Best Evidence Summaries of Topics in Mental Healthcare

BEST *in* MH *clinical question-answering service*

Question

In adults with a diagnosis of psychotic / delusional depression how effective is electroconvulsive therapy compared to treatment as usual (antidepressants and/or antipsychotics) in achieving improvement of symptoms, relapse rates, admission rates and physical and social functioning?

Clarification of question using PICO structure

Patients: Adults with psychotic/delusional depression
Intervention: Electroconvulsive therapy (ECT)
Comparator: Treatment as usual
Outcome: Improvement of symptoms, relapse rates, admission rates, physical and social functioning.

Clinical and research implications

No definite clinical implications can be made from the available evidence. There is a paucity of randomised controlled trials that evaluate the effectiveness of ECT in comparison with treatment as usual. Only one trial was found in the literature that appeared to address this BEST question. This study, however, compared ECT with combined nortriptyline hydrochloride and lithium carbonate – a treatment which may not be currently used in routine practice. Thus, more studies are required with different study medication combinations (such as a selective serotonin reuptake inhibitor and an anticonvulsant). The authors of the trial further suggested that more research is needed to explore individual patient characteristics (either historical or potential biomarkers) that can be used to predict which patients would do best with the different treatments available. They also suggested that more research is needed to identify effective strategies, including the possibility of combined modalities, for relapse prevention in mood disorders.

What does the evidence say?

Number of included studies/reviews (number of participants)
One systematic review (Parker 1992) and one randomised controlled trial (Kellner 2006) with two associated publications (Petrides 2001; 2011) appeared to meet the inclusion criteria for this BEST summary.

Main Findings
The authors of one review attempted to calculate a mean effect size for ECT in general (Parker 1992). As the authors did not report comparisons with other treatments evaluated in the included

studies (although they did attempt to conduct naïve indirect comparisons), or present data for specific outcomes, this review will not be considered further in this BEST abstract.
One RCT assessed the efficacy and tolerability of C-ECT compared with 50mg of nortriptyline hydrochloride and 600mg of lithium carbonate on relapse prevention in participants with unipolar major depression (Kellner 2006). The authors reported that there was no significant difference in relapse prevention between treatment groups and that more than half of the patients either experienced relapse or dropped out of the study – suggesting a somewhat limited efficacy. A subgroup analysis found that relapse rates after ECT were lower in patients with psychotic depression than in patients with non-psychotic depression (Petrides 2011). The authors also reported that in patients with psychotic depression, relapse rates were lower in those who received medication therapy than in those who received ECT, but statistical comparisons were not reported.

Authors Conclusions
The authors of the RCT concluded that both the C-Pharm and C-ECT demonstrated moderate protection against depressive relapse and that there was no statistical evidence to suggest that one treatment arm had greater efficacy in relapse prevention than the other. Based on subgroup analyses however, the authors concluded that psychotic and non-psychotic depression represent different nosologic entities and may require different treatment algorithms.

Reliability of conclusions/Strength of evidence
The included RCT had some methodological limitations, so that the reliability of the results are uncertain.

What do guidelines say?

NICE clinical guideline CG90 *Depression in adults* (2010) was consulted, no direct recommendations are made in respect to the treatment of psychotic depression with ECT.

Date question received: 12/04/2013
Date searches conducted: 18/04/2013
Date answer completed: 06/05/2013

References

SR

1. Parker G, Roy K, Hadzi-Pavlovic D, Pedic F. *Psychotic (delusional) depression: a meta-analysis of physical treatments*. Journal of Affective Disorders, 24 (1992) 17-24

Primary Studies

2. Kellner C, Knapp R, Petrides G, Rummans T, Husain M, Rasmussen K, Mueller M, Bernstein H, O'Connor K, Smith G, Biggs M, Bailine S, Malur C, Yim E, McClintock S, Sampson S, Fink M. *Continuation Electroconvulsive Therapy vs Pharmacotherapy for Relapse Prevention in Major Depression. A Multisite Study From the Consortium for Research in Electroconvulsive Therapy (CORE)***.** Arch Gen Psychiatry. 2006;63:1337-1344

3. Petrides, G., et al. (2001). "ECT remission rates in psychotic versus nonpsychotic depressed patients: a report from CORE." Journal of ECT 17(4): 244-253.

4. Petrides, G., et al. (2011). "Relapse rates in psychotic depression are lower than in non-psychotic depression after a successful course of Electroconvulsive Therapy (ECT)." Neuropsychopharmacology 36. http://www.nature.com/npp/journal/v36/n1s/full/npp2011293a.html

Results

Systematic Reviews

Author (year)	Search Date	Inclusion criteria	Number of included studies	Summary of results	Risk of bias
Parker (1992)	1988	Studies were eligible for inclusion in this review if they examined a population who were 'depressives' whose symptoms had psychotic features. The trials were required to have a common denominator. Treatments studied were limited to RCT, tricyclic antidepressants, monoamine oxidase inhibitors, antipsychotics, or a combination of these treatments.	44 studies were included in this review: 21 included an EC treatment arm.	The included studies were published between 1959 and 1988. Of the 21 studies that evaluated ECT, one explicitly also evaluated ECT in combination with a tricyclic antidepressant. The authors, however, stated that it was likely that a number of the ECT studies also involved unreported concurrent psychotropic medication. The systematic review authors calculated pre-post effect measures; they also derived a single effect size for each study if there were multiple outcomes. For ECT, the mean effect size was 2.30 (SD 1.52). (Outcome measures were not reported; the authors only reported a general measure of effect)	High

RCTs

Author (year)	Inclusion criteria	Number of participants	Summary of results	Risk of bias
Kellner (2006)	*Study Design* – Multisite randomised, parallel design, 6 months controlled trial (CORE). *Population* – Aged 18 – 85 years old. Participants were referred for ECT, determined by an attending level ECT psychiatrist. Those	Phase 1 N = 531 Phase 2 N = 201	Ten patients (3 in the C-ECT group and 7 in the C-Pharm group) did not receive a treatment and 7 patients (6 in the C-ECT group and 1 in the C-Pharm group) received 1 treatment but did not return for at least 1 postbaseline visit, yielding a modified intention-to-treat (ITT) efficacy evaluable sample of 184 patients	Unclear

	included in this study met DSM IV criteria for primary major depressive disorder, unipolar type, single or recurrent, and with or without psychosis. Additional inclusion criteria were pretreatment 24 item Hamilton Rating Scale for Depression (HRSD24) total score of 21 or higher and the ability to provide informed consent. *Intervention* – ECT standardised across all trial centres using the Thymatron DGX ECT device with bilateral electrode placement. Dose titration was employed in order determine seizure threshold at initial treatment, and stimulus dosing at subsequent treatments of 1.5 times the seizure threshold. Treatments were 3 times per week in phase 1 and weekly for 4 weeks, bi-weekly for 8 weeks, and monthly for 2 months in phase 2 (10 ECT sessions throughout 6 months, with the final session at week 20). *Comparison* – Participants received an initial dose of 50mg of nortriptyline hydrochloride and 600mg of lithium carbonate. Blood levels obtained 24 hours later were used to make recommendations regarding doses needed to achieve steady-state levels of 125ng/mL of nortriptyline and 0.7mEq/L of lithium. *Outcomes* - Depressive symptoms were measured with the HRSD24, administered at baseline and after each ECT treatment in phases 1 and 2. The primary outcome measure was time to relapse. Relapse was declared if at 2 consecutive ratings a patient's HRSD24 total	(randomised phase)	(89 in the C-ECT group and 95 in the C-Pharm group). In the C-ECT group, 37.1% relapsed, 46.1% remained remitted at study end, and 16.8% dropped out. In the C-Pharm group, 31.6% relapsed, 46.3% remained remitted, and 22.1% dropped out, with no statistically significant difference among groups in the 3 outcome categories (relapse, no relapse, and dropout). Among study completers (74 in the C-ECT group and 74 in the C-Pharm group), the relapse proportions were 44.6% (95% CI, 33.3%-55.9%) for C-ECT and 40.5% (95% CI, 29.4%-51.7%) for C-Pharm. Mean (SD) time to relapse for the C-ECT group was 9.1 (7.0) weeks compared with 6.7 (4.6) weeks for the C-Pharm group (*P*=.13) A Cox proportional hazards model regression analyses demonstrated that there was no significant difference between the two treatment groups for relapse rates (unadjusted hazard ratio: 1.1; 95% CI, 0.7-1.9; *P*=.63). These results were similar in adjusted analyses (adjustment for clinical centre, psychosis status, age, and sex): hazard ratio 1.2; 95% CI, 0.7-1.9; *P*=.53) The adjusted mean mMMSE scores for C-Pharm vs C-ECT were not significantly different at study end (6 months) among those who had not relapsed or dropped out (C-ECT: 48.4 (SE 0.5); C-Pharm: 49. (SE 0.5); *P*=.54). The mMMSE scores for both groups improved, on average, during the 6-month period, with a mean change from baseline not significantly different for the C-ECT and C-Pharm groups. The adverse effect profile of ECT included cognitive effects and minor adverse effects on treatment days of headache, nausea, and muscle aches (not described in further detail). The most common adverse events in the C-Pharm group were dry mouth (27.4%), tremor (17.9%), drowsiness and fatigue (14.7%), and	

	score was 16 or higher, with a minimum increase of 10 points from phase 2 baseline. The impact of ECT and Pharm on neurocognitive performance was measured by an extensive battery of neuropsychological tests measured at phase 2 baseline, 3 months, and 6 months. Patient performance on the mMMSE is reported as a measure of the neurocognitive effects of C-ECT and C-Pharm. The mMMSE is an expanded instrument that broadens the range of scores from a maximum of 30 on the standard MMSE to a maximum of 57. The mMMSE is a measure of global cognitive impairment that has shown sensitivity to ECT induced deficits, including recovery of functioning after. The Treatment Emergent Symptom Scale, although administered to both treatment arms, was used mainly to assess medication adverse effects in the C-Pharm arm. The Antidepressant Treatment History Form was used to determine degree of prior medication treatment failure. Compliance in the C-Pharm arm was assessed by measuring blood levels of nortriptyline and lithium at each study visit.		constipation (13.7%).	
Petrides 2001	This study reports phase 1 results of the CORE study (see Kellner 2006), therefore the inclusion criteria are as above. This study examined those participants with psychotic depression, looking at the comparative remission rates between psychotic and non-psychotic patients.	N = 253 (N=77 with psychotic depression & N=176 with non-psychotic depression)	For the full analysis set (treating premature exits as non-remitters), 75% of patients reached full remission status after the acute course of ECT, with an average of 7.8 (±3.3) treatments. Among psychotic depressed patients, 83% remitted compared with 71% of the non-psychotic depressed patients ($p < 0.04$); the odds of becoming a remitter was two times higher among the psychotic depressed than among the non-psychotic depressed patients (odds ratio [OR] 2.0; 95% CI: 1.02, 3.96).	NA

			For the completers of the acute ECT course (n =217), the overall remission rate was 87%. The remission rate for the psychotic patients was 95%, while for the non-psychotic patients it was 83% ($p < 0.01$). The number of ECTs received during the acute phase for psychotic and non-psychotic depressed were similar.	
Petrides 2011 (abstract)	This study reports a subgroup analysis of phase 2 resuclts of the CORE study (see Kellner 2006), therefore the inclusion criteria are as above. This study examined those participants with psychotic depression, looking at the comparative remission rates between psychotic and non-psychotic patients.	N = 184 (N=66 with psychotic depression & N=118 with non-psychotic depression)	The six month relapse rates were 28.8% (N=19) among the psychotic patients and 44.9% (N=53) among the non-psychotic (p =0.009), while 26.3% did not complete the study or exited prematurely. Among the patients in the C-ECT group, 32.3% of the psychotic patients relapsed, compared to 44.8% of the non-psychotic patients (p=0.159). In the C-PHARM group, the relapse rates were 25.7% and 45% respectively (p=0.22). Among patients with psychotic depression who received C-ECT, 48.4% remained remitted and among those who received the combination of lithium and nortriptyline, 65.7% remained remitted.	NA

Risk of Bias: SRs

Author (year)	Risk of Bias				
	Inclusion criteria	Searches	Review Process	Quality assessment	Synthesis
Parker 1992	☹	☹	☹	☹	☹

RCTs

Study	RISK OF BIAS					
	Random allocation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting
Kellner (2006)	☺	?	Not applicable	☺	☺	☹

☺Low Risk ☹High Risk ? Unclear Risk

Search Details

Source	Search Strategy	Number of hits	Relevant evidence identified
SRs and Guidelines			
NICE	ECT OR electroconvulsive	34	0
DARE	((psychosis OR psychotic OR schizo*) adj5 depress*) in DARE	66	1
Primary studies			
CENTRAL	#1 MeSH descriptor: [Affective Disorders, Psychotic] explode all trees 1468 #2 Enter terms for search psychosis or psychoticpsychosis or psychotic 4570 #3 Enter terms for search hallucinat*hallucinat* 1012 #4 Enter terms for search	67	2

	delusion*delusion* 580 #5 MeSH descriptor: [Depressive Disorder, Major] explode all trees 2006 #6 Enter terms for search depression or depressivedepression or depressive 31480 #7 Enter terms for search #1 or #2 or #3 or #4#1 or #2 or #3 or #4 6487 #8 Enter terms for search #5 or #6#5 or #6 31480 #9 Enter terms for search #7 and #8#7 and #8 2391 #10 MeSH descriptor: [Electroconvulsive Therapy] explode all trees 473 #11Enter terms for searcelectroconvulsive or ECT1060 #12Enter terms for searc#10 or #111060 #13Enter terms for searc#9 and #12169 (78 in CENTRAL)		
PsycINFO	1. PsycINFO; "psychotic depression".ti,ab; 907 results. 2. PsycINFO; (depression adj3 psychosis).ti,ab; 1081 results. 3. PsycINFO; (depression adj3 hallucinations).ti,ab; 188 results. 4. PsycINFO; (depression adj3 delusion*).ti,ab; 443 results. 5. PsycINFO; (depression AND "mood incongruent").ti,ab; 52 results. 6. PsycINFO; (depression AND "mood congruent").ti,ab; 172 results. 7. PsycINFO; (psychotic adj5 depression).ti,ab; 1825 results. 8. PsycINFO; 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7; 3469 results. 9. PsycINFO; ELECTROCONVULSIVE SHOCK THERAPY/; 4889 results. 10. PsycINFO; ECT.ti,ab; 5498 results. 11. PsycINFO; electroconvulsive.ti,ab; 5389 results. 12. PsycINFO; 9 OR 10 OR 11; 7558 results. 13. PsycINFO; 8 AND 12; 329 results. 14. PsycINFO; CLINICAL TRIALS/; 6674 results.	56	

	15. PsycINFO; random*.ti,ab; 117636 results. 16. PsycINFO; groups*.ti,ab; 342095 results. 17. PsycINFO; (doubl* adj3 blind*).ti,ab; 17160 results. 18. PsycINFO; (singl* adj3 blind*).ti,ab; 1460 results. 19. PsycINFO; EXPERIMENTAL DESIGN/; 8599 results. 20. PsycINFO; controlled.ti,ab; 73371 results. 21. PsycINFO; (clinical adj3 study).ti,ab; 7249 results. 22. PsycINFO; trial.ti,ab; 61920 results. 23. PsycINFO; "treatment outcome clinical trial".md; 23767 results. 24. PsycINFO; 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23; 526965 results. 25. PsycINFO; 13 AND 24; 56 results.		
Embase	26. EMBASE; "psychotic depression".ti,ab; 934 results. 27. EMBASE; (depression adj3 psychosis).ti,ab; 1379 results. 28. EMBASE; (depression adj3 hallucinations).ti,ab; 305 results. 29. EMBASE; (depression adj3 delusion*).ti,ab; 517 results. 30. EMBASE; (depression AND "mood incongruent").ti,ab; 54 results. 31. EMBASE; (depression AND "mood congruent").ti,ab; 132 results. 32. EMBASE; (psychotic adj5 depression).ti,ab; 1968 results. 33. EMBASE; DEPRESSIVE PSYCHOSIS/; 673 results. 34. EMBASE; 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33; 4364 results. 35. EMBASE; ELECTROCONVULSIVE SHOCK THERAPY/; 14772 results. 36. EMBASE; ECT.ti,ab; 7686 results. 37. EMBASE; electroconvulsive.ti,ab; 7806 results. 38. EMBASE; ELECTROCONVULSIVE THERAPY/; 14772 results. 39. EMBASE; 35 OR 36 OR 37 OR 38; 18262 results. 40. EMBASE; 34 AND 39; 540 results. 41. EMBASE; random*.tw; 795047 results. 42. EMBASE; factorial*.tw; 20523 results. 43. EMBASE; placebo*.tw; 187097 results.	67	

	44. EMBASE; (crossover* OR cross-over*).tw; 65083 results. 45. EMBASE; (doubl* adj3 blind*).tw; 135657 results. 46. EMBASE; (singl* adj3 blind*).tw; 15251 results. 47. EMBASE; assign*.tw; 219160 results. 48. EMBASE; allocat*.tw; 74396 results. 49. EMBASE; volunteer*.tw; 166113 results. 50. EMBASE; CROSSOVER PROCEDURE/; 36637 results. 51. EMBASE; DOUBLE-BLIND PROCEDURE/; 114019 results. 52. EMBASE; SINGLE-BLIND PROCEDURE/; 17227 results. 53. EMBASE; RANDOMIZED CONTROLLED TRIAL/; 340260 results. 54. EMBASE; 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53; 1297136 results. 55. EMBASE; 40 AND 54; 67 results.		
Medline	56. MEDLINE; "psychotic depression".ti,ab; 739 results. 57. MEDLINE; (depression adj3 psychosis).ti,ab; 973 results. 58. MEDLINE; (depression adj3 hallucinations).ti,ab; 199 results. 59. MEDLINE; (depression adj3 delusion*).ti,ab; 400 results. 60. MEDLINE; (depression AND "mood incongruent").ti,ab; 44 results. 61. MEDLINE; (depression AND "mood congruent").ti,ab; 105 results. 62. MEDLINE; (psychotic adj5 depression).ti,ab; 1477 results. 63. MEDLINE; 56 OR 57 OR 58 OR 59 OR 60 OR 61 OR 62; 2944 results. 64. MEDLINE; ECT.ti,ab; 5574 results. 65. MEDLINE; electroconvulsive.ti,ab; 6475 results. 66. MEDLINE; ELECTROCONVULSIVE THERAPY/; 9244 results. 67. MEDLINE; 64 OR 65 OR 66; 12808 results. 68. MEDLINE; 63 AND 67; 298 results. 69. MEDLINE; "randomized controlled trial".pt; 347102 results. 70. MEDLINE; "controlled clinical trial".pt; 85770 results.	33	

	71. MEDLINE; placebo.ab; 143370 results. 72. MEDLINE; random*.ab; 627981 results. 73. MEDLINE; trial.ti; 113189 results. 74. MEDLINE; CLINICAL TRIALS AS TOPIC/; 163996 results. 75. MEDLINE; 69 OR 70 OR 71 OR 72 OR 73 OR 74; 983432 results. 76. MEDLINE; exp ANIMALS/ NOT HUMANS/; 3802339 results. 77. MEDLINE; 75 NOT 76; 898588 results. 78. MEDLINE; 68 AND 77; 33 results.		
Summary	**NA**	**NA**	

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