RAPID REVIEWS FOR THE HTA PROGRAMME

Electroconvulsive therapy (ECT) for depressive illness, schizophrenia, catatonia and mania

A. **This protocol is provisional and subject to change**

B. Details of review team

Lead: Greenhalgh, Joanne, Research Officer, Nuffield Institute for Health, 71-75 Clarendon Road, Leeds, LS2 9PL
Tel: 0113 233 6792
Fax: 0113 233 6880
Email: j.greenhalgh@leeds.ac.uk

Knight, Chris, Senior Operational Research Analyst, Operational Research Unit, ScHARR, Regent Court, 30 Regent Street, Sheffield, S1 4DA
Tel: 0114 2220688
Fax: 0114 2220785
Email: c.knight@sheffield.ac.uk

Warren, Emma, Operational Research Analyst, Operational Research Unit, ScHARR, Regent Court, 30 Regent Street, Sheffield, S1 4DA
Tel: 0114 2220788
Fax: 0114 2220785
Email: e.warren@sheffield.ac.uk

Beverley, Catherine, Systematic Reviews Information Officer, ScHARR, Regent Court, 30 Regent Street, Sheffield, S1 4DA
Tel: 0114 222 0725
Fax: 0114 272 4095
Email: c.a.beverley@sheffield.ac.uk

C. Full title of research question

To establish the clinical and cost effectiveness of electroconvulsive therapy (ECT) for depressive illness, schizophrenia, catatonia and mania.

D. **Clarification of research question and scope**

Population

The review will consider the evidence regarding the clinical and cost effectiveness of ECT in people with depressive illness (including those with reactive depression to other chronic illnesses such as Parkinson's disease and stroke), schizophrenia, catatonia and mania (including bipolar disorder). The review will include the use of ECT in older people, young people and children. The review will also consider the general medical fitness of the person from these populations to undergo ECT treatment. It is likely that separate evaluations will be undertaken for each different clinical group.

If the evidence allows, the review will attempt to identify people for whom the treatment is particularly effective or suitable and those for whom it is not, or for whom there are particular contraindications. This will include consideration of clinical features, age, sex and ethnicity and its use in pregnant women.

Intervention

ECT has been available for use since the 1930s. It is currently a standard treatment for a specific group of people. The therapy involves the passage of an electric current through a person's brain while they are under a general anaesthetic and have been given a muscle relaxant. This normally produces a convulsion, but not always. A course of ECT usually consists of six to twelve treatments given twice a week.

The review will consider a number of aspects relating to the settings in which ECT is used and the methods used to administer the treatment including:

- The impact of ECT stimulus parameters (including dosage, frequency of electricity, number of treatments and electrode placement) and technique of administration on the effectiveness of ECT
- The duration of the effects of ECT
- The use of ECT as a maintenance therapy, emergency therapy and the role of concomitant therapy (including seizure enhancers) in the overall effectiveness of ECT
- The setting in which ECT is administered and its impact on the clinical and cost effectiveness of ECT
- The costs of additional infrastructure and training required for the optimal delivery of ECT
- Patient acceptability and choice in ECT treatment and how these may affect outcomes

Although issues around consent to treatment fall outside the remit of the review, if the evidence allows, the impact of compulsory treatment on effectiveness will be considered.

Comparators

The review will consider the use of ECT (alone or in combination with other therapies) in comparison to any appropriate pharmacological or psychological treatment within the population for which ECT is currently a standard treatment.

Outcomes

It is likely that a wide range of outcome criteria will have been used to evaluate the clinical and cost effectivess of ECT in the literature. These might include both condition specific criteria such as symptomatology and more generic criteria such as physical, psychological and social functioning, ability to live independently, employment status, overall health status, quality of life and life satisfaction. They might also include process indicators such as re-admission to hospital, residential status, contact with inpatient, outpatient and specialist mental health services. An important aspect of the review will be to consider the impact of patient acceptability and choice on the effectiveness of ECT, and to consider its side effects including suicide and memory loss. Avoidance of adverse events such as suicide and self-harm would also be important outcome criteria in their own right

E. Report Methods

Search strategy

The search will aim to identify all studies relating to electroconvulsive therapy (ECT) for depression, schizophrenia, catatonia and mania. Key papers identified through initial scoping searches will be used to develop combined thesaurus and free-text search strategies. The following databases will be searched: Medline, Embase, Biological Abstracts, PsycINFO, Web of Science (Science and Social Sciences Citation Indexes), Cochrane Library, NHS CRD DARE, NHS EED and HTA, OHE HEED and Premedline. Where possible, searches will not be restricted by publication or study type. However, due to the large number of potentially relevant references in the field, searches in the major databases (e.g. Medline and Embase) will be restricted to the highest level of evidence (i.e. randomised controlled trials). This will be supplemented by specific searches designed to identify other study types and outcomes, such as economic evaluations, adverse effects, patient acceptability, etc. Current research registers and the websites and publications registers of relevant professional bodies will also be consulted. Citation searches of included studies will be undertaken using the Web of Science citation search facility. Finally, the reference lists of included studies, relevant reviews and sponsor submissions will be handsearched.

Inclusion and exclusion criteria

Population
The review will include people with depressive illness (including those with reactive depression to other chronic illnesses such as Parkinson's disease and stroke), schizophrenia, catatonia and mania (including bipolar disorder) for whom ECT is indicated as a standard treatment alongside drug or psychological therapy, or where ECT is indicated when drug therapy has proved ineffective or is not suitable. No age limits will be imposed on this population and the review will also consider the use of ECT in pregnant women.

Intervention
Electroconvulsive therapy at all doses and frequency of administration, by any technique, in all settings, and administered by any health professional. The review will include the use of ECT on its own or in conjunction with other appropriate pharmacological or psychological treatment.

Comparators
The review will include ECT in comparison with any pharmacological or psychological treatment that is appropriate to the population for whom ECT is indicated as a standard treatment alongside drug or psychological treatment, or where drug or psychological treatment has proved not effective or not suitable.

Outcomes
The review will consider the impact of ECT on condition specific symptoms, psychological, physical and social functioning, quality of life and life satisfaction, suicide both as a preventable adverse event and as a side effect of treatment. The review will also consider the impact of patient choice and acceptability on outcomes and side effects such as suicide and memory loss. Where appropriate, the impact of ECT on outcomes will be considered with respect to patient characteristics such as age and ethnicity. . Although issues around

consent to treatment fall outside the remit of the review, if the evidence allows, the impact of compulsory treatment on the effectiveness of ECT will be considered.

Methodology
Published papers will be included in the review according to the accepted hierarchy of evidence, whereby meta-analyses of randomised controlled trials are taken to be the most authoritative forms of evidence, with uncontrolled observational studies the least authoritative. In the first instance, the study will include systematic reviews, randomised controlled trials and economic evaluations. Where no randomised controlled trial evidence is available, non randomised comparator studies (for example non randomised trials, controlled cohort studies and case control studies) will be included in the review. Where no evidence from non randomised comparator studies is available, non randomised, non comparator studies (for example case series, case reports, non controlled cohort studies) will be included in the review. Qualitative studies will also be used and are likely to be a valuable source of evidence in exploring issues such a patient choice and acceptability of ECT.

Language
Any studies not available in English will be excluded as the time scale of the review precludes time for translation.

Data extraction strategy

All abstracts will be read and studies meeting inclusion criteria will be identified. Data from identified studies, reviews and other evidence will be extracted by one reviewer using a standardised data extraction form.

Quality assessment strategy

Published papers will be assessed according to the accepted hierarchy of evidence, whereby meta-analyses of randomised controlled trials are taken to be the most authoritative forms of evidence, with uncontrolled observational studies the least authoritative.

- Any randomised controlled trials will be assessed with respect to randomisation procedures, blinding, handling of withdrawals and dropouts, using Jadad's scoring system (Controlled Clinical Trials 1996;17:1-12).
- Non randomised studies using quantitative data, such as case-control, cohort, case series and case reports will be assessed with respect to validity using guidelines from the Centre for Health Evidence based upon the Users Guides to Evidence-Based Medicine (JAMA 1994;271:1615-1619).
- Qualitative evidence will be assessed using the CASP checklist for qualitative research (Institute of Human Sciences, Oxford).

In most instances, use of data from non-randomised studies will only be considered if there is insufficient evidence from good quality randomised controlled trials. The quality of the economic literature will be assessed according to the Guidelines for authors and peer reviewers of economic submissions to the BMJ (Drummond MF, Jeffereson TO, BMJ 1996;313:275-283).

Methods for estimating qualify of life, costs and cost-effectiveness and/or cost/QALY

A systematic review of the health economic literature relating to ECT and its comparators will be undertaken for each of the four diseases in question. If the cost-effectiveness of ECT cannot be determined fully from the existing literature, an economic model will be developed to assess the marginal cost-effectiveness of ECT compared to standard treatment. If the treatment outcomes differ in the four different diseases to be studied, it may be necessary to develop separate models for the separate diseases. Ideally the model will calculate the marginal cost-utility of ECT over its comparator. However, if the relationship between clinical outcomes and utility is not well established, it may only be feasible to estimate a disease specific cost-effectiveness of ECT. Cost data from published sources, where available, or derived from published or other sources of resource and cost data, will be incorporated in order to allow the economic, as well as clinical, implications of ECT to be assessed.

A sensitivity analysis will be undertaken to identify the key parameters that determine the cost-effectiveness of the intervention with the objective of identifying how secure the results of the economic analyses are given the available evidence.

F. **Handling the company submission**(s)

If any economic models are included within the sponsor submissions, the review team will undertake a detailed critical appraisal analysis of the industry models. This will allow a comparison of the sponsor and the review team models. The industry dossier will also be used to identify any RCTs or cost-effectiveness studies omitted from the systematic review.

Any 'commercial in confidence' data taken from the company submission will be <u>underlined</u> in the HTA report (followed by an indication of the relevant company name in brackets) so that the NICE secretariat can negotiate (before and during the Institute's consultation process) with industry the subsequent inclusion of such data in the HTA monograph publication or subsequent peer-review publications.

G. **Project Management**

a. ***Timetable/milestones*** *- submission of:*

Draft protocol:	19th November 2001
Finalised protocol	10th December
Consultees meeting	17th January 2002
Progress report:	4th March 2002
Final draft assessment report:	13th May 2002

b. ***Competing Interests***

None

c. ***External reviewers****:*

The rapid review will be subject to external peer review by at least two experts. These reviewers will be chosen according to academic seniority and content expertise and will be agreed with NCCHTA. We recognise that methodological review will be undertaken by the NICE secretariat and Appraisal Committee, but if the rapid review encounters particularly challenging methodological issues we will organise independent methodological reviews. External expert reviewers will see a complete and near final draft of the rapid review and will understand that their role is part of external quality assurance. Where the review contains data that is regarded as 'commercial in confidence' we will require peer reviewers to sign a copy of the NICE Confidentiality Acknowledgement and Undertaking. We will return peer reviewers' signed copies to NCCHTA. Comments from external reviewers and our responses to these will be made available to NCCHTA in strict confidence for editorial review and approval.