Electroconvulsive therapy for depressive illness, schizophrenia, catatonia and mania

Clinical and cost-effectiveness of electroconvulsive therapy for depressive illness, schizophrenia, catatonia and mania: systematic reviews and economic modelling studies

J Greenhalgh,[1*†] C Knight,[2] D Hind,[2] C Beverley[2] and S Walters[2]

[1] Sheffield Institute for Health, University of Leeds, UK
[2] The School of Health and Related Research (ScHARR), University of Sheffield, UK

* Corresponding author

† Current affiliation: Health Care Practice R&D Unit, University of Salford, UK

Executive summary

Health Technology Assessment 2005; Vol. 9: No. 9

Health Technology Assessment
NHS R&D HTA Programme

How to obtain copies of this and other HTA Programme reports.
An electronic version of this publication, in Adobe Acrobat format, is available for downloading free of charge for personal use from the HTA website (http://www.hta.ac.uk). A fully searchable CD-ROM is also available (see below).

Printed copies of HTA monographs cost £20 each (post and packing free in the UK) to both public **and** private sector purchasers from our Despatch Agents.

Non-UK purchasers will have to pay a small fee for post and packing. For European countries the cost is £2 per monograph and for the rest of the world £3 per monograph.

You can order HTA monographs from our Despatch Agents:

– fax (with **credit card** or **official purchase order**)
– post (with **credit card** or **official purchase order** or **cheque**)
– phone during office hours (**credit card** only).

Additionally the HTA website allows you **either** to pay securely by credit card **or** to print out your order and then post or fax it.

Contact details are as follows:

HTA Despatch
c/o Direct Mail Works Ltd
4 Oakwood Business Centre
Downley, HAVANT PO9 2NP, UK

Email: orders@hta.ac.uk
Tel: 02392 492 000
Fax: 02392 478 555
Fax from outside the UK: +44 2392 478 555

NHS libraries can subscribe free of charge. Public libraries can subscribe at a very reduced cost of £100 for each volume (normally comprising 30–40 titles). The commercial subscription rate is £300 per volume. Please see our website for details. Subscriptions can only be purchased for the current or forthcoming volume.

Payment methods

Paying by cheque
If you pay by cheque, the cheque must be in **pounds sterling**, made payable to *Direct Mail Works Ltd* and drawn on a bank with a UK address.

Paying by credit card
The following cards are accepted by phone, fax, post or via the website ordering pages: Delta, Eurocard, Mastercard, Solo, Switch and Visa. We advise against sending credit card details in a plain email.

Paying by official purchase order
You can post or fax these, but they must be from public bodies (i.e. NHS or universities) within the UK. We cannot at present accept purchase orders from commercial companies or from outside the UK.

How do I get a copy of *HTA on CD*?

Please use the form on the HTA website (www.hta.ac.uk/htacd.htm). Or contact Direct Mail Works (see contact details above) by email, post, fax or phone. *HTA on CD* is currently free of charge worldwide.

The website also provides information about the HTA Programme and lists the membership of the various committees.

Executive summary

Objective

The aim of this review is to establish the clinical effectiveness and cost-effectiveness of electroconvulsive therapy (ECT) for depressive illness, schizophrenia, catatonia and mania.

Background

ECT has been available for use since the 1930s. It involves passing an electric current through a person's brain after they have been given a general anaesthetic and muscle relaxants, to produce a convulsion. There is a complex interplay between the stimulus parameters of ECT, including position of electrodes, dosage and waveform of electricity, and its efficacy.

ECT is rarely used as a first line therapy, except in an emergency where the person's life is at risk as a result of refusal to eat or drink or in cases of attempted suicide. Current guidelines indicate that ECT has a role in the treatment of people with depression and in certain subgroups of people with schizophrenia, catatonia and mania. In England between January and March 1999 there were 16,482 administrations of ECT to 2835 patients, 85% of which were in an inpatient setting. There were important variations in the rates of administration of ECT by gender, age and health region. Women received ECT more frequently than men and the rates of administration for both genders increased with age. In England, rates of administration of ECT are highest in the North West and lowest in London.

Methods

Seventeen electronic bibliographic databases were searched, covering biomedical, health-related, science, social science and grey literature. In addition, the reference lists of relevant articles were checked and 40 health services research-related resources were consulted via the Internet. These included health technology assessment organisations, guideline-producing bodies, generic research and trials registers, and specialist psychiatric sites. All abstracts were examined to ascertain whether they met the inclusion criteria for the review. The study quality of relevant articles was assessed using standard checklists and data were abstracted by two people using standardised forms in a Microsoft Access database. Where relevant, results from studies were pooled for meta-analysis.

Results and conclusions

Number and quality of studies

Two good-quality systematic reviews of randomised evidence of the efficacy and safety of ECT in people with depression, schizophrenia, catatonia and mania were identified. Four systematic reviews on non-randomised evidence were also identified, although only one of these could be described as good quality. There was no randomised evidence of the effectiveness of ECT in specific subgroups including older people, children and adolescents, people with catatonia and women with postpartum exacerbations of depression or schizophrenia.

Summary of benefits/direction of evidence

In people with depression, real ECT is probably more effective than sham ECT, but stimulus parameters have an important influence on efficacy, low-dose unilateral ECT is no more effective than sham ECT. ECT is probably more effective than pharmacotherapy in the short term, but the evidence on which this assertion is based was of variable quality and inadequate doses of pharmacotherapy were used. Limited evidence suggests that ECT is more effective than repetitive transcranial magnetic stimulation (rTMS). Limited data suggest that tricyclic antidepressants (TCAs) may improve the antidepressant effect of ECT during the course of ECT, and that continuation pharmacotherapy with TCAs combined with lithium in people who have responded to ECT reduces the rate of relapses. Overall, gains in the efficacy of the intervention depending on the stimulus parameters of ECT are achieved only at the expense of an increased risk of cognitive side-effects. Limited evidence suggests these effects do not last beyond 6 months, but there is no evidence examining the longer term ▶

cognitive effects of ECT. There is little evidence of the long-term efficacy of ECT. There was much less evidence regarding the efficacy of ECT in schizophrenia and mania, and no randomised evidence of the effectiveness of ECT in catatonia. ECT either combined with antipsychotic medication or as a monotherapy is not more effective than antipsychotic medication in people with schizophrenia. The evidence did not allow any firm conclusions to be drawn regarding the efficacy of ECT in people with mania or catatonia, older people, younger people and women with psychiatric problems, or the impact of ECT on all-cause mortality. There was limited non-randomised evidence regarding the impact of patient acceptability and choice on the outcomes of ECT, and this produced mixed results.

Cost-effectiveness

No previous analysis has been undertaken on the cost-effectiveness of ECT in depression or schizophrenia. Two economic models were developed primarily based on evidence from the clinical effectiveness analysis and limited quality of life studies.

Depression

The economic model for depression was based on a severely depressed population requiring hospitalisation. As clinical opinion differs to whether ECT should be used only as a last resort treatment or whether it could be used earlier in the treatment hierarchy, the model was constructed to allow the evaluation of the cost-effectiveness of ECT being provided as a first, second or third line therapy.

Different scenarios that incorporated ECT as a treatment were compared with a pharmacological only treatment. The economic modelling results did not demonstrate that any of the scenarios had a clear economic benefit over the others. The main reason for this was the uncertainty surrounding the clinical effectiveness of the different treatments and the quality of life utility gains. Sensitivity analysis surrounding the cost of ECT and the quality of life utility values had little effect on the overall results.

Further economic analysis, such as expected value of perfect information, may be able to identify areas in which research would be best targeted by identifying parameters where reducing the level of uncertainty would have the most effect in helping to make the decision on whether ECT is a cost-effective treatment in the hospitalised severely depressed population.

Schizophrenia

The main schizophrenic population for which ECT is indicated in the guidelines of the American Psychiatric Association and the Royal College of Psychiatrists is patients resistant to pharmacotherapy. Therefore, the economic model constructed for schizophrenia was based on a pharmacological model previously constructed which was the only cost–utility study identified in the treatment of schizophrenia. This model analysed the cost-effectiveness of clozapine compared with haloperidol/chlorpromazine treatment in treatment-resistant schizophrenia. The model was adapted to incorporate an ECT arm to the decision tree analysis. The results of the adapted model including ECT suggest that clozapine is a cost-effective treatment compared with ECT. For patients who fail to respond to clozapine, ECT treatment may be preferred to the comparative treatment of haloperidol/chlorpromazine. However, the clinical evidence underpinning the ECT assumptions in the model is weak and the results should be interpreted with caution.

Recommendations for further research

Clinical effectiveness

There is a need for further, high-quality randomised controlled trials (RCTs) of the use of ECT in specific subgroups that are most likely to receive this treatment. These include older people with depression, women with postpartum exacerbation of depression or schizophrenia and people with catatonia. There is also a lack of good quality randomised evidence of the effectiveness of ECT in people with mania and people who are resistant to pharmacotherapy in schizophrenia and depression.

There is currently no randomised evidence comparing ECT with, or in addition to newer antipsychotic drugs (e.g. clozapine and risperidone) and antidepressants (e.g. venlafaxine) that are currently used in clinical practice. Further work is needed in these areas. More research is also needed to compare ECT with rTMS, especially in people with schizophrenia. Again, there is a need for further, high-quality RCTs comparing the use of ECT with these treatments.

More research is needed to examine the long-term efficacy of ECT and the effectiveness of post-ECT pharmacotherapy. There is only limited evidence regarding the efficacy of supplementing ECT with pharmacotherapy in people with ▶

depression and the continuation of pharmacotherapy following successful response to ECT to prevent relapses. In most trials, the aftercare of people receiving ECT was not randomised and people were rarely followed up beyond the course of ECT. Future work in the area requires longer follow-up periods. Further work is also needed to develop ways of incorporating patients' perspectives on the impact of ECT into future RCTs. Consideration should be given to the use of both quantitative and qualitative methods. The outcome measures used should reflect both clinical and patient perspectives on the impact of ECT.

There is also little good-quality quantitative evidence of the short-term and longer term cognitive side-effects of ECT. Cognitive functioning should be measured using well-validated instruments, and methods need to be developed that also reflect patients' concerns regarding personal memory loss. These instruments should be incorporated into trial design at the outset, and hypotheses set and results interpreted using a well-developed theory or set of theories from cognitive psychology. Again, longer term follow-up is needed as memory losses may only become apparent in the longer term. There is also a need for longer term follow-up within RCTs to explore the impact of ECT on suicide and all-cause mortality.

Further work is needed to examine the information needs of people deciding whether to accept ECT and how their decision-making can be facilitated. The influence of these choices on the perceived efficacy of ECT also requires further exploration.

Despite over 50 years of research into ECT, there is still no agreement on the mechanism of action of ECT. More research is needed in this area.

Finally, the quality of reporting of trials in this area would be vastly improved by strict adherence to the Consolidated Standards of Reporting Trials (CONSORT) recommendations.

Cost-effectiveness

Further economic analysis, such as expected value of perfect information, may identify areas in which research would be best targeted by identifying parameters where reducing the level of uncertainty would have the most effect in helping to make the decision on whether ECT is a cost-effective treatment.

Publication

Greenhalgh J, Knight C, Hind D, Beverley C, Walters S. Clinical and cost-effectiveness of electroconvulsive therapy for depressive illness, schizophrenia, catatonia and mania: systematic reviews and economic modelling studies. *Health Technol Assess* 2005;**9**(9).

NHS R&D HTA Programme

The research findings from the NHS R&D Health Technology Assessment (HTA) Programme directly influence key decision-making bodies such as the National Institute for Clinical Excellence (NICE) and the National Screening Committee (NSC) who rely on HTA outputs to help raise standards of care. HTA findings also help to improve the quality of the service in the NHS indirectly in that they form a key component of the 'National Knowledge Service' that is being developed to improve the evidence of clinical practice throughout the NHS.

The HTA Programme was set up in 1993. Its role is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care, rather than settings of care.

The HTA programme commissions research only on topics where it has identified key gaps in the evidence needed by the NHS. Suggestions for topics are actively sought from people working in the NHS, the public, consumer groups and professional bodies such as Royal Colleges and NHS Trusts.

Research suggestions are carefully considered by panels of independent experts (including consumers) whose advice results in a ranked list of recommended research priorities. The HTA Programme then commissions the research team best suited to undertake the work, in the manner most appropriate to find the relevant answers. Some projects may take only months, others need several years to answer the research questions adequately. They may involve synthesising existing evidence or designing a trial to produce new evidence where none currently exists.

Additionally, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme is able to commission bespoke reports, principally for NICE, but also for other policy customers, such as a National Clinical Director. TARs bring together evidence on key aspects of the use of specific technologies and usually have to be completed within a limited time period.

Criteria for inclusion in the HTA monograph series
Reports are published in the HTA monograph series if (1) they have resulted from work commissioned for the HTA Programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this monograph was commissioned and funded by the HTA Programme on behalf of NICE as project number 01/48/01. The authors have been wholly responsible for all data collection, analysis and interpretation and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

ISSN 1366-5278

Published by Gray Publishing, Tunbridge Wells, Kent, on behalf of NCCHTA.
Printed on acid-free paper in the UK by St Edmundsbury Press Ltd, Bury St Edmunds, Suffolk.