Cost-effectiveness analysis of a lidocaine 5% medicated plaster compared with gabapentin and pregabalin for treating postherpetic neuralgia: a German perspective
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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.

CRD summary
The objective was to examine the cost-effectiveness of the lidocaine 5% medicated plaster versus gabapentin and pregabalin for the treatment of patients with post-herpetic neuralgia. The authors concluded that the lidocaine plaster was the most cost-effective treatment. The methodology had several limitations, so the authors' conclusions should be treated with caution.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The aim was to assess the cost-effectiveness of four options for the treatment of post-herpetic neuralgia in patients who did not experience pain relief when administered standard analgesics, and who displayed contraindications to tricyclic antidepressants.

Interventions
The treatment options compared were: the antiepileptic drug gabapentin at a dose of 1,800mg per day in monotherapy; gabapentin at 1,200mg per day in combination with other medication; lidocaine 5% medicated plaster; and pregabalin. Two doses of pregabalin were compared: 300mg per day (150mg twice daily), and 600mg per day (300mg twice daily, reduced to 150mg when in combination therapy).

Location/setting
Germany/primary care.

Methods
Analytical approach:
A Markov model with a six-month time horizon was used in the economic analysis. The authors stated that the third party payer perspective (Statutory Health Insurance scheme) was taken.

Effectiveness data:
The clinical data were derived from a systematic review of the literature from MEDLINE and EMBASE databases. Two randomised controlled trials (RCTs) and one open-label non-randomised study were the main sources of evidence. In addition, in cases where no published data were available, a Delphi panel made up of 11 clinical specialists was used to estimate the doses of other drugs used in combination with the treatments under study, the medications used in case of discontinuation of treatment, and the probability of necessitating additional medications or discontinuation of treatment in the long-run. The primary clinical outcome was adequate pain relief based on the Patients’ Global impression of Self Improvement scale and the Patients’ Global Impression of Change scale.

Monetary benefit and utility valuations:
Utility values were derived from previous studies. Utility values assigned to certain health states were briefly reported.

Measure of benefit:
Quality-adjusted life-years (QALYs) and time without pain or intolerable adverse effects were used as the summary measures of benefit. The latter was an adaptation of a measure of benefit used in a previous study, namely the Time
Without Symptoms or Toxicity (TWIST) study.

Cost data:
The economic analysis included the costs of medications, general practitioner and specialist visits. Resource use was either obtained from published sources or from the Delphi panel, while costs were obtained from official national sources. Medication costs reflected the true cost to the Statutory system (i.e. patient co-payment, the pharmacy part payment and manufacturer discounts were excluded). Unit costs and resource use was reported separately. All costs were reported in Euros (EUR) for the price year 2007.

Analysis of uncertainty:
Parameter uncertainty was investigated using one-way sensitivity analyses on all the model parameters, except for the price of lidocaine plaster and consultation costs. Each input was varied across its 95% confidence interval. Multivariate deterministic analysis was also conducted, testing three different scenarios by simultaneously varying specific model parameters. All prior assigned distributions were reported in detail. A 12- and a 42-month time horizon were tested and an annual discount rate of 5% was used for both costs and benefits.

Results
The average total therapy costs per patient for the six-month period were EUR 911 for the lidocaine plaster, EUR 728 for gabapentin, EUR 875 for pregabalin 300mg, and EUR 977 for pregabalin 600mg. The expected QALYs were 0.3 with lidocaine-medicated plaster, 0.247 with gabapentin, 0.253 with pregabalin at 300mg, and 0.256 with pregabalin at 600mg.

The lidocaine plaster dominated pregabalin 600mg, as it was more effective and less costly. The incremental cost-effectiveness ratio for the lidocaine plaster was EUR 3,453 per QALY gained over gabapentin and EUR 766 per QALY gained over pregabalin 300mg. The TWIST analysis showed similar results.

The probabilistic sensitivity analysis demonstrated that there was a probability greater than 99% that the lidocaine plaster was the most cost-effective strategy, at a willingness-to-pay threshold of EUR 20,000 per QALY. The deterministic and scenario analyses also demonstrated that the results were robust.

Authors' conclusions
The authors concluded that the lidocaine medicated plaster was the most cost-effective option in comparison with gabapentin and pregabalin for the treatment of patients with post-herpetic neuralgia, who did not experience pain relief with standard analgesics, and could not tolerate tricyclic antidepressants.

CRD commentary
Interventions:
The rationale for the choice of comparators was explicitly reported. The study was thorough in the coverage of available alternatives for the particular study population.

Effectiveness/benefits:
A systematic literature review was performed to obtain clinical data, and the methodology was reported. The basic characteristics of the primary data sources (the study population, design and so on) were not given, although it appeared from the references that the data were mainly obtained from two RCTs and one open-label non-randomised study. But the lack of explicit details on the sources for these data made it difficult to objectively assess the validity of the effectiveness data. The issue of heterogeneity among the sources of data was not addressed. The Delphi panel techniques were reported, but the use of such a method as a primary source of evidence was appropriately acknowledged by the authors as a limitation to their study. For example, one-month pregabalin effectiveness was determined by the Delphi panel, based on a study that reported three-month effectiveness. In addition, two different scales from different studies were combined to estimate outcomes. It seemed doubtful whether the method used could provide reliable estimates. Equally, little information on the derivation of the utility valuations was provided. The authors used a disease-specific benefit measure as well as QALYs, which represented a validated benefit measure that allowed cross-disease comparisons.
Costs:
The costs included in the analysis reflected the perspective stated by the authors. A breakdown of costs items was provided, as well as information on the resource consumption. There may be a problem regarding the sources used to obtain resource use. For example, the number of plasters was based on US observational data, and it was unclear whether this level of resource use produced the same level of effectiveness assumed in the model. Secondly, the authors appropriately acknowledged that gabapentin efficacy might have been overestimated, as the dosage included in the model was less than that reported in clinical trials. The sources used to derive unit costs and the price year were reported. In the sensitivity analyses, where the impact of a longer time horizon was investigated, discounting was appropriate. In general, the economic analysis was well reported.

Analysis and results:
The synthesis of costs and benefits was appropriately performed using incremental analysis. The issue of uncertainty was extensively investigated using deterministic and probabilistic approach. The results of the base case and the sensitivity analysis were well reported. The results of the deterministic sensitivity analyses were only briefly discussed. Cost-effectiveness acceptability curves were generated. The authors compared their results with those from other studies and highlighted important similarities.

Concluding remarks:
The methodology was characterised by several limitations, so the authors' conclusions should be treated with caution.

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