Cost-effectiveness analysis of stratified versus stepped care strategies for acute treatment of migraine: the disability in strategies for care (DISC) study

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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.

Health technology
The health interventions examined in the study were three strategies for the management of patients suffering from migraine: stepped care across attacks, stepped care within attacks, and stratified care. With stepped care across attacks, patients begin with a simple or combination analgesic and if, after treating a number of attacks, the patient is not satisfied with the treatment, the clinician is contacted to change therapy until an acceptable therapy is identified. Stepped care within attacks consists of the patient starting off each attack with a simple or combination analgesic but, if the patient is not happy with the treatment during the attack (usually 2 hours after attack onset), another medication, usually migraine-specific, is taken. Finally, with stratified care, the choice of the initial medication follows an assessment of each individual patient's needs and those patients experiencing the greatest disability during attacks usually receive migraine-specific therapy. Drug dosages and types of medications varied in each strategy and were reported.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised adult patients graded II to IV in the Migraine Disability Assessment Scale (MIDAS) questionnaire. Patients were also required to fulfil the International Headache Society criteria for migraine, with or without aura. Exclusion criteria were a medical or psychiatric condition increasing risk when exposed to trial medications, or interfering with efficacy and safety assessment; a history of basilar, ophthalmoplegic or hemiplegic migraine; and a history of heart disease, stroke, or significant medical illness.

Setting
The setting was primary care. The economic study was conducted in the UK.

Dates to which data relate
Data on effectiveness and resource use were derived from a study published in 2000. Prices were estimated in 1999 and 2000 values.

Source of effectiveness data
The effectiveness evidence came from a single study (see Lipton et al in ‘Other Publications of Related Interest’ below).
Link between effectiveness and cost data
The costing was conducted prospectively on the same sample of patients as that used in the effectiveness study.

Study sample
The overall study sample comprised 835 patients: 279 in the stratified care group, 271 in the stepped care across attacks group, and 285 in the stepped care within attack group.

Study design
This was a prospective, randomised, parallel group, open label, multiple migraine attack trial, which was undertaken in 88 centres across 13 countries. Patients were followed until 6 attacks were treated or for a maximum of 6 months. No other information on the design was provided.

Analysis of effectiveness
The analysis of the clinical study was based on intention to treat. Two primary outcome measures were used in the effectiveness analysis: the headache response rate at 2 hours over 6 attacks, where a response was defined as a reduction in pain intensity from severe or moderate at the time of drug administration to mild or absent; and the disability adjusted time over 4 hours per 6 attacks, calculated on the basis of each patient recording their level of functioning pre-treatment and at 1, 2, and 4 hours post-treatment.

Effectiveness results
The mean headache response rate at 2 hours over 6 attacks was 51.37% (95% confidence interval (CI): 47.30% - 55.68%; median: 50%; interquartile range (IQR): 16.67% - 83.33%) for stratified care; 38.97% (95% CI: 35.14% - 42.84%; median: 33.33%; IQR: 0 - 60%) for stepped care across attacks; and 36.48% (95% CI: 32.46% - 40.31%; median: 33.33%; IQR: 0 - 66.67%) for stepped care within attacks.

In terms of headache response, stratified care was significantly more effective than either stepped care strategy.

The mean disability adjusted time over 4 hours per 6 attacks was 12.90 hours (95% CI: 12.38 hours - 13.47 hours; median: 13.14 hours; IQR: 10.04 hours - 16.40 hours) for stratified care; 11.43 hours (95% CI: 10.92 hours - 12 hours; median: 11.50 hours; IQR: 8.20 hours - 14.68 hours) for stepped care across attacks; and 12.02 hours (95% CI: 11.43 hours - 12.56 hours; median: 12.28 hours; IQR: 8.54 hours - 15.33 hours) for stepped care within attacks.

In terms of mean disability adjusted time, stratified care was significantly more effective than stepped care across attacks but not against stepped care within attacks.

Clinical conclusions
The effectiveness analysis showed that better outcomes were generally associated with the stratified care strategy.

Measure of benefits used in the economic analysis
The summary benefit measures used in the analysis were the headache response rate at 2 hours over 6 attacks and the disability adjusted time over 4 hours per 6 attacks, which were both derived directly from the effectiveness study. No discounting was applied.

Direct costs
Discounting was not relevant as costs were incurred over a short time frame. Unit costs were presented separately from quantities of resources used. The health services included in the economic evaluation were study drugs, rescue medications, and adverse events. The cost/resource boundary reflected the societal perspective of the study; therefore all direct costs were included, irrespective of the subject who bore them. The estimation of resource use was based on
actual individualised data derived from the effectiveness trial. Resources used for the treatment of adverse events were not estimated alongside the trial and were assessed by one of the authors, who described in a blinded manner the optimal management of patients suffering from each event considered in the study. Costs were obtained from the British National Formulary for study drugs and rescue medications, and published sources for treatment of adverse events. Prices were estimated in 1999 and 2000 values.

**Statistical analysis of costs**
Costs were presented as mean values, confidence intervals, median values, and IQRs.

**Indirect Costs**
Indirect costs were considered in the analysis to reflect the societal perspective of the study. Productivity costs were considered as both time off work and reduced effectiveness while at work. The estimation of productivity losses was based on the lost work equivalent (LWE), which relied on the information patients reported in their diary cards. Standard average wage rates in 2000 were used to apply a unit cost to LWE. Discounting was not relevant and so was not applied.

**Currency**
UK pounds sterling (,).

**Sensitivity analysis**
Sensitivity analyses were not conducted but confidence intervals for cost-effectiveness ratios were calculated using non-parametric bootstrapping techniques. Accordingly, a cost-effectiveness acceptability curve was calculated to show the probability of each of the three alternative strategies being more cost-effective than the other two for a range of alternative maximum threshold values corresponding to the society's willingness to pay for the intervention.

**Estimated benefits used in the economic analysis**
Please refer to the effectiveness results reported above.

**Cost results**
The analysis of costs showed that the number of LWEs was lower with stratified care (mean: 11.19 hours), followed by the stepped care within attacks (mean: 12.72 hours), and the stepped care across attacks (mean: 14.43 hours).

Productivity costs per patient were the greatest cost item and were 112.22 (median: 67.70; IQR: 0 - 144.43) for stratified care, 144.70 (median: 98.54; IQR: 0 - 192.20) for stepped care across attacks, and 127.53 (median: 60.18; IQR: 12.54 - 157.97) for stepped care within attacks.

Total costs per patient were 138.95 (95%CI: 122.38 - 158.93; median: 88.61; IQR: 32.43 - 170.85) for stratified care, 157.19 (95% CI: 134.50 - 184.93; median: 91.19; IQR: 12.87 - 196.81) for stepped care across attacks, and 148.53 (95% CI: 123.04 - 179.41; median: 80.19; IQR: 29.93 - 173.38) for stepped care within attacks.

The overlapping between confidence intervals suggested that total costs were not significantly different across groups.

**Synthesis of costs and benefits**
An incremental cost-effectiveness analysis was used to combine costs and benefits of the interventions under evaluation. The stratified care approach dominated both stepped care approaches, because it was both more effective (in terms of both outcome measures) and less expensive. The results of the cost-effectiveness acceptability curve showed that stratified care had the highest probability of being cost-effective in comparison with the two stepped care strategies. Even if decision makers were not interested in clinical outcomes, the stratified care strategy still had the
highest (greater than 50%) probability of being cost-saving.

Authors' conclusions
The authors concluded that stratified care for patients with migraine was unequivocally a cost-effective strategy in comparison with stepped care strategies from the societal point of view.

CRD COMMENTARY - Selection of comparators
The authors justified their choice of comparators on the grounds that the three options represented recommended strategies for the management of migraine. The interventions were satisfactorily described. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness was based on a prospective, multicentre, randomised trial, which was appropriate for the study question. Limited information on the study design and methods was provided as the study had been previously published in a separate paper. Therefore it is difficult to evaluate the internal validity of the study, which appears to have been high due to the randomised and multicentre design and the use of intention to treat as the basis for the analysis of the clinical study.

Validity of estimate of measure of benefit
The summary benefit measures were derived from the effectiveness study and were specific to the disease considered in the study. They are usually selected for the assessment of the impact of the intervention on patient health in the case of migraine, but may be difficult to compare with the benefits of other health care interventions.

Validity of estimate of costs
The adoption of the societal perspective permitted the inclusion of costs borne by different payers. The analysis of costs was carried out satisfactorily and detailed information on sources of data was reported. Unit costs were presented separately from quantities of resources used for almost all cost items. The years during which prices were estimated were provided. This would facilitate the replication of the study and reflation exercises in other settings. Some of the resources used, which had not been collected alongside the clinical trial, were estimated in a blinded manner by one of the study investigators. Descriptive statistics were used to present costs. All economic estimates were specific to the study setting and no sensitivity analyses were conducted. However, bootstrapped cost estimates were calculated.

Other issues
The authors did not compare their findings with those from other studies. With respect to the issue of the generalisability of the study results to other settings, the authors stated that the results of the analysis should not be extrapolated to the general population of patients with migraine since those with MIDAS Grade I were not included in the study. Other aspects of the study appear more generalisable to other settings. Sensitivity analyses were not conducted, but the issue of uncertainty was addressed by assessing probabilistic estimates of cost-effectiveness ratios. Therefore, the external validity of the analysis appears high.

Implications of the study
The study results suggest that stratified care for migraine has the highest probability of being cost-effective and cost-saving from the perspective of society.

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Other publications of related interest

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