Decision analysis of the cost-effectiveness of repetitive transcranial magnetic stimulation versus electroconvulsive therapy for treatment of nonpsychotic severe depression
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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
Repetitive transcranial magnetic stimulation (rTMS) was compared with electroconvulsive therapy (ECT) for the treatment of non-psychotic severe depression.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised adults (more than 18 years old) with non-psychotic severe depression, who were resistant to routine pharmacological treatment and were eligible for ECT in the USA.

Setting
The setting was tertiary care. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness evidence was obtained from studies published in 2000-2002. The dates to which the resource data related and the price year were not stated.

Source of effectiveness data
The effectiveness data were derived from a review or synthesis of completed studies.

Modelling
A decision analytic model was developed to compare the relative cost-effectiveness of rTMS and ECT in the treatment of non-psychotic resistant depression, both acutely and in a maintenance setting. The rationale for developing the model was the lack of actual data that would enable a direct comparison of the cost-effectiveness of the two interventions. A hypothetical cohort of 13,162 patients with severe depression (i.e. an estimated number of the US adult population with severe depression receiving ECT) was treated with rTMS, ECT, or rTMS-to-ECT. The time horizon was 52 weeks in total since patients received acute treatment for 3 weeks and maintenance treatment for 49 weeks. Following acute treatment, patients moved to states of response to treatment or no response, based on transition probabilities taken from the literature.

Outcomes assessed in the review

The outcomes assessed were the response rates in the acute and maintenance phase of treatment for both rTMS and ECT.

**Study designs and other criteria for inclusion in the review**
The effectiveness data were taken from the results of clinical trials, where available. One of the clinical trials was an open study in which the patients were randomised to either rTMS or ECT. Additional data were based on a retrospective case-control study.

**Sources searched to identify primary studies**
Not stated.

**Criteria used to ensure the validity of primary studies**
The authors reported that the rates of antidepressant response to prefrontal rTMS have varied across the literature, partly because of small sample sizes, heterogeneous clinical samples (particularly for the degree of treatment resistance), and the multiple different treatment parameters used across the various studies. Thus, the authors chose to use the rTMS response rate from the same population from which the ECT response rate was obtained for the initial model, and then to test this value using a sensitivity analysis.

**Methods used to judge relevance and validity, and for extracting data**
The results of a meta-analysis of primary studies were considered when judging the relevance of the parameters assessed.

**Number of primary studies included**
Approximately 3 primary studies were included in the review.

**Methods of combining primary studies**
The results of the primary studies were combined in a narrative.

**Investigation of differences between primary studies**
The authors investigated differences between the primary studies in the meta-analysis included in the review. They discussed potential reasons for these differences and gave a justification for the estimate they chose to use in their economic analysis.

**Results of the review**
The acute response rate was 0.64 for rTMS, and 0.60 for ECT or ECT following unsuccessful rTMS.

The maintenance response rate was 0.50 for rTMS, and 0.93 for ECT or ECT following unsuccessful rTMS.

**Methods used to derive estimates of effectiveness**
Calculations were conducted to derive the number in the US population with severe non-psychotic depression who might receive ECT.

**Estimates of effectiveness and key assumptions**
An insured population of 253,866 individuals was used to determine the percentage that suffered from severe depression without psychosis (0.360%) and the percentage that suffered from severe depression and went for ECT.
(1.75%). These data were applied to the adult US population (n=209,128,094) to obtain an estimate of the number of patients with severe depression (n=752,105) and the number of patients with severe depression receiving ECT (n=13,162) for the model.

Measure of benefits used in the economic analysis
The measure of benefit used was the number of quality-adjusted life-years (QALYs) gained, associated with each of the strategies assessed. The utility values for depressed and recovered depressed patients were taken from a published study (Feeny et al., see "Other Publications of Related Interest" for bibliographic details).

Direct costs
The costs included in the analysis comprised the health service costs for providing the interventions evaluated, plus associated patient and carer costs. The direct costs were medical costs (costs of the procedures under assessment) and patient travel costs. The costs and the quantities were not analysed separately. The cost of ECT was derived from typical charges in a tertiary care centre, which included facility, medication, psychiatrist, anaesthesiologist and nursing fees. As no data existed for the cost of rTMS, this was based on authors' estimates, after taking the resources required into consideration (i.e. nursing and physician's time, machine cost, and facility fee). The patients' travel costs were taken from typical travel costs for patients seen in the tertiary care centre. The costs associated with the management of patients not responding to treatment were not included in the analysis. The total costs were derived using modelling. Discounting was not undertaken since the costs were incurred within one year. The price year was not stated.

Statistical analysis of costs
The costs were treated deterministically. No statistical analysis of the costs was undertaken.

Indirect Costs
Indirect costs reflected the time of a companion required to accompany a patient treated with ECT to the health care centre and remain with him or her for the rest of the day. A companion was considered necessary in the case of ECT, owing to the adverse cognitive side effects following treatment. Patients undergoing rTMS did not require a companion because of the lack of such side effects following this treatment. The amount of companion's time required, as well as the costing of this time, was based on authors' assumptions. The time of patients themselves undergoing treatment was not considered in the estimation of the indirect costs. Discounting was not necessary since the costs were incurred within one year. The date to which the prices referred was not reported.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was carried out to investigate the impact of various parameter changes on the results. In addition, to determine which economic- or treatment-associated assumptions, if any, might drastically alter the results. One-way sensitivity analyses were undertaken by varying the ECT and rTMS acute response rates, the rTMS maintenance response rate, the costs of both ECT and rTMS, and the companion costs. The parameters examined were selected from those that were felt to be critical in the model and/or had the least data support. The range of values was based on published data for ECT response rate, the lowest allowable Medicare charge for ECT cost, and authors' assumptions for the rest of the parameters used.

Estimated benefits used in the economic analysis
ECT resulted in 7,793 QALYs, rTMS in 7,514 QALYs, and rTMS-to-ECT in 9,331 QALYs. ECT provided 279 additional QALYs compared with rTMS, while rTMS-to-ECT provided 1,538 additional QALYs compared with ECT alone.
The total benefits were estimated for a 52-week period. These referred to a population of 13,162 adult patients with severe (resistant) depression.

Cost results
The total costs, incurred during the 52-week period were $57,845,347 for rTMS, $186,359,571 for ECT, and $124,934,792 for rTMS-to-ECT. ECT incurred an additional cost of $128,514,224 compared with rTMS, while rTMS-to-ECT was less costly by $61,424,778 in comparison with ECT.

The total costs referred to a population of 13,162 adult patients with severe (resistant) depression.

The costs of adverse events were not included in the analysis, nor were the costs of treating patients not responding to the strategies examined.

Synthesis of costs and benefits
The costs and benefits were combined in the form of incremental cost-effectiveness ratios (ICERs).

The ICER of ECT versus rTMS was $460,031 per QALY gained. rTMS-to-ECT dominated ECT, as it was both more effective and less costly, leading to cost-savings of $39,949 per QALY gained.

The sensitivity analysis demonstrated that these results were quite robust across a broad range of parameter values for both comparisons. The largest QALY difference for ECT versus rTMS was achieved when the rTMS response was dropped from 0.64 to 0.40. This still produced a high ICER for ECT versus rTMS, equal to $76,858 per QALY gained. rTMS-to-ECT dominated ECT under all ranges of values used in the sensitivity analysis.

Authors' conclusions
If repetitive transcranial magnetic stimulation (rTMS) were to be made widely available in the USA, it would offer a substantial economic benefit over electroconvulsive therapy (ECT) in treating resistant depression. rTMS would be a cost-effective treatment for depression in comparison with the routine treatment option of ECT alone.

CRD COMMENTARY - Selection of comparators
The choice of the comparator used (ECT) was implicitly justified, as it represented the only treatment for resistant depression widely available in the USA. You should decide whether this intervention also reflects widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
It was not stated that a systematic review of the literature had been undertaken. The authors used data from the available studies selectively. Although this is a common practice with models, it does not always ensure that the best data available are used in the model. One cannot be sure that all relevant literature was identified, although the estimates of effectiveness were derived credibly from the studies identified. The effectiveness estimates were combined using narrative methods. The authors justified the choice of effectiveness rates they used in their analysis. Differences between the results of the primary studies were discussed and possible explanations were provided.

Validity of estimate of measure of benefit
The estimation of benefits was modelled. The decision analytic model used for this purpose was appropriate since it included potential states of response, nonresponse and relapse following the treatment of severe depression, with transition probabilities based on published literature. Quality of life was derived from a published study that used the health utilities index mark 3 system to assess utility value for depressed patients.
Validity of estimate of costs
The perspective of the study was not stated. The analysis included intervention costs, patient travel costs, and the companion time required in the case of a patient treated with ECT suffering adverse cognitive side effects. The costs associated with the management of patients not responding to treatment were omitted from the analysis, as were travel costs for the companion and the patients' time. It is not known whether the inclusion of such costs, in particular those related to treating nonresponders, would affect the results considerably. The costs and the quantities were not reported separately, which hinders the reproducibility of the results. A sensitivity analysis of the costs was undertaken using ranges that appear to have been appropriate. In the case of ECT, charges were used to proxy costs. However, charges do not reflect true opportunity costs (due to profit margin) and, in the absence of a cost-to-charge ratio, may limit the generalisability of the results beyond the authors' clinical setting. Discounting was not applied, but it was not required since the costs were incurred within 52 weeks. The date to which the prices related was not reported and this limits the generalisability of the results.

Other issues
The authors did not compare their findings with those of other studies. It is possible, though, that no other studies comparing rTMS with ECT in terms of cost-effectiveness had been published at the time of the study. The issue of the generalisability of the results to other settings was not discussed. The authors reported a number of limitations of their study. First, the lack of effectiveness data derived from clinical trials with large study samples. Second, the oversimplification of clinical care assumed in the decision-analytic model, owing to limitations in the model structure and available evidence. Finally, the population with severe depression who were eligible for ECT may have been underestimated. However, the latter would affect only the values of the total costs and benefits associated with each strategy assessed, and not the relative cost-effectiveness of the interventions. The results of the study were reported in full. The authors' conclusions reflected the scope of the analysis.

Implications of the study
It can be inferred from the results of the study that rTMS should be widely available in the USA for the treatment of resistant depression, as it represents a cost-effective option compared with routine treatment with ECT. The authors suggested that more research should be undertaken to clarify the acute response rates in resistant depression for both treatment modalities, as well as to define the best methods to maintain wellness after successful treatment.

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Bibliographic details

PubMedID
15162090

Other publications of related interest

Li X, Nahas Z, Oliver NC, et al. Initial results using left prefrontal rTMS as a maintenance treatment for bipolar depression. Biological Psychiatry 2001;49:36S.


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Cost-Benefit Analysis; Decision Making; Depressive Disorder, Major /economics /epidemiology /therapy; Electroconvulsive Therapy /economics /instrumentation /statistics & numerical data; Electromagnetic Phenomena /economics /instrumentation /statistics & numerical data; Humans; Periodicity; Severity of Illness Index

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