TITLE: Electroconvulsive Therapy Performed Outside of Surgical Suites: A Review of the Clinical Effectiveness, Safety, and Guidelines

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CONTEXT AND POLICY ISSUES

Major depression is a mental disorder characterised by severe depression which lasts for at least two consecutive weeks. Symptoms include feelings of worthlessness or guilt; lack of enjoyment of once pleasurable activities; difficulties concentrating or making decisions; suicidal thoughts; and changes in weight, appetite, or sleep patterns.[1] It is a leading cause of morbidity and mortality. In Canada, lifetime prevalence rates are about 12%.[1]

Treatment options for major depression include pharmacotherapies, psychotherapies and neuro-modulation therapies. Pharmacotherapies include a variety of drugs such as antidepressants, antipsychotics and mood stabilizers.[2] Psychotherapies include various therapies such as cognitive behavioural therapy (CBT) or interpersonal psychotherapy (IPT). Neuro-modulation therapies include electroconvulsive therapy (ECT), repetitive transcranial magnetic stimulation (rTMS), vagus nerve stimulation (VNS), and magnetic seizure therapy (MST).[3] rTMS involves stimulation of brain cells through the scalp using an electromagnetic coil and does not require the use of anesthesia.[2] VNS involves surgically placed electrodes around the left vagus nerve and requires a battery powered generator which is implanted in the chest wall.[2] MST involves brain stimulation using alternating magnetic fields to induce seizures under general anesthesia.[4] In comparison to ECT, MST allows a more focal stimulation so regions responsible for memory function are spared from stimulation.[4] ECT has been in use since the 1930s and is still used for treating psychiatric conditions.[5,6] ECT is generally undertaken in a dedicated ECT suite, a hospital post-anesthesia care unit, or an ambulatory surgery suite and may be performed on an inpatient or outpatient basis.[7] It is a procedure in which an electrical stimulus is used to induce a cerebral seizure and is performed under general anesthesia.[6,7] Typically, the ECT team comprises a psychiatrist, an anesthesiologist, and a nurse.[7] ECT has demonstrated efficacy in a variety of psychiatric conditions including patients with treatment-resistant depression (TRD).[8,9] However, ECT is thought to be associated with stigma, and memory and learning impairment.[10,11] There is some concern that use of surgical suites for ECT impacts availability of surgical suites for other needed surgeries.

The purpose of this report is to review the available evidence on clinical effectiveness and safety of treating patients with depression with ECT conducted outside of a surgical suite and the associated evidence based guidelines. In addition the clinical effectiveness of ECT compared with other non-pharmacological modalities will be reviewed.

RESEARCH QUESTIONS

1. What is the clinical effectiveness and safety of performing electroconvulsive therapy (ECT) outside of a surgical suite for patients with depression?

2. What is the comparative clinical effectiveness of ECT to alternate non-pharmacological forms of mental health interventions for patients with depression?

3. What are the evidence-based guidelines associated with the use of ECT outside of a surgical suite for patients with depression?

KEY FINDINGS

No studies on the clinical effectiveness and safety of performing electroconvulsive therapy (ECT) outside of a surgical suite for patients with depression were identified.

Three systematic reviews were identified comparing ECT with repetitive transcranial magnetic stimulation (rTMS). One found greater improvement in depressive symptoms with ECT but did not report statistical significance. One SR showed that response and remission were statistically significantly better with ECT. One SR presented results for separate groups of studies according to extent of previous treatment failure. Results for depressive severity, response, remission and cognitive functioning in the studies included in this SR appeared to be inconsistent; some studies showed that ECT was statistically significantly better with respect to reducing depressive severity, and achieving response and remission and worse with respect to cognitive functioning whereas some studies showed there were no statistically significant differences between the two treatment modalities for these outcomes.

One RCT comparing ECT with cognitive behavioural therapy (CBT) as continuation therapy after ECT treatment at the acute phase found that sustained response rates were significantly lower with ECT compared with CBT and that the cognitive side effects were not significantly different between the two.

One RCT found were no significant differences between ECT and magnetic seizure therapy in responses, measured using various scales. One RCT found that recall of memorized words were statistically significantly worse with ECT compared to MST, on the treatment day but not on a day when there was no treatment while another found no statistically significant difference between the two modalities.

One guideline, though not specifically on conduct of ECT outside of a surgical suite, provided some general guidance regarding a treatment site that would be conducive for ECT.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including Medline, PsycINFO, PubMed, The Cochrane Library (2014, Issue 12), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2010 and December 8, 2014.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Adults dealing with depression (from any cause)
Intervention	Electroconvulsive therapy (ECT)
Comparator	Any alternative intervention (excluding pharmacotherapy) Trauma Release Exercises (TRE) ECT (not performed in a surgical suite) No comparator
Outcomes	Q1: Clinical effectiveness, and patient safety Q2: Comparative clinical effectiveness with alternatives or with ECT in a different location Q3: Guidelines
Study Designs	Health technology assessment (HTA), systematic review (SR), meta-analysis (MA), randomized controlled trial (RCT), and non-randomized study (NRS).

Exclusion Criteria

Studies were excluded if they did not satisfy the selection criteria, if they were duplicate publications, or were published prior to 2010. Studies comparing ECT with a combination of ECT and other therapies were excluded. Studies already included in a selected systematic review were excluded. Systematic reviews with all studies included in a selected systematic review which was more recent were excluded. Case series or case reports were excluded.

Critical Appraisal of Individual Studies

Critical appraisal of a study was conducted based on an assessment tool appropriate for the particular study design. The AMSTAR checklist[12] was used for systematic reviews and the Downs and Black checklist[13] for RCTs.

For the critical appraisal, a numeric score was not calculated. Instead, the strengths and limitations of the study were described narratively.

SUMMARY OF EVIDENCE

Quantity of Research Available

A total of 386 citations were identified in the literature search. Following screening of titles and abstracts, 356 citations were excluded and 30 potentially relevant reports from the electronic search were retrieved for full-text review. One potentially relevant publication was retrieved from the grey literature search. Of these potentially relevant articles, 24 publications were excluded for various reasons, while seven publications met the inclusion criteria and were included in this report. These seven publications comprised of three systematic reviews,[2,5,14] three RCTs,[12,15,16] and one guideline.[17] Appendix 1 describes the PRISMA flowchart of the study selection.

Additional references that did not meet the inclusion criteria but may be of potential interest are included in Appendix 2.

Summary of Study Characteristics

Characteristics of the included systematic reviews (SRs), randomized controlled trials (RCTs) and guideline are summarized below and details, including number of and duration of ECT sessions, are provided in Appendix 3.

Systematic reviews

Three relevant SRs[2,5,14] including comparisons of ECT with rTMS in adults with depression were identified. Of the three SRs, one[5] was published in 2014 from Malta, one[14] was published in 2014 from China and one[2] was published in 2011 from USA.

Of these three SRs, two SRs[5,14] each included nine RCTs published between 2000 and 2011. There was overlap in seven of the nine studies included in these two SRs. The third SR[2] included five RCTs and two cohort studies published between 2000 and 2011. The total number of patients in the SRs varied between 231 and 429. The patient ages in the studies included in these three SRs ranged between 25 years and 73 years. In two SRs the proportions of males in the individual included studies were reported and ranged between 23% and 53%. One SR[2] categorized studies into three types: Tier 1, Tier 2 and Tier 3. Tier 1 was studies including patients with ≥ 2 previous treatment failures; Tier 2 was studies including patients with ≥ 1 previous treatment failures; and Tier 3 was studies with the number of treatment failures not specified. The main focus of this SR was Tier 1 studies. The other two SRs did not specify any criteria around previous treatment failures.

All three SRs compared ECT with rTMS. Of the three SRs, one SR[2] mentioned the settings where ECT or rTMS were conducted for the individual studies and the settings were university hospitals or medical centres but further details were not presented.

Outcomes reported varied between studies. Changes in depressive severity based on Hamilton rating scale for depression (HRSD) scores were reported in the three SRs. Response, remission, and side effects or adverse events were reported in two SRs.[2,14] Cognitive functioning was reported in one SR[2] and discontinuation was reported in one SR.[14] Definitions

of response and remission were not always provided and varied across studies. Response was defined as reduction in Hamilton rating scale for depression (HRSD) score of 50% or more or as a score of ≤ 10 on HRSD (17 item). The definition of remission was based on achieving a pre-defined score such as HRSD (17 item) score of ≤ 7, ≤8 or <12 or HDRS (21 item) score ≤ 10.

Randomized controlled trials

Three relevant RCTs,[4,15,16] comparing ECT with other non-pharmacologic therapies in patients with depression were identified; two[4,16] compared ECT with MST and one[15] compared ECT with CBT.

ECT versus CBT

One RCT[15] compared ECT with CBT as continuation therapy, after all patients had received ECT in the acute phase. It was published in 2014 from Germany. ECT was conducted at the Department of Psychiatry and Psychotherapy, Charité University Hospital, Berlin. It included 42 patients of mean age 59 years and 63 years in the ECT and CBT groups respectively. The proportions of males were 36% and 12% in the ECT and CBT groups respectively. In both groups, patients also received at least one antidepressant. Outcomes assessed included response, relapse, dropouts and cognitive side effects.

ECT versus MST

Two RCTs[4,16] compared ECT with MST and were published from Germany; one[4] in 2014 and one[16] in 2010.

In one RCT,[4] ECT was conducted at the Department of Psychiatry and Psychotherapy, University Hospital, Bonn. The RCT included 20 patients of mean age 55 years and 44 years in the ECT and MST groups, respectively. The proportions of males were 40% and 70% in the ECT and MST groups, respectively. All patients had treatment resistant depression. Treatment resistant depression was defined as being unresponsive to two different antidepressant treatments of adequate length and dosage during the current episode of depression. This RCT reported on memory performance (recall).

In one RCT,[16] ECT was conducted at the Department of Psychiatry and Psychotherapy, University Hospital, Bonn. The RCT included 20 patients of mean age 53 years and 49 years in the ECT and MST groups respectively. The proportions of males were 30% and 40% in the ECT and MST groups respectively. All patients had treatment resistant depression. Treatment resistant depression was defined as failure to respond to two different treatment categories during the current major depressive episode. The RCT reported on psychopathological measures (e.g., HRSD and Beck depression inventory [BDI]) and adverse events.

Guidelines

One guideline,[17] providing recommendations on the personnel and treatment site requirements for performing electroconvulsive therapy, was identified. It was prepared by the New York State Office of Mental Health (OMH) and was accessed from their website in December 2014. OMH oversees Psychiatric centres across New York State and regulates the programs used by the centres.

Summary of Critical Appraisal

Critical appraisal of the included SRs, RCTs and guideline are summarized below and additional details for the SRs and RCTs are provided in Appendix 4.

Systematic reviews

In all the three SRs, objectives, inclusion and exclusion criteria were stated, a comprehensive literature search was conducted, a list of included studies was provided, and appropriate methods for analyses were used. The SRs described characteristics of the individual included studies but details regarding the settings where ECT was conducted were lacking. Article selection was done in duplicate in one SR and not specified in two SRs. A list of excluded studies was provided in one[2] of the three SRs. Data extraction was done in duplicate in two SRs[2,14] and not specified in one SR.[5] Quality assessments were conducted in all the SRs but results of the assessment were reported in two[2,14] of the three SRs. One SR[2] assessed quality of the studies based on the Methods Guide for Comparative Effectiveness Reviews of the Agency for Healthcare Research and Quality (AHRQ) and one SR[14] assessed quality of the studies based on criteria in the Cochrane handbook and Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. In one SR[2] the studies were mostly of fair quality and the strength of evidence was generally low and in one SR[14] the studies were mostly of moderate quality and the strength of evidence was generally moderate. The assessment method was different in the two SRs. Publication bias was assessed in the three SRs. Two SRs[5,14] reported there was low risk for publication bias and one SR[2] reported that as the number of included studies was small, there was lack of sensitivity to detect publication bias. Two SRs[2,5] mentioned that there were no conflicts of interest and one SR[14] did not mention conflict of interest.

Randomized controlled trials

In all the three RCTs, objectives, inclusion and exclusion criteria were stated and patient characteristics, interventions and outcomes were described but details regarding the settings where ECT was conducted were lacking. Due to nature of the interventions, blinding of patients and clinicians was not possible, hence there is potential for bias. Sample size calculations were not described so it is unclear if there was sufficient power to detect a clinically important difference. Analysis appeared to be intent-to-treat (ITT) in two RCTs[4,15] but was unclear in one RCT.[16] *P*-values were provided for some, but not all, outcomes. Conflict of interest was not mentioned in two RCT reports.[4,15] In one RCT,[16] from the authors' disclosures, there did not appear to be any conflicts of interest, however it should be noted that the study was partially funded by the manufacturer of the MST apparatus. Generalizability of the findings was limited considering the RCTs were conducted at single centres.

Guidelines

One relevant guideline[17] was identified. It was a brief document and did not contain enough information to conduct a critical appraisal. However, in the document it was stated that this guideline was based on an earlier guideline (The Practice of Electroconvulsive Therapy: Recommendations for Treatment, Training, and Privileging, 2001) from the American Psychiatric Association (APA). The process followed by APA for developing guidelines appears to be rigorous.[18,19] An APA guideline is developed by a team comprising psychiatrics in active clinical practice including academics and researchers. Team members are required to disclose

their conflict of interest and if there is potential of bias, the member is requested to decline participation. The APA guideline development is not supported by any commercial organization. The recommendations are based on a systematic review of available evidence from the literature on efficacy and safety of the intervention, and on clinical consensus. Implementation issues are also taken into consideration.

Summary of Findings

The overall findings are summarized below and details of the findings of included systematic reviews and RCTs are provided in Appendix 5 and details of the included guideline are provided in Appendix 6.

What is the clinical effectiveness and safety of performing electroconvulsive therapy (ECT) outside of a surgical suite for patients with depression?

No evidence on the clinical effectiveness and safety of performing ECT outside of a surgical suite for patients with depression was identified.

What is the comparative clinical effectiveness of ECT to alternate forms of mental health interventions (e.g. trauma release exercises) for patients with depression?

Systematic reviews

Three relevant SRs[2,5,14] including comparisons of ECT with rTMS in adults with depression were identified.

One SR[5] showed that compared to baseline values, both ECT and rTMS produced a statistically significant decrease in depressive symptoms as measured by HRSD (15.4, $P \leq 0.0005$ for ECT and 9.3, $P \leq 0.0005$ for rTMS). The extent of improvement with ECT was numerically greater compared with rTMS but whether the difference was statistically significant or not was not mentioned.

One SR[14] presented relative risk (RR) and 95% confidence interval (CI) and showed that the risk of lack of response or remission were statistically significantly higher in the rTMS group compared with the ECT group (RR [95% CI] 1.52 [1.18 to 1.96] for lack of response and 1.42 [1.16 to 1.75] for lack of remission). The mean difference (MD) in HRSD scores for rTMS versus ECT was statistically significant (MD [95% CI] 2.81 [0.17 to 5.46]). The mean difference (MD) in mini-mental status examination (MMSE) scores for rTMS versus ECT was not statistically significant (MD [95% CI] 0.65 [-0.51 to 1.82]). The mean difference in side effects for rTMS versus ECT was not statistically significant (MD [95% CI] 0.19 [-1.84 to 2.22]).

One SR[2] presented results separately for three categories of studies (Tier 1, Tier 2 and Tier 3 based on previous treatment status). For Tier 1 and Tier 2 studies, no significant difference was observed between the rTMS and ECT groups for response or remission. For Tier 3 studies, statistically significant differences were observed between the rTMS and ECT groups for response and remission, favouring ECT (for response, response rate difference [95% CI] 0.37 [0.14 to 0.59] in one RCT and 59% versus 17%, $P = 0.005$ in one RCT; and for remission response rate difference [95% CI] 0.26 [0.03 to 0.51] in one RCT and 59% versus 17%, $P = 0.005$ in one RCT; percentages refer to the proportions of patients). Change in depressive severity between the two groups was not significantly different in Tier 1 and Tier 2 studies but

was statistically significantly better with ECT compared to rTMS in the only Tier 3 study for which it was reported. Results for cognitive functioning were inconsistent in the Tier 1 studies. There were no statistically significant differences in cognitive function in ECT and rTMS groups in the Tier 2 and Tier 3 studies. There was no difference in withdrawals due to adverse events in the Tier 1 study that reported this outcome. No treatment related adverse events were reported in a Tier 3 study.

Randomized controlled trials

ECT versus CBT

One RCT[15] compared ECT with CBT as continuation therapy, after all patients had received ECT in the acute phase. At six months follow up, sustained response was statistically significantly lower with ECT compared with CBT (40% versus 77%, *P* = 0.02). At six months follow up, relapses and dropouts were numerically higher with ECT compared with CBT (32% versus 24% for relapses and 28% vs 0% for dropouts); *P*-values were not reported. Similar trends were observed at 12 months follow up. Cognitive side effects were reported to be non-significant in both groups.

ECT versus MST

One RCT[4] comparing ECT with MST reported on memory function assessed by recall ability. Recall of memorized words with ECT compared with MST, was statistically significantly lower (23% versus 51%. *P* = 0.02) on treatment day and numerically lower (47% versus 56%, *P* = NS) on control day. Control day refers to a testing day without treatment.

One RCT[16] comparing ECT with MST reported on psychopathological measures (HDRS, BDI, Montgomery Ashberg depression scale [MADRS], Hamilton anxiety scale [HAMA], and symptom checklist [SCL-90]). The decrease in HDRS score from baseline was numerically less in the ECT group compared with the MST group (11.9 versus 12.4, *P* = NS). The decrease in BDI score from baseline was numerically less in the ECT group compared with the MST group (7.3 versus 10.7, *P* = NS). Similar results were obtained for the other pathological measures. No statistically significant differences were observed in memory function between the ECT and MST groups. Some patients in the ECT group experienced headache, nausea, or muscle pain after treatment. No side effects were observed in the MST group.

<u>What are the evidence-based guidelines associated with the use of ECT outside of a surgical suite for patients with depression?</u>

One guideline,[17] though not specifically on conduct of ECT outside of a surgical suite, provided general guidance with respect to a treatment site for ECT. It recommended that the treatment site should be conducive to the delivery of ECT treatment for both the patient and the staff. It should have adequate quantities of required and optional equipment, medications, and supplies for safe administration of ECT which should be available in the treatment area. The guidelines state that the treatment site should have equipment such as devices to deliver positive oxygen pressure, monitors for vital signs, and equipment for intubation, resuscitation and seizure induction. Further details are presented in Appendix 6. The ECT team should comprise of a ECT privileged psychiatrist, an anesthesia provider, and a recovery nurse.

Limitations

No studies on the clinical effectiveness and safety of performing ECT outside of a surgical suite for patients with depression were identified.

Descriptions of the settings where ECTs were conducted lacked details. In most studies, ECT was conducted at a hospital however it was not specified if the ECT was conducted at the surgical suite of the hospital or at a different facility of the hospital.

There was overlap between the studies included in the selected SRs, hence the results of the SRs are not completely exclusive and effects may be over-emphasized.

Definitions for response and remission were not always provided and there was variability in the definitions used in individual studies, hence comparability between studies was difficult. Not all outcomes were reported in all studies. Reporting of adverse events was sparse.

The studies were generally small in size (number of patients varied between 20 and 73 in the individual studies) Also, it should be noted that for the SR categorizing studies as Tier 1, Tier 2 and Tier 3 depending on the specifics of previous treatment failure and providing separate results, the number of studies contributing to a particular outcome in each category were few and varied between one and three studies. Results need to be interpreted with caution.

Lack of blinding in the RCTs is a potential source of bias, however it is recognized that blinding is not possible for studies on these types of interventions.

Due to paucity of data as well as inconsistencies in the results, definitive conclusions are not possible.

For the studies included in the SRs, the countries where the studies were conducted were not always specified and the individual RCTs included in this report were not conducted in Canada hence results may not be generalizable to the Canadian setting.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

No studies on the clinical effectiveness and safety of performing ECT outside of a surgical suite for patients with depression were identified.

Three SRs comparing rTMS with ECT, one RCT comparing ECT with CBT and two RCTs comparing ECT with MST for treating patients with depression were identified.

The three SRs presented results in different formats. One SR showed that extent of improvement in depressive symptoms was numerically greater with ECT compared with rTMS but statistical significance was not reported. One SR presented pooled estimates and showed that response and remission were statistically significantly better with ECT compared with rTMS. One SR presented results for separate groups of studies according to extent of previous treatment failure. Results for depressive severity, response and remission in studies included this SR appeared to be inconsistent; some studies showed ECT was statistically significantly better compared to rTMS whereas some studies showed there were no statistically significant differences between the two treatment modalities. Results for cognitive functioning were also inconsistent; some studies found ECT had a negative impact on cognitive functioning compared

to rTMS and some studies found no significant differences between the two treatment modalities.

One RCT comparing ECT with CBT as continuation therapy after ECT treatment at the acute phase found that sustained response rates were significantly lower with ECT compared with CBT and that the cognitive side effects were not significantly different between the two modalities.

One RCT found that there were no significant differences in responses, measured using various scales, between ECT and MST. One RCT found that recall of memorized words were statistically significantly worse with ECT compared to MST on the treatment day but that there was no statistically significant difference between the two modalities on a day without treatment. A second RCT found no statistically significant difference in memory function between the two modalities.

One guideline though not specifically on conduct of ECT outside of a surgical suite provided some general guidance regarding a treatment site that would be conducive for ECT.

There is lack of evidence on comparative clinical effectiveness and safety of conducting ECT at various types of treatment facilities, hence at this time it remains unclear as to which setting would be minimally adequate.

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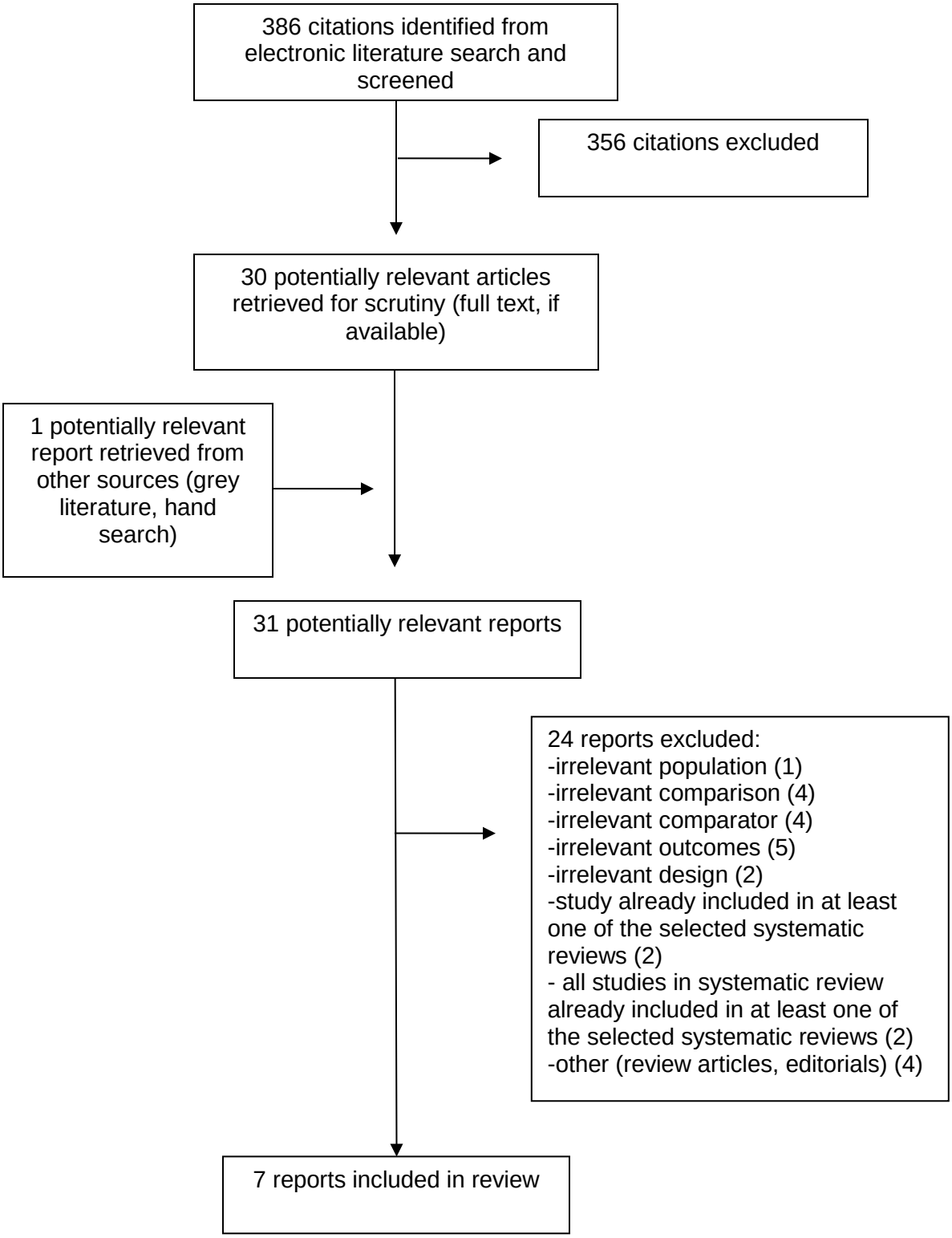
ABBREVIATIONS

AHRQ	Agency for Healthcare Research and Quality
BDI	Beck depression inventory
BP	bipolar
BP-D	bipolar depression
CBT	cognitive behavioral therapy
CI	confidence interval
DLPFC	dorsolateral prefrontal cortex
ECT	electroconvulsive therapy
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HAMA	Hamilton anxiety scale
HRSD	Hamilton rating scale for depression
HRQoL	Health related quality of life
HTA	Health technology assessment
IPT	Interpersonal psychotherapy
ITT	intent to treat
LDLPFC	left dorsal prefrontal cortex
MA	meta-analysis
MADRS	Montgomery Ashberg depression scale;
MDD	major depressive disorder
Med	medication
MMSE	mini-mental status examination
MST	magnetic seizure therapy
NA	not available
NRS	non-randomized study
NS	not significant
OMH	Office of Mental Health
QoL	quality of life
RCT	randomized controlled trial
RDLPFC	right dorsal prefrontal cortex
RR	relative risk
rTMS	repetitive transcranial magnetic stimulation
SCL	symptom checklist
SD	standard deviation
SR	systematic review
TRD	treatment resistant depression
UP-D	uni-polar depression
VNS	vagus nerve stimulation
vs	versus

APPENDIX 1: Selection of Included Studies



APPENDIX 2: References of potential interest

SR with studies already included in a more recent SR:

Berlim MT, Van den EF, Daskalakis ZJ. Efficacy and acceptability of high frequency repetitive transcranial magnetic stimulation (rTMS) versus electroconvulsive therapy (ECT) for major depression: a systematic review and meta-analysis of randomized trials. Depress Anxiety. 2013 Jul;30(7):614-23.

Xie J, Chen J, Wei Q. Repetitive transcranial magnetic stimulation versus electroconvulsive therapy for major depression: a meta-analysis of stimulus parameter effects. Neurol Res. 2013 Dec;35(10):1084-91.

APPENDIX 3: Characteristics of Included Studies

First Author, Publication Year, Country	Study Design, Duration	Patient Characteristics, Sample Size[a] (N)	Comparison[a]	Outcomes[a] Measured
Systematic reviews				
Micallef-Trigona,[5] 2014, Malta	SR comparing rTMS with ECT for treatment of depression. Included 9 RCTs published between 2000 and 2011 Setting for conducting ECT or rTMS in individual RCTs: NR	Adults with MDD N = 384 (total for 9 RCTs; N in individual RCTs ranged between 25 and 73) Age (years) (range): 34 to 68 % Male: NR HRSD score: NR	ECT vs rTMS Number of ECT sessions ranged between 6 and 12; unilateral in 4 RCTs, bilateral in 2 RCTs, and unilateral or bilateral in 3 RCTs Number of rTMS sessions ranged between 10 and 20	Depressive severity using HRSD
Ren,[14] 2014, China	SR comparing rTMS with ECT for treatment of major depression. Included 9 RCTs published between 2000 and 2011 Setting for conducting ECT or rTMS in individual RCTs: NR	Adults with MDD or bipolar depression N = 429 (total for 9 RCTs; N in individual RCTs ranged between 26 and 73) Age (years) (mean ± SD): 49.8 ± 12.6 in ECT, 47.6 ± 12.4 in rTMS Male: 38.2% in ECT 42.9% in rTMS HRSD score: NR	ECT vs rTMS Number of ECT sessions ranged between 6 and 12; unilateral in 2 RCTs, bilateral in 3 RCTs, and unilateral or bilateral in 4 RCTs Number of rTMS sessions ranged between 7 and 20; LDLPFC rTMS in 8 RCTs and RDLPFC rTMS in 1 RCT.	Response, remission, depressive severity using HRSD, discontinuation, side effects
Gaynes,[2] 2011, USA (AHRQ report)	SR on non-pharmacologic interventions (ECT, rTMS VNS, CBT or IPT) and pharmacologic therapy Included 5 RCTs and 2 cohorl studies for ECT vs rTMS published between	Adults with TRD N = 231 (N varied between 40 and 60 in the individual RCTs and between 28 and 30 in the individual cohort studies) Age (years) varied	ECT vs rTMS Number of ECT sessions ranged between 2 and 10 in the RCTs and between 6 and 12 in the cohort studies Number of rTMS sessions ranged	Response, remission, depressive severity using HRSD, cognitive functioning, AE

First Author, Publication Year, Country	Study Design, Duration	Patient Characteristics, Sample Size[a] (N)	Comparison[a]	Outcomes[a] Measured
	2000 and 2011 Setting for conducting ECT or rTMS in individual RCTs: University hospital or medical centre	between 42 to 68 in the RCTs and between 47 and 51 in the cohort studies Male: 23% to 53% in the RCTs and 53% in one cohort study and not reported for one cohort study HRSD score: 24 to 32 in the RCTs and 28 to 30 in the cohort studies	between 15 and 20 in the RCTs and was 10 in one cohort study and was 2 to 3 per week in one cohort study	
Randomized controlled trials				
Brakemeier,[15] 2014, Germany	RCT, single centre, 3-arm: ECT vs CBT vs med. Duration/ setting: 2004 to 2010 at Department of Psychiatry and Psychotherapy, Charité University Medicine, Berlin	Adults with UP-D N = 42 Age (year) (Mean ± SD): 59.0 ± 13.9 in ECT, 62.6 ± 12.4 in CBT Male: 36% in ECT, 11.8% in CBT HRSD (24 item) score: 8.8 ± 3.9 in ECT, 8.2 ± 4.5 in CBT	ECT vs CBT; in continuation phase. (All patients had received ECT in the acute phase. During continuation phase patients received pharmacotherapy [at least one antidepressant] and either ECT or CBT as add on therapy) ECT: ultra-brief pulse device, Mecta 5000Q. Right unilateral ECT administered weekly for 4 weeks, biweekly for 8 weeks and monthly for 3 months	Response, relapse, dropout, cognitive side effects
Polster, [4] 2014, Germany	RCT, single centre, 3-arm: ECT vs CBT vs healthy controls.	Adults with TRD (UP-D) *N* = 20	ECT vs MST Patients were treated 3 times a	Memory performance (delayed recall, cued

First Author, Publication Year, Country	Study Design, Duration	Patient Characteristics, Sample Size[a] (N)	Comparison[a]	Outcomes[a] Measured
	Duration/ setting: June 2009 to December 2012 at Department of Psychiatry and Psychotherapy, University Hospital Bonn	Age (year) (Mean ± SD): 54.7 ± 13 in ECT, 43.7 ± 11 MST Male: 40% in ECT, 70% in MST HRSD-28 score: 23.2 ± 8 in ECT, 25.3 ± 7 in MST	week and received a total of 10 to 12 treatments. One month before and during treatment, antidepressant medication was kept stable ECT: Thymatron IV used. Stimulus parameters were bipolar wave form, square wave, brief pulse current, duration and frequency 5 to 8 seconds MST: MagPro used. Stimulus parameters were biphasic waveform, amplitude 100%, frequency 100 MHz, duration 5 to 8 seconds	recall)
Kayser,[16] 2010, Germany	RCT, single centre Duration/ setting: July 2006 to November 2008 at Department of Psychiatry and Psychotherapy, University Hospital Bonn	Adults with TRD (mainly [80%] MDD and few BP) *N* = 20 Age (year) (Mean ± SD): 52.8 ± 11.43 in ECT, 48.80 ± 8.35 in MST Male: 30% in ECT, 40% in MST HRSD-28 score: 25.8 ± 2.62 in ECT, 30.7 ± 5.03 in MST	ECT vs MST Patients were treated 2 times a week and received a total of 12 treatments. Antidepressant medication was not stopped or changed during treatment ECT: Thymatron IV used. Stimulus parameters were bipolar wave form, square wave, brief pulse current, duration	Psychopathological measures (MADRS, HRSD-28, HAMA, BDI, SCL), memory function and AE

First Author, Publication Year, Country	Study Design, Duration	Patient Characteristics, Sample Size[a] (N)	Comparison[a]	Outcomes[a] Measured
			and frequency 5 to 8 seconds MST: MagPro used. Stimulus parameters were biphasic waveform, amplitude 100%, frequency 100 MHz, duration up to 6 seconds	

AHRQ = Agency for Healthcare Research and Quality; AE = adverse event; BDI = Beck depression inventory; CBT = cognitive behavioral therapy; ECT = electroconvulsive therapy; HAMA = Hamilton anxiety scale; HRSD = Hamilton rating scale for depression; HRSD-28 = Hamilton rating scale for depression – 28 item; HTA = health technology assessment; IPT = interpersonal psychotherapy; LDLPFC = left dorsal prefrontal cortex; MADRS = Montgomery Ashberg depression scale; MDD = major depressive disorder; med = medication; MST = magnetic seizure therapy; QoL = quality of life; RLDPFC = right dorsal prefrontal cortex; TMS = repetitive transcranial magnetic stimulation; TRD = treatment resistant depression; SCI = symptom checklist; SD = standard deviation; SOC = sense of coherence scale of Antonovsky; TRD = treatment resistant depression; UP-D = uni polar depression; VNS = vagus nerve stimulation; vs = versus

[a]In case of reports with multiple comparisons only comparisons of relevance for this report and the corresponding characteristics, sample size and outcomes are mentioned here.

APPENDIX 4: SUMMARY OF STUDY STRENGTHS AND LIMITATIONS

First Author, Publication Year, Country	Strengths	Limitations
Systematic reviews (SR)		
Micallef-Trigona,[5] 2014, Malta	• The objective was clearly stated. • The inclusion and exclusion criteria were stated. • Multiple databases were searched, 1974 to 2013. PsycINFO was stated to have been searched between 1806 and 2013. Also reference list of the identified studies were manually searched. • List of included studies was provided • Characteristics of the individual studies were provided but but details of settings where ECT and rTMS were conducted were lacking • Quality assessments of studies were conducted but results of assessment were not reported • Methods used to combine the findings of studies were appropriate • Publication bias was explored and there appeared to be low risk of publication bias • The author stated that there was no conflict of interest.	• Study selection not described and flow chart not presented • List of excluded studies not provided • Article selection and data extraction were not done in duplicate • Details of settings where ECT or rTMS were performed were lacking • Though quality assessment appears to have been conducted, results of assessments were not reported.
Ren,[14] 2014, China	• The objective was clearly stated. • The inclusion and exclusion criteria were stated. • Multiple databases were searched up to November 2013. • Study selection was described and flow chart was presented • List of included studies was provided • Data extraction was done in duplicate • Characteristics of the individual studies were provided but details of settings where ECT and rTMS were conducted were lacking • Quality assessments of studies	• List of excluded studies was not provided • Unclear if article selection was done in duplicate • Conflict of interest was not stated

First Author, Publication Year, Country	Strengths	Limitations
	were based on the Cochrane Handbook. The risk of bias was judged to be moderate and the overall quality of evidence assessed by the GRADE criteria appeared to be moderate • Methods used to combine the findings of studies were appropriate • Publication bias was explored and there appeared to low risk of publication bias	
Gaynes,[2] 2011, USA (AHRQ report)	• The objective was clearly stated. • The inclusion and exclusion criteria were stated. • Multiple databases were searched, 1980 to November 2010. Grey literature search was conducted. Also reference list of the relevant articles were manually searched. • Study selection was described but no flow chart was presented • List of included and excluded studies was provided • Article selection and data extraction were done in duplicate • Characteristics of the individual studies were provided • Quality assessments of studies were conducted using the AHRQ's Methods guide. Majority of the studies were judged to be of fair quality and the strength of evidence was mostly low. • Methods used to combine the findings of studies were appropriate • Publication bias was explored using Funnel plots and Kendell's test. However, considering the numbers of studies were small these tests have low sensitivity to detect publication bias. • The authors stated that there was no conflict of interest.	• The flow chart of the study selection process was not provided

First Author, Publication Year, Country	Strengths	Limitations
Randomized controlled trials (RCT)		
Brakemeier,[15] 2014, Germany	• Objectives were stated. • Inclusion/ exclusion criteria were stated. • Patient characteristics, interventions, and outcomes were described. • Patient characteristics appeared to be balanced as indicated by P-values • Randomized but method of randomization not described • Analysis was stated to be ITT • P values provided in some cases and in other cases mentioned as significant or not significant	• Patients and therapists were aware of treatment but the clinical evaluation team and outcome assessors were blinded • All patients had received ECT in the acute phase and hence the comparison between ECT and CBT is for add on therapy during continuation phase • Although antidepressant medications were distributed nearly equally across treatment groups, potential influences of concomitant medication and comorbidities cannot be ruled out • Sample size calculations not described • Conflict of interest was not mentioned • Generalizability limited as conducted at a single centre; uncertain as to whether study patients were representative of all patients.
Polster, [4] 2014, Germany	• Objectives were stated. • Inclusion/ exclusion criteria were stated. • Patient characteristics, interventions, and outcomes were described. • Randomized (stratified by age and gender) but method of randomization not described • Analysis appeared to be ITT though not explicitly stated • P values provided in some cases and in other cases mentioned as significant or not significant	• Proportion of males was much lower in the ECT group compared with the MST group. For other patient characteristics, there is uncertainty in comparability between the groups as p-values for were not provided. • Possible influences of concomitant medication and comorbidities cannot be ruled out • No blinding • Sample size calculations not described • Conflict of interest was not mentioned • Generalizability limited as conducted at a single centre; uncertain as to whether study patients were representative of all patients.

First Author, Publication Year, Country	Strengths	Limitations
Kayser,[16] 2010, Germany	• Objectives were stated. • Inclusion/ exclusion criteria were stated. • Patient characteristics, interventions, and outcomes were described. • Patient characteristics were stated to be comparable between groups • Randomization was stated to be done according to the Consolidated standards of reporting trials (CONSORT) but details of the randomization method were not described. • P values provided in some cases and in other cases mentioned as significant or not significant	• Possible influences of concomitant medication and comorbidities cannot be ruled out • No blinding • Sample size calculations not described • Unclear if the analysis was ITT • Authors disclosed their conflict of interest and apparently there were none. However the study was partially funded by the manufacturer of MST and the device was provided on loan for the study. • Generalizability limited as conducted at a single centre; uncertain as to whether study patients were representative of all patients.
AHRQ = = Agency for Healthcare Research and Quality; GRADE = Grading of Recommendations Assessment, Development and Evaluation		

APPENDIX 5: Main Study Findings and Authors' Conclusions

<table>
<tr><th>First Author, Publication Year, Country</th><th>Main Findings and Authors' Conclusion</th></tr>
<tr><td>Systematic reviews</td><td></td></tr>
<tr><td>Micallef-Trigona,[5] 2014, Malta</td><td>Main Findings:

Reduction in HRSD scores with treatment with ECT or rTMS in adults with MDD, considering 9 RCTs
<table>
<tr><th>Treatment (tx)</th><th>Reduction in HRSD score (mean ± SD)</th><th>P-value (after tx vs at baseline</th></tr>
<tr><td>ECT</td><td>15.42 ± 4.55</td><td>≤ 0.0005</td></tr>
<tr><td>rTMS</td><td>9.3 ± 4.45</td><td>≤ 0.0005</td></tr>
</table>
Combined effect sizes with treatment with ECT or rTMS in adults with MDD, considering 9 RCTs
<table>
<tr><th>Treatment (tx)</th><th>Model</th><th>Effect size</th><th>Standard error</th><th>95% CI</th></tr>
<tr><td>ECT</td><td>Fixed</td><td>2.17</td><td>0.13</td><td>1.90 to 2.43</td></tr>
<tr><td></td><td>Random</td><td>2.15</td><td>0.16</td><td>1.85 to 2.46</td></tr>
<tr><td>rTMS</td><td>Fixed</td><td>1.24</td><td>0.11</td><td>1.01 to 1.46</td></tr>
<tr><td></td><td>Random</td><td>1.28</td><td>0.15</td><td>0.97 to 1.58</td></tr>
</table>
Definitions:
Response and remission were measured using HRSD.
Response was defined as reduction in HRSD score by 50% or more.
Remission was defined as a final HRSD score of eight or less.

Authors' Conclusion:
"The results of this meta-analysis show that patients who undergo either rTMS or ECT have statistically significant reductions in their depressive symptoms, as measured by HDRS. …… When the degree of improvement between rTMS and ECT participants was analysed, those participants undergoing ECT showed significantly lower HDRS scores compared to those undergoing rTMS. When the effect size was factored into the comparison, the difference became even more significant in favour of ECT." P.5</td></tr>
<tr><td>Ren,[14] 2014, China</td><td>Main Findings:

Relative risks with rTMS versus ECT in adults with MDD or bipolar depression
<table>
<tr><th>Outcome[a]</th><th>No. of RCTs</th><th>No. of patients</th><th>RR (95% CI)</th><th>Heterogeneity I^2 value (%)</th></tr>
<tr><td>Response</td><td>7</td><td>279</td><td>1.52 (1.18 to 1.96)</td><td>34</td></tr>
<tr><td>Response[b]</td><td>6</td><td>219</td><td>1.41 (1.04 to 1.90)</td><td>36</td></tr>
<tr><td>Remission</td><td>7</td><td>275</td><td>1.42 (1.16 to 1.75)</td><td>38</td></tr>
<tr><td>Remission[b]</td><td>6</td><td>215</td><td>1.38 (1.10 to</td><td>43</td></tr>
</table></td></tr>
</table>

<table>
<tr><th>First Author, Publication Year, Country</th><th>Main Findings and Authors' Conclusion</th></tr>
<tr><td></td><td>
<table>
<tr><td></td><td></td><td></td><td>1.74)</td><td></td></tr>
<tr><td>Discontinuation</td><td>7</td><td>286</td><td>1.17 (0.66 to 2.08)</td><td>0</td></tr>
<tr><td>Discontinuation[b]</td><td>6</td><td>226</td><td>1.11 (0.49 to 2.53)</td><td>0</td></tr>
<tr><td colspan="5">[a]Outcomes refer to lack of response, remission and all-cause discontinuation
[b]Excluding one RCT that used low frequency rTMS. The other 6 RCTs used high frequency rTMS</td></tr>
</table>

Mean differences for rTMS versus ECT in adults with MDD or bipolar depression
<table>
<tr><th>Outcome</th><th>No. of RCTs</th><th>No. of patients</th><th>MD (95% CI)</th><th>Heterogeneity I^2 value (%)</th></tr>
<tr><td>HRSD score</td><td>8</td><td>311</td><td>2.81 (0.17 to 5.46)</td><td>64</td></tr>
<tr><td>HRSD score[a]</td><td>7</td><td>251</td><td>2.15 (-0.50 to 4.81)</td><td>50</td></tr>
<tr><td>MMSE score</td><td>3</td><td>NR</td><td>0.65 (-0.51 to 1.82)</td><td>20</td></tr>
<tr><td>Side effects</td><td>2</td><td>NR</td><td>0.19 (-1.84 to 2.22)</td><td>76</td></tr>
<tr><td colspan="5">[a]Excluding one study that used low frequency rTM. The other 7 RCTs used high frequency rTMS</td></tr>
</table>

Definitions:
Response was defined as reduction in HRSD score by 50% or more.
It was stated that the individual studies had pre-defined remission criteria.</td></tr>
<tr><td></td><td>Authors' Conclusion:
"In conclusion, ECT seemed more effective than and at least as acceptable as rTMS in the short term, especially in the presence of psychotic depression. This review identified the lack of good quality trials comparing the long-term outcome and cognitive effects of rTMS and ECT, especially using approaches to optimize stimulus delivery and reduce clinical heterogeneity." P.181</td></tr>
<tr><td>Gaynes,[2] 2011, USA (AHRQ report)</td><td>Main Findings:
Outcomes for rTMS versus ECT in adults with TRD (Tier1 studies: patients with ≥2 treatment failures)
<table>
<tr><th>Outcome</th><th>No. of studies</th><th>No. of patients</th><th>Strength of evidence</th><th>Finding</th></tr>
<tr><td>Response</td><td>1 (RCT)</td><td>42</td><td>low</td><td>No significant difference between the 2 groups (P =0.35)</td></tr>
<tr><td>Remission</td><td>1 (RCT)</td><td>42</td><td>low</td><td>No significant difference between the 2 groups (P = 0.65)</td></tr>
<tr><td>Change in depressive severity</td><td>1 (RCT)</td><td>42</td><td>low</td><td>Symptom severity improved with both ECT and rTMS but no significant difference between them (P = 0.86)</td></tr>
</table></td></tr>
</table>

First Author, Publication Year, Country	Main Findings and Authors' Conclusion

Cognitive functioning	2 (1 RCT & 1 cohort study)	72	insufficient	Some evidence indicates negative impact on cognitive function with ECT compared with rTMS however some evidence indicates no difference between the two treatments (one study showed significant effect in 1-week recall but both studies showed no significant effect on all other measures).
Withdrawal due to AE	1 (cohort study)	30	low	No difference in withdrawals between the ECT and rTMS groups (P value: NR).
Overall withdrawals	2 (1 RCT & 1 cohort study)	72	low	More withdrawals in the ECT group compared with rTMS group (P value: NR).

Outcomes for rTMS versus ECT in adults with TRD (Tier2 studies: patients with ≥1 treatment failures)

Outcome	No. of studies	No. of patients	Strength of evidence	Finding
Response	1 RCT	40	NR	No significant difference between the 2 groups (P = NS)
Remission	1 RCT	40	NR	No significant difference between the 2 groups (P = NS)
Change in depressive severity	1 RCT	40	NR	No significant difference between the 2 groups (P = NS)
Cognitive functioning	1 RCT	40	NR	No significant difference between the 2 groups (P = NS)

Outcomes for rTMS versus ECT in adults with TRD (Tier3 studies: patients with treatment failures not specified)

Outcome	No. of studies	No. of patients	Strength of evidence	Finding
Response	2 RCTs	106	NR	Response was significantly better in the ECT group compared with the rTMS group. For one RCT the response rate difference was 0.37 (95% CI 0.14 to 0.59) and for one RCT the response was 59% vs 17% (P= 0.005).

First Author, Publication Year, Country	Main Findings and Authors' Conclusion

Remission	2 RCTs	106	NR	Remission was significantly better in the ECT group compared with the rTMS group. For one RCT the partial remission rate difference was 0.26 (95% CI 0.03 to 0.51) and for one RCT the remission was 59% vs 17% (P= 0.005).
Maintenance of remission	3 RCT	147	NR	No significant difference between the 2 groups (P = NS in one RCT, P = 0.20 in one RCT and remission maintained at 50% in both groups in one RCT)
Change in depressive severity	1 RCT	45	NR	Significantly better improvement with ECT compared with rTMS (P = 0.017)
Cognitive functioning	2 (1 RCT & 1 cohort study)	74	NR	No significant differences between the two groups.
Withdrawals due to AE	2 (1 RCT & 1 cohort study)	74	NR	None in either group
AE	1 RCT	46	NR	No treatment related major AEs (i.e., seizure, induction, anesthetic complications, mania) were reported

Definition:
Response was defined as a decrease ≥ 50% or HRSD (17 item) score ≤ 10
Remission: Definitions of remission varied among the studies. The HRSD definition for the 17-item version was ≤7, ≤ 8, or <12 and for the 21-item version was ≤ 10. For the MADRS, the remission definition was a score of ≤ 8.

Authors' Conclusion:
"Our review suggests that comparative clinical research on nonpharmacologic interventions in a TRD population is early in its infancy, and many clinical questions about efficacy and effectiveness remain unanswered. Interpretation of the data is substantially hindered by varying definitions of TRD and the paucity of relevant studies. The greatest volume of evidence is for ECT and rTMS. However, even for the few comparisons of treatments that are supported by some evidence, the strength of evidence is low for benefits, reflecting low confidence that the evidence reflects the true effect and indicating that further research is likely to change our confidence in these findings. This finding of low strength is most notable in two cases: ECT and rTMS did not produce different clinical

<table>
<tr><th>First Author, Publication Year, Country</th><th>Main Findings and Authors' Conclusion</th></tr>
<tr><td></td><td>outcomes in TRD, and ECT produced better outcomes than pharmacotherapy. No trials directly compared the likelihood of maintaining remission for nonpharmacologic interventions. The few trials addressing adverse events, subpopulations, subtypes, and health-related outcomes provided low or insufficient evidence of differences between nonpharmacologic interventions. "
P. ES-16</td></tr>
<tr><td colspan="2">Randomized controlled trials (RCT)</td></tr>
<tr><td>Brakemeier,[15] 2014, Germany</td><td>Main Findings:
Outcomes with add on ECT compared to add on CBT during continuation phase for patients who were responders to ECT in the acute phase
<table>
<tr><th>Outcome</th><th>ECT
n (%)</th><th>CBT
n (%)</th><th>P value</th></tr>
<tr><td>Sustained response[a] - 6 month FU</td><td>10 (40)</td><td>13 (77)</td><td>0.02</td></tr>
<tr><td>Sustained response[a] - 12 month FU</td><td>7 (28)</td><td>11 (65)</td><td>0.02</td></tr>
<tr><td>Relapse[b] - 6 month FU</td><td>8 (32)</td><td>4 (24)</td><td>NA</td></tr>
<tr><td>Relapse[b] - 12 month FU</td><td>11 (44)</td><td>5 (30)</td><td>NA</td></tr>
<tr><td>Dropouts[c] 6 month FU</td><td>7 (28)</td><td>0 (0)</td><td>NA</td></tr>
<tr><td>Dropouts[c] 12 month FU</td><td>7 (28)</td><td>1 (6)</td><td>NA</td></tr>
<tr><td>Cognitive side effects</td><td>NA</td><td>NA</td><td>NS</td></tr>
<tr><td colspan="4">[a]Sustained response was defined as "the absence of relapse and dropout" P.198.
[b]Relapse was defined as "1) hospitalization of the patient for symptomatic worsening and/or when 2) increase of Hamilton scores apart by ≥18 points or higher at a continuation measurement time point or 3) increase from baseline ≥10 points." P. 198
[c]Dropout was defined as "discontinuation of the continuation therapies or not attending study visits" P. 198.</td></tr>
</table>
Authors' Conclusion:
"These results suggest that ultra-brief pulse ECT as a continuation treatment correlates with low sustained response rates. However, the main finding implicates cognitive-behavioral group therapy in combination with antidepressants might be an effective continuation treatment to sustain response after successful ECT in MDD patients." P. 194</td></tr>
<tr><td>Polster, [4] 2014, Germany</td><td>Main Findings:
Percentage recall of memorized words compared to baseline values; presented as mean ± SD
<table>
<tr><th>Outcome</th><th>ECT</th><th>MST</th><th>P value</th></tr>
<tr><td>Delayed recall on treatment day</td><td>23.2% ± 24.6%</td><td>51.1% ± 21.8%</td><td>0.015</td></tr>
<tr><td>Delayed recall on control[a] day</td><td>46.7% ± 21.6%</td><td>56.4% ± 24%</td><td>NS</td></tr>
<tr><td>Cued[b] recall on treatment day</td><td>86.3%</td><td>104.8%</td><td>NS</td></tr>
<tr><td>Cued[b] recall on control[a] day</td><td>104.5%</td><td>98.9%</td><td>NS</td></tr>
<tr><td colspan="4">[a] control refers to testing day without treatment
[b] provided cue to assist in recall</td></tr>
</table></td></tr>
</table>

<table>
<tr><th>First Author, Publication Year, Country</th><th>Main Findings and Authors' Conclusion</th></tr>
<tr><td></td><td>Authors' Conclusion:
"….our results confirm and extend a favorable side effect profile of MST compared to ECT with regard to acute memory function. We hope that the confirmed advantages of MST will improve therapy options for patients with severe depression." P.6</td></tr>
<tr><td>Kayser,[16] 2010, Germany</td><td>Main Findings:
Responses with ECT and MST using psychopathological measures
<table>
<tr><th rowspan="2">Outcome</th><th colspan="2">ECT</th><th colspan="2">MST</th><th rowspan="2">P value comparing mean difference with ECT vs MST</th></tr>
<tr><th>Baseline mean ± SD</th><th>Mean difference post treatment ± SD</th><th>Baseline mean ± SD</th><th>Mean difference post treatment ± SD</th></tr>
<tr><td>MADRS</td><td>26.3 ± 3.83</td><td>-10.2 ± 8.7</td><td>31.2 ± 6</td><td>-15.3 ± 8.8</td><td>NS</td></tr>
<tr><td>HDRS-28</td><td>25.8 ± 2.62</td><td>-11.9 ± 7.33</td><td>30.7 ± 5.03</td><td>-12.4 ± 11.9</td><td>NS</td></tr>
<tr><td>BDI</td><td>31.8 ± 12.97</td><td>-7.3 ± 6.17</td><td>36.5 ± 10.96</td><td>-10.7 ± 12.94</td><td>NS</td></tr>
<tr><td>HAMA</td><td>17.7 ± 4.29</td><td>-6.9 ± 5.65</td><td>22.4 ± 4.38</td><td>-9.5 ± 8.58</td><td>NS</td></tr>
<tr><td>SCL-90</td><td>102.1 ± 58.06</td><td>-29.4 ± 58.44</td><td>133.78 ± 59.47</td><td>-46.22 ± 54.18</td><td>NS</td></tr>
</table>
No statistically significant differences were observed in memory function between the ECT and MST groups.

Adverse effects: Some patients in the ECT group experienced headache, nausea or muscle pain after treatment. No side effects were observed in the MST group.

Authors' Conclusion:
"In conclusion, preliminary data have demonstrated equal antidepressant effect in MST as compared to ECT and no cognitive side effects. Further studies should clarify if MST could become an alternative treatment for patients suffering from treatment-resistant depression." P. 575</td></tr>
</table>

AHRQ = Agency for Healthcare Research and Quality; AE = adverse event; BDI = Beck depression inventory; CI = confidence interval; CBT = cognitive behavioral therapy; ECT = electroconvulsive therapy; HAMA = Hamilton anxiety scale; HRSD = Hamilton rating scale for depression; HRSD-28 = Hamilton rating scale for depression – 28 item; IPT = interpersonal psychotherapy; MADRS = Montgomery Ashberg depression scale; MD = mean difference; MDD = major depressive disorder; med = medication; MMSE = mini-mental status examination; MST = magnetic seizure therapy; NA = not available; NS = not significant; QoL = quality of life; rTMS = repetitive transcranial magnetic stimulation; TRD = treatment resistant depression; SCL = symptom checklist; SD = standard deviation; RD = treatment resistant depression; UP-D = uni polar depression; VNS = vagus nerve stimulation; vs = versus

APPENDIX 6: Guidelines and Recommendations

Guideline Society, Country, Author, Year	Recommendations
OMH guideline,[17] USA, 2012	"An ECT treatment team should be appropriately trained and consist of at least an ECT privileged psychiatrist, an anesthesia provider, and a recovery nurse. In addition, an ECT treatment nurse or assistant in the treatment room is recommended…." p. NA but refers to p. 109-112, 241-243 of APA[a] "The treatment site should include separate areas for waiting, treatment, and recovery. If outpatient ECT treatment is provided, there should also be space identified for patients and those accompanying the patient during the post recovery period. Policies should identify where ECT related equipment and supplies are stored within the treatment site……. Since ECT differs from other "typical" operative procedures, hospitals who designate general operating rooms, surgical suites, and/or common recovery rooms for ECT treatment should identify any additional equipment that is specific to the delivery of ECT and should be available during treatment. When such treatment sites are used, providers should delineate any additional steps that may be needed to assure patient privacy……" p.NA but refers to p. 117-118 of APA[a] "……Equipment should be available in both the ECT treatment area and the recovery area to provide suction; deliver intermittent positive-pressure oxygen; monitor vital signs, including cardiac rhythm and hemoglobin oxygen saturation. The treatment area should also contain equipment for intubation, seizure induction (brief pulse waveform ECT device), physiologic monitoring including EEG, and resuscitation. The recovery area should also contain ECG monitoring and pulse oximetry devices. More specifically, standard equipment in the treatment area includes: 1) stretcher or bed with side rails and the capacity to raise both the head and feet, 2) automatic or manual blood pressure monitoring device, 3) stethoscope, 4) ECT device with built-in EEG monitoring, 5) ECG monitoring equipment, 6) sphygmomanometer cuff to permit detection of ictal motor duration, 7) pulse oximeter, 8) oxygen delivery system, 8) suction apparatus, 9) intubation set for managing airways, and 10) reflex hammer. When treating patients who are at significantly increased risk of musculoskeletal injury (e.g. severe osteoporosis) or when using nondepolarizing muscle relaxant agents (e.g. curare, atracurium, mivacurium, rocuronium), it is recommended that a peripheral nerve stimulator be available to ensure the adequacy of muscle blockade before delivering the electrical stimulus. A defibrillator should be readily available. Access to a backup ECT device and additional cables is suggested; however, because of cost, this may not be reasonable in smaller hospitals/facilities. Staff responsibilities relating to equipment should be delineated including its availability in the treatment area, safety checks and general care and maintenance." p.NA but refers to p. 118 of APA[a] "Pharmacologic agents that may be required during ECT treatment should be identified. Such medications include: 1) primary anesthetic agent, 2) primary muscle relaxant, 3) an anticholinergic agent, 4) medications for first-line management of arrhythmias, hyper- or hypotension, and cardiac arrest, 5) medications for the initial management of severe bronchospasm or anaphylactic shock, other agents for managing status epilepticus, 6) antinausea medications,

Guideline Society, Country, Author, Year	Recommendations
	and 7) non-narcotic analgesics……..” p.NA but refers to p. 122-123 of APA[a] “Providers should assure availability of supplies needed in the ECT treatment area to induce anesthesia, monitor physiologic functions, and provide ventilation and resuscitation. ……” p.NA but refers to p.123-124 of APA[a]

APA = American Psychiatric Association; NA = not available

[a] APA’s The Practice of Electroconvulsive Therapy: Recommendations for Treatment, Training, and Privileging (2001)