Cost-effectiveness of oral triptans for acute migraine: mixed treatment comparison
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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
To objective was to assess cost-effectiveness of oral triptans therapy for acute migraine attacks in Finland. The authors concluded eletriptan 40mg was cost-effective beyond a willingness-to-pay for a sustained pain-free period with no adverse events of €44 (QALY €20,000). Sumatriptan was cost-effective below these thresholds. The analysis was generally well conducted and reported transparently but issues and limitations make the results uncertain; it is unclear whether this uncertainty is reflected in the conclusions.

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

Study objective
To assess the cost-effectiveness of oral triptans therapy for acute migraine attacks in Finland.

Interventions
The analysis included oral triptans: almotriptan 12.5mg, eletriptan 40mg, frovatriptan 2.5mg, naratriptan 2.5mg, rizatriptan 5mg or 10mg, sumatriptan 50mg or 100mg and zolmitriptan 2.5mg or 5mg. All interventions were compared to each other and placebo.

Location/setting
Finland/Secondary Care

Methods
Analytical approach:
A previous systematic review and meta-analysis and model were updated and extended for a Finnish context (see Other Publications of Related Interest). The model was conducted from a societal perspective and evaluated treatments over a 24-hour period. Two analyses were presented based on a clinical outcome and a health-related quality-of-life outcome.

Effectiveness data:
The updated systematic review included double blind randomised controlled trials that compared any interventions and dosages in adult patients with moderate or severe intensity migraines.

The network meta-analysis simultaneously evaluated four outcomes using a fixed-effect model: reduction from 2 or 3 on the four-point International Headache Severity (IHS) scale to 0 or 1 (defined as response) (R2); pain free at two hours (PF2); recurrence at 24 hours (Rec24); and adverse events (AE). Treatment effects were evaluated using log-odds ratio and then transformed into probabilities.

The primary effectiveness outcome in the cost-effectiveness analysis was sustained pain-free with no adverse events (SNAE); a composite outcome that combined PF2, Rec24, and adverse events. The formula for SNAE was as follows: SNAE = PF2 * (1-Rec24) * (1-AE).

A cost-utility analysis was conducted using health-related quality-of-life as the outcome.

Monetary benefit and utility valuations:
Two sets of utility scores were used. The primary analysis used utility scores from the quality of well-being self-administered instrument (QWB-SA). A sensitivity analysis was conducted using EQ-5D from another study.
Measure of benefit:
Two measures of benefit were used: the composite SNAE derived from the three clinical outcomes for the cost-effectiveness analysis; and quality-adjusted life-years (QALYs) for the cost-utility analysis.

Cost data:
Costs included acquisition costs of drugs and the cost of productivity losses derived from a published Finnish study. Costs were presented in euros (€). The price year was 2010. Data were derived from a post-hoc analysis of a published report.

Analysis of uncertainty:
Data from the mixed treatment comparison were presented with 95% credible intervals. Sensitivity analyses were conducted that simulated drug purchasing by the cheapest packet instead of the cheapest price per tablet, quality of life using EQ-5D utilities instead of QWB-SA utilities and using the effectiveness results from the previously published meta-analysis rather than the update. The model was fully probabilistic.

Results
For the base-case cost-effectiveness analysis, eletriptan was cost-effective at a willingness-to-pay of €44 per SNAE. When the price per packet (assumes drug wastage) was used instead of the price per tablet eletriptan was cost-effective at €70 per SNAE.

In the base-case cost-utility analysis: sumatriptan dominated zolmitriptan 2.5mg, sumatriptan 50mg, almotriptan 12.5mg, frovatriptan 2.5mg and naratriptan 2.5mg for the cost-utility analysis; and eletriptan 40mg dominated rizatriptan 10mg and zolmitriptan 5mg.

The incremental cost-effectiveness ratio (ICER) for eletriptan 40mg compared to sumatriptan 100mg was €19,659/QALY, which was under the proposed €20,000/QALY willingness-to-pay threshold estimated for Finland.

In sensitivity analyses, the drug wastage did not change the ranking of treatments but increased the ICER for eletriptan 40mg to €31,500/QALY. Similarly, an analysis using EQ-5D utilities did not change rankings but raised the ICER for eletriptan 40mg to €29,806/QALY.

An analysis using the previously published systematic review results would still place sumatriptan as the least costly option, but would change rankings between eletriptan, rizatriptan and zolmitriptan, with a possibility of rizatriptan being cost-effective at a €22,500/QALY willingness-to-pay threshold.

Authors’ conclusions
The authors concluded that eletriptan 40mg was cost-effective beyond a willingness-to-pay of €44 (QALY €20,000) and that sumatriptan was the most cost-effective below these thresholds.

CRD commentary
Interventions:
These were derived from an appropriate search of the literature with sufficient description of the interventions. The authors appropriately considered different dosages of the same drug as separate interventions and had appropriately inclusive intervention and comparator criteria.

Effectiveness/benefits:
Methods for the systematic review and meta-analysis were clearly stated and generally appropriate. Inclusion criteria were presented for the patient population, interventions, comparators, outcomes and study designs. Unpublished studies were excluded and the impact of publication bias was unclear. The network meta-analysis was appropriate given the lack of head-to-head trials. It was unclear whether the uncertainty in the estimates obtained was propagated through the decision model. The time horizon of the model was extremely short. Patients with migraines may have effects that last for more than one day and migraines may be recurrent, so it was unlikely that benefits of triptans were captured fully in the analyses.

Costs:
As acknowledged by the authors, the time horizon was only 24 hours and migraines and subsequent use of drugs may occur beyond this time horizon. The source of productivity costs was referenced but the methods for producing these productivity costs was not reported. No costs beyond lost work productivity and drug acquisition costs were included.

Some sensitivity analysis was undertaken regarding drug wastage but it was likely that the scenarios presented were insufficient to deal with this issue. The impact of wastage on the ICER remains uncertain. Patients with migraines may have expenses due to visits to general practitioner, specialist or hospital; the authors acknowledged this limitation. Overall, the perspective was very limited and may limit the transferability and generalisability of the results.

### Analysis and results:
Generally, the analyses were well reported and conducted with appropriate meta-analytical techniques. However the findings are uncertain and there were insufficient sensitivity analyses. The authors indicated that there may have been between-study variation in the placebo arms of the trials but did not conduct a random-effects meta-analysis to incorporate this heterogeneity.

### Concluding remarks:
The analysis was generally well conducted and reported transparently. However, the issues and limitations highlighted mean that the results are uncertain. It is unclear where this uncertainty is reflected in the conclusions.

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