Cost effectiveness of topiramate in the prevention of migraines in the United States: an update


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 investigated the use of topiramate (100 mg/day) in the prevention of migraine. This intervention was compared with no preventive treatment.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised working adults who were appropriate candidates for migraine prevention with topiramate. This included those with a mean monthly migraine frequency of 5.6, and an established history (of 6 months or more) of consistent migraines conforming to International Headache Society criteria for the diagnosis of migraine. Patients were excluded if their total monthly headache-days exceeded 15 during the prospective baseline period and/or if they had a previous failure of more than two adequate regimens of preventive migraine medication.

Setting
The study setting was primary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published in 2004. The resource use data were derived from studies published between 2001 and 2005. The price year was 2004.

Source of effectiveness data
The clinical and epidemiological data included in the model were:

- the baseline monthly migraine rate;
- the topiramate discontinuation rate;
- the probability of response to topiramate;
- the reduction in migraine days by response category;
- the probability of response for topiramate drop-outs;
- the probability of response for patients not receiving preventive treatment;
the probability of migraine occurring on a paid workday; and
the probability of migraine being treated with a triptan.

Modelling
An analytic decision tree model was updated with new clinical and economic data to assess the cost-effectiveness of topiramate versus no preventive treatment for patients with migraines. The time horizon was one year. A sub-group analysis was performed to assess the model outcomes for all patients who continued the treatment.

The model was based on various assumptions. It was assumed that patient who dropped out discontinued the treatment during the first month. In addition, treatment drop-outs and patients receiving no preventive treatment were assumed to receive no clinical benefit.

Sources searched to identify primary studies
Pooled clinical trial data for the effectiveness of topiramate were derived from two randomised, double-blind, placebo-controlled trials. These data were then confirmed by two 6-month open-label extension findings of these two studies. The probability of response for topiramate drop-outs and patients not receiving preventive treatment was based on authors' assumptions.

Methods used to judge relevance and validity, and for extracting data
The authors reported that data used to populate the decision analysis model were obtained from published and unpublished clinical trial data on topiramate and from published literature accessed through the National Library of Medicine's PubMed database. However, the methods of the review were not reported. The authors reported that clinical data from different trials were pooled, but the methods used to do so were not reported. In some instances (i.e. response rates for topiramate drop-outs and for those not receiving treatment) data were assumed by the authors, but no arguments were provided to support their assumptions.

Measure of benefits used in the economic analysis
The measures of benefits used were the monthly migraine-days averted and monthly disability-hours averted. The number of migraine-days averted was based on the number of monthly migraine-days at baseline, the probability of each response category, and the average reduction in migraine rate for each response category. Total disability-hours were calculated as the product of the number of migraine-days and the estimated number of disability-hours per migraine-day, given the acute treatment regimen.

Direct costs
The direct costs to the health care payer were included in the analysis. These comprised the costs of hospitalisation for migraine, emergency room and outpatient care visits, computed tomography (CT) scans and magnetic resonance imaging (MRI), and medications (including topiramate, no preventive treatment, triptan acute treatment and usual care treatment). Estimates of resource use were derived from the medical literature. The unit cost of physician visits, emergency department visits and hospitalisations were based on health care claims data. The unit costs of medications were derived from average wholesale prices and/or wholesale acquisition costs. Since the costs were incurred over one year, discounting was not relevant and was therefore not applied. The price year was 2004. The study reported the average costs. The unit cost and quantity of each resource use were appropriately reported.

Statistical analysis of costs
Resource use and the costs were treated as point estimates (i.e. the data were deterministic).

Indirect Costs
The authors included the costs of lost productivity due to migraine. The costs of lost productivity were based on US Bureau of Labour Statistics data for the median hourly wage of women aged 25 to 54 during the fourth quarter of 2004. Since the costs were incurred during one year, discounting was not relevant and was therefore not applied.

**Currency**

US dollars ($).

**Sensitivity analysis**

Sensitivity analyses were performed to assess the effect of changing key model parameter values along plausible ranges. The model parameters varied were the baseline number of migraine days, the rate of triptan use, the discontinuation rate, and the efficacy of topiramate.

**Estimated benefits used in the economic analysis**

Topiramate patients experienced an average of 55.3 migraine-days, compared with 84.0 migraine-days experienced by patients receiving no preventive treatment.

Topiramate patients experienced an average of 51.8 leisure time disability-hours and 99.6 work time disability-hours. No-preventive treatment patients experienced an average of 78.6 leisure time disability-hours and 151.2 work time disability-hours.

**Cost results**

The total direct medical annual costs incurred by topiramate patients were $2,508 per patient, compared with $1,672 per patient receiving no preventive treatment.

The annual lost productivity costs incurred by topiramate patients were $1,502 per patient, compared with $2,278 per patient receiving no preventive treatment.

Overall, the total annual cost was $4,010 for patients receiving topiramate and $3,950 for those receiving no preventive treatment.

**Synthesis of costs and benefits**

The costs and benefits were combined using an incremental cost-effectiveness ratio (i.e. the additional cost per migraine-averted day).

From a health care payer perspective the additional cost per migraine-day averted when topiramate was compared with no preventive treatment was $59.

From a societal perspective, the additional cost per migraine-day averted was $2.

The results of the sensitivity analysis showed that, from a societal perspective, topiramate became dominant (i.e. both less costly and more effective than no preventive treatment) when the baseline migraine-days were 9 or more, the topiramate discontinuation rate was 0%, the proportion of topiramate patients with a response rate lower than 50% was 17.95%, or the probability of migraine being treated with a triptan was 100%.

The results of the sensitivity analysis also showed that under no scenario evaluated did topiramate become dominated (i.e. both more costly and less effective than no preventive treatment).

**Authors' conclusions**

Topiramate use was predicted to result in fewer migraine-days for patients at an incremental cost to their health care plans.
CRD COMMENTARY - Selection of comparators
The use of no preventive treatment as the comparator was justified on the grounds that recent clinical trials had been placebo controlled. You should decide if the comparator used represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The authors reported that the data used to populate the decision analysis model were obtained from published and unpublished clinical trial data of topiramate and published literature accessed through the National Library of Medicine's PubMed database. It was clear from the article that some synthesis of the study results took place. However, no details of the methods used were provided. Further, the authors did not report any of the review methodology, such as search methods or inclusion criteria. The treatment effect parameters would appear to be internally valid as they were derived from the pooling of two randomised controlled trials, which are considered to be the ‘gold’ standard study design when comparing health care interventions.

Validity of estimate of measure of benefit
The estimation of health benefits (migraine-days and disability-hours) was derived appropriately using a decision tree model. Discounting was not relevant since the benefits were incurred during a short time (one year). The use of these measures of benefit will limit the generalisability of the authors' results, as these narrow disease-specific measures make comparisons with the benefits from other interventions difficult.

Validity of estimate of costs
The authors reported that the study had been conducted from health care payer and societal perspectives. All the relevant cost categories for these two perspectives, and all relevant major costs, appear to have been included. Resource use and the unit costs were derived from published sources. Since the costs were incurred during one year, discounting was not relevant and was therefore not applied. The authors did not perform any sensitivity analyses on the resource use or cost data. The cost data were reported adequately, with the authors reporting the price year, resource dates, and costs and quantities separately.

Other issues
The authors compared their results with those of a previous model on the cost-effectiveness of topiramate, and found similar results to those presented in this article. The issue of generalisability to other settings was not addressed, although the use of the model and sensitivity analyses improves generalisability. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors reported a number of further limitations to their study. First, results from clinical trials may not be representative of all patients eligible for topiramate therapy, owing to selection bias. Second, when published data were not available, estimates had to be assumed or derived from databases.

Implications of the study
The authors reported that their results suggest that topiramate may be a cost-effective treatment for migraine patients who are candidates for preventive therapy. They did not provide explicit recommendations relating to the need for further research.

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Other publications of related interest
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