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The cost utility analysis of riluzole for the treatment of amyotrophic lateral sclerosis in the UK

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Abstract

This study reports the results of a long-term economic evaluation of riluzole in the treatment of amyotrophic lateral sclerosis (ALS) versus best supportive care in the United Kingdom. The aim was to assess the cost implications of the life extension offered by riluzole through cost utility analysis based on patient assessed utilities of different health states.

A Markov model was used to assess the cost–effectiveness of Rilutek with best supportive care. Transition possibilities and the distribution of patients by health states were taken from a cohort of 954 patients drawn from a large randomised, double blind, placebo–controlled, multicentre trial between 1992 and 1994 in the first 18 months and used to extrapolate the model to assess the long-term prolongation of life. Four distinct health states were used corresponding to mild, moderate, severe and terminal states. Costs associated with Rilutek included the acquisition cost and bi-monthly monitoring for raised ALT levels. Patient assessed utilities were collected by use of the standard gamble technique. 77 patients were entered into the study from two centres (King's, London and Preston) in the UK. Mean utilities for each of the health states was generated and, given that the data were skewed, a sensitivity analysis was undertaken with the median utility values.

The implications of life extension offered by riluzole versus best supportive care were assessed both in terms of life extension projected and quality adjusted survival using patient based utilities. Using the Markov model and the transitional probabilities the base case cost per life year gained was estimated at £14,370 and applying Standard Gamble utility scores, the base case cost per QALY was assessed as £20,904. The effect of discounting costs and benefits altered the cost effectiveness analysis to £17,760 per life year gained while a sensitivity analysis around median or mean scores for the utility weight resulted in a range of £19,020 to £25,794 per QALY gained.

Keywords: ALS; Cost utility; Cost effectiveness; Markov models; Riluzole

1. Introduction

This study provides an updated assessment of the cost effectiveness of riluzole (Rilutek® Aventis Pharma) in the treatment of amyotrophic lateral sclerosis (ALS), commonly known as motor neurone disease (MND) in the UK. This is an update on an earlier paper by Tavakoli et al. [1]. This analysis uses Markov modelling, a method introduced to this area by Riviere et al. [2]. The analysis included in this paper provides an update of the cost effectiveness analysis, as well as an assessment of the cost utility of riluzole in this indication. The main aim of this study is to review and assess the cost implications of the life extension offered by riluzole by taking into account the patients' utility score with updated cost figures.

Amyotrophic lateral sclerosis (ALS) is a chronic, progressive and fatal neurodegenerative disorder. It is characterised by progressive muscle degeneration called amyotrophy and rapid deterioration of alpha and cortical motor neurones. It is the most frequently occurring form of motor neurone disease (MND) and usually affects patients over the age of 50 [3,4]. There is also a certain amount of evidence suggesting that incidence continues to increase once the age of 75 is reached [5], i.e. this is a chronic disease that extends over the lifetime of the patient. ALS is caused by a degeneration of both lower and upper motor neurones of indeterminate aetiology. At present, there is no known cure [2,6–8] and death of the patient is most commonly caused by respiratory failure [2]. Once ALS has been diagnosed, life expectancy ranges from a few months to decades. Estimates of median survival range between 2.5 and 5 years from the date of diagnosis [9–11].

The disease is found predominantly amongst the male population [12], and international estimates of prevalence

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range between 4 and 10 cases per 100,000 population, with annual incidence estimated between 1 and 3 cases per 100,000 population [2–4]. In the United Kingdom, it is estimated that there are currently between 2400 and 5400 people suffering from ALS [3,13].

ALS occurs in two forms: sporadic and familial, although familial accounts for only 5–10% of all cases. Both forms require palliative care and treatment subscribed for both forms of the disease is identical as they are clinically indistinguishable [4,14].

Common symptoms are muscle weakness and atrophy, muscle fasciculations, cramps and spasticity, dysarthria, dysphagia, drooling, dyspnoea and emotional lability [3]. Although there are several hypotheses regarding the cause of ALS [4,15–17], the exact pathogenic mechanisms governing the onset of ALS are still unknown. However, one of the theories put forward argues that the excessive accumulation of glutamate to toxic levels causes neurones to die via a calcium dependant pathway [18,19]. This has resulted in the development of drugs such as riluzole, which are designed to decrease the exitotoxic potential of glutamate [13]. It has been shown that riluzole can alter glutamatergic transmission [20], retard disease progression [13] and improve survival in ALS patients [19,21]. In the clinical trials, the beneficial effects of riluzole appear to be time-related. A post hoc analysis [2] concluded that the benefits of riluzole were greatest for patients in the early stages of disease. As a consequence of this, there has been a call for earlier diagnosis and subsequent treatment.

2. Aims

The principal aim of this study is to update the cost implications of the effect of riluzole by estimating both the cost per life year, as well as the cost per QALY of treatment in comparison with best supportive care in the UK. The viewpoint considered is that of the National Health Service so indirect costs and nonmedical direct costs have not been considered. Whilst this may lead to an underestimation of the benefit of riluzole in the treatment of ALS, this is consistent with the perspective of the study and removes any debate regarding the most appropriate measure of these outcomes.

The probable balance of costs and outcomes as a basis for assessing value for money in treating people with ALS with riluzole is clearly important information for healthcare purchasers. The provision of such information for decision makers in the UK leads to the issue of interpretation of the results gained from economic analysis. An attempt is made in the paper to assess the potential implications of the cost per life year and cost per QALY results by drawing comparisons with other interventions, which have been considered worthwhile and cost effective through the use of published decision making criteria [22].

3. Methods

3.1. Model and data

There are various parametric and nonparametric techniques [23,24] to estimate the life expectancy. Markov processes have been shown to be effective and appropriate methods of modelling life expectancy. Markov models are useful for modelling stochastic processes (random processes that evolve over time). They are particularly suited to modelling the progression of chronic diseases in which the risk changes over time, and have also been widely used in economic evaluation [23–26].

The Markov model in this study uses the transitional probabilities observed in the clinical trial. The model is then used to extrapolate the trial data, assess duration in specific states and also to estimate cost and effectiveness over the lifetime of the treated patients.

Markov models in health services research are well documented [23,27]. First, the natural history of a disease is divided into a number of distinct states. The time horizon of the process is then divided into equal fixed time periods (usually dictated by the clinical trial) called Markov cycle or stage. Transition probabilities between these states for each cycle are then calculated using clinical observations. The transition probabilities are either assumed to be constant or allowed to be time dependent [23]. Here, the state transition probabilities are time dependent and the clinical trial data indicated a 2-month cycle period. Throughout each cycle, the patient may stay in one state or transfer to another state, and it is assumed that only one transition can be made per cycle. Calculation of the Markov process gives the average amount of time spent in each state. The simple life expectancy (duration of survival) is the sum of the average times spent in each of the individual states.

The model in this study draws on an earlier work by Riviere et al. [2], who introduced the Markov model into ALS therapy assessment, and uses previously published data [13]. The patient data are based on a cohort of 954 patients drawn from a randomised double-blind, placebo-controlled multicentre (France, Belgium, North America, UK, Germany and Spain) trial, which took place between December 1992 and December 1994 [2,21]. The transition probabilities in the first 18 months and the distribution of patients by health states were, therefore, derived from observed data. Extrapolation of the transition probabilities was undertaken to model the expected life experience of patients on each arm. The average months and the proportion of patients remaining in each state over the lifetime of all patients in both groups were estimated in order to capture all the differential effects of the strategies.

Table 1 shows the Markov states that were defined to represent the progression through disease states to eventual death and has been described in detail elsewhere [2]. The

Table 1
States of health defined for ALS

States	Definition
State 1: mild	Recently diagnosed
	Mild deficit in only one of three regions (i.e. speech, arm and leg)
	Functionally independent in speech, upper extremity activities of daily living and ambulation
State 2: moderate	Mild deficit in all three regions; or
	Moderate to severe deficit in one region, while the other two regions are normal or mildly affected
State 3: severe	Needs assistance in two or three regions
	Speech is dysarthric and/or patient needs assistance to walk and/or needs assistance with upper extremity activities of daily living
State 4: terminal	Nonfunctional use of at least two regions and moderate or nonfunctional use of the third region
State 5: death	

Source: Ref. [2].

model structure was developed through interviews with ALS experts who identified four clinically distinct health states: mild, moderate, severe and terminal. These states were chosen to represent both clinically and economically important events in the disease progression. A simple illustrative figure of state transitions representing the Markov model of disease progression is shown in Fig. 1. States from which it is not possible to leave are known as absorbing states, the only absorbing state in this model being death. In addition, the backward bending arrows indicate that it is possible for patients to remain in a specific state for a whole cycle.

3.2. Survival analysis

Table 2 shows the starting distribution of patients for both arms of the Markov model. It was based on the number of patients in each health state reported by Riviere et al. [2], while Tables 3a and 3b show the patients transitional probability data used in the Markov model.

To assess the long-term effects of riluzole on survival, the 18-month transition probabilities for both riluzole and best supportive care groups were extended using linear interpolation between successive probabilities [28] and the process was ended when more than 99% of patients from the cohort entered the dead state. The results showed a close fit in terms of percentage survival rates for both arms of the model for the first 18 months (within the sample period). However, the model tends to underestimate the actual survival rate in the riluzole arm post-18 months, compared with the additional observational data over the next 2.5 years (see Fig. 2). Given this fact, the predicted survival gain and so the quality adjusted life year (QALY) is likely to be underestimated for the riluzole arm over the lifetime of the treated patients.

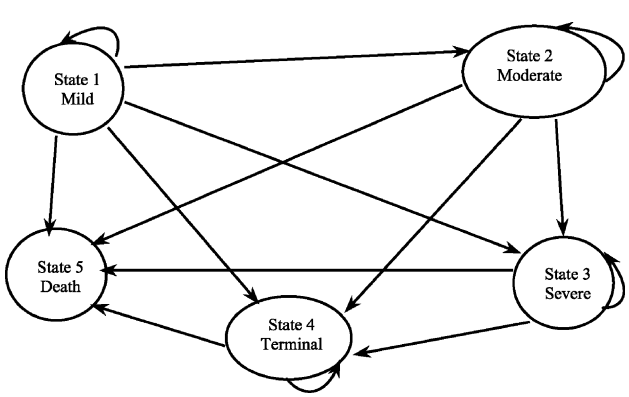

Fig. 1. State transition diagram for Markov model. The backward bending arrows indicate that it is possible for patients to ramain in a spicific state for a whole cycle.

3.2.1. Utility assessment

All cost utility studies should always use valuations derived from a choice-based method. The term utility has always been synonymous with preference; the more desirable or preferable an outcome, the higher the utility associated with that outcome. The term preference is used to describe the level of satisfaction or stress with a health outcome when the outcome is known in advance (certainty). Measured preferences may be ordinal or cardinal. When preferences for different health states are assessed under the conditions of uncertainty they are called utilities [29]. The modern utility theory under uncertainty is based upon von Neumann–Morgenstern expected utility theory [30,31]. Utilities provide an approach to the measurement of health-related quality of life [32]. Measuring health utilities involves first defining a set of health states, then identifying individuals who participate in preference measurement in each health state, decide on a choice-based method such as standard gamble (SG) or time trade-off (TTO), and finally aggregating across the individuals to yield utility scores for each health state [33].

Table 2
Distribution of patients by health state at baseline

Health state	Percentage
Mild	19.18
Moderate	67.29
Severe	12.57
Terminal	0.96

Source: Ref. [2].

Table 3a
Patients' transitional probabilities: riluzole group

	State 1 (%)	State 2 (%)	State 3 (%)	State 4 (%)	State 5 (%)
Cycle 1					
State 1	60.58	4.01	0.00	0.00	0.00
State 2	37.96	78.48	1.27	0.00	0.00
State 3	0.00	15.40	73.42	0.00	0.00
State 4	0.00	0.00	18.99	100.00	0.00
State 5	1.46	2.11	6.33	0.00	100.00
Cycle 2					
State 1	63.73	0.96	0.00	0.00	0.00
State 2	36.27	82.17	3.31	0.00	0.00
State 3	0.00	13.25	75.21	6.25	0.00
State 4	0.00	0.96	7.44	37.50	0.00
State 5	0.00	2.65	14.05	6.25	100.00
Cycle 3					
State 1	75.00	2.45	0.00	0.00	0.00
State 2	25.00	83.65	5.71	0.00	0.00
State 3	0.00	11.44	71.43	0.00	0.00
State 4	0.00	0.27	14.29	66.67	0.00
State 5	0.00	2.18	8.57	33.33	100.00
Cycle 4					
State 1	66.67	3.14	0.00	0.00	0.00
State 2	33.33	81.45	3.68	0.00	0.00
State 3	0.00	11.64	69.85	5.88	0.00
State 4	0.00	0.00	13.97	82.35	0.00
State 5	0.00	3.77	12.50	11.76	100.00
Cycle 5					
State 1	70.21	0.73	0.00	0.00	0.00
State 2	29.79	79.93	3.14	0.00	0.00
State 3	0.00	15.69	79.07	4.65	0.00
State 4	0.00	0.36	11.63	86.05	0.00
State 5	0.00	3.28	6.16	9.30	100.00
Cycle 6					
State 1	71.43	3.02	0.00	0.00	0.00
State 2	28.57	78.88	5.00	0.00	0.00
State 3	0.00	16.38	72.86	2.08	0.00
State 4	0.00	0.00	9.29	64.58	0.00
State 5	0.00	1.72	12.86	33.33	100.00
Cycle 7					
State 1	83.87	1.05	0.00	0.00	0.00
State 2	16.13	77.49	5.34	0.00	0.00
State 3	0.00	17.28	78.63	7.89	0.00
State 4	0.00	0.00	5.34	76.32	0.00
State 5	0.00	4.19	10.69	15.79	100.00
Cycle 8					
State 1	88.46	0.69	0.00	0.00	0.00
State 2	11.54	82.07	3.60	0.00	0.00
State 3	0.00	16.55	75.68	6.25	0.00
State 4	0.00	0.00	8.11	78.13	0.00
State 5	0.00	0.69	12.61	15.63	100.00
Cycle 9					
State 1	73.68	4.21	0.00	0.00	0.00
State 2	26.32	82.11	2.50	0.00	0.00
State 3	0.00	12.63	77.50	3.85	0.00
State 4	0.00	0.00	8.75	69.23	0.00
State 5	0.00	1.05	11.25	26.92	100.00

Table 3b
Patients' transitional probabilities: usual care group

	State 1 (%)	State 2 (%)	State 3 (%)	State 4 (%)	State 5 (%)
Cycle 1					
State 1	67.44	1.91	0.00	0.00	0.00
State 2	32.56	77.07	5.71	0.00	0.00
State 3	0.00	17.83	85.71	0.00	0.00
State 4	0.00	0.00	5.71	100.00	0.00
State 5	0.00	3.18	2.86	0.00	100.00
Cycle 2					
State 1	62.50	3.70	0.00	0.00	0.00
State 2	37.50	72.59	0.00	0.00	0.00
State 3	0.00	18.52	81.03	0.00	0.00
State 4	0.00	0.74	5.17	80.00	0.00
State 5	0.00	4.44	13.79	20.00	100.00
Cycle 3					
State 1	60.00	1.89	0.00	0.00	0.00
State 2	40.00	81.13	1.45	0.00	0.00
State 3	0.00	12.26	71.01	0.00	0.00
State 4	0.00	0.00	13.04	71.43	0.00
State 5	0.00	4.72	14.49	28.57	100.00
Cycle 4					
State 1	62.50	5.43	0.00	0.00	0.00
State 2	31.25	75.00	1.69	0.00	0.00
State 3	0.00	14.13	77.97	0.00	0.00
State 4	0.00	0.00	10.17	69.23	0.00
State 5	6.25	5.43	10.17	30.77	100.00
Cycle 5					
State 1	66.67	0.00	0.00	0.00	0.00
State 2	33.33	81.33	1.82	0.00	0.00
State 3	0.00	14.67	76.36	0.00	0.00
State 4	0.00	0.00	9.09	69.23	0.00
State 5	0.00	4.00	12.73	30.77	100.00
Cycle 6					
State 1	70.00	3.08	0.00	0.00	0.00
State 2	30.00	76.92	1.89	0.00	0.00
State 3	0.00	20.00	75.47	7.14	0.00
State 4	0.00	0.00	13.21	64.29	0.00
State 5	0.00	0.00	9.43	28.57	100.00
Cycle 7					
State 1	66.67	1.89	0.00	0.00	0.00
State 2	33.33	81.13	6.00	0.00	0.00
State 3	0.00	13.21	74.00	0.00	0.00
State 4	0.00	0.00	14.00	93.33	0.00
State 5	0.00	3.77	6.00	6.67	100.00
Cycle 8					
State 1	71.43	2.27	0.00	0.00	0.00
State 2	82.57	79.55	2.56	0.00	0.00
State 3	0.00	13.64	71.79	6.25	0.00
State 4	0.00	0.00	23.08	81.25	0.00
State 5	0.00	4.55	2.56	12.50	100.00
Cycle 9					
State 1	66.67	0.00	0.00	0.00	0.00
State 2	33.33	70.37	4.17	0.00	0.00
State 3	0.00	25.93	75.00	0.00	0.00
State 4	0.00	0.00	8.33	68.75	0.00
State 5	0.00	3.70	12.50	31.25	100.00

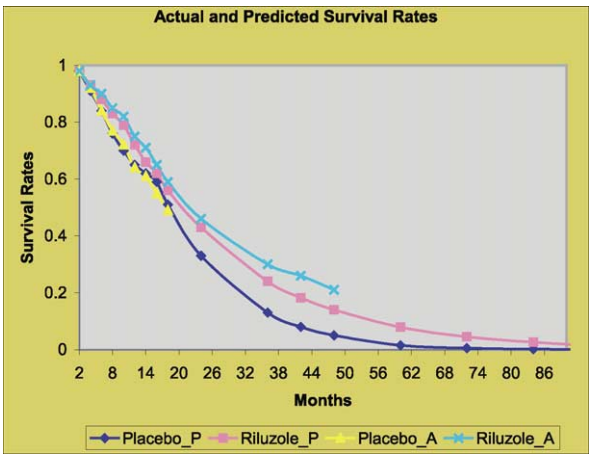

Fig. 2. Actual predicted survival rates. After 18 months patients in the placebo arm of the trial were offered riluzole. Therefore there are no follow-up data available for the placebo group. Placebo_A = actual survival rates; Placebo_P = survival prediction rates from the Markov model; Riluzole_A = actual survival rates including follow-up data; Riluzole_P = survival prediction rates from the Markov model.

There are a number of methods used to assess patients' utility directly (e.g. SG) or indirectly (e.g. EuroQol EQ-5D) for different health states. The utilities/values used in this study are those derived by Kiebert et al. [34], who elicited standard gamble and VAS responses from a sample of MND patients. Kiebert et al. [34] interviewed 77 patients with different levels of disease severity from two centres (King's, London and Preston) in the UK. Patients were asked to complete a number of measures including standard gamble exercise and visual analogue scale (VAS) rating of current health for their own health state (for more details, see Kiebert et al. [34] in this special issue). In standard gamble (SG), the utility of the current ith health state is assessed by asking patients to make a choice between two alternatives. The first choice is an intervention/treatment which would lead either to full health with a probability p, or death with a probability $1-p$. The other choice has the certain outcome/knowledge that they would continue in their present health state, i. Probability p is varied until the point at which the patient can not decide between the two alternatives and this would be taken as the utility of the health state, i.

EQ-5D is a generic health instrument. It consists of five health attributes/dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression with each dimension being divided into three levels: no problems, some problems, major problems; thus, resulting in 243 possible health states. Preferences are then measured using time trade-off (TTO) technique on a random sample of over 3000 members of adult population of the UK [35]. The scores on value scale range from 0 for death to 1.0 for perfect health. The results from the EQ-5D descriptive system suggest that although patient HRQL decreases systematically with increasing severity of disease, the classification system may not be sensitive enough to detect subtle changes over time within the ALS/MND patient group, thus, indicating a floor effect with the majority of ALS patients clustering at the lower boundaries [34].

Table 4
Utility scores

ALS severity level	Visual analogue scale (VAS)	Standard gamble (SG)	
	Mean	Mean	Median
1	0.74	0.79	0.8
2	0.63	0.67	0.75
3	0.51	0.71	0.78
4	0.37	0.45	0.5

Source: Ref. [34].

The VAS component of EQ-5D allows patients to mark their current health state, under the condition of certainty, on a scale between "worst imaginable health state" and "best imaginable health state," and not "full health" and "death" as required for estimating QALYs [31]. In this sense, the VAS values give only preference values and are not utilities. Although, theoretically, it is possible to transform VAS scores into von Neumann–Morgenstern utilities, results suggest that the corrected scores and SG utilities are not stable [36]. The EQ VAS measures the respondent's self-rated health status. It is a quantitative measure and differences in the scale can be used as an outcome measure. It is also used in conjunction with the five-digit classification of EQ-5D to generate a profile of the respondent's health status. For this reason, VAS values in this study are used only for illustrative purposes (sensitivity analysis).

On the other hand, SG is based on expected utility theory with an underlying theoretical base, which captures the individual's risk attitude. Because future health outcomes are uncertain in the real world, it is argued that utilities are preferable to values in the setting of decision analysis [31]. The SG has been used extensively as a method of utility measurement [32,37–39] and is generally considered to be reliable. However, the SG can be confusing to administer and, hence, can lead to some inconsistencies as shown in this study, whereas the VAS is not. For this reason, the base case results for cost utility analysis report the mean SG utilities, but the effects of using median SG results (although they are still inconsistent but

Table 5
Annual costs of the best supportive care for each ALS health state (£, 1998)

	State 1: mild	State 2: moderate	State 3: severe	State 4: terminal
Average (baseline)	1224	805	1754	3231
Maximum	1343	868	1871	11,819
Minimum	889	640	1376	1895

Source: Refs. [13,40].

Table 6
The cost per life year gained and cost per QALY (quality adjusted life-year) gained (Munsat et al. [13]; 1998 prices) (costs discounted at 6%)

The cost per life-year gained (£)	The cost per QALY (£)	
	Standard gamble	
	Mean	Median
14,370	20,904	19,092

to a lesser degree) or VAS values are explored in the sensitivity analysis.

Table 4 shows values and utility scores obtained from the VAS and SG techniques. The mean values for VAS, although, look on a low magnitude for the mild states, they are a priori in the right direction. However, the mean (and the median) values for the SG scores are rather unexpected as the utility value in state 2 is lower than the utility score in state 3. A possible reason for this may be that in the severe stage of disease patients are typically receiving more dedicated medical attention and, hence, their level of satisfaction could be slightly elevated since they might feel that their disease is being managed.

3.3. Costs

The cost data were obtained from Munsat et al. [13] and updated using the NHS price deflator. The deflator was calculated using the Government Health Expenditure Series from the Blue Book [40]. Whilst there is no doubt that the health-related costs of life in the face of disabling disease could be substantial, in this study, as in Tavakoli et al. [1], we have focused on direct costs. Other costs such as those associated with community care are ignored due to lack of data. Consequently, the model estimates only direct health service costs and not the full economic costs of care, which may provide greater cost offsets from the decrease in dependency associated with riluzole. The direct medical costs were derived from resource utilisation patterns associated with treatment of ALS in the United Kingdom [13].

Table 5 shows the updated average, maximum and minimum annual costs for each ALS health state. There is a clear pattern of rising costs, starting with diagnosis and testing and then increasing further with disease severity and progression, with the exception of the moderate state. This can be attributed to a reduction in hospitalisation after the extensive diagnosis phase is completed.

The annual cost of treatment with riluzole has remained the same as that quoted in the paper by Tavakoli et al. at £3742, which includes the cost of the product [41] in addition to the cost of bimonthly serum ALT testing (taken from Ninewells Hospital, Dundee, Scotland). The cost of side effects was assumed to be zero as patients were taken off treatment until symptoms were relieved (personal communication with a consultant neurologist in Ninewells Hospital, Dundee, Scotland).

4. Results

It is standard practice for long-term economic evaluations to adjust the costs and outcomes by applying a discount rate to bring them to their present values for comparison. The treasury recommended rate of 6%, used across Central government including the NHS, is applied in this study. However, although there is no controversy regarding the discounting of variables such as costs and income expressed in monetary terms, discounting nonmonetary variables or health benefits has remained controversial [42,43]. In this study, the base case results include discounting of only the costs; however, sensitivity analysis is used to explore the effects of discounting both costs and benefits for both analyses (see Table 7).

By applying the Markov model to the transitional probabilities, SG utility scores and the updated costs, Table 6 shows discounted incremental costs of riluzole treatment per life year gained and per QALY gained (using SG utility scores). The cost per life year gained is estimated at £14,370 and the cost per QALY is estimated as £19,092 and £20,904, depending on whether the median or mean SG are used, respectively (Table 6).

5. Sensitivity analysis

Table 7 shows costs per QALY when costs or both costs and benefits are discounted under various scenarios. The results suggest that the cost per QALY ranges from £19,092 to £28,674 depending on the scenario used, al-

Table 7
Sensitivity of results to discounting both costs and benefits

The cost per life-year gained (£)		The cost per QALY (£)					
		Visual analogue scale		Standard gamble			
		Mean		Mean		Median	
Only costs discounted	Both costs and outcomes discounted	Only costs discounted	Both costs and utility discounted	Only costs discounted	Both costs and utility discounted	Only costs discounted	Both costs and utility discounted
14,370	17,760	23,400	28,674	20,904	25,794	19,092	23,556

though it should be mentioned that the figures for VAS should be treated with caution, as they do not strictly reflect cost per QALY as explained previously.

A sensitivity analysis was also conducted on the costs of each of the health states experienced by patients with ALS. The findings suggested that cost effectiveness and cost utility analysis are not sensitive to the cost of care using maximum and minimum values reported in Table 5.

Finally, the effectiveness of riluzole in comparison with best supportive care in terms of life-year gained suggested that patients on riluzole would gain an additional 6.3 months over best supportive care. In terms of quality adjusted life-year gained, using the standard gamble utility scores, patients on riluzole will gain at least an extra 3.5 months to approximately 5 months of equivalent perfect health depending on whether discounting is applied.

6. Conclusions

This study updated the findings of the earlier paper by Tavakoli et al. [1], which assessed the phases of the disease that were prolonged by riluzole and concluded that riluzole was effective in prolonging life. It was also established that more patients would remain in states 1–3 where functional status is the least impaired, thus, providing a higher quality of life than with no treatment. The results from the present study support these findings by demonstrating an increase in QALYs over the lifetime of patients treated with riluzole versus best supportive care.

Again, although randomised controlled trials have established the efficacy of riluzole, the cost implications have remained an important issue for some health providers. Although Rilutek is associated with higher healthcare costs, it is also accompanied by 6.3 months of additional life gained, or an equivalent of an extra 4–5 months of perfect health in the base case, depending on whether mean or median utility scores are used, when compared with best supportive care over the lifetime of the treated patients. This is important when one considers that the median survival is between 2.5–5 years from the date of diagnosis. Thus, ultimately, the question is whether treating ALS patients with riluzole can be considered to be cost effective, or more loosely is it value for money when it is compared with other progressive and fatal illnesses?

The cost effectiveness of riluzole has been addressed in other countries and published economic evaluations. A similar study to ours by Messori et al. [44] reported a higher cost per life-year gained (by replacing the English, the Italian and the US price of riluzole) of £27,028 for UK (US$45,048, exchange rate of US$1.0 = £0.60), £32,500 for Italy (US$54,166) and £37,565 for USA (US$62,609), while a study in Israel by Ginsber and Lev [45] suggests that riluzole is cost effective. However, the variation in the cost per life-year gained between our study and Messori et al. can be explained by a number of factors. Our study has incorporated specific costs associated with each stage of the disease, used actual patient transitional probability data and patient reported utility data, and reported a higher additional life gained (5 versus 2.3 months) and a lower medication cost.

Furthermore, on how to interpret and to use the outcome of cost per QALY in healthcare decision making, according to Stevens et al. [22] the findings of Messori's study and our own indicate that riluzole intervention merits supporting. This conclusion has also been echoed in a recent appraisal by the National Institute for Clinical Excellence (NICE) Guidance[46] for "Riluzole to be used to treat patients suffering from the Amyotrophic Lateral Sclerosis (ALS) form of Motor Neurone Disease (MND)," and a recent HTA report (part 2) suggests that revised analysis provide "a more attractive cost effectiveness profile for riluzole" [47].

However, like all other studies, these results are only a guide rather than an exact measurement of the cost effectiveness of riluzole. Furthermore, the indirect cost to carers, their families as well as the direct cost to the community services can be significant. These costs could not be included in the present study since no data were available, but the incremental QALYs gained could be interpreted as potential savings in these areas.

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