Economic evaluation of systemic therapies for moderate to severe psoriasis

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 examined the cost-effectiveness of biologic and non-biologic treatments for moderate to severe psoriasis. It was found that methotrexate and cyclosporin were cost-effective, but required monitoring for toxicities. Adalimumab was the most cost-effective of the biologic treatments for those with conventional systemic treatment failure or inadequate response. The analysis was well conducted and clearly presented and the sensitivity analysis confirmed that the authors’ conclusions were robust.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of biologic and non-biologic treatments for moderate to severe psoriasis. The sequence of treatments that would be the most cost-effective was also assessed.

Interventions
The biologic treatments included adalimumab, efalizumab, etanercept, and infliximab. The dosages were adalimumab at 40mg every other week (after a loading dose of 80mg), efalizumab at 1mg/kg each week, etanercept at 25mg twice a week intermittently or continuously, or 50mg twice weekly intermittently, and infliximab at 5mg/kg every eight weeks (after doses of 5mg/kg at weeks zero, two, and six). The non-biologic treatments included methotrexate (15 to 25mg per week) and cyclosporin (3mg/kg per day). These treatments were compared with supportive care.

Location/setting
UK/secondary care.

Methods
Analytical approach:
This economic evaluation was based on a decision analytic model, with a long-term time horizon. The authors stated that the viewpoint of the UK National Health Service (NHS) was taken.

Effectiveness data:
The clinical data came from a systematic review, which identified 22 randomised controlled trials (RCTs). The evidence from these was combined using a mixed-treatment analysis, as there was a lack of head-to-head comparisons for some treatments. The key clinical endpoint was the change in Psoriasis Area and Severity Index (PASI) score. Given the relatively short follow-up in the RCTs, the long-term benefit of therapy was calculated on the basis of some published evidence, the details of which were not reported, and assumptions on the duration of the treatment effect.

Monetary benefit and utility valuations:
The utility valuations were derived by linking PASI scores to published valuations of health-related quality of life elicited using the European Quality of life (EQ-5D) questionnaire. These data were taken from two RCTs conducted in the UK.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and no discounting of future QALYs was reported.
Cost data:
The economic analysis included the costs of drug acquisition and administration as well as hospitalisations. The unit costs of drugs were obtained from the British National Formulary and recommended dosages were used. The unit costs for laboratory tests and out-patient visits were derived from NHS reference costs and the York NHS Trust. The number and length of hospitalisations were based on published evidence. The price year was 2005 to 2006. All costs were in UK pounds sterling (£) and the use of a discount rate was not reported.

Analysis of uncertainty:
In an alternative scenario, a societal perspective was adopted and the costs associated with productivity losses were included. A deterministic, one-way sensitivity analysis and a probabilistic sensitivity analysis were carried out using plausible ranges of values (deterministic) and probability distributions (probabilistic) for the model inputs.

Results
The annual incremental QALYs over supportive care were 0.129 (95% CI: 0.078 to 0.185) with methotrexate; 0.079 (95% CI: 0.044 to 0.116) with cyclosporin; 0.110 (95% CI: 0.070 to 0.153) with etanercept 25mg intermittently; 0.123 (95% CI: 0.081 to 0.166) with etanercept 50mg intermittently; 0.124 (95% CI: 0.077 to 0.173) with efalizumab; 0.164 (95% CI: 0.110 to 0.219) with adalimumab; 0.134 (95% CI: 0.085 to 0.186) with etanercept; and 0.182 (95% CI: 0.126 to 0.240) with infliximab. Thus, infliximab was the most effective treatment.

Annually, both methotrexate and cyclosporin were found to be cost-saving due to reduced hospitalisations, which saved more than the drug-related costs. The costs were £0 for supportive care, £4,114 for etanercept 25mg intermittently, £4,699 for etanercept 50mg intermittently, £4,942 for efalizumab, £4,993 for adalimumab, £5,058 for etanercept, and £7,736 for infliximab.

Compared with supportive care, both methotrexate and cyclosporin were dominant treatments (more effective and less costly), while the incremental cost per QALY gained was £37,284 with etanercept 25mg intermittently, £38,358 with etanercept 50mg intermittently, £39,948 with efalizumab, £30,538 with adalimumab, £37,676 with etanercept, and £42,492 with infliximab. Comparing biologic treatments only and excluding dominated ones, the incremental cost per QALY was £30,538 with adalimumab and £147,906 with infliximab.

Methotrexate and cyclosporin were the first and second treatments in the optimal treatment sequence, followed by adalimumab, which was the most cost-effective biologic therapy. This finding was confirmed in the probabilistic sensitivity analysis.

The most influential model input was the length of hospital stay for a patient who did not respond to treatment. The use of alternative data improved the cost-effectiveness of intermittent etanercept therapy. In a patient population with less severe psoriasis at baseline, the cost-effectiveness of biologic treatments decreased. If the patient weight was set at 60kg (80kg in the base case) infliximab became the most cost-effective biologic. The inclusion of productivity losses increased the cost-effectiveness of all treatments.

Authors' conclusions
The authors concluded that methotrexate and cyclosporin were cost-effective, but required monitoring for toxicities. Adalimumab was the most cost-effective of the biologic treatments for those with conventional systemic treatment failure or inadequate response.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear in that all the available systemic therapies were considered and were compared against best supportive care. The authors stated that some alternatives were excluded because a comparison with placebo was not available and it was not possible to include these options in the mixed treatment comparison.

Effectiveness/benefits:
The systematic review of RCTs was a valid source of evidence, not only because this approach identifies all the relevant
studies, but also because it was restricted to RCTs, which are considered to be the most robust study design. The authors did not describe these RCTs in terms of their patient population or other methodological features (randomisation or blinding), but they were similar in terms of length of follow-up. A mixed-treatment analysis was used to pool the clinical endpoints due to the lack of head-to-head comparison studies, which would be the most appropriate option. The authors described the approach used to derive the treatment benefits. The instrument used appears to have been appropriate for this patient population. QALYs allow cross-disease comparisons of the treatment benefits to be made.

Costs:
The analysis of costs reflected the perspective in terms of both their sources and the categories of costs. A broader perspective was considered in the sensitivity analysis. Details of the cost calculation were clearly reported. Some data on the unit costs and quantities of resources used were given and the fiscal year for the economic data was reported. Confidence intervals were calculated for the average annual total costs. The use of discounting was not explicitly reported, but it is likely that the recommended rate for the UK was used.

Analysis and results:
The findings were clearly presented for both annual costs and benefits. The time horizon was not clearly reported, but a long-term horizon was used. The use of an incremental approach to synthesise the costs and benefits was appropriate and highlighted the superior profile (dominance) of some treatments, especially in the comparison between biologic treatments. The issue of uncertainty was extensively investigated and both the approaches used (deterministic and probabilistic) were appropriate for different aspects of uncertainty. The authors acknowledged some limitations such as the exclusion of potential side effects of biologic treatments, which are quite rare, assumptions on the long-term efficacy of treatments, and the assumed identical efficacy, for treatments, wherever they were in the treatment sequence.

Concluding remarks:
In general, the analysis was well conducted and clearly presented. The sensitivity analysis confirmed that the authors’ conclusions were robust.

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