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COST-EFFECTIVENESS OF ORAL TRIPTANS FOR ACUTE MIGRAINE: MIXED TREATMENT COMPARISON

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Background: The cost-effectiveness of triptans in the treatment of migraine has not been assessed since generic sumatriptan entered the Finnish market in 2008.
Methods: Using systematic review and mixed treatment comparison, the effectiveness of triptans was estimated with regard to 2-hour response, 2-hour pain-free, recurrence, and any adverse event, using published clinical data. Direct and indirect costs (2010 EUR, societal perspective) and quality-adjusted life-years (QALYs) were evaluated over one acute migraine attack using a decision-tree model.
Results: The meta-analysis combined data from fifty-six publications. The highest probability of achieving the primary outcome, "sustained pain-free, no adverse event" (SNAE), was estimated for eletriptan 40 mg (20.9 percent). Sumatriptan 100 mg was the treatment with lowest estimated costs (€20.86), and the incremental cost-effectiveness ratio of eletriptan 40 mg compared with sumatriptan 100 mg was €43.65 per SNAE gained (€19,659 per QALY gained).
Conclusion: Depending on the decision-maker's willingness-to-pay threshold, either sumatriptan 100 mg or eletriptan 40 mg is likely to be cost-effective.

Keywords: Triptans, Migraine disorders, Comparative effectiveness research, Cost-benefit analysis, Meta-analysis

Migraine is a debilitating neurological disorder that manifests usually in recurring severe headaches, which may include nausea and altered bodily perceptions (10). However, the pathophysiology of migraine is not fully understood (6), and patients may need to try different treatments before achieving adequate response (7). Triptans (selective serotonin 5-$HT_{1B/1D}$ receptor agonists) were introduced in the early 1990s (2) and are recommended as first-line treatment of severe migraine. Several triptans are currently marketed for migraine, but their cost-effectiveness has not been assessed in Finland. Such a study is even more warranted after the expiry of the sumatriptan patent in 2008, when cheaper generic rivals were introduced.

Almost a decade ago, an earlier review and meta-analysis of triptans in migraine (5) found that riza-, ele-, and almotriptan show favorable results in terms of efficacy, and that the rate of adverse events in the almotriptan studies was relatively low compared with those seen in other studies. A more recent Swedish review and cost-effectiveness model (16) also found that riza- and eletriptan had the highest probabilities of being cost-effective, a conclusion that was in large part due to the use of the earlier evidence synthesis results (5).

The aim of this study is to assess the efficacy and cost-effectiveness of different triptans in the treatment of an acute migraine attack in patients at the point of initiating their first triptan therapy. We present the results of a systematic review and meta-analysis regarding the effectiveness of the different triptans available in Finland in 2009: almo-, ele-, frova-, nara-, riza-, and sumatriptan. We also present an economic evaluation of these pharmacotherapies from a societal perspective. For that purpose, we use a decision-tree model and evaluate the costs of treatment and health outcomes associated with the different treatment options. The key outcome of interest is the incremental cost per additional "sustained pain-free, no adverse event" (SNAE), and estimation of the incremental cost per quality-adjusted life-year (QALY) gained is our second objective.

METHODS

Using systematic review and mixed treatment comparison (MTC), we estimated the effectiveness of triptans with regard to four clinical endpoints (2-hour response, 2-hour pain-free, recurrence, any adverse event) using data from published clinical trial reports, thereby updating an earlier meta-analysis (5).

This study was conducted at the University of Eastern Finland and funded by the Finnish Medicines Agency. C.A. and J.M. are employed by ESiOR Oy, and J.M. holds shares in ESiOR Oy.

The cost-effectiveness model extends an earlier model used for the evaluation of oral triptan therapies in Sweden (16).

Systematic Review

The aims of the systematic review were to identify randomized controlled clinical trials (RCTs) on the efficacy and adverse events profiles associated with the triptans available in Finland to treat acute migraine attacks in adults (18 to 65 years old), and to update the review conducted by Ferrari et al. (5). Studies were included in the systematic review if they met the following inclusion and exclusion criteria:

- Patient criteria inclusion: Age 18–65, migraine diagnosed using International Headache Society (IHS) criteria on a 4-point severity scale (0–3), attacks of moderate (2) or severe (3) intensity. Studies in patients refractory to triptan therapy are excluded.
- Intervention inclusion: Oral triptan at following dosing: almotriptan 12.5 mg, eletriptan 40 mg, frovatriptan 2.5 mg, naratriptan 2.5 mg, rizatriptan 5 or 10 mg, sumatriptan 50 or 100 mg, zolmitriptan 2.5 or 5 mg.
- Comparator inclusion: Placebo or another triptan at the listed dosing.
- Outcome inclusion: One or more of response 2 hours, pain-free 2 hours, recurrence, sustained pain-free, adverse events.
- Study design inclusion: randomized, double-blind, controlled clinical trial.

PubMed and Cochrane databases were searched on December 16, 2010. Studies published before year 2000 were assumed to be covered by the previous review (5). Because parallel double data extraction helps avoid errors (4), data from all the articles were extracted independently by two researchers (T.O. and P.P.). Results from intention-to-treat (ITT) analyses were preferred. The following five outcomes were identified.

- Response at 2 hours (R2), that is, the headache severity grade improved from grade 2 or 3 on the (IHS) scale to grade 0 or 1.
- Pain-free at 2 hours (PF2), that is, the headache severity grade improved from 2 or 3 to 0.
- Recurrence at 24 hours (Rec24), that is, following an initial response the headache severity worsened again to grade 2 or 3 in hours 3–24. This is usually measured in treatment responders only (R2).
- Sustained pain-free 24 hours (SPF24), that is, the pain disappeared and the patient remained pain-free until 24 hours. In some studies, the definition of this outcome included the non-use of rescue medication, that is, in some studies patients who used additional medication and then remained pain-free were counted as meeting this end point, in others these patients were considered not to meet SPF24.
- Any adverse events (AE). In this study, we do not distinguish adverse events by type.

Mixed Treatment Comparison

MTC models, also known as network meta-analyses, provide a methodology that combines evidence on treatment effects from both direct and indirect comparisons (17). Lu and Ades (11) explore different representations of variance within a random-effects framework for mixed treatment comparison that generalizes to multiple treatment alternatives. Arends et al. (1) show how multiple outcomes can be included in the same meta-analysis, which allows for a methodologically sound analysis of the relations between, for example, a baseline risk and treatment effects. Here, we combine these two methodological advances into a network meta-analysis involving four outcomes with baselines correlated across the different outcomes, but with no explicit correlation between the treatment effect estimates.

SPF24 was excluded from the meta-analysis because few studies included it and different definitions of SPF24 were used. Probabilities are mathematically conveniently represented on the log-odds scale, that is, using baseline risk and additive treatment effects. Treatment effects are parameterized as log-odds ratios relative to placebo (11). Fixed treatment effects are applied for all treatments.

Noninformative priors were used in this Bayesian analysis, and noninformativeness was tested by varying the means of these priors and checking that the results are only minimally affected by this (that is, the data dominates the prior). The analysis presented here was fitted in OpenBUGS 3.0.3 (18) (the code is available as Supplementary Material 1, which can be viewed online at www.journals.cambridge.org/thc2012042). Performance of the numerical fitting method was assessed by verifying that chains with different initial values converge to the same region of posterior density, and inspecting the Brooks-Gelman-Rubin diagnostic provided by the software. To ensure adequate sampling of the posterior, burn-in was set to 5,000 draws and every tenth subsequent draw was recorded (thinning) for a total of 10,000 recorded draws each from three parallel chains.

Cost-Effectiveness Model

A previously published decision-tree model (16) was applied to evaluate the cost-effectiveness of oral triptans for acute migraine. In the model, SNAE was the primary end point. Several different definitions exist (14) for deriving SNAE from the above primary outcomes of our meta-analysis, and here we use the following definition (16): Pain-free at 2 hours, no recurrence until 24 hours, and no adverse events, that is, the probability of $\text{SNAE} = \text{PF2} \times (1-\text{Rec24}) \times (1-\text{AE})$. For two treatments that have a different probability of achieving an outcome, the number needed to treat (NNT) to obtain (or prevent) an additional outcome is defined as the inverse of the incremental probability. Cost-effectiveness between different triptans was then expressed as the incremental cost per additional SNAE. Here, we adapt the model (16) to the Finnish setting and extend it by incorporating additional treatment arms and by evaluating also the quality of life associated with the different treatments. The model structure is shown in Supplementary Figure 1, which can be viewed online at www.journals.cambridge.org/thc2012043.

Costs (2010 EUR) included acquisition costs for the initial triptan (Table 1) and productivity losses (Supplementary Table 1, which can be viewed online at

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Table 1. Drug Acquisition Costs

Active ingredient	Dose (mg)	Package size	Price (incl. VAT), €/package	Price (excl. VAT), €/dose	Trade name in Finland
Almotriptan	12.5	9	62.26	6.30	Almogran
Eletriptan	40	18	106.77	5.40	Relert
Frovatriptan	2.5	6	35.58	5.44	Migard
Naratriptan	2.5	6	41.92	6.36	Naramig
Rizatriptan	5	–	–	–	Not available
Rizatriptan	10	18	144.95	7.33	Maxalt
Sumatriptan	50	12	10.37	0.77	Several generic providers
Sumatriptan	100	18	18.38	0.93	Several generic providers
Zolmitriptan	2.5	6	42.03	6.37	Zomig
Zolmitriptan	5	6	58.29	8.84	Zomig

Note. For sumatriptan, which is available as a generic, the reference price (i.e., the highest price that can be reimbursed) was used. Because rizatriptan 5 mg is unavailable in Finland, it was excluded from the health-economic analysis. Where packages in different sizes are available, the package with the lowest cost per dose was chosen for the base-case analysis.

www.journals.cambridge.org/thc2012004) obtained from a post-hoc analysis based on data published in Martikainen et al. (12). Rescue medication is not used. Acquisition costs were based on the price of one tablet (matching the specified dose), assuming that the patient would buy the package with the cheapest price per tablet and that additional tablets would not go to waste. However, the assumption of no wastage may be inappropriate for the first use of a triptan. In a sensitivity analysis, we apply the entire price for the cheapest available package (which may be a smaller and cheaper package) and assume that the left-over tablets will remain unused. Utility values (see Supplementary Table 1) were incorporated into the model to estimate QALYs using the Quality of Well-Being scale self-administered, (QWB-SA). For health states 1 to 3, the mean utility weights estimated by Thompson et al. (19) were used, and uncertainty in these estimates was addressed by setting the 95 percent confidence intervals to ±10 percent. Utility values for health states 4 to 6 were derived from states 1 to 3 by applying a utility decrement corresponding to a typical adverse event. This resulted in a reduction in quality of life by 0.15 for 5 hours. Alternative inputs on QALYs elicited using the EuroQol EQ-5D scale (20) were derived for a sensitivity analysis (see Supplementary Table 1). The model time horizon was one acute migraine attack (24 hours). The model was evaluated using R version 2.11.0 (15).

For a health outcome (E) and associated costs (C), the net monetary benefit (NMB) is defined as $NMB = E \times WTP - C$. Here, WTP denotes the willingness-to-pay for one additional health outcome. Reimbursement decisions should be made according to which treatments provide an estimated positive incremental net monetary benefit (when compared with cheaper treatments), given the decision-maker's WTP per additional outcome. If treatment A has better effect and higher costs than treatment B, its incremental cost effectiveness ratio (ICER) is defined as $ICER = (C_A - C_B) / (E_A - E_B)$.

RESULTS

Systematic Review

A total of 1,765 abstracts were identified in the literature search. Of the fifty-three studies included in Ferrari et al. (5), twelve unpublished abstracts were excluded. Finally, thirty-eight additional references were obtained from (5), including two references describing more than one study each. An unpublished review (Joakim Ramsberg and Martin Henriksson, personal communication December 17, 2008) yielded two further references. In total, 122 full-text publications were assessed and 56 publications (Supplementary Material 2, which can be viewed online at www.journals.cambridge.org/thc2012045) qualified for inclusion in the evidence base (see PRISMA flow diagram, Figure 1), two of which reported on more than one clinical study, that is, a total of fifty-eight studies. Of these studies, thirty-three compared an active agent against placebo alone and twenty-five included more than one active treatment arm. The tables of evidence extracted from these studies are available from the authors at http://esior.fi/images/PDFt/ijtahc-11-094.doc. The entire evidence base contains aggregate-level data on 31,094 patients, with an average age of 39.9 years and a high proportion of female patients (83.8 percent). In the double data extraction, most disagreements concerned whether or not a study reported a certain outcome, for example when the proportion of responders had to be read off from a diagram because it was not presented in numeric form. All disagreements were resolved by consensus (P.P., J.M., and C.A.). Figure 2 illustrates the number of patients recruited for different comparisons between the treatment alternatives under consideration.

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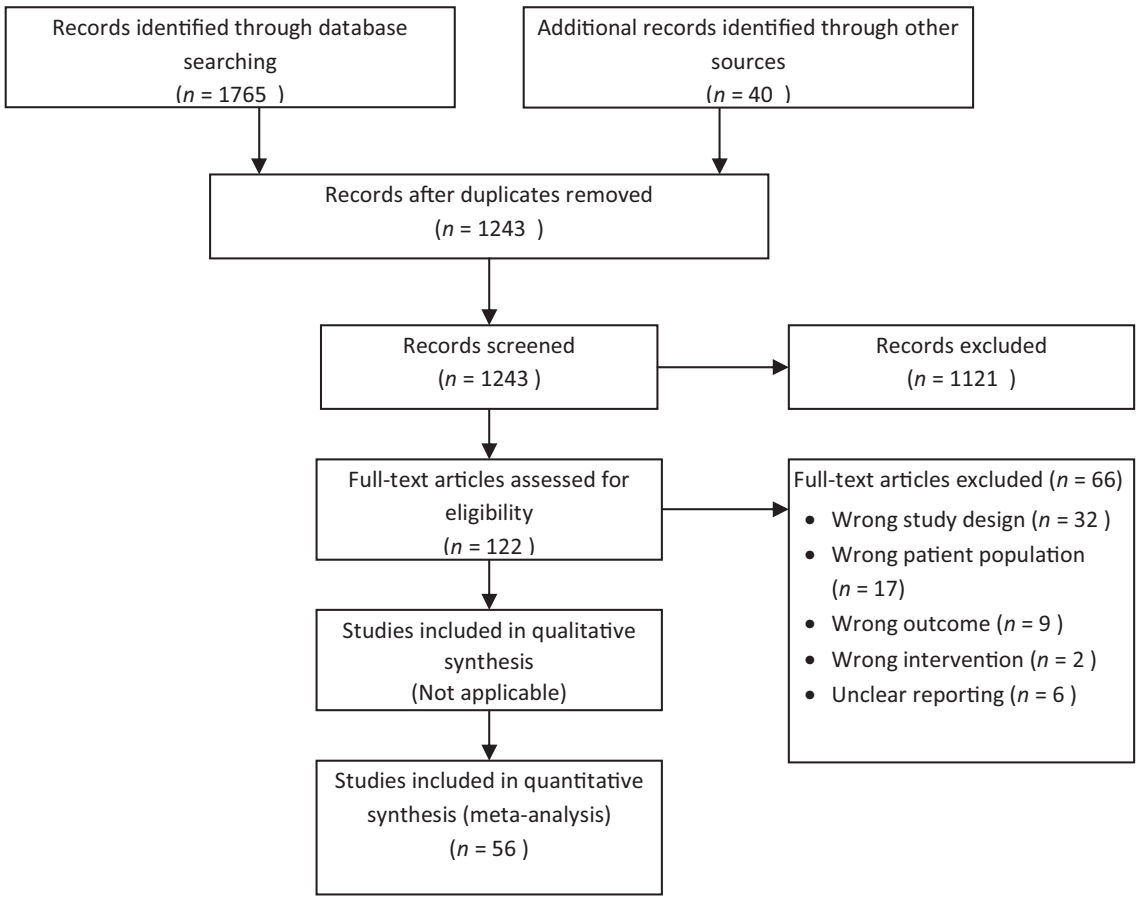

Figure 1. PRISMA flow diagram (9), illustrating the flow of articles screened in the literature search.

Mixed Treatment Comparison

Results of the evidence synthesis are presented in Supplementary Table 2, which can be viewed online at www.journals.cambridge.org/thc2012046. The highest probability of 2-hour pain-free was estimated for eletriptan 40 mg (0.388, 95 percent credibility interval [CrI], 0.349 to 0.429), and the lowest probability of recurrence was estimated for naratriptan 2.5 mg (0.196, 95 percent CrI, 0.142 to 0.258). The probability of achieving sustained pain-free and no adverse events (SNAE, Supplementary Figure 2, which can be viewed online at www.journals.cambridge.org/thc2012047) was estimated to be highest with eletriptan 40 mg (0.209, 95 percent CrI, 0.182 to 0.239).

Cost-Effectiveness

In the health-economic model, sumatriptan 100 mg was estimated as the treatment option with the lowest total costs, that is, €20.86 per attack (95 percent CrI, €15.75 to 27.25). Treatments estimated to provide a higher probability of SNAE are sumatriptan 50 mg, rizatriptan 10 mg, and eletriptan 40 mg. Whereas sumatriptan 50 mg and rizatriptan are extendedly dominated and dominated, respectively, the ICER of eletriptan 40 mg relative to sumatriptan 100 mg was estimated at €43.65 per additional SNAE. The corresponding number of attacks needed to treat with eletriptan 40 mg instead of sumatriptan 100 mg to obtain one additional SNAE was estimated at 16.1 (95 percent CrI, 11.7 to 23.2). At an additional cost of €2.79 per attack (95 percent CrI, €1.83 to 3.55), eletriptan 40 mg provided a QALY gain of 0.00014 (95 percent CrI, 0.00008 to 0.00021), resulting in an ICER of around €19,659 per QALY gained (Table 2). The other treatments were dominated.

In the sensitivity analysis regarding drug acquisition costs, if costs for the cheapest packet size are used instead of cheapest costs per tablet, sumatriptan 100 mg remains the cheapest treatment option at a cost of €26.85 (that is, €6.92 acquisition costs and €19.93 in indirect costs). The most effective treatment alternative in terms of SNAE and QALYs, eletriptan 40 mg, costs €31.31 (that is, €13.25 acquisition costs and €18.06 in indirect costs), which results in an ICER per SNAE of around €70 and per QALY around €31,500. Other treatments are dominated or extendedly dominated. In the sensitivity analysis regarding quality of life weights, if the EQ-5D weights (20) are used, the ranking of treatments by health outcome remains unchanged, but total QALY estimates are generally higher (sumatriptan 100 mg: mean 0.001581, eletriptan 40 mg: mean 0.001674) than in the base-case. The differences in terms of QALYs between different treatments are narrower and the ICER of eletriptan versus sumatriptan 100 mg is estimated as €29,806 per QALY gained.

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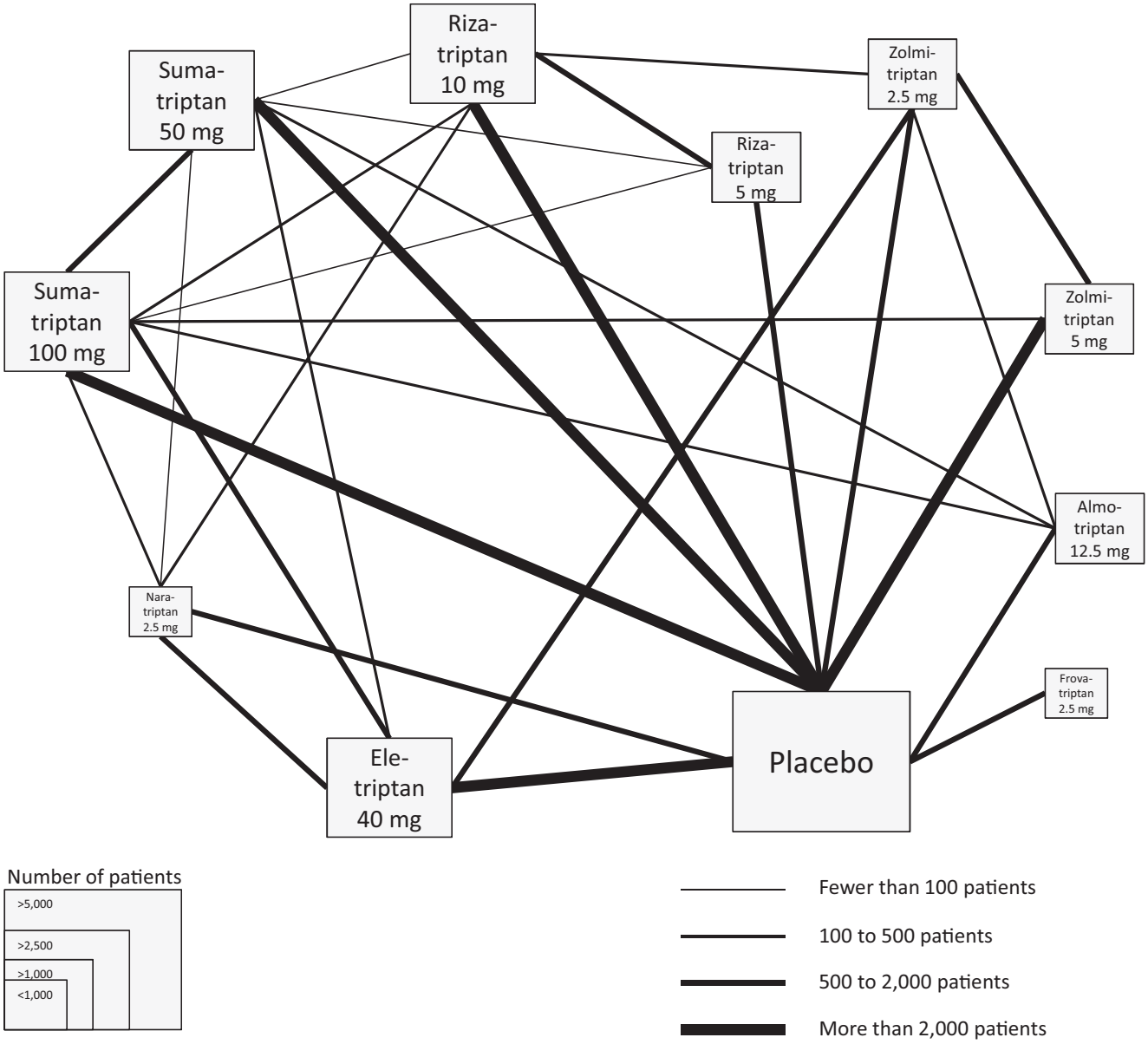

Figure 2. Connections show which treatments have been compared directly and indicate how many patients inform each of these direct comparisons. The nodes correspond to treatment arms and node size indicates how many patients have been recruited to receive each of the treatments.

DISCUSSION

Our analysis suggests that, depending on whether a payer's WTP per additional SNAE is below or above approximately €44 per SNAE, sumatriptan 100 mg or eletriptan 40 mg, respectively, may be the best treatment choice when considering cost-effectiveness only. In terms of QALYs, eletriptan 40 mg has the highest probability of being the most cost-effective option at WTP thresholds of €20,000 per QALY gained or above (Supplementary Figure 3, which can be viewed online at www.journals.cambridge.org/thc2012048). It also provides the highest expected NMB and should therefore be chosen for the reimbursement budget. At lower willingness-to-pay thresholds sumatriptan 100 mg has the highest probability of being cost-effective. The cost-effectiveness of each triptan in terms of achieving SNAE necessarily depends on the payer's willingness-to-pay for this outcome.

Potential weaknesses of the economic evaluation presented here include the short time horizon of 24 hours, the exclusion of rescue medication, and the uncertainty regarding data sources on quality of life. In clinical practice, the treatment of migraine is undoubtedly influenced by other factors not included in the underlying assumptions made in this study, and may additionally affect rescue therapy or future treatment episodes. Furthermore, the ranking of treatments by SNAE (eletriptan 40 mg best, followed by rizatriptan 10 mg, sumatriptan 50 mg and 100 mg) does not match the ranking by QALY exactly (eletriptan 40 mg, followed by rizatriptan 10 mg, zolmitriptan 5 mg, and sumatriptan 100 mg), suggesting that research is required to

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Table 2. Health-Economic Outcomes

Treatment	Total costs (€)	Direct costs only (€)	Total utility (QALYs)	Health-economic summary (using total costs)
Naratriptan 2.5 mg	28.91 (23.10, 36.15)	6.36	0.000127 (0.000044, 0.000224)	Dominated
Frovatriptan 2.5 mg	27.46 (21.72, 34.72)	5.44	0.000178 (0.000068, 0.000315)	Dominated
Almotriptan 12.5 mg	27.66 (22.22, 34.49)	6.30	0.000252 (0.000184, 0.000327)	Dominated
Sumatriptan 50 mg	21.31 (16.06, 27.90)	0.77	0.000311 (0.000247, 0.000382)	Dominated
Zolmitriptan 2.5 mg	26.81 (21.56, 33.36)	6.37	0.000326 (0.000252, 0.000409)	Dominated
Sumatriptan 100 mg	20.86 (15.75, 27.25)	0.93	0.000370 (0.000300, 0.000447)	Base-case
Zolmitriptan 5 mg	28.46 (23.41, 34.78)	8.84	0.000383 (0.000293, 0.000483)	Dominated
Rizatriptan 10 mg	26.37 (21.48, 32.46)	7.33	0.000473 (0.000390, 0.000565)	Dominated
Eletriptan 40 mg	23.64 (18.94, 29.52)	5.40	0.000511 (0.000422, 0.000610)	ICER to Sumatriptan 100 mg: €19,659

Note. The treatment alternatives are sorted from low to high utility. Means and 95% credibility intervals are shown.

overcome a slight mismatch between clinical treatment targets and patient preferences. The sensitivity analysis on quality of life weights has shown that choice of evidence source can have a considerable impact on the resulting cost per QALY gained. This suggests that additional research into quality of life during an ongoing migraine attack is required to support these findings.

The sensitivity analysis shows that, if unused tablets do go to waste in real clinical practice in patients trying out their first triptan, eletriptan 40 mg is a somewhat more costly option relative to sumatriptan 100 mg (at an ICER of €70 per SNAE gained, compared with an ICER of €44 in the base-case).

It is assumed that the trials included in the mixed treatment comparison do not differ in terms of the characteristics that are modifiers of the relative treatment effect (similarity assumption). While we have tried to select a relatively homogeneous set of trials in the systematic review, it is unlikely that this assumption is strictly true. However, in the absence of direct head-to-head trials that compare all comparators, a mixed treatment comparison is a commonly used method for synthesizing evidence indirectly. To test model goodness-of-fit, predicted and observed probabilities for all the outcomes reported in the trials were compared in a probability-probability plot (13), which verifies the model fit and distributional assumptions and is easily generalized to the situation where each data point is associated with its own predictive distribution. There was no indication of better or worse goodness-of-fit with regard to particular outcomes or particular active treatments, but higher heterogeneity was observed between the outcomes on placebo arms than between those on active treatment arms. A plausible explanation may be that active comparators are usually well-defined interventions, whereas the treatment protocol specifying placebo may differ between studies. It would be possible to represent the additional variability that seems to be associated with placebo arms, for example using a random-effects model for the treatment effects (8), which takes into account the heterogeneity between studies explicitly (3). However, some of the comparators included in the present study were used in a small number of trials only, and random-effects between-trial variances of their treatment effects could not be estimated. Using a random-effects model for the placebo arms only would, thus, come at the expense of giving up the assumption that all trial arms can be modeled in structurally the same way. Furthermore, with a higher between-trials variance on the placebo arms, placebo-controlled studies would be down-weighted in such a modified model, relative to studies including only active treatment arms. For these reasons, a model as used here, with the same structural assumption of fixed effects on all treatment arms, appears more appealing than a modified, nonstandard model.

PF2 in the above definition of outcomes can be interpreted as conditional on R2 (that is, if a patient's headache does not respond to treatment, the patient cannot be pain-free at 2h either), and we constructed an exploratory model that establishes stochastic independence by conditioning PF2 on R2. However, for the analysis presented here, a model was chosen that includes the outcomes R2, PF2, Rec24, and AE as defined above (and does not condition PF2 on R2), because the evidence on PF2 is usually reported for the entire patient population and there were no important differences between the results of these two models. Theoretically, correlations could be observed (a) between baselines for different outcomes, and (b) between baselines and treatment effects. Our model explicitly includes correlated baselines (a). Trial-specific baseline risk can be assumed uncorrelated with the trial-specific treatment effects (1), and this type of correlation (b) is not modeled here.

When comparing the results of the present evidence synthesis with those presented by Ferrari et al. (5) in 2002, there is broad overall agreement in terms of all four endpoints. However, some discrepancies stand out. More than 10 percentage points difference in probability of outcome between our estimates and those in Ferrari are found for: probability of pain-free 2h with almotriptan 12.5 mg (here: 0.248, Ferrari et al.: 0.612) and with eletriptan 40 mg (here: 0.388, Ferrari et al.: 0.272). Additionally,

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discrepancies by more than 5 percentage points appear in the results of initial response for four drugs (almo-, ele-, frova-, and sumatriptan 50 mg) and in the results of recurrence for two drugs (almo- and eletriptan). A main reason for these discrepancies is due to the analytical methodology used in the Ferrari et al. meta-analysis (5), which does not fully adjust for baseline heterogeneity. The MTC methods address this weakness (11). Another explanation for the observed discrepancies are different sources of evidence used in this updated evidence synthesis. In particular, eight studies informed the estimates of eletriptan in the earlier evidence synthesis (5). Four of these were unpublished, and two did not meet our inclusion criteria, so only two of these were included in the present review. Also, none of the three studies used by Ferrari et al. to inform estimates related to almotriptan were included in the present review (one was available as a conference abstract only, the other two did not meet our inclusion criteria). An evaluation of the present health-economic model using the earlier evidence synthesis results would agree with our main results that sumatriptan is the least costly alternative, but there would be disagreement on the role of ele-, riza-, and zolmitriptan, with a possibility of rizatriptan 10 mg being cost-effective at willingness-to-pay thresholds of above €22,500 per QALY gained. Our updated evidence base does not support such an assessment.

The earlier Swedish health-economic assessment of triptans (16) from 2007 concluded that eletriptan 40 mg and rizatriptan 10 mg have considerable probability of being cost-effective in terms of the SNAE outcome. In terms of eletriptan, this agrees with the assessment presented here. A key reason why the health-economic evaluation of sumatriptan is much more favorable in our results than in the Swedish assessment (16) is the availability of generic sumatriptan in Finland since 2008. Additional differences concern the evidence base on effectiveness as discussed above and differences in the unit costs of several triptans between Swedish (16) and current Finnish prices.

This analysis may differ from other economic models of migraine in that costs of rescue medication, physician visits and other direct costs are not included. However, such costs are unlikely to be relevant in the Finnish evaluation context of the first severe migraine attack to be treated with triptans. These types of resource use should be considered in a cost-effectiveness model of triptan treatment over a longer time horizon.

In summary, the study presented here gives an updated overview of the evidence base on efficacy and adverse events associated with the use of triptans in the treatment of acute migraine attacks. Direct clinical comparisons of all study drugs in the Finnish target population would constitute a "gold standard" of evidence, but in the absence of all-encompassing direct comparisons, meta-analytic approaches such as the one presented here are required and useful. Its results are only as good as the available evidence base, and we cannot exclude the possibility of biases related to incomplete or selective publication of clinical study results. The health-economic evaluation suggests that sumatriptan 100 mg is an attractive first treatment due to its generic price and acceptable efficacy and that eletriptan 40 mg should also be considered as a first treatment alternative in triptan-naive patients because of better efficacy at reasonable additional costs. However, when making individual treatment decisions, it is important to recall that the data presented here are derived from population-based estimates (that is, how large a proportion of patients can be expected to respond to a particular triptan, how large a proportion of patients is likely to suffer from adverse events) and do not take into account individual differences between patients that may be deemed relevant in selecting the optimal triptan. Response to treatment varies considerably between patients (with none of the triptans studied here achieving response in more than 70 percent of patients); therefore, it is prudent to have a selection of triptans available.

CONCLUSIONS

At a willingness-to-pay threshold of €44 per SNAE (alternatively, €20,000 per QALY) or higher, eletriptan 40 mg appears to provide the best cost-effectiveness, whereas sumatriptan 100 mg appears to be the most cost-effective triptan at lower willingness-to-pay thresholds. The ranking of treatments by effectiveness differs somewhat if SNAE is used instead of QALY, which suggests a mismatch between available data on patient preferences and clinical consensus on the "gold standard" of treatment success.

SUPPLEMENTARY MATERIAL

Supplementary Material 1: www.journals.cambridge.org/thc2012042
Supplementary Figure 1: www.journals.cambridge.org/thc2012043
Supplementary Table 1: www.journals.cambridge.org/thc2012044
Supplementary Material 2: www.journals.cambridge.org/thc2012045
Supplementary Table 2: www.journals.cambridge.org/thc2012046
Supplementary Figure 2: www.journals.cambridge.org/thc2012047
Supplementary Figure 3: www.journals.cambridge.org/thc2012048

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CONFLICTS OF INTEREST

Christian Asseburg and Janne Martikainen have received salary or funding for consultancy from ESiOR Oy where Janne Martikainen also is a shareholder. Timo Purmonen has received funding from Pfizer, Finland and grants from Pharma Industry Finland research trust. The other authors report no potential conflicts of interest.

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