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Comparison of the cost-effectiveness of infliximab in the treatment of ankylosing spondylitis in the United Kingdom based on two different clinical trials

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Objectives: To compare the cost-effectiveness of the treatment of ankylosing spondylitis (AS) with infliximab in the United Kingdom over lifetime estimated from two different clinical trials and adjusted for clinical practice guidelines.
Methods: A cost-effectiveness model was developed to incorporate clinical, epidemiological, and economic data and allow extrapolation of trial results and incorporation of long-term treatment. Assumptions regarding treatment beyond the trials were based on open extensions from the trials and treatment guidelines by the British Society for Rheumatology. Results are presented for both the societal perspective and the perspective of the National Health Service (UK £, discounted 3.5 percent).
Results: Under the assumption that disease activity would be controlled and functional capacity would remain stable while on drug, treatment with infliximab (5 mg/kg every 6 weeks) dominates standard treatment in the societal perspective. In the National Health Service perspective, the cost per quality-adjusted life-year (QALY) gained over lifetime was £28,300 and £26,800 for the two trials. If functional capacity were to deteriorate at half the rate of untreated patients, the cost per QALY gained would be £35,300 and £34,100, respectively. The results are sensitive to the dosing regimen adopted, the discontinuation rate, and assumptions concerning disease progression while on treatment.
Conclusions: The two clinical trials yield the same cost-effectiveness results and the cost per QALY gained with treatment was found to be in the acceptable range.

Keywords: Cost-effectiveness, QALY, Infliximab, Ankylosing spondylitis, United Kingdom

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The impact of ankylosing spondylitis (AS), in particular of the physical and functional impairment, on healthcare costs and work capacity has been shown in several studies both in Europe and in North America (3;4;21;22;30). Functional capacity has been identified as the main cost-driver overall in all studies, but particularly in late disease (21;22). In the largest of these studies in the United Kingdom, the mean annual costs ranged from £2,400 for patients with mild functional disability, defined as a score equal or less than 1 on the Bath Ankylosing Spondylitis Functional Index, BASFI (10), to £38,400 for patients with a BASFI score of 10 (21).

Similarly, the impact on AS patients' quality of life (QoL) is considerable (14;21;22;29), and strongly correlated with both disease activity and functional impairment. In the study in the United Kingdom, mean utility ranged from .80 for a BASFI <3 to .47 for BASFI ≥7. Using the disease activity score (Bath Ankylosing Spondylitis Disease Activity Index, BASDAI) (17), the scores ranged from .80 for BASDAI <3 to .39 BASDAI ≥7 (21).

Cost-effectiveness analysis in AS is based on the concept that, as costs increase and QoL decreases as the disease worsens, a treatment that prevents or slows disease progression and controls disease activity will avoid or delay the high healthcare costs and productivity losses combined with low QoL associated with severe disease. Initially, cost-effectiveness analyses for new treatments can only be based on clinical data, and results can, thus, differ depending on the patients included in the trials. The purpose of this analysis was, therefore, to model the cost-effectiveness of infliximab compared with standard care based on the small double-blind registration trial with open extension by Braun and colleagues (6–8) and confirm the results using a more recent trial in a larger and slightly different patient population with a longer double-blind period (ASSERT) (28).

MATERIALS AND METHODS

Data

Cost-effectiveness models in chronic progressive disease generally combine data on treatment effect (clinical trials) with epidemiological data on the natural course of the disease and data on costs and QoL related to disease severity. The main data sets used in this analysis have been described in detail elsewhere (7;8;12;21;25) and are, therefore, only summarized here.

Effectiveness Data. The two international clinical trials compared infliximab with placebo in patients with active AS according to the ASAS criteria (8;9;28). The first trial by Braun and colleagues randomized 70 patients for a double-blind period of 12 weeks (8), followed by open treatment with infliximab for all patients thereafter (7;28). ASSERT included 279 patents for a double-blind period of 24 weeks (28) and open follow-up thereafter (not available at the time of this analysis). The demographics of the patients used in the model are summarized in Table 1.

Disease Progression. Disease progression in the model is expressed with changes in BASFI. Average annual disease progression was estimated from two epidemiological surveys in 1,110 patients at the University of Bath (UK) 10 years apart (1992 and 2002) (21;27). The mean absolute annual change in BASFI was +.07 for patients in the

Table 1. Clinical Trial Populations Used in the Models

	Braun trial		ASSERT trial	
	Placebo	Infliximab	Placebo	Infliximab
	Baseline[a]		Baseline[a]	
	$N = 35$	$N = 35$[b]	$N = 78$	$N = 201$
Male (%)	62.9%	68.6%	87.2%	78.1%
Age	39.0 (9.1)	40.1 (8.2)	41.0 (34–47)	40.0 (32–47
Disease duration	14.9 (9.3)	16.4 (8.3)	13.2 (3.7–17.9)	7.7 (3.3–14.9)
BASDAI	6.3 (1.4)	6.5 (1.1)	6.5 (5.2–7.1)	6.6 (5.3–7.6)
BASFI	5.1 (2.2)	5.5 (1.8)	6.0 (4.1–7.2)	5.7 (4.5–7.1)
	End of double-blind period (ITT)		End of double-blind period (ITT)	
BASDAI		3.4 (.4)		4.0 (2.6)
BASFI		3.2 (.4)		3.7 (2.6)
	Start of extension		Start of extension	
	$N = 34$[c]	$N = 18$ (responders)	$N = 75$[d]	$N = 100$ (responders)
BASDAI	6.3 (1.5)	1.8 (1.0)	6.4 (1.6)	1.4 (1.0)
BASFI	5.4 (1.7)	2.0 (1.3)	5.8 (2.0)	1.9 (1.5)

[a] Results as published.
[b] Two patients that had been randomized but had not received treatmentwere incorporated into the placebo group in the model.
[c] Three patients withdrew during the double-blind period; two patientsfrom the active group are added.
[d] Three patients withdrew during the double-blind period.
BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, BathAnkylosing Spondylitis Functional Index; ITT, intention to treat.

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mid-range of the scale (4–7), and BASDAI did not show any progression over time. Due to the limited data points available, the same rate of progression was used in the model for all patients regardless of age or level of disability.

Cost and Utility Data. Resource utilization and cost data are based on a cross-sectional retrospective survey conducted in 2004 at the University of Bath, United Kingdom (21). The survey included all consumption of healthcare and community services, out-of-pocket expenses, and informal care related to AS, as well as data on work capacity. A total of 1,413 patients with a mean age of 57 years (range, 28–89 years) participated in the study. The sample covered the full range of BASDAI and BASFI (1–10). With increasing functional impairment, costs increased steeply, whereas the increase due to disease activity was moderate. Costs were adjusted to reflect prices for 2005 using the consumer price index.

Utility had been collected in the same survey using the EQ-5D five-dimensional health status classification from the United Kingdom (15;16). The EQ-5D is widely used in studies in rheumatology and has been shown to be very sensitive to changes in function and inflammation (18;23). Also, the simplicity of the instrument makes it an ideal tool to use in large cross-sectional surveys.

The annual cost of treatment with infliximab was based on 5 mg/kg body weight (weeks 0, 2, 6, and then every 6 weeks). The list price for infliximab was £419.62 per 100 mg vial, as of January 2005. For each infusion, the cost of an outpatient visit was included in the cost. The cost of all adverse events possibly related to treatment was estimated from the Braun trial and based on routine care for such events. A mean cost of £79.25 was assigned to all patients starting treatment.

The Model

Structure. Cost-effectiveness is modeled by combining a decision tree representing the double-blind periods of the trials with a subsequent Markov model with annual cycles to estimate disease progression with and without treatment beyond the trials (see Supplemental Figure 1 [http://www.journals.cambridge.org/jid_thc] for the "model structure"). In the decision tree, means of the clinical variables at each data point in the trials are used. At the start of the Markov model, individual BASFI and BASDAI scores are incorporated and used in the extrapolation. The Markov model uses three states: "on treatment," "off treatment," and "dead." Only standardized population mortality for the United Kingdom is incorporated, to avoid modeling an effect of treatment on mortality for which there are no data. Natural disease progression is represented by changes in BASFI only, as BASDAI fluctuates with patients experiencing flares, but did not show a progression over time in the data sets used (21).

Only patients responding to treatment as defined by the British Society of Rheumatology (BSR) (26), that is, a BASDAI ≤ 4 or a ≥ 50 percent improvement in BASDAI, remain on treatment. Thus, at the end of the double-blind periods, 12 and 100 patients are withdrawn from treatment in the Braun and ASSERT trials, respectively.

Utilities and costs are assigned to individual patients at each data point or cycle using regression analyses controlling for age, gender, BASDAI, and BASFI, and bootstrapping the regression coefficients from the observational study (21). This strategy allows combining the clinical and observational data despite demographic differences of the samples and accounting for advancing age. (See Supplemental Table 1 [http://www.journals.cambridge.org/jid_thc] for regression models to estimate "utilities" and "costs per patient.")

Assumptions. Although the model is based on extensive and detailed data sets for all variables, several assumptions were required, as summarized in Table 2. The double-blind phase of the model is based directly on BASFI and BASDAI measurements in the clinical trial, but no information was available for patients after withdrawal from treatment during the trials. In the short-term decision tree, patients who discontinue treatment are assumed to revert to their baseline score at the next measurement point. This assumption is supported by data on discontinuation of treatment after 3 years in 42 patients. All but one of these patients had a relapse within 52 weeks and had to be treated again (1).

After the trials, a further 15 percent of remaining patients are assumed to withdraw from treatment every year, estimated from the second year extension in the Braun trial. These patients revert to the BASFI and BASDAI scores of the no treatment arm at the same time point to account for underlying disease progression. A small additional cost for adverse events was assigned to these patients at discontinuation, to account for potential adverse events.

One of the most important assumptions relates to the effect of treatment on disease progression. Patients in the standard care arm progress at a rate of .07 BASFI points every year. For patients on treatment, three hypotheses are used. The first analysis assumes that functional disability does not progress while on treatment, supported by the extensions of the Braun trial (2;6). Of those patients who qualified for further treatment according to the BSR criteria at the end of the 12-week double-blind period, 72 percent completed 2 years of treatment and even appeared to improve further. Indeed, for these patients, BASDAI decreased from 1.9 at 12 weeks to 1.5 at 1 and 2 years, whereas BASFI decreased from 2.2 to 2.1 at 1 year and 2.0 at 2 years. The two alternative scenarios assume a 50 percent reduced progression while on treatment and no effect of treatment on progression.

Simulations. Results are presented for both the societal and the National Health Service (NHS) perspectives,

Table 2. Summary of Data Inputs and Assumptions in the Markov Model

	Data inputs and assumptions
Basic model	
Markov states	"On treatment," "off-treatment," "death"
Cycle length	1 year
Time horizon	Lifetime
Discount rate	3.5%
Mortality	Normal mortality
Disease progression	Based on BASFI only, annual progression .07 points
Disease activity	BASDAI assumed to be stable
Costs	Assigned with two-step multiple regression based on the mean BASFI/BASDAI score and demographic characteristics of the group at each cycle
Utility	Assigned with regression analysis and bootstrapping from the full distribution of values
Intervention	5 mg/kg every 6 weeks, no drug wastage
Simulations	
Sample	Mean age of 40 years, 80% male
Starting state (Braun)	"Off treatment": BASFI 5.4, BASDAI 6.3 (average) "On treatment"(responders): BASFI 2.0, BASDAI 1.8 (average)
Starting state (ASSERT)	"Off treatment": BASFI 5.8, BASDAI 6.4 (average) "On treatment"(responders): BASFI 1.9, BASDAI 1.4 (average)
Disease progression on treatment	1) No progression while on treatment 2) 50% of natural history (.035/yr) 3) Same as natural history (.07/yr)
Transitions (dropout)	15% of patients withdraw from treatment every year
Dropouts (BASDAI)	Patients return to mean score of the nontreated group (Within trial: to their own baseline)
Dropouts (BASFI)	Patients return to the mean score of the nontreated group, adjusted for a reduction in the underlying natural progression during the years of treatment (−.07* years of treatment) (Within trial: to their own baseline)

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index.

over lifetime. Estimates are based on first-order Monte Carlo simulations (10,000 simulations).

Sensitivity Analyses. All sensitivity analyses are presented for the NHS perspective, as infliximab treatment dominates no treatment in the societal perspective for both trials. One-way sensitivity analysis is performed for a large number of parameters, and the comparison of the results with the two trials provides additional insight into the uncertainty of patient outcomes.

The uncertainty in the cost-effectiveness results is explored with acceptability curves. Such curves indicate the probability that cost-effectiveness estimates fall below a certain threshold of willingness to pay for a QALY gained. Estimates are based on second-order Monte Carlo simulations (10,000 for each case), varying costs, utilities, progression rates, and BASFI values.

In addition to different levels of effect of treatment on disease progression, sensitivity analyses are presented, varying the discontinuation rate, the time horizon, the discount rate, and the dosing regimen of infliximab.

In the main analysis, the treatment regimen from the clinical trials was used. However, arguments have been made for using lower doses. Collantes-Estevez et al. (12;13) used 5 mg/kg every 8 weeks; Myckatyn and colleagues treated patients on an "as needed" basis and over the 4 years of the study, 75 percent of patients are treated with 3 mg/kg every 8 weeks, 15 percent with 3 mg/kg every 6 weeks, and 10 percent with 5 mg/kg every 8 weeks ("Canadian regimen") (20;25). Another study in the United Kingdom followed up patients treated with 3 mg/kg every 8 weeks for 12 months (19). All studies showed an improvement of disease activity of around 50 percent or more.

Infliximab is presented in vials, but administered by body weight. This situation leads potentially to either wastage or use of a reduced dose to limit the number of vials and thus costs. A patient weighing 70 kg would need 3.5 vials with the dosing regimen of the registration trials, or 2.1 vials with the Canadian dosing regimen. Data from the registry of the BSR indicate an average use of two or three vials per patient, which would correspond either to a lower body weight than what we used in our analysis (60 kg compared with 73.6 kg), or a lower dose (confidential information, BSRBR, University of Manchester, www.arc.man.ac.uk/webbiologicsreg.htm). In our base case, we use the actual amount of drug required, thus assuming that vials can be shared among patients infused during the same day, but we present sensitivity analysis for different numbers of vials used.

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Table 3. Cost per QALY Gained over Lifetime

(5 mg/kg every 6 weeks)	Incremental cost[a]	QALY gain[a,b]	ICER (£/QALY)[a]
	BRAUN TRIAL		
	No progression while on treatment		
Societal perspective, all costs	−16,862	1.28	Dominance
NHS and PSS costs only	36,378	1.28	28,332
	50% progression while on treatment		
Societal perspective, all costs	−3,975	1.01	Dominance
NHS and PSS costs only	35,756	1.01	35,332
	Same progression in both groups		
Societal perspective, all costs	12,156	.81	15,045
NHS and PSS costs only	39,336	.80	49,417
	ASSERT		
	No progression while on treatment		
Societal perspective, all costs	−15,927	1.27	Dominance
NHS and PSS costs only	33,920	1.27	26,751
	50% progression while on treatment		
Societal perspective, all costs	−5,233	1.01	Dominance
NHS and PSS costs only	34,408	1.01	34,067
	Same progression in both groups		
Societal perspective, all costs	10,540	.88	11,937
NHS and PSS costs only	39,242	.86	46,167

[a] Cost and effects discounted with 3.5%.
[b] Small differences in QALY gains between the two cost perspectives as estimates are based on stochastic simulation procedures.
QALY, quality-adjusted life-year; ICER, incremental cost-effectiveness ratio; NHS, National Health Service; PSS, Personal Social Services.

RESULTS

For the flow of patients between the three states over the lifetime horizon both for the Braun trial and ASSERT, see Supplemental Figure 2 [http://www.journals. cambridge. org/jid_thc] on "cohort movements." Table 3 presents the results for the three scenarios. In the societal perspective, where all costs are included, treatment with infliximab dominates in both trials in the first two scenarios. Under the assumption that treatment has no effect on disease progression, the cost per QALY gained was estimated at £15,045 and £11,937 for the Braun and ASSERT trials, respectively. In the NHS perspective, the cost per QALY gained ranged from £28,332 and £26,751 (no progression while on treatment) £49,417 to £46,167 (no effect of treatment on progression), respectively.

The model is most sensitive to the treatment cost and the time horizon (Table 4). When using the regimen from the Spanish study, the cost per QALY is reduced by 30 percent to 32 percent in the NHS perspective. Using the individualized Canadian regimen reduces the ratios by as much as 63 percent to 65 percent, while using two vials for all patients reduces the cost per QALY by 62 percent to 65 percent. Reducing the time horizon to 10 years more than doubles the cost-effectiveness ratios.

Stochastic analyses indicate that there is an 80 percent probability that the cost per QALY falls below the threshold of £30,000, and all estimates fall below £32,000. (See Supplemental Figure 3 [http://www.journals.cambridge.org/jid_thc] for "acceptability curves.") When patients progress at half the rate of untreated patients, all estimates fall below £40,000. In the societal perspective (curves not shown), 100 percent of the estimates are cost-saving in the first scenario (Braun trial), 70 percent of all estimates remain cost-saving in the second scenario (50 percent progression), and 100 percent of the simulations remain under the threshold of £30,000 assuming no effect of treatment on progression.

DISCUSSION

Estimating the cost-effectiveness of treatments in AS requires modeling for several reasons. Although functional capacity is the major driver of costs, it may take many years to progress to severe impairment. However, effectiveness data are limited both in terms of the duration and sample size in clinical trials. Functional impairment and disease activity are highly correlated ($r^2 = .7$), but they affect costs and utility at different times in the disease course. Thus, both measures, as well as age, need to be taken into account at every time point for calculation of costs and utility. This approach makes it necessary to adopt a long-term perspective using disease models that, by definition, suggest several assumptions.

We present our results from both the societal and the NHS perspective. However, the social cost of the disease is

Table 4. Sensitivity Analyses

	Assumptions	Braun and ASSERT Trials
		% change in ICER
Reference case		
Dosing regimen	5 mg/kg, 6 weeks	
Longterm dropout	15% per year	
Time horizon	Lifetime	
Costs	NHS and PSS costs	
Discount rate	3.5% cost, effect	
Incremental cost per QALY gained		£28,332 /£26,751
Sensitivity		
Dosing regimen	5 mg/kg, 8 weeks	−30%/−32%
	3 mg/kg, 6 weeks	−53%/−50%
	3 mg/kg, 8 weeks	−69%/−66%
	75% 3 mg/kg, 8 weeks 15% 3 mg/kg, 6 weeks	
	19% 5 mg/kg, 8 weeks	−71%/−63%
	4 vials per patient	+7%/+12%
	3 vials per patient	−34%/−28%
	2 vials per patient	−65%/−62%
Dropout rate	10%	+12%/+17%
	5%	+22%/+33%
	0%	+39%/+47%
Time horizon	60 years	No change
	50 years	+2%/+6%
	40 years	+7%/+14%
	30 years	+15%/+27%
	20 years	+37%/+46%
	10 years	+63%/+66%
Discount rate	5%, cost, effect	+14%/+21%
	0%	−51%/−46%

QALY, quality-adjusted life-year; ICER, incremental cost-effectiveness ratio; NHS, National Health Service; PSS, Personal Social Services.

substantially higher than NHS costs only, arguing for using a societal perspective for the main analysis. The deterioration of function often leads to loss of work capacity and need for informal care. Productivity losses have been estimated at almost 60 percent of total costs in the United Kingdom (21). Also, if family members were unable to provide the support and care, estimated at almost 10 percent of total costs (21), social services would have to do it, likely at a substantially higher cost.

Based on the open extension period in the Braun trial, we can argue for a sustained effect of infliximab over time (6). There was no functional decline seen in patients on treatment, once inflammation was controlled (6). Our own analysis of patients responding according to the BSR criteria showed not only that BASFI scores were stable, but that they actually improved slightly over time. In addition, magnetic resonance imaging data showed a 75 percent improvement of active spinal lesions in patients treated for 2 years with etanercept, with the majority of patients having no disease activity flares (1;2). This finding supports our base case assumption that BASFI does not progress for patients on treatment, or at least not at the same rate as untreated patients. Our most conservative scenario, where patients' function declines after the clinical trials according to natural history, regardless of treatment or not, suggests that only an effect on disease activity is maintained and that this does not affect the progression of functional disability. This appears overly conservative, as it is generally thought that it is persistent inflammation that leads to functional decline. Also, it is not supported by the data used in the model, or radiographic studies of patients on treatment (23). Considering the difference of post-trial disease progression in the three scenarios explored, the difference in the mean QALY gain appears small. The reason for this finding is that patients on treatment retain the initial within trial changes to BASDAI and BASFI and, hence, have a higher utility score from the beginning. The QALY gain of .86–.88 in the most pessimistic scenario where both groups progress at the same rate is, thus, due to the maintenance of the trial gains for as long as patients remain on treatment.

Recently, evidence is increasing that infliximab has comparable effects with alternative treatment regimens. In our main analyses, patients receive 5 mg/kg every 6 weeks, but other regimens have been successfully tested, particularly in Canada, Spain, and the United Kingdom (12;13;19;20;25). These studies have shown that effective treatment can be provided with lower dose and more individualized dosing schedules ranging between 3 and 5 mg/kg every 6–8 weeks. Almost 60 percent of patients in the Canadian observational cohort demonstrated a reduction of 50 percent in the BASDAI by week 14. Furthermore, all 15 (45 percent) patients in this cohort that continued on infliximab (median follow-up of 1,209 days) maintained a $\geq$50 percent decrease in the BASDAI during follow-up. In the Spanish study, over 70 percent of patients achieved a 50 percent response in BASDAI at 30 weeks and the response was fully maintained in patients continuing to 62 weeks. In the study in the United Kingdom, 54 percent of patients achieved a 50 percent response in BASDAI at 3 months, and response was maintained with the low dose in 63 percent of patients remaining on treatment for 12 months (19). We, therefore, explore the effect of these reduced regimens on the cost-effectiveness. However, in the absence of patient level data for all trials, it is impossible to compare the effectiveness. We, therefore, assumed that it would be the same as in the Braun and ASSERT trials, and results can thus be likened to sensitivity on treatment cost.

Results are sensitive to the withdrawal rate in the extension period. In the Braun trial and its extension, around 10 percent of patients discontinued treatment every year. In ASSERT, only 4 of 100 patients in ASSERT discontinued during the 6 months double-blind phase. Among responders entering the long-term extension in our model, the rate was 15 percent, and we used this value in the base case. It is difficult to explain why the persistence rate is lower in responders, as one would expect the opposite. However, in the study by Collantes and colleagues (13), several very good responders declined to enter the second phase of the clinical study, which

may indicate that some patients may withdraw, possibly only temporarily, when they have a very good response. Clearly our sample in the extension phase was very small, and these findings would, therefore, have to be confirmed further in clinical practice. Continuation rates with infliximab in rheumatoid arthritis in Sweden in patients exceeding 1 year of treatment (66 percent) have been estimated at 77 percent in the second year, and in those patients continuing beyond 2 years, at 88 percent (24). This finding supports our withdrawal rate of more than 10 percent. However, persistence rates in patients with AS have been reported to be higher over a period of 3 years (hazard ratio for discontinuation, .66) (11).

Another study evaluating the cost-effectiveness of infliximab in AS was conducted in the Netherlands (5). Boonen et al. compared infliximab and etanercept with usual care over a time frame of 5 years. The analysis for infliximab was based on the same clinical data as our study, and the researchers estimated cost-effectiveness ratios ranging from €67,000 to €237,000. This large difference can be explained by several factors related to the underlying data and the modeling approach used. Within a 5-year time horizon, the benefit of treatment is much more limited, as can bee seen in our sensitivity analysis (Table 4). Potential long-term effects of treatment are excluded, while the cost of treatment is high with a very limited effect of discounting. Ratios in our model more than double when the time horizon is reduced to 5 years. Similarly, natural progression to functional impairment over 5 years is limited, and the short time horizon excludes thus one of the major cost-drivers of the disease. The analysis by Boonen and colleagues is based on BASDAI only and, hence, does not incorporate the effect of treatment on BASFI observed in the trials. Also, only two levels for costs and utilities are used, above and below BASDAI 4, and smaller changes could thus not be incorporated. The authors also incorporate a stronger focus on toxicity of treatment than our analysis. Information from other sources than the efficacy trials was incorporated, while our analysis limited toxicity to the data observed in these trials. Finally, the authors use the friction cost method to estimate production losses as mandated by the Dutch reimbursement guidelines. This method ignores long-term production losses and, hence, leads to very low indirect costs, de facto limiting possible cost offsets.

The cost per QALY gained in our analyses ranges from around £27,000 in the most optimistic to £49,000 in the most pessimistic scenario (NHS perspective), while treatment is dominant in the societal perspective. The stochastic analyses show that there is relatively little uncertainty around the cost-effectiveness results obtained from the two trials (see Supplemental Figure 3 [http://www.journals.cambridge.org/jid_thc]). In the optimistic scenario, 80 percent of cost-effectiveness estimates fall below a threshold of £30,000 (NHS perspective), while 100 percent of simulations are cost-saving in the societal perspective.

POLICY IMPLICATIONS

This analysis highlights the importance of selecting those patients for treatment who are likely to benefit most, and of deciding when to start and when to stop treatment to use resources in a cost-effective way. In the United Kingdom, the BSR has issued guidelines that define the level of disease activity at which treatment is indicated, as well as the response criteria required to continue treatment. In clinical practice, this may be difficult to achieve. However, our analysis indicates that, if these criteria were applied, the use of biological drugs such as infliximab would be cost-effective.

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