Cost effectiveness of adalimumab for the treatment of ankylosing spondylitis in the United Kingdom

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Introduction

Ankylosing spondylitis (AS) is an inflammatory disease of unknown aetiology and is one of a group of conditions known as seronegative spondyloarthropathies\cite{1}. The hallmark of AS is inflammation of the sacroiliac joint at the base of the spine (sacroilitis), followed by inflammation along the spine resulting in back pain and stiffness. Inflammation at enthesis, the sites where ligaments and tendons attach to bone, can lead to new bone development and joint fixation (ankylosis)\cite{1}. The large peripheral joints (hips, shoulders and knees) may also be involved\cite{2}. The prevalence of AS is reported to be between 0.1% and 0.8%, with nearly three times more males affected than females\cite{2,3}. On occasion, the disease is severe, resulting in spinal fusion with pronounced incapacity and significant deformities in peripheral joints, which in turn may necessitate joint replacement surgery for some patients. Approximately one-third of AS patients may be unable to work at any one time, with another 15% reporting some type of change to their working lives\cite{4,5}. There is currently no cure for AS. Until recently, there were only a limited number of treatments available for AS, including non-steroidal anti-inflammatory drugs (NSAIDs) and physiotherapy. NSAIDs and physiotherapy provide short-term symptomatic relief. Traditional disease-modifying antirheumatic drugs (DMARDs), such as methotrexate and sulphasalazine, have demonstrated only limited effectiveness\cite{1}. Recent studies have shown that AS is an immunologically mediated disease in which tumour necrosis factor (TNF) is present in increased concentrations in joints\cite{6}. Several clinical trials have demonstrated the significant and sustained efficacy of TNF antagonists in the treatment of AS\cite{7–12}. Previous published analyses have suggested that TNF antagonists for AS are marginally cost-effective. However, one of these studies was probably conducted prior to the publication of British treatment guidelines\cite{2}, and therefore assumed that patients would continue therapy despite responding inadequately\cite{13}. Another study apparently assumed that patients who do not respond adequately derive no benefit at all from their therapies\cite{14}.

The purpose of the present analysis was to determine the cost effectiveness of the TNF antagonist adalimumab (HUMIRA\textsuperscript{\textregistered}, Abbott Laboratories, Abbott Park, IL, USA)\textsuperscript{32} vs conventional therapy for the management of active AS from the perspective of the National Health Service (NHS) in the United Kingdom. The analysis focused on the cost effectiveness of TNF antagonists when used according to existing treatment guidelines\cite{2}, and in consideration of relevant benefits and costs of adalimumab. As such, this analysis adopted the treatment guidelines’ principle that patients responding adequately to therapy (i.e. those who experience significant benefits) should be allowed to continue therapy, whereas those who failed to do so should not. The underlying economic rationale for this approach is that it is less cost-effective to continue therapy in patients who are not benefiting significantly from therapy.

Methods

Overview

In line with National Institute for Clinical Excellence (NICE) methodology guidance for manufacturers and sponsors, the analysis was conducted from the perspective of the NHS.
Adapting trial data to routine clinical practice

The model simulates individual patient histories of patients enrolled in two adalimumab clinical trials: the Adalimumab Trial Evaluating Long-Term Efficacy and Safety in AS (ATLAS) and the M03-606 trial, details of which have been published [11, 15]. By applying the continuation/stopping rules from the British Society of Rheumatology (BSR) guidelines [2] for the use of TNF antagonists in AS directly to the data from these trials, it was possible to simulate treatment decisions that would normally take place. In particular, Bath AS Disease Activity Index (BASDAI), Bath AS Functional Index (BASFI) and spinal pain visual analogue scale (VAS) scores were used to evaluate the trial data. The BSR guidelines were followed as closely as possible within the confines of the trial data to define eligibility for TNF-antagonist therapy, what is an adequate or inadequate response, when to assess response, and whether and when to cease therapy.

Application of BSR guidelines

Patients included in the analysis were those in the adalimumab trials who would also be candidates for TNF-antagonist therapy based on BSR guidelines. These patients had active AS and an inadequate response to NSAIDs. The inclusion/exclusion criteria from the trials differed from the BSR guidelines in two respects. First, the definition of active AS in the adalimumab trials required patients to fail at least two of three criteria: (i) BASDAI $\geq 4.0$ (scale $0–10$ cm); (ii) VAS score for total back pain $\geq 4$ (scale $0–10$ cm); and (iii) morning stiffness $\geq 1$ h. The BSR guidelines have a more restrictive definition that requires patients to meet both criteria (i) and (ii) on two separate occasions at least 4 weeks apart. For the present analysis, the BSR definition of active AS was used, and trial patients who did not fulfill the criteria were excluded. Second, patients enrolled in the adalimumab trials were required to have had a previous inadequate response to or intolerance of $\geq 1$ NSAIDs. The BSR guidelines require failure of conventional treatment with $\geq 2$ NSAIDs, each taken sequentially at maximum tolerated/recommended dosage for 4 weeks. Since the majority of patients at the study entry had already failed $\geq 2$ NSAIDs, no adjustment was performed. Adalimumab trial patients were allowed to continue their baseline NSAIDs or DMARDs, and therefore, the placebo group was considered to represent conventional AS therapy.

In the clinical trials, patients were kept on active treatment even when there was an insufficient treatment response. In contrast, within the economic analysis, when patients were assessed as non-responders, it was assumed that they would be taken off therapy and that, at their next visits, efficacy measures would rebound to averages of conventional-therapy–only patients. In accordance with BSR guidelines, a response in the model was defined as a reduction of BASDAI to 50% of the pre-treatment value or a decrease of $\geq 2$ cm accompanied by reduction of the spinal pain VAS of $\geq 2$ cm. Assessment of initial response was performed 8 weeks after treatment initiation. At that point, if response criteria were not met, a second therapy response evaluation was assumed to have been made at 12 weeks. Failure to achieve response on both occasions led to cessation of TNF-antagonist therapy as per BSR guidelines (i.e., patients were assumed to receive conventional therapy subsequently).

Therapeutic responses were then reviewed every 3 months until the end of the simulation at Year 30. Failure to maintain the original response led to repeat assessments after 6–12 weeks in the first 48 weeks (depending on the visit schedule from the trials). Again, failure to maintain response on both occasions led to cessation of treatment. After 48 weeks, inadequate response was defined on the basis of the BASDAI scores only, as no published data are available on the progression of VAS spinal pain scores over time. Specifically, lack or loss of response after week 48 was defined as a reduction of BASDAI of $<50\%$ of the pre-treatment value or a decrease of $<2$ cm.

Missing observations

For patients who had baseline and subsequent observed values but were missing BASDAI, spine pain, or BASFI measures during one or more trial visits, missing scores were imputed using last observation carried forward (LOCF) until the next actual observation was available. This was also performed when patients discontinued therapy prematurely because of a serious adverse event. In the trials, patients who did not achieve a 20% response according to the AS assessment in Ankylosing Spondylitis International Working Group criteria for improvement (ASAS20) at weeks 12, 16 or 20 were eligible to receive early-escape, open-label treatment with adalimumab 40 mg ( Biol). In addition, at week 24, all patients in the treatment and placebo groups switched to open-label therapy. In the model, BASDAI, VAS and BASFI values for patients who switched to open-label therapy were replaced with LOCF values at time of switch.

Additional data adjustments

At baseline in the trials, patients randomly assigned to adalimumab arms had slightly better (albeit non-statistically significant) BASDAI, BASFI and spinal pain scores than placebo patients (i.e., conventional therapy only). Since treatment decisions, cost and utilities in the model were based on BASDAI, BASFI and spinal pain VAS scores, these differences could have led to a potentially biased estimation of the cost-effectiveness of adalimumab. Therefore, a conservative approach was adopted: BASDAI, BASFI and spinal pain scores of every patient randomized to adalimumab were adjusted accordingly at all time points by a fixed value equal to the average difference in scores between adalimumab and conventional-therapy–alone patients at baseline. For the economic analysis, patients were assumed to be all of the same age and racial composition based on trial patient characteristics. Disease outcomes were based on directly observed trial scores (until week 48) and additional assumptions about disease progression (after week 48).

The model’s conceptual structure is presented in Fig. 1. For patients receiving conventional therapy only, BASDAI scores from week 48 on were assumed to have remained stable (drift $=0$ BASDAI units/yr) based on the observation reports that BASDAI is independent of disease duration and age [14, 16, 17]. In contrast, BASFI score was assumed to worsen (increase) by 0.05 units (on a 0–10 scale) per year, consistent with the assumption from published economic models.
Utilities

The impact of AS and its treatment on quality of life was assessed using the economic concept of utility. Utility measures the preference for, or desirability of, a specific degree of health or specific health outcome, ranked on a scale 0–1, with ‘1’ representing ‘perfect health’ and ‘0’ representing ‘death’.

Cost data

Costs associated with ankylosing spondylitis. Estimates of AS costs by disease activity groups were based on the 2-yr data from the Outcomes in Ankylosing Spondylitis International Study (OASIS) conducted in the Netherlands, Belgium and France [16]. In this longitudinal study registry, disease activity measures such as the BASDAI and BASFI were evaluated every 2 months in 208 patients. In addition, economic questionnaires assessing resource use were also completed. In the cost analysis, each resource use was multiplied with price information from published unit cost sources. To estimate the incremental cost associated with a change in BASDAI, trend lines (using ordinary least-squares regression) were fitted to the estimated cost by BASDAI. Each incremental change in one unit of BASDAI (0–10 scale) was estimated to have been associated with a direct medical cost increase of approximately £750 based on: Cost = £708.45 + £750.00 × BASDAI. The use of the BASFI, as opposed to BASDAI, to predict costs was tested in a sensitivity analysis.

Monitoring and administration. Adalimumab costs were £357.50 per injection [23]. No additional administration cost was included as patients were assumed to have been able to self-administer adalimumab. AS patients were expected to incur at least two rheumatologist visits per year regardless of whether or not they were receiving TNF-antagonist therapy, with an assumed cost of £108 [13, 24]. Routine safety monitoring was based on the Prodigy Guidance [25], and cost estimates were derived from the literature [26] and adjusted for inflation. Nursing time cost to administer monthly tests (10 min at £34/h) [27] and physician time to read and report the monthly test results (10 min at £100/h) [29] were also included (total cost per month £24.14). The model also included the cost of routine tuberculosis (TB) screening via

Discontinuation

In the base-case analyses, since the disease progression rate based on BASDAI for patients receiving adalimumab was assumed to be equal to zero beyond week 48, discontinuation of therapy due to loss of response did not occur. However, it was assumed that patients would withdraw from therapy for reasons other than loss of response (e.g. adverse events) at a rate of 10% per year, which is consistent with the rates of discontinuation used in previous economic analyses [13, 14].
chest X-ray (one before initiation of therapy and one 6 months after therapy initiation) and TB skin testing before initiation of therapy, as recommended for the use of all TNF antagonists [27, 29].

**Adverse events.** Adverse events (AEs) were collected from the two clinical trials [11, 15]. All AEs were assumed to require a physician visit (£28.00) [30], liver function test (£6.70) [26], a full blood count (£12.06) [26] and, in case of an infectious AE, a course of antibiotics (£21.90) [23].

**Sensitivity analyses**

The incremental differences between treatment groups in costs and QALY were computed and the ratio of incremental cost to QALY gained (i.e. ICER) was used to measure cost effectiveness.

Sensitivity analyses were conducted to estimate the uncertainty surrounding the long-term (30 yrs) ICER. Multivariate sensitivity analysis was addressed by a combination of bootstrapping and probabilistic sensitivity analysis, which involved 1000 model simulations using input values drawn from probability distributions in Table 2. This provides an indication of degree of confidence associated with the results (e.g. in what percentage of the model replications is a strategy saving costs compared with the other). Finally, several scenario analyses were conducted to test the impact of changing key model assumptions.

**Results**

**Patients characteristics**

A total of 397 patients comprised the trial dataset. Of those, 354 met the spinal pain VAS and BASDAI criteria at baseline, and 315 met both criteria at baseline and pre-baseline and were therefore included in the simulation. This reflects application of the BSR guidelines to the trial dataset. Compared with the trial patient population, those included in the simulation were very comparable in average baseline age (42.0– vs 42.2-yrs-old, respectively), sex (76 vs 75% male, respectively) and race (96 vs 95% white). However, as expected, patients in the simulation had greater average baseline spinal pain VAS, BASDAI and BASFI scores (75.15 vs 66.22 mm, 6.94 vs 6.29 cm and 6.04 vs 5.39 cm, respectively).

**Disease projection**

In the model, BASDAI and BASFI for both adalimumab and conventional therapy groups improved initially during the first few weeks. However, the improvement was significantly more pronounced for adalimumab patients. Modelled over the long term, the average BASDAI score of the adalimumab group slowly increased as more patients discontinued therapy and results converged with the conventional therapy group. A similar pattern was observed for the BASFI score, except that it drifted upward (worsened) over time (Fig. 2).

**Cost effectiveness**

Base-case cost-effectiveness results are presented in Table 3. QALYs, costs and ICER were estimated for 1-yr, 5-yr and 30-yr time horizons. Overall, the ICER improved with longer time horizons. After 1 yr (48 weeks), adalimumab led to savings of £1164 per patient from offsetting AS-related treatment costs (visits to general practitioners, specialists and physiotherapists, para-medical visits, hospitalization, technical examinations, adaptation and aids, and formal care). Additional costs associated with adalimumab therapy were (per patient): drug (£5233), para-medical visits, technical examinations and aids, and formal care. Additional costs associated with adalimumab therapy were (per patient): drug (£5233), para-medical visits, technical examinations and aids, and formal care. Additional costs associated with adalimumab therapy were (per patient): drug (£5233), para-medical visits, technical examinations and aids, and formal care. Additional costs associated with adalimumab therapy were (per patient): drug (£5233), para-medical visits, technical examinations and aids, and formal care. Additional costs associated with adalimumab therapy were (per patient): drug (£5233), para-medical visits, technical examinations and aids, and formal care. Additional costs associated with adalimumab therapy were (per patient): drug (£5233), para-medical visits, technical examinations and aids, and formal care. Additional costs associated with adalimumab therapy were (per patient): drug (£5233), para-medical visits, technical examinations and aids, and formal care. Additional costs associated with adalimumab therapy were (per patient): drug (£5233), para-medical visits, technical examinations and aids, and formal care. Additional costs associated with adalimumab therapy were (per patient): drug (£5233), para-medical visits, technical examinations and aids, and formal care. Additional costs associated with adalimumab therapy were (per patient): drug (£5233), para-medical visits, technical examinations and aids, and formal care. Additional costs associated with adalimumab therapy were (per patient): drug (£5233), para-medical visits, technical examinations and aids, and formal care.

**Sensitivity analyses**

Figure 3 presents the univariate sensitivity analyses testing the impact of change in values of model parameters. These analyses indicate that the model appears to be generally robust, with no single parameter dramatically affecting the results when set to
a maximum or minimum value listed in Table 2. All sensitivity results were below £30 000 per QALY. Among the variables tested, the model results were relatively more sensitive to (in decreasing order) discounting method, regression coefficient of BASDAI to predict cost and regression coefficients of BASDAI and BASFI to predict utilities.

Probabilistic sensitivity analyses confirmed that adalimumab is cost-effective vs conventional therapy. The median ICER was £23 142. The incremental cost per QALY gained was below £30 000 and £40 000 in 69.7 and 85.6% of the 1000 probabilistic sensitivity analysis simulations, respectively, indicating a relatively narrow confidence interval.

Additional scenario analyses

Several additional scenario analyses were conducted for which changes in key model assumptions were considered (Fig. 4). These results indicate that the model is relatively robust even when important modelling decisions are modified. Two exceptions were:

1. When indirect costs were included in the analysis, the ICER decreased dramatically from £23 097 per QALY to £5093 per QALY; and
2. When all patients were assumed to remain on therapy regardless of response (i.e. when BSR guidelines were not followed), ICER increased significantly to £62 679 per QALY.

Finally, in one set of analyses, the BASFI score was used instead of the BASDAI to link costs to disease progression. In this analysis, a unit decrease in BASFI was associated with a slightly lesser cost than a corresponding decrease in BASDAI (£680 v. £750). Nevertheless, the cost-effectiveness ratio remained acceptable, at £25 252, in part because the BASFI score was assumed to worsen over time in patients not receiving adalimumab.

Discussion

The present analysis suggests that active adalimumab is cost-effective for the treatment of AS according to BSR guidelines relative to conventional therapy from the perspective of the UK
the benefits are small are quite cost-effective. guideline recommendations to stop treating the patients in whom gain in utility in responders (who by then are the only ones still which require that: (i) patients have sufficiently severe disease the BSR recommendations for the use of TNF antagonists in AS, sensitivity analysis generated a relatively narrow confidence interval for the ICER (e.g. 70% of model replicates were generally robust in that, while the ICER was sensitive to several key parameters, no change in a single parameter resulted in £23,097 over 30 yrs. This estimate of cost effectiveness was NHS. The central estimate of the cost per QALY gained was £23,097 over 30 yrs. This estimate of cost effectiveness was generally robust in that, while the ICER was sensitive to several key parameters, no change in a single parameter resulted in qualitatively different conclusions. In addition, the probabilistic sensitivity analysis generated a relatively narrow confidence interval for the ICER (e.g. 70% of model replicates were <£30,000 per QALY for the 30-yr time horizon).

The results of this analysis support the fundamental tenets of the BSR recommendations for the use of TNF antagonists in AS, which require that: (i) patients have sufficiently severe disease (≥4 BASDAI) and (ii) those who do not exhibit a sufficient response discontinue therapy. Based on the present analysis, allowing patients to remain on therapy regardless of response appears to be less cost-effective vs adopting some form of response criteria. In other words, when all patients in the simulation were allowed to continue therapy regardless of response, the cost effectiveness was significantly worse (£62,679) than when patients were required to show adequate response to remain on therapy (£23,097).

In this analysis, the ICER of adalimumab vs conventional therapy improved when the timeframe of the analysis was extended (£47,000 per QALY at 48 weeks to approximately £26,000 per QALY and £23,000 per QALY at years 5 and 30, respectively). This is consistent with the expectation that, as responders continue to benefit from therapy, they continue to offset the initial ‘sunk’ costs associated with a trial of therapy in patients who (i) eventually do not respond at all or do not respond adequately, (ii) lose an initial response or (iii) discontinue prematurely. As a consequence, the ICER improves when more people with little or no benefit discontinue. In line with this, one might also read the long-term cost-effectiveness ratio as a weighted average over the various years. During the first year—with many patients finding out whether they respond—it is greatest (here about £48,000). Subsequently, when most non-responders have stopped using it, it decreases to approximately £23,000 during the subsequent years. For instance, after the second year, for the non-responders have been filtered out, this corresponds with an ~0.25 gain in utility in responders (who by then are the only ones still being treated). One might come to the conclusion that the current guideline recommendations to stop treating the patients in whom the benefits are small are quite cost-effective.

From a policy perspective, these findings suggest that the appropriate analytical time horizon for the assessment of cost effectiveness for TNF antagonists should be a minimum of 5 yrs and perhaps as long as 30 yrs. Shorter horizons lead to the exclusion of important treatment benefits in patients who continue to respond.

To a large extent, health economic benefits of TNF antagonists for AS may be a result of initial impact on improving BASDAI and BASFI from baseline, and may be less dependent on changes in these scores over time. Patients receiving conventional therapy were assumed to experience an upward drift of 0.05 BASFI units per year vs no progression among adalimumab patients, which resulted in the ICER at £23,097 per QALY. This was only marginally better than when both groups were assumed to have had the same BASFI progression rate (0.05 units per year; £23,812 per QALY saved) or neither group had BASFI progression (£23,802 per QALY saved). A similar finding was reached even when both BASDAI and BASFI were assumed to have worsened over time. For instance, if one assumes that BASFI and BASDAI worsen at a rate of 0.05 in the conventional therapy group but do not worsen in the adalimumab group, the ICER only marginally improved to £21,676 per QALY.

The necessity of extrapolating long-term results (30 yrs) from a short-term clinical trial may be seen as a limitation. The main expectation, however, is that adalimumab will be used if it renders significant quality-of-life improvement. This may be subject to uncertainty. However, policy decisions about the use of this therapy have to be made conditional on some assumption about this. Rather than developing national or local formulary decisions in a vacuum, decision-makers may use this analysis as a starting point to form an opinion on the likely value of adalimumab. Nevertheless, the results of the significantly shorter 5-yr analysis were comparable with those of the longer term projection, suggesting perhaps that the overall conclusions are robust despite the uncertainty inherent in this analysis.

Additional limitations were more technical. The resource utilization data were taken from an observational study of 208 AS patients from the Netherlands, France and Belgium conducted in the late 1990s (OASIS). The limitations of this source of data and type of analysis have been discussed elsewhere [24], and include the small size (n = 208 total, of which only 79 had BASDAI > 4), the limited external validation of the cost data
and the focus on AS-related resource utilization alone. The data are representative of AS patients followed by a hospital-based rheumatologist. If there is one particular concern regarding the use of the OASIS for the present study, it certainly is that the patterns of care in the countries covered by OASIS differ from the patterns of care of the UK. For this reason, the present analysis may over- or underestimate the cost of conventional therapy. On the other hand, since both the clinical trials and the resource use data were multinational, the results of this analysis may be viewed as relevant from a perspective broader than the UK’s.

Despite these limitations, the OASIS has several advantages, including that patients had to have met a strict clinical definition of AS. Inclusion in OASIS was irrespective of age, disease duration and/or disease severity/activity. In addition, this was a 2-yr longitudinal study in which patients were assessed every 2 months. Therefore, the resource utilization estimates derived from this study may be somewhat more robust than the estimates reported from larger cross-sectional studies (e.g. Kobelt et al. [13]). Nevertheless, because of these concerns, a sensitivity analysis was conducted to test how changes in the value of the regression coefficient of BASDAI level (along its estimated 95% confidence interval) predicting cost could lead to different results. As shown in Fig. 3, the model was very sensitive to this cost coefficient. However, it is also very likely that the regression across the aggregate results (only eight observations) significantly overestimated the confidence interval around the cost coefficient of a BASDAI unit. Nevertheless, even in these circumstances, the cost-effectiveness ratio was less than £28,000.

The use of the BSR guidelines rather than the international ASAS guidelines [31] also raises the question of the generalizability of the findings to other settings in which the ASAS guidelines may be used. The response criteria from ASAS are somewhat less restrictive than the BSR guidelines, as they require an improvement in BASDAI of 50% (relative change) or two units (absolute change), but do not require minimum improvements in spinal pain VAS (and instead require expert opinion that therapy should be continued). Although expert opinion was not modelled in this analysis, the present analysis suggests that when the spinal pain requirement is excluded from the analysis, the ICER at 30 yrs is estimated at just greater than £25,000 (results not shown). This figure is naturally very close to the base case, since the BASDAI includes the spinal pain VAS. Nevertheless, these findings suggest that both sets of guidelines may actually produce broadly comparable results.

In addition to the present analysis, several published peer-review and other cost-effectiveness assessments of TNF-antagonist therapy exist. In a peer-reviewed analysis for the Netherlands [5], the incremental direct cost per QALY gained after 5 yrs of therapy with etanercept or infliximab vs usual care was €115,169 (£79,863 based on an exchange rate of 1 euro = £0.6935) [range in sensitivity analyses: €42,914 (£29,758) to €123,761 (£85,803) per QALY] and €187,522 (£130,010) [range: €67,207 (£46,605) to €237,010 (£164,356)], respectively. These estimates are appreciably greater than in the present analysis and might result from several important methodological differences including adopting a 5-yr perspective; using a significantly more restrictive definition of response than used in the present analysis; using a simplified Markov model instead of a patient-level simulation; apparently assuming that patients not achieving a response experience little benefits from therapy; including less severe patients at baseline; and linking both utilities (and costs) to BASDAI only. In a UK analysis [13], it was reported that the direct costs per QALY gained for infliximab was £73,000 at 2 yrs and £33,500 using a 30-yr perspective. This model, like the present model, was a patient-level simulation. However, this analysis assumed that therapy would be continued regardless of response. In addition, this analysis focused on infliximab, which was significantly more expensive (£451.20/100-mg vial × 5 mg/kg every 6 weeks × 73.7 kg, or about £14,410 per year not including the cost of out-patient visit for administration) than the cost of adalimumab (40-mg pre-filled syringe = £357.50 used every other week, or £929.50 per year). One additional difference between the present model and the above-mentioned analyses lies in the

![Fig. 4. Incremental cost-effectiveness ratio (30-yr perspective) for additional model scenario analyses. Additional scenario analyses tested the impact of adopting different assumptions for the analysis (each bar represents the result of a separate analysis).](https://academic.oup.com/rheumatology/article-abstract/46/8/1320/1784948/1326_M._F._Botteman et al)
assumption used to model the disease progression of patients failing and stopping TNF-antagonist therapy.

In the present model, patients receiving conventional therapy were assumed to have stabilized at the level of disease severity observed at the end of the first 12 weeks of the trial. In addition, patients failing and stopping TNF-antagonist therapy were assumed to have ‘caught up’ with the conventional therapy group. These assumptions are more conservative than those used by Kobelt et al. [13], who apparently assumed that all patients receiving conventional therapy lost their responses within 6 weeks of the end of the trials and returned to their baseline values. Disease activity scores for patients on conventional therapy are generally worse at baseline than at the end of trials. Therefore, assuming that patients would return to baseline scores, in effect, resulted in a wider difference in disease scores between conventional-therapy and TNF-antagonist therapy groups than if the assumption were that conventional-therapy disease activity scores would be lower (improved) at the end of the trials. As a result, although both the present analysis and the Kobelt et al. analysis assumed patients stopping therapy ‘catch up’ to the conventional-therapy group, the gap in the disease activities between the TNF-antagonist and conventional-therapy groups was likely greater in the Kobelt et al. model. Adopting the Kobelt et al. set of assumptions in the present analysis would have resulted in a more favourable ICER for adalimumab at £12,434 per QALY over 30 yrs (a significant decrease from the original base case result at £23,097 per QALY). However, the assumptions adopted in the present analysis are less conservative than those used in Boonen et al. [14], who used a different modelling approach. Thus, the model approach in this analysis, although imperfect, is reasonable and balanced overall.

Finally, the present economic assessment relied on the BASDAI alone (as opposed to BASFI alone or BASDAI and BASFI in combination) to predict the economic impact of TNF-antagonist therapy. This approach may underestimate the benefits of therapy as BASFI, not BASDAI, is often considered the major driver of costs [14]. However, the decision to anchor costs with the BASDAI is justified on three grounds. First, from a practical standpoint, the authors only had access to data sets linking BASDAI and BASFI separately to costs, but not in tandem with costs. Second, the inclusion of the BASFI to estimate costs is mostly relevant in the estimation of productivity costs rather than direct costs. Since the perspective adopted was that of the NHS, the inclusion of the productivity costs is less relevant. Since the BASFI is included in the utility regression, the impact of BASFI was not completely ignored. Finally, the approach adopted here was also used in a previous economic analysis [14]. Nevertheless, the sensitivity analysis also showed that implementing BASFI instead of BASDI in the regression of costs led to similar estimates of direct cost per QALY (£25,252 vs £23,097 in the base-case analysis), thus suggesting that the results are reasonably robust.

In conclusion, this analysis suggests that adalimumab is cost-effective relative to conventional therapy for the treatment of AS when used according to widely accepted treatment guidelines such as the UK BSR guidelines.

Rheumatology key messages

- When used according to the British Society of Rheumatology treatment guidelines, adalimumab appears cost-effective compared to conventional therapy in patients with ankylosing spondylitis.
- Adalimumab therapy in ankylosing spondylitis patients experiencing an adequate response is predicted to result in gains in quality of life and reductions in health care costs (before inclusion of adalimumab drug costs).
- The economic benefits of therapy are particularly large when potential reductions in lost productivity are included.

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