

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Aged; Antirheumatic Agents /economics /therapeutic use; Arthritis, Rheumatoid /drug therapy /economics; Computer Simulation; Cost-Benefit Analysis; Drug Costs /statistics & numerical data; Epidemiologic Methods; Female; Great Britain; Health Care Costs /statistics & numerical data; Humans; Immunologic Factors /economics /therapeutic use; Male; Middle Aged; Models, Econometric; Quality-Adjusted Life Years; Severity of Illness Index; Treatment Outcome; Tumor Necrosis Factor-alpha /antagonists & inhibitors

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