The cost-effectiveness of newer drugs as add-on therapy for children with focal epilepsies

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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 study considered the addition of newer anti-epileptic drugs (AEDs) as an add-on therapy following the failure of monotherapy with carbamazepine and sodium valproate. The newer AEDs studied were lamotrigine, gabapentin, topiramate and oxcarbazepine.

Type of intervention
Treatment.

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

Study population
The study population comprised children (aged 3 to 18 years old) with newly diagnosed epilepsy.

Setting
The setting was outpatient care. The economic study was carried out in the UK.

Dates to which data relate
The clinical effectiveness and resource use data were derived from a paper published in 2006. The price year was 2002.

Source of effectiveness data
The clinical data used in the model included the probability of each stage in the treatment strategy resulting in each of the six health states for children with a learning difficulty and children without a learning difficulty. The six health states were:

- intolerable adverse effects leading to discontinuation;
- lack of an effect on seizure rate leading to discontinuation;
- partial efficacy with tolerable or no adverse effects;
- complete freedom from seizures with tolerable or no adverse effects;
- seizure free following withdrawal of the drug therapy;
- not seizure free but patient prefers to remain untreated.

Modelling
A patient-level simulation model was used to model the clinical outcomes and costs associated with the treatment strategies until the child reached the age of 18 years. Patients were assigned the characteristics of gender, age and presence of learning difficulties at entry into the model. It was unclear whether these characteristics affected the probabilities in the model. The model used 10,000 simulations.

**Sources searched to identify primary studies**
The clinical data were taken from a systematic review of RCTs, other RCTs and clinical experts.

**Methods used to judge relevance and validity, and for extracting data**
The authors indicated that they took the clinical data from a systematic review of RCTs, but did not report the methods of the review. They also reported that data were combined from more than one RCT but, again, did not indicate the methods used to achieve this.

**Measure of benefits used in the economic analysis**
The main measure of health benefit used was the quality-adjusted life-years (QALYs). The health states were valued by a panel of 25 clinicians using a modified version of the Euro-QoL EQ-5D. Future benefits were discounted at a rate of 1.5% per annum. The authors also reported the average time spent with intolerable adverse effects, lack of an effect on seizure rate, partial efficacy with tolerable adverse effects, and complete seizure freedom with tolerable adverse effects.

**Direct costs**
The study identified the direct costs to the NHS. The cost of drugs, general practitioner and outpatient consultations, accident and emergency visits, advice telephone calls and inpatient stays were identified. The unit cost of the drugs was taken from the British National Formulary. Department of Health reference costs and costs identified by PSSRU, University of Kent were used to identify other unit costs. The resource use data for each health state in the model were obtained from clinical experts. The unit costs of the drugs and some resource use data were presented in the paper. Future costs were discounted at a rate of 6% per annum. The price year was 2002.

**Statistical analysis of costs**
No statistical analysis of the resource use or cost data was undertaken.

**Indirect Costs**
No productivity costs were included in this study.

**Currency**
UK pounds sterling (£).

**Sensitivity analysis**
Parameter uncertainty was measured using multi-way sensitivity analyses. The discount rates for costs and health benefits were varied, toxicity and efficacy rates were altered, and the "best" and "worst" utility values were used.

**Estimated benefits used in the economic analysis**
The summary health benefits derived from the model were not reported in the paper.

**Cost results**
The total costs were not reported in the paper.
Synthesis of costs and benefits
Assuming a willingness-to-pay of 150,000 per QALY gained, the probability that any of the new AED treatment strategies would have an acceptable cost-utility was less than 50%. The sensitivity analyses did not substantially alter the results.

Authors' conclusions
There was no strong evidence that newer anti-epileptic drugs (AEDs) resulted in greater benefit than older AEDs. In addition, the newer AEDs were more costly.

CRD COMMENTARY - Selection of comparators
This study compared a treatment strategy based on the newer AEDs with a treatment strategy based on the older AEDs for the treatment of epilepsy in children. Flow diagrams were used to report the sequence of treatments in each strategy.

Validity of estimate of measure of effectiveness
The model parameters were derived from a published systematic review of RCTs and data from other RCTs. Although the authors indicated that data from two RCTs were combined, they did not report the methods used. The authors did not detail the search methods or the inclusion criteria used to identify studies to populate the model.

Validity of estimate of measure of benefit
The estimates of health benefit used in the economic analysis were derived from the model. Health state valuations were assessed by clinical experts, using an appropriate valuation method, and were appropriately discounted.

Validity of estimate of costs
The economic perspective of the study was that of the UK NHS, and all appropriate costs for this perspective appear to have been included. Sensitivity analyses were performed to assess uncertainty in resource use and cost data. A breakdown of the drug unit costs and the mean costs for each health state was provided in the paper. Future costs were appropriately discounted. These factors enhance the generalisability of the study findings. A price year could be ascertained from the paper, which will enable future reflation exercises.

Other issues
The authors noted that there were no other directly comparable studies, but compared their findings with those from similar studies. The study sought to identify the costs from an NHS perspective, thus the generalisability of the findings to other countries was not considered. The authors did not present their results in a comprehensive way (e.g. the total costs and health benefits were not stated), which makes it difficult to generalise the study findings to other settings. The authors' conclusion reflected the scope of their analysis.

Implications of the study
The authors stated that better information on the clinical effectiveness and costs of the newer AEDs is required before an accurate assessment of the trade-off between the two treatment strategies can be made. The authors indicated that RCTs with long-term follow-up are needed to determine the effectiveness of newer AEDs in comparison with older AEDs.

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Other publications of related interest
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