Efficacy and safety of electroconvulsive therapy in depressive disorders: a systematic review and meta-analysis

UK ECT Review Group

CRD summary
This review assessed the benefits and harms of electroconvulsive therapy (ECT) in patients with depressive disorders. ECT was shown to be an effective short-term treatment for depression and is probably more effective than drug therapy. Bilateral ECT was moderately more effective than unilateral ECT, while high-dose ECT was more effective than low-dose. The evidence presented supports the authors' conclusions.

Authors' objectives
To review the efficacy and safety of electroconvulsive therapy (ECT) with simulated ECT, ECT versus pharmacotherapy, and different forms of ECT for patients with a depressive illness.

Searching
The following sources were searched: the controlled trials registers of the Cochrane Depression Anxiety and Neurosis Group and the Cochrane Schizophrenia Group, the Cochrane Controlled Trials Register, Biological Abstracts, CINAHL, EMBASE, LILACS, MEDLINE, PsycINFO, SIGLE, reference lists, and specialist textbooks. The search strategy was described in the appendix of the paper, as found on the Lancet website.

Study selection

Study designs of evaluations included in the review
The review included randomised, unconfounded controlled trials for comparisons of ECT with no ECT, ECT versus pharmacotherapy, or different forms of ETC. Non randomised studies investigating mortality after ECT, and case-control neuroimaging and post-mortem studies looking at the possibility of structural brain changes after ECT, were also identified.

Specific interventions included in the review
The interventions included ETC. ECT versus pharmacotherapy or studies of different forms of ECT, such as bilateral ECT, unipolar ECT and high- and low-dose ECT, were eligible.

Participants included in the review
Participants with a diagnosis of depressive illness were included in the review. Participant subgroups were identified by clinical or demographic factors: psychotic depression, retarded depression, and the effect of age, treatment resistance, gender and severity of depression.

Outcomes assessed in the review
The primary outcome used to estimate the efficacy of ECT was the change in symptoms on a continuous depressive symptom scale at the end of the course of ETC.

Changes in depressive symptoms, cognitive functioning (especially memory functioning) and other outcomes such as premature discontinuation of ECT and mortality were assessed. The change in symptoms at 6 months' follow-up was also investigated.

How were decisions on the relevance of primary studies made?
Two reviewers independently checked the search results. Any disagreements were resolved by discussion within the study team.

Assessment of study quality
The quality of the identified trials was assessed through the reporting of the allocation concealment, masking, loss to follow-up and length of follow-up. Cohort studies were assessed by accounting for the likelihood of measurement bias, handling of confounding factors and number of cases, and loss to follow-up. Case-control studies were quality assessed by accounting for the likelihood of measurement bias, handling of confounding factors and number of cases. When RCTs were available, only they were considered. Paired members of the review team performed the data validation process. Any disagreements were resolved by discussion with the whole review team.

**Data extraction**
Paired members of the review team extracted the data. Any disagreements were resolved by discussion with the whole review team.

**Methods of synthesis**
How were the studies combined?
When appropriate, the data from individual trials were pooled by a meta-analysis. Continuous data were combined to produce standardised weighted mean differences, while dichotomous data were merged to produce estimates of odds ratios and absolute risk differences. Odds ratios and standardised mean differences were combined with numerical simulation techniques based on Gibbs sampling (reference cited in paper). In trials in which multiple doses of unilateral ECT were compared with bilateral ECT, the unilateral groups were combined for analysis.

Funnel plots were used to investigate publication bias. A meta-regression was undertaken to investigate the possibility of an interaction between dose and electrode position. Analyses were based on intention-to-treat when these data were available.

How were differences between studies investigated?
The results from applying fixed-effect and random-effects models were reported. Differences between the groups were described qualitatively. Patient subgroups such as psychotic depression, retarded depression, effect of age, treatment resistance, gender and severity of depression were used to describe the differences between the studies.

**Results of the review**
Seventy-three RCTS were included in the review. In addition, four cohort studies and three observational studies were also identified.

The authors noted that a meta-analysis of the data on short-term efficacy from RCTs was possible. Real ECT was significantly more effective than simulated ECT in reducing depressive symptoms (6 RCTs, n=256); the standardised effect size (SES) was -0.91 (random-effects) (95% confidence interval, CI: -1.27, 0.54). At 6 months, no significant difference was noted. There was no significant difference between the ECT and simulated ECT for premature discontinuation (3 trials). No deaths were reported.

Treatment with ECT was significantly more effective than pharmacotherapy in reducing depressive symptoms (n=1,144; SES -0.80, 95% CI: -1.29, 0.29). Discontinuation was typical in both groups, but significantly lower in the ECT arm (risk difference 0.03, 95% CI: -0.09, 0.03). Four trials in this group had discontinuations in the pharmacotherapy arm only. One trial reported a death in each group.

Bilateral ECT was more effective than unipolar ECT (n=1,408; SES 0.32, 95% CI: -0.46, 0.19). Six trials reported that the times to orientation were longer for patients treated with bilateral ECT than for those treated with unilateral ECT. Four trials reported the results from testing retrograde memory within a week of the course of ETC.

Observational studies: four non-randomised cohort studies were found, of which three reported lower overall mortality in patients treated with ECT and one showed no difference. Funnel plots did not reveal any publication bias.

**Authors' conclusions**
ECT was shown to be an effective short-term treatment for depression and is probably more effective than drug.
therapy. Bilateral ECT is moderately more effective than unilateral ECT, while high-dose ECT is more effective than low-dose ECT.

CRD commentary
A reasonable literature search was conducted. However, since the authors did not attempt to locate unpublished studies, it is possible that some studies may have been missed. The inclusion criteria were reported but more study details would have been helpful, in particular details of the participants included. The authors performed a quality assessment, although the results were not used in the review. They used appropriate methods to synthesise the data. The main results were presented clearly in forest plots, but no formal statistical test for heterogeneity was reported. Funnel plots were not presented. The evidence presented supports the conclusions.

Implications of the review for practice and research
Practice: The authors state that ECT remains an important treatment option for the management of severe depression.

Research: The authors state that trials to assess different doses of ECT would be specifically useful to inform practice in older patients or those with treatment-resistant illnesses, or in subgroups in whom ECT is thought to be especially effective (post partum disorders).

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Other publications of related interest
This additional published commentary may also be of interest. Andrade C. Review: electroconvulsive therapy reduces depressive symptoms. Evid Based Med 2003;8:138.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.