A cost-effectiveness decision model for antiepileptic drug treatment in newly diagnosed epilepsy patients


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.

CRD summary
The study assessed the cost-effectiveness of six antiepileptic drugs for the treatment of newly diagnosed epilepsy patients, including carbamezepine (CBZ), lamotrigine (LTG) and valproate (VPA) as first- and second-line drugs. The study demonstrated the cost-effectiveness of conventional first-line CBZ-VPA therapy and suggested that first-line LTG was not likely to be cost-effective. However, the study results also depended on the inclusion criteria used to select trials. The study was well conducted with sound methodology and good reporting of the methods and results.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The aim of the study was to determine the cost-effectiveness of six alternative strategies of treatment in newly diagnosed epilepsy patients. Treatment was based on older antiepileptic drugs (AEDs) such as carbamazepine (CBZ) and valproate (VPA) and new AEDs such as lamotrigine (LTG) used as first- and second-line therapies.

Interventions
The six strategies were as follows:

CBZ first-line monotherapy followed by either VPA or LTG if CBZ failed because of either a lack of seizure control or adverse effects;

VPA first-line monotherapy followed by either CBZ or LTG if VPA failed because of either a lack of seizure control or adverse effects; and

LTG first-line monotherapy followed by either CBZ or VPA if LTG failed because of either a lack of seizure control or adverse effects.

Location/setting
Netherlands/secondary care.

Methods
Analytical approach:
A decision tree analysis populated with published clinical evidence was developed in order to simulate the outcomes of the six alternative options. The time horizon was 1 year of treatment. The authors stated that a societal perspective was adopted.

Effectiveness data:
A review of the literature was undertaken in order to identify relevant sources of clinical estimates. The inclusion criteria were reported in detail. Most of the clinical data were derived from randomised clinical trials (RCTs), but no direct comparison among the drugs under study was available. Some observational studies were also used. It appears that the authors have used their judgement to select the most appropriate estimate from the available evidence found in the literature. The key clinical input was treatment effectiveness, i.e. the success rate (freedom from seizure).
Monetary benefit and utility valuations:
The summary benefit measure was treatment success (patient being seizure free). This was derived from the literature and calculated using the decision model for the entire treatment period (1 year).

Measure of benefit:
None

Cost data:
The cost categories included in the analysis were general practitioner visits, physician and hospital services, diagnostic tests (both laboratory and imaging), drugs, unpaid care, and productivity losses due to absence from work. The resource use data were derived from a survey of 71 adult epilepsy patients treated in two local hospitals. Average doses used in RCTs were selected for the analysis. The unit costs were derived from guideline prices relevant to the Netherlands. When no guideline price was available, these items were valued using official tariff lists for allowable reimbursement rates. The costs were in euros (EUR) and the price year was 2002.

Analysis of uncertainty:
The issue of uncertainty was addressed by running second-order Monte Carlo simulations with probability distributions assigned to all model inputs. Cost-effectiveness acceptability curves were generated. Alternative models were populated by introducing clinical data that did not meet the inclusion criteria set for the review of the literature.

Results
The expected 1-year costs were EUR 975 for CBZ-VPA, EUR 1,111 for VPA-CBZ, EUR 1,230 for CBZ-LTG, EUR 1,255 for VPA-LTG, EUR 1,861 for LTG-VPA and EUR 2,036 for LTG-CBZ.

The expected probability of complete success was 0.684 for CBZ-VPA, 0.635 for VPA-CBZ, 0.726 for CBZ-LTG, 0.722 for VPA-LTG, 0.742 for LTG-VPA and 0.706 for LTG-CBZ.

CBZ-VPA was thus the reference strategy and only two treatment alternatives (i.e. CBZ–LTG and LTG–VPA) were non-dominated. All the other options were more expensive and less effective than a compared strategy (dominated).

The incremental cost per additional patient classified as complete success was EUR 6,079 for CBZ–LTG relative to the CBZ–VPA strategy, and EUR 40,422 for LTG–VPA relative to CBZ–LTG.

The sensitivity analysis basically confirmed the results of the base-case analysis, suggesting that there was a high probability that CBZ-VPA was cost-effective at relatively low values of willingness-to-pay (about EUR 6,000) for a successfully treated patient. Second-line LTG options were cost-effective only for high willingness-to-pay, while first-line LTG was likely not to be cost-effective. The use of data from studies not initially included in the review did not alter the conclusion that CBZ-VPA is the reference strategy, but it had a strong impact on the other strategies, and CBZ-LTG or LTG-VPA were also dominated in some cases.

Authors’ conclusions
The authors concluded that conventional first-line CBZ-VPA therapy is potentially the most cost-effective treatment for newly diagnosed epilepsy patients in the Netherlands. Further research should be based on prospective real-life studies.

CRD commentary
Interventions:
The authors justified their choice of the treatments under examination, which are likely to be relevant in their own setting. They compared conventional AEDs with newer options. A description of all alternatives was given.

Effectiveness/benefits:
The identification of clinical estimates was based on a review of the literature, the inclusion criteria for which were extensively described. However, other details such as sources searched and methods used to select the primary estimates from among those available were not reported. Details of selected studies were provided instead, including sample size, doses and success rates. The authors highlighted the lack of head-to-head comparisons between the strategies compared,
thus an extensive sensitivity analysis was performed and alternative scenarios were considered. The rate of successfully treated patients may not be easy to compare with the benefits of other health care interventions, although it does represent a commonly used benefit measure for these patients.

**Costs:**
The analysis of the costs was consistent with the authors’ stated perspective. A breakdown of cost categories was provided. The analysis showed that the impact of productivity losses was negligible. The use of patient-level data for the derivation of resource consumption was appropriate and reflected actual consumption of health services and patient expenses. The costs were derived from national databases. Statistical analyses of the costs were performed in the sensitivity analysis. The price year was reported, which will help if carrying out reflation exercises in other time periods.

**Analysis and results:**
The costs and benefits were appropriately synthesised. The results of the base-case analysis and sensitivity analyses were clearly presented. The issue of uncertainty was fully addressed, with the presentation of cost-effectiveness acceptability curves. Dominated alternatives were excluded from the final analysis. Extensive details of both the clinical and economic sides of the analysis were given, which enhances the possibility of transferring the analysis to other settings.

**Concluding remarks:**
Overall, the analysis appears to have been carried out satisfactorily, with extensive reporting of the methods and results. The authors’ conclusions appear appropriate.

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**Bibliographic details**

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
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