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

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of riluzole for the treatment of amyotrophic lateral sclerosis (ALS), also known as motor neurone disease.

Type of intervention
Palliative treatment.

Economic study type
Cost-effectiveness analysis; cost-utility analysis.

Study population
The study population comprised patients with ALS.

Setting
The setting of the study was not explicitly stated. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness data were derived from studies published in 1996, 1998 and 2001. The resource use data were derived from a study published in 1998. The price year was 1998.

Source of effectiveness data
The effectiveness data were derived from published studies.

Modelling
A Markov model was constructed to extrapolate transition probabilities from observational data, and then to estimate the costs and effectiveness over the lifetime of treated patients. Transitional probabilities were time-dependent and each cycle lasted 2 months. Nine cycles were included in the model since the period of observation was 18 months. Five health states were considered in the model according to disease stage. These were mild, moderate, severe, terminal and death. The model was constructed through interviews with ALS experts.

Outcomes assessed in the review
The health outcomes assessed from the published study were the distribution of patients by health states at baseline. Also, all the transitional probabilities involved in moving across health states in the treatment and BSC group. Published utility values, assessed using the standard gamble method and the visual analogue scale, were also reported. These were used as utility weights to derive quality-adjusted life-years (QALYs).
Study designs and other criteria for inclusion in the review
The transitional probabilities were derived from a randomised, multi-centre, double-blind placebo-controlled trial involving 954 patients. The utility values were derived from a study in which interviews were conducted with 77 patients with different levels of disease.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
The data on transitional probabilities and utility values were derived from three primary studies.

Methods of combining primary studies
Narrative methods were used to combine the primary studies.

Investigation of differences between primary studies
Not carried out.

Results of the review
The distribution of patients by health states at baseline was 19.18% in the mild state, 67.29% in the moderate state, 12.57% in the severe state, and 0.96% in the terminal state.

Transitional probabilities were reported in detail in the paper.

The mean utility values measured using the standard gamble method were 0.79 in disease level 1, 0.67 in disease level 2, 0.71 in disease level 3, and 0.45 in disease level 4. The corresponding median utility values were 0.8 in disease level 1, 0.75 in disease level 2, 0.78 in disease level 3, and 0.5 in disease level 4.

The mean utility values measured using the visual analogue scale were 0.74 in disease level 1, 0.63 in disease level 2, 0.51 in disease level 3, and 0.37 in disease level 4.

Measure of benefits used in the economic analysis
The benefit measures used in the effectiveness analyses were survival and QALYs, which were obtained using the Markov model. No discounting was carried out in the base-case.

Direct costs
A 6% discount rate, as recommended by the UK Treasury, was used to assess the long-term costs. The unit costs and the quantities of resources were not reported separately. A detailed breakdown of the costs was not reported, but the health services included in the analysis were both diagnosis and treatment. The cost/resource boundary adopted was that of the NHS. The costs of side effects were not included as they were irrelevant. The costs and quantities were estimated from a published study. The total costs were obtained using modelling. The costs were updated to 1998.
using the NHS price deflator, which was calculated using the Government Health Expenditure Series from the Blue Book.

**Statistical analysis of costs**
The costs were treated deterministically in the base-case.

**Indirect Costs**
The indirect costs were not included in the analysis, due to the lack of data.

**Currency**
UK pounds sterling (€).

**Sensitivity analysis**
One-way sensitivity analyses were performed to assess the robustness of the estimated cost-effectiveness ratios to variations in the parameters used in the main analysis. These included the minimum and maximum values of costs, discounting of both the costs and benefits, use of utility values derived using the visual analogue scale or the median (rather than the mean) values in the standard gamble approach.

**Estimated benefits used in the economic analysis**
Total survival and QALYs were not reported. However, the authors reported that patients on riluzole gained an additional 6.6 months over BSC, and approximately 3.5 to 5 quality-adjusted life-months.

**Cost results**
The mean annual costs of BSC were 1,224 (minimum 889, maximum=1,343) in state 1, 805 (minimum 640, maximum 868) in state 2, 1,754 (minimum 1,376, maximum 1,871) in state 3, and 3,231 (minimum 1,895, maximum 11,819) in state 4.

The annual costs of the intervention with riluzole were not reported. The total costs were not indicated.

**Synthesis of costs and benefits**
Incremental cost-effectiveness and cost-utility analyses were performed.

The cost per life-year gained with riluzole over BSC was 14,370, which became 17,760 when both the costs and outcomes were discounted.

The cost per QALY gained with riluzole over BSC was 20,904 in the base-case, and 25,794 when both the costs and outcomes were discounted.

When the visual analogue scale approach was used, the cost per QALY gained with riluzole over BSC was 23,400 in the base-case (28,904 when both the costs and outcomes were discounted).

When the median values of the standard gamble method were used, the cost per QALY gained with riluzole over BSC was 19,092 in the base-case (23,556 with both the costs and outcomes discounted).

Variations in the costs did not affect the study results.

**Authors' conclusions**
The treatment with riluzole was cost-effective in comparison with best supportive care (BSC). It improved (quality-
adjusted) survival at an acceptable cost to the National Health Service (NHS).

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparator was clear. BSC was selected as representing the routine intervention for patients with ALS. You should decide whether it represents a widely used procedure in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness estimates were derived from three published studies, although a formal review of the literature was not undertaken. The study design and main details of the primary studies were reported. Also, sensitivity analyses were performed in which the utility values used to derive QALYs were varied.

**Validity of estimate of measure of benefit**
The benefit measures used in the effectiveness analyses were survival and QALYs. These were derived using a decision model, which appears to have been appropriate to describe the development and treatment of the disease. The use of QALYs allows the cost-effectiveness of the treatment to be compared with that of other interventions funded in the health care system.

**Validity of estimate of costs**
The cost analysis was carried out from the perspective of the NHS. The indirect costs were not included due to the lack of data, although the authors stated that their inclusion may have been relevant. Indirect costs to the patients' families and community may be significant and their inclusion would probably favour the riluzole treatment. The unit costs and the quantities of resources were not reported separately, and a breakdown of the costs was not provided. The source of the cost and resource data was reported, as was the price year.

**Other issues**
The authors compared their findings with those from studies carried out in other countries. The issue of the generalisability of the study results to other settings was not addressed, and the external validity of the analysis was limited. The study referred to patients with ALS and this was reflected in the conclusions of the analysis. The authors reported their results selectively.

**Implications of the study**
The results of the study suggest that, compared with BSC, riluzole should be the treatment of choice in patients with ALS. The authors noted that their findings represent only a guide rather than an exact measurement of the cost-effectiveness of riluzole.

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None stated.

**Bibliographic details**

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**Other publications of related interest**
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**MeSH**
Amyotrophic Lateral Sclerosis /drug therapy /economics; Cost-Benefit Analysis /statistics & numerical data; Disease Progression; Drug Costs /statistics & numerical data; Forecasting; Great Britain; Health Status; Humans; Markov Chains; Models, Econometric; Multicenter Studies as Topic /statistics & numerical data; Neuroprotective Agents /economics /therapeutic use; Palliative Care /economics; Quality-Adjusted Life Years; Randomized Controlled Trials as Topic /statistics & numerical data; Riluzole /economics /therapeutic use; Sensitivity and Specificity; Survival Analysis; Survival Rate /trends; Treatment Outcome; Value of Life /economics

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