Safety and Effectiveness of Maintenance ECT: the UK perspective

NACT, Gjøvik, Norway, May 22-24 2019

Prof George Kirov Cardiff University Cardiff & Vale NHS Trust





MRC An

Centre for Neuropsychiatric Genetics and Genomics



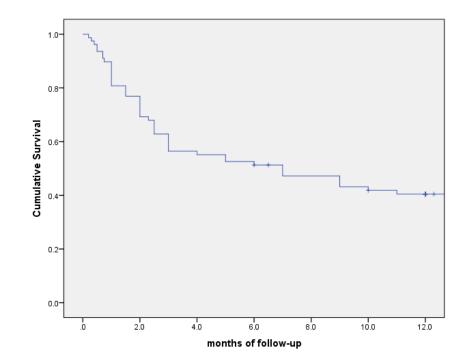
Relapse rate: Cardiff

2010:

Audited the outcomes of 49 patients who responded to ECT

40% relapsed in 3 months

60% relapsed in 12 months



Relapse Following Successful Electroconvulsive Therapy for Major Depression: A Meta-Analysis

Neuropsychopharmacology (2013) 38, 2467-2474

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b	Study	Relapse proportion	Lower limit	Upper limit	N relapses / valid N		se proportio 95% CI)	n
	Krog-Meyer 1984	0.182	0.046	0.507	2/11		- 1	
	Sackeim 1993	0.457	0.345	0.574	32 / 70		-	
	Grunhaus 1994	0.550	0.336	0.747	11/20	- 2	- • -	
	Shapira 1995	0.333	0.176	0.539	8/24	-	•	
	Lauritzen 1996	0.333	0.215	0.477	16/48	- L -	• I	
	Sackeim 2000	0.500	0.378	0.622	31/62		-	
	Meyers 2001	0.250	0.124	0.439	7/28	-	-	
	Sackeim 2001	0.500	0.362	0.638	24/48		- -	
	Dannon 2002	0.200	0.077	0.428	4/20		_	
	Birkenhager 2004	0.286	0.150	0.476	8/28	- I - I		
	Kellner 2006	0.405	0.300	0.520	30/74		- I	
	van den Broek 2006	0.182	0.046	0.507	2/11	-	_	
	Eranti 2007	0.500	0.244	0.756	6/12		→	
	Tew 2007	0.509	0.377	0.640	27 / 53		- -	
	Navarro 2008	0.125	0.031	0.386	2/16	-	- 1	
	Martinez-Amoros 2012	2 0.205	0.131	0.305	17/83			
	Prudic 2013	0.598	0.500	0.688	61 / 102	10075	•	
	Overall	0.377	0.307	0.452	288 / 710		 ↓ ↓ 	710 patients,
						0.00	0.50 1.0	0

6 months follow-up: 37.7% relapsed



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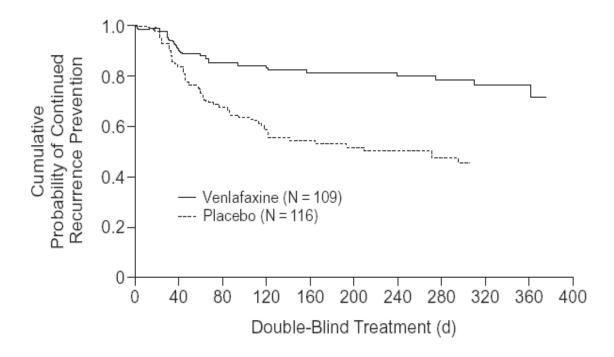
Study	Relapse proportion	Lower limit	Upper limit	N relapses / valid N	Relapse proportion (95% CI)
Spiker 1985	0.500	0.333	0.667	16/32	1 + 1
Sackeim 1993	0.586	0.468	0.695	41 / 70	- - -
Sackeim 2000	0.532	0.409	0.652	33 / 62	- → -
Birkenhager 2004	0.357	0.204	0.546	10/28	
Birkenhager 2005	0.418	0.296	0.551	23 / 55	
Navarro 2008	0.375	0.179	0.623	6/16	
Sackeim 2008	0.567	0.440	0.685	34 / 60	
Nordenskjold 2013	0.640	0.440	0.801	16 / 25	
Overall	0.511	0.447	0.574	179 / 348	+
					0.00 0.50 1.00

12-months follow-up, 51.1% relapsed



Relapse rates are high after stopping antidepressants

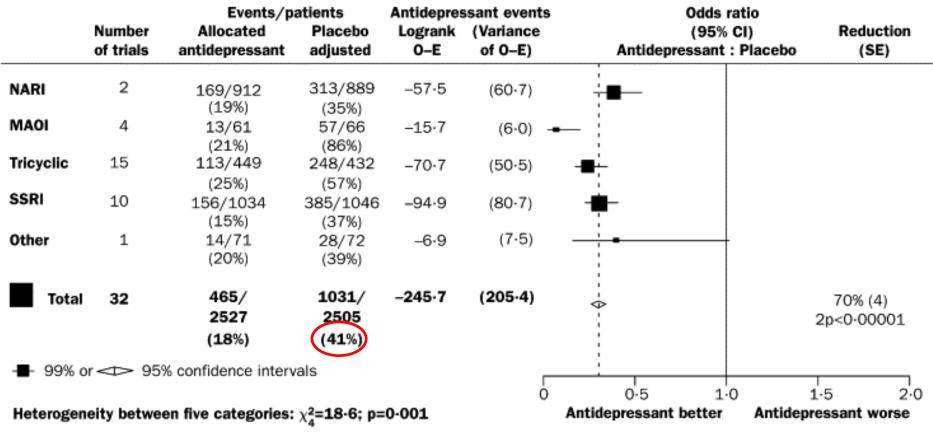
Figure 1. Cumulative Probability of Continued Recurrence Prevention Accounting for All Months of Double-Blind Treatment^a



J Clin Psychiatry 2004, 65:328-336. Venlafaxine v placebo in the preventive treatment of recurrent major depression

^ap < .001, venlafaxine vs. placebo.

Abrupt cessation of antidepressants triggers relapse



Treatment effect 2p<0.00001

John Geddes: Lancet 2003, 361:653-661

m-ECT in the UK: NICE guidelines, 2009

- Given the relative lack of data, the continuation/maintenance ECT is not recommended as a routine treatment
- Establish a national audit for the collection of data on all people receiving maintenance ECT

APA Guidelines

- APA Task Force Report (2001), reaffirmed 2015
- established the indications for c-ECT and m-ECT for patients who responded to an acute ECT course
- ...maintenance ECT may be considered

Use of c/m-ECT in different countries

Norway: 14% of patients in 88% of units
New York: 16% of ECT patients
Spain: 16% of patients
UK: 9% of patients in 68% of units

Manic switch

- A patient achieved remission after 8 ECTs. He develops a manic switch. What do we do?
- A: stop ECT
- B: continue twice a week
- C: continue at weekly intervals

Prospective studies support the effectiveness of m-ECT: Petrides *et al*, 2011

Study	Ν	duration	effect		
Wijkstra 2000	12	6 months	50% remain well		
Swoboda 2001	13	2-24 months	Stable MMSE, fewer hospitalisations		
Datto 2001	16	6+ months	Cognitive problems the day after ECT		
Rami-Gonzalez 2003	11	27 months	Poor cognitive frontal function, stable HDRS scores		
Vothknecht 2003	9	15 months	Stable cognitive function, improved depression		
Rami 2004	14	12 months	Stable cognitive and depression ratings		
Kellner 2006	89	6 months	Similar efficacy and tolerability to medication		
Odeberg 2008	16	4+ months	87% in remission		
Navarro 2008	16	2 years	Stable MMSE, only 1 relapse		
Nordenskjold 2013	28	12 months	32% relapse. Stable cognitive tests		

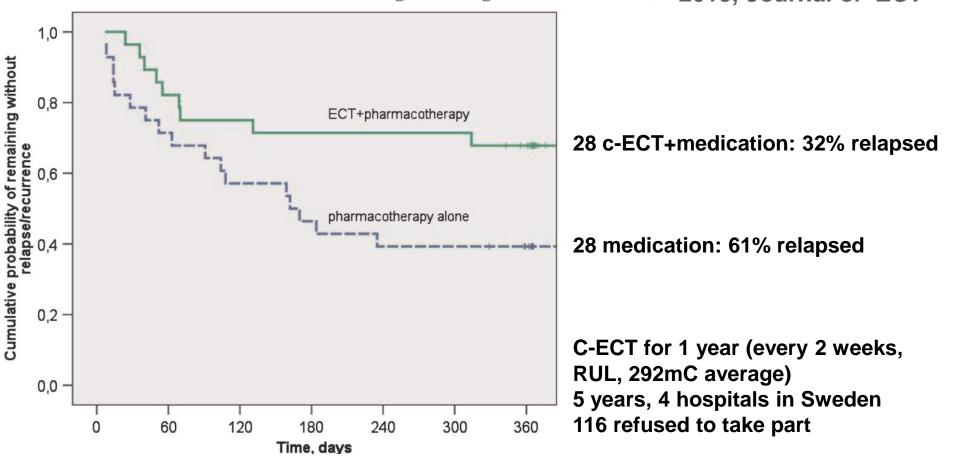
M-ECT: prospective studies

- Different frequencies of ECTs
- Variable duration
- Outcome: N admissions, N episodes, N days in hospital
- 30-50% relapse, stable depression ratings
- Patients did not present any serious adverse effects
- Cognitive function stable
- Concomitant antidepressants provide better efficacy

Continuation Electroconvulsive Therapy With Pharmacotherapy Versus Pharmacotherapy Alone for Prevention of Relapse of Depression

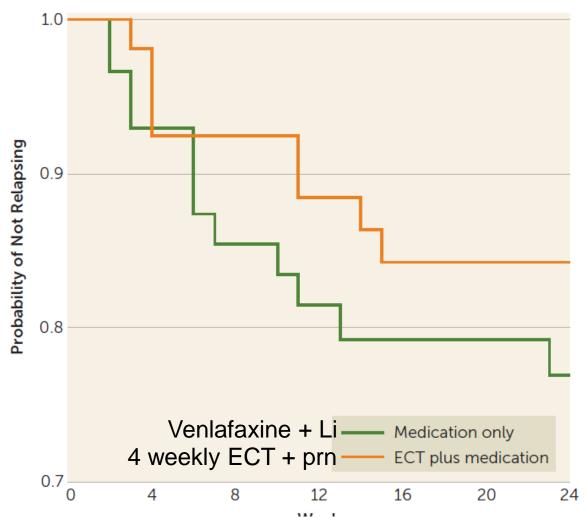
A Randomized Controlled Trial

Axel Nordenskjöld, MD, *† Lars von Knorring, MD, PhD, *‡ Tomas Ljung, MD,§ Andreas Carlborg, MD, PhD,//¶ Ole Brus, Msc, *# and Ingemar Engström, MD, PhD*† **2013, Journal of ECT**



A Novel Strategy for Continuation ECT in Geriatric Depression: Phase 2 of the PRIDE Study

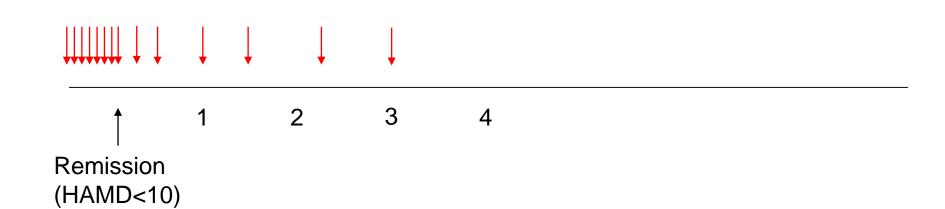
FIGURE 2. Time to Relapse for Patients in the ECT Plus Medication and Medication Only Treatment Arms in a Study of Continuation ECT in Geriatric Depression^a



McCall et al *J Psych Res* 2018. (Prolonging Remission in Depressed Elderly)

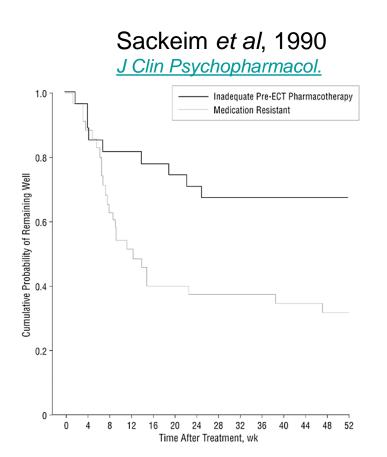
RUL, 120 patients 4 additional ECTs in weekly intervals, followed by more, if needed (4.5 average) Continuation ECT: Cardiff protocol, 2010

- Indications: high relapse risk (previous relapse, multiple episodes, chronic course)
- 6 continuation ECTs after reaching remission
- Follow-up for 12 months

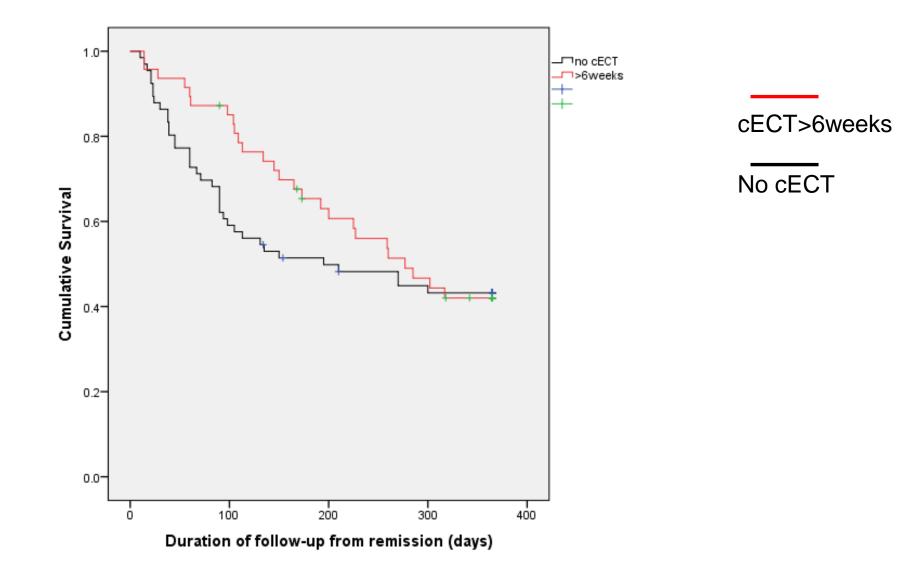


Who should be offered c-ECT?

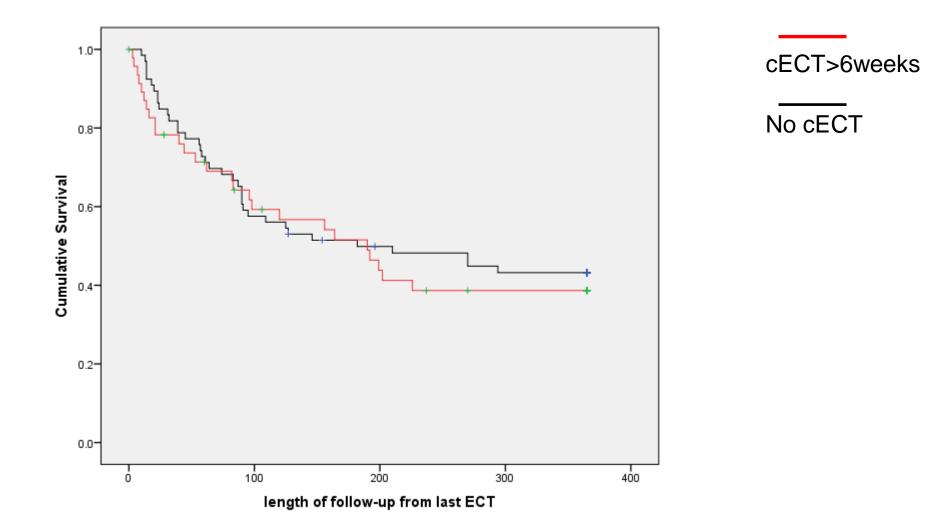
- Factors predicting relapse:
- Long duration of illness
- Delayed response
- Previous relapses
- Treatment resistance



Results: duration of remission



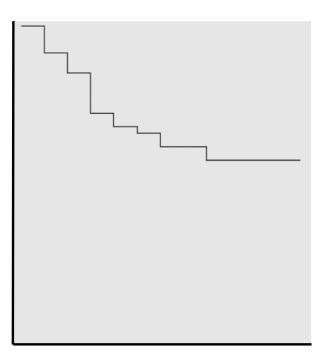
Duration of remission from last ECT: Effect is limited for the duration of c-ECT



One-Year Follow-Up After Discontinuing Maintenance Electroconvulsive Therapy

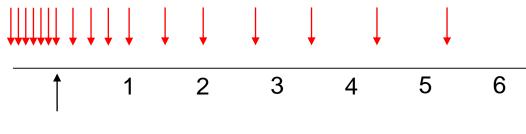
Kaija Huuhka, MD, PhD,* Merja Viikki, MD, PhD,†‡ Tarja Tammentie, RN, PhD,* Kati Tuohimaa, RN,* Minna Björkqvist, RN,* Hanna-Mari Alanen, MD, PhD,* Esa Leinonen, MD, PhD,*† and Olli Kampman, MD, PhD†§

45 patients from Finland28 ECTs on average, >1 year44% relapsed within one year.All 20 relapses within 8 months



Continuation ECT: Cardiff protocol, 2018

- Indications: high relapse risk (previous relapse, chronic course)
- Start continuation after achieving remission
- Continue c-ECT for 6 months
- Follow-up for 12 months



Remission (HAMD<10)

How to manage relapse? (SB)

56 y male patient achieves remission after 10 sessions. We give him 2 sessions once per week, then one every two weeks. After 4 weeks he relapses, feels suicidal. What should we do?

Continue at 2 week intervals Give weekly sessions Give twice a week sessions Stop ECT, as it is not working

How to manage relapse? (SB)

- He has ECT twice a week for 3 weeks. No response. What do we do?
- After 4 weeks achieves remission. Move to weekly again. Stabilises. After 6 months doing well, moving to 4-week intervals.

ECT does not cause cumulative cognitive deficits:

Kirov et al, 2016, Brit J Psychiatry

Evaluation of cumulative cognitive deficits from electroconvulsive therapy

George G. Kirov, Laura Owen, Hazel Ballard, Adele Leighton, Kara Hannigan, Danielle Llewellyn, Valentina Escott-Price and Maria Atkins

Background

Electroconvulsive therapy (ECT) is the most effective acute treatment for severe depression, but widely held concerns about memory problems may limit its use.

Aims

To find out whether repeated or maintenance courses of ECT cause cumulative cognitive deterioration.

Method

Analysis of the results of 10 years of cognitive performance data collection from patients who have received ECT. The 199 patients had a total of 498 assessments, undertaken after a mean of 15.3 ECT sessions (range 0–186). A linear mixed-effect regression model was used, testing whether an increasing number of ECT sessions leads to deterioration in performance.

Results

The total number of previous ECT sessions had no effect on cognitive performance. The major factors affecting performance were age, followed by the severity of depression at the time of testing and the number of days since the last ECT session.

Conclusions

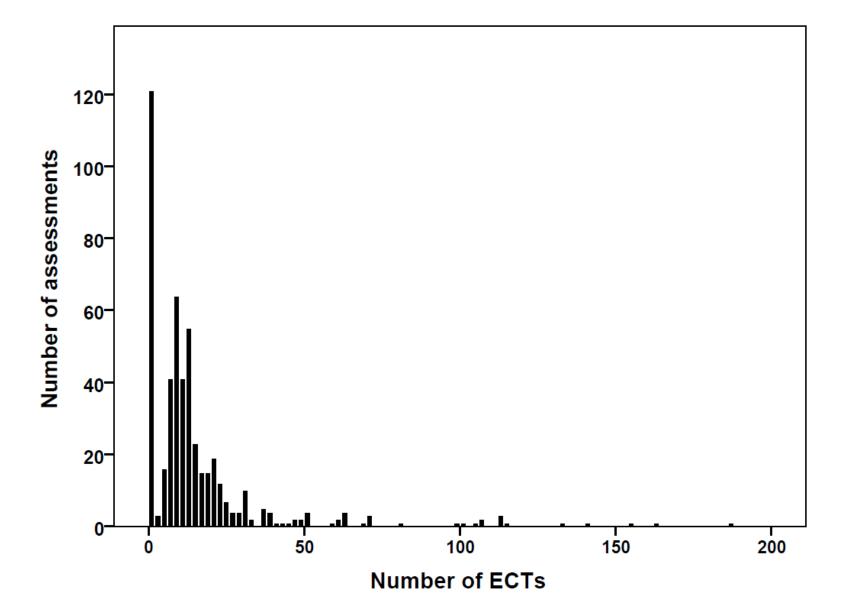
Repeated courses of ECT do not lead to cumulative cognitive deficits. This message is reassuring for patients, carers and prescribers who are concerned about memory problems and confusion during ECT.

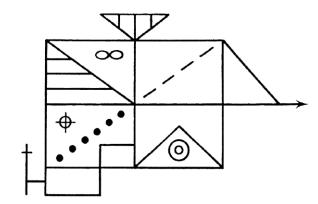
Declaration of interest

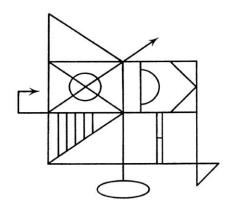
None.

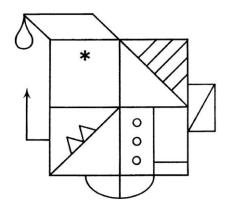
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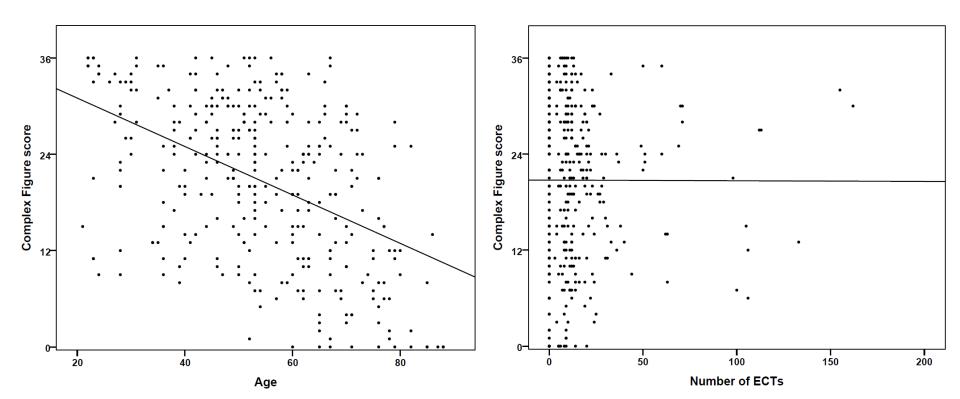
© The Royal College of Psychiatrists 2015.











Lack of cumulative cognitive deficits

Table 1 Statistical significance and effect size of the number of electroconvulsive therapy (ECT) sessions and the four covariates on the cognitive tests^a

	Digit Span	Recognition (memory)	Verbal fluency	MMSE	Complex figure	CFQ	Reaction time	Trail making A	Trail making B
Assessment, n	460	455	479	493	384	360	418	340	332
ECT sessions, <i>n</i> Effect size <i>P</i>	0.005 ns	-0.008 ns	-0.004 ns	0.005 ns	-0.004 ns	-0.02 ns	- 1.0 ns	0.02 ns	-0.5 ns
HRSD Effect size <i>P</i>	-0.01 0.03	-0.05 0.0006	-0.02 ns	-0.03 0.002	-0.03 ns	-0.5 9 × 10 ⁻¹⁰	-2.9 0.0007	-0.4 0.002	-1.8 0.003
Age Effect size <i>P</i>	-0.01 0.005	-0.08 6×10^{-10}	-0.05 0.005	-0.07 10 ⁻¹²	-0.3 8 × 10 ⁻¹⁴	0.3 8×10 ⁻⁶	-4.9 4×10^{-11}	-1.2 4 × 10 ⁻¹⁷	-4.7 3×10 ⁻¹⁵
Days since ECT Effect size P	-0.002 ns	0.5 0.0003	0.3 ns	0.1 ns	0.4 ns	-0.6 ns	6.8 ns	3.1 0.006	6.7 ns
Practice (repetition of test) Effect size P	0.05 ns	0.1 ns	0.1 ns	-0.02 ns	0.7 ns	0.2 ns	20.2 0.04	4.6 0.006	13.1 ns

MMSE, Mini-Mental State Examination, CFQ, Cognitive Failures Questionnaire; HRSD, Hamilton Rating Scale for Depression.

a. Results with P > 0.05 are shown as non-significant (ns). No correction for multiple testing is applied. Effect size indicates the degree of change on the cognitive test score by each unit of the variable. For example for the variable age, each year reduces the performance on the MMSE by 0.07 points, i.e. a patient who is 50 years older than another one, scores on average 3.5 points lower. All effect sizes have been converted so that a minus (-) sign always denotes a deterioration.

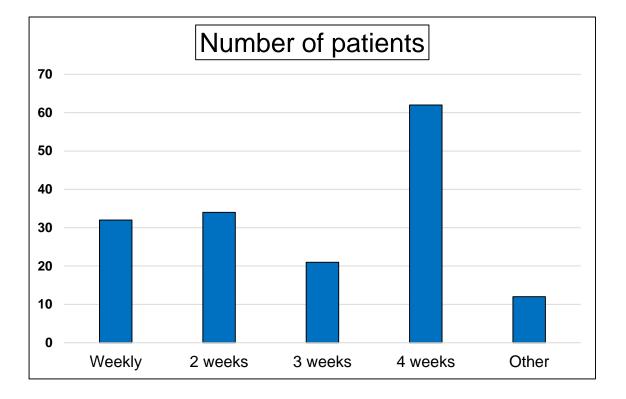
ECT Minimum Dataset 2014-15

Activity Data Report – England, Wales, Northern Ireland & Republic of Ireland

Editors: Nicky Buley, Sophie Hodge, Emma Hailey

Domain	2013	2015	2017
Number of people receiving maintenance ECT	160	155 (3% decrease)	161
Gender	76% female; 24% male	74% female; 25% male	74%
Mean age	67	65	66
Most common reason for referral	Recurrent symptoms of depression 92%	Recurrent symptoms of depression 92%	
Patient status	82% outpatients	83% outpatients	
Mental health act/capacity status	82% informal and capacitous	85% informal and capacitous	80%

Frequency of m-ECT sessions, 2017





Complete survey about (Subject)	7. Frequency of treatments: C Weekly Every 2 weeks Every 3 weeks Every 3 weeks Monthly Other If other, please state:
Data Set Questionnaire - Maintenance ECT Pat Please complete one questionnaire for each patient receiving maintenance or continuation ECT in March 2	 Inpatient Outpatient
1. Name of Trust	9. Clinical Global Impression (CGI) score at the time of the assessment:
2. ECT Clinic 3. Age of patient	10. Is ECT helping you? (patient's own assessment) Definitely Some benefit No effect
4. Gender of patient C Female Male	11. Do you have memory problems? (patient's own assessment) O No problems Occasionally Severe problems
5. Reason for Maintenance ECT: C Recurrent symptoms of depression Recurrent symptoms of mania Other If other, please state:	13. MOCA or MMSE used: MOCA MMSE Score:
6. Patient status: ^C Detained, capacitious ^C Detained, non-capacitous ^C Informal, capacitous ^C Informal, non-capacitous	Thank you for completing this questionnaire. Please press 'Submit' to send your responses to ECTAS.



CGI score	n
1 Normal, not at all ill	20
2 Borderline mentally ill	27
3 Mildly ill	11
4 Moderately ill	15
5 Severely ill	3
6 Amongst the most severely ill	1

Is ECT helping you? (patient report)				
Definitely	64			
Some benefit	26			
No effect	3			

Do you have memory problems?				
(patient report)				
No problems	28			
Occasionally	60			
Severe problems	5			

How to start maintenance? JM 80

- Achieved remission after 8 ECTs. This is his 3rd course, he relapsed before after 3-4 months. Ctarts m-ECT. His consultant suggests to start with 6-week intervals. Do we agree?
- Agreed. 5 months later still in remission
- Family worried about severe memory problems. What should we do?
- Switch to RUL, working and memory much improved

Safety of m-ECT Case study

- Maintenance patient, female, 70 y, needs weekly ECTs and high electric charges
- Each time has 3-4 minutes bigeminy
- Developed salvos of 4 ventricular complexes, uneventful recovery.