



Title	Adalimumab, Etanercept, and Infliximab for the Treatment of Ankylosing Spondylitis: A Systematic Review and Economic Evaluation
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Aim

To assess the comparative clinical effectiveness and cost effectiveness of adalimumab, etanercept, and infliximab in treating ankylosing spondylitis (AS).

Conclusions and results

The review of clinical effects included 2 studies of adalimumab, 5 of etanercept, and 2 of infliximab in comparison with placebo (along with conventional management). No RCTs directly comparing anti-tumor necrosis factor- α (TNF- α) agents were identified. Meta-analyses were conducted for data on Assessment in Ankylosing Spondylitis (ASAS), mean change in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and mean change in Bath Ankylosing Spondylitis Functional Index (BASFI) at 12 weeks following initiation of anti-TNF- α therapy or placebo for all 3 drugs. Meta-analyses were also conducted at 24 weeks for etanercept and infliximab. Each meta-analysis of anti-TNF- α therapy demonstrated statistically significant advantages over placebo, although there was no significant difference between individual anti-TNF- α agents. At 12 weeks, ASAS 50% responses were 3.6-fold more likely with anti-TNF- α treatment than placebo. Compared with baseline, BASDAI scores were reduced by close to 2 points at 12 weeks. Functional scores (BASFI) were reduced at 12 weeks.

The review included 6 full economic evaluations. Conclusions were mixed, but the evidence in the short term indicates that anti-TNF- α therapies are unlikely to be considered cost effective. Limitations in clinical outcome data restrict the assessment of cost effectiveness. Direct unbiased RCT evidence is only available in the short term. Currently BASDAI and BASFI are the best available assessment tools, but not ideal for economic evaluations. A review of the 3 models identified several inherent flaws and errors. Incremental cost-effectiveness ratios (ICERs) of etanercept and adalimumab were similar, falling below an assumed willingness-to-pay threshold of GBP 30 000. The ICER for infliximab

ranged between GBP 40 000 and GBP 50 000 per QALY. The short-term model confirmed large front-loading of costs with a result that none of the 3 anti-TNF- α agents appears cost-effective at the current acceptable threshold, with infliximab yielding much poorer economic results (GBP 57 000–120 000 per QALY). Assumptions of the short-term model were used to explore the cost effectiveness of using anti-TNF- α agents in the long term (far more speculative). Sensitivity analyses show wide variations in long-term cost estimates, but it is unlikely that costs will decrease over time.

Recommendations

The review of clinical data related to the 3 drugs (including conventional treatment) compared with conventional treatment plus placebo indicates that in the short term (12–24 weeks), the 3 treatments are clinically effective in relation to assessment of ASAS, BASDAI, and BASFI. Indirect comparisons of treatments were limited and did not show a significant difference in effectiveness between the 3 agents. The short-term economic assessment indicates that none of the 3 anti-TNF- α agents is likely to be considered cost effective at current acceptability thresholds, with infliximab consistently the least favorable option.

Methods

See Executive Summary link above.

Further research/reviews required

To obtain robust estimates of the longer term clinical and cost effectiveness of anti-TNF- α agents for AS, clinical trials should address several limiting factors related to patients suffering from AS, the disease itself, and its treatment.