C/M ECT in Different Patient Populations

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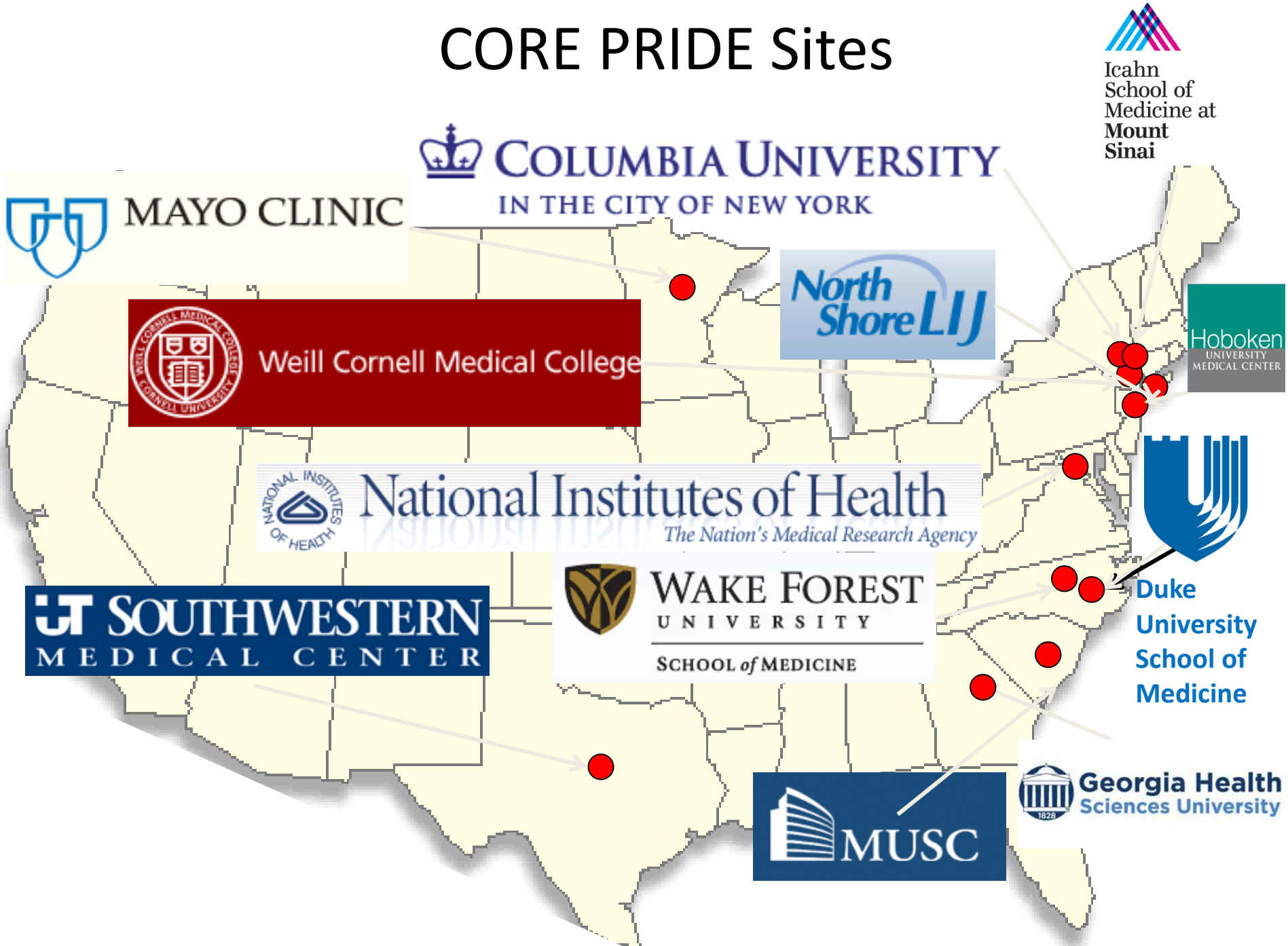
Disclosures

- NIMH (prior grant support)
- UpTo Date (honoraria for writing ECT sections)
- Cambridge University Press Royalties
- NorthWell Health System
- (honoraria for teaching ECT course)
- Psychiatric Times (honoraria for writing ECT sections)

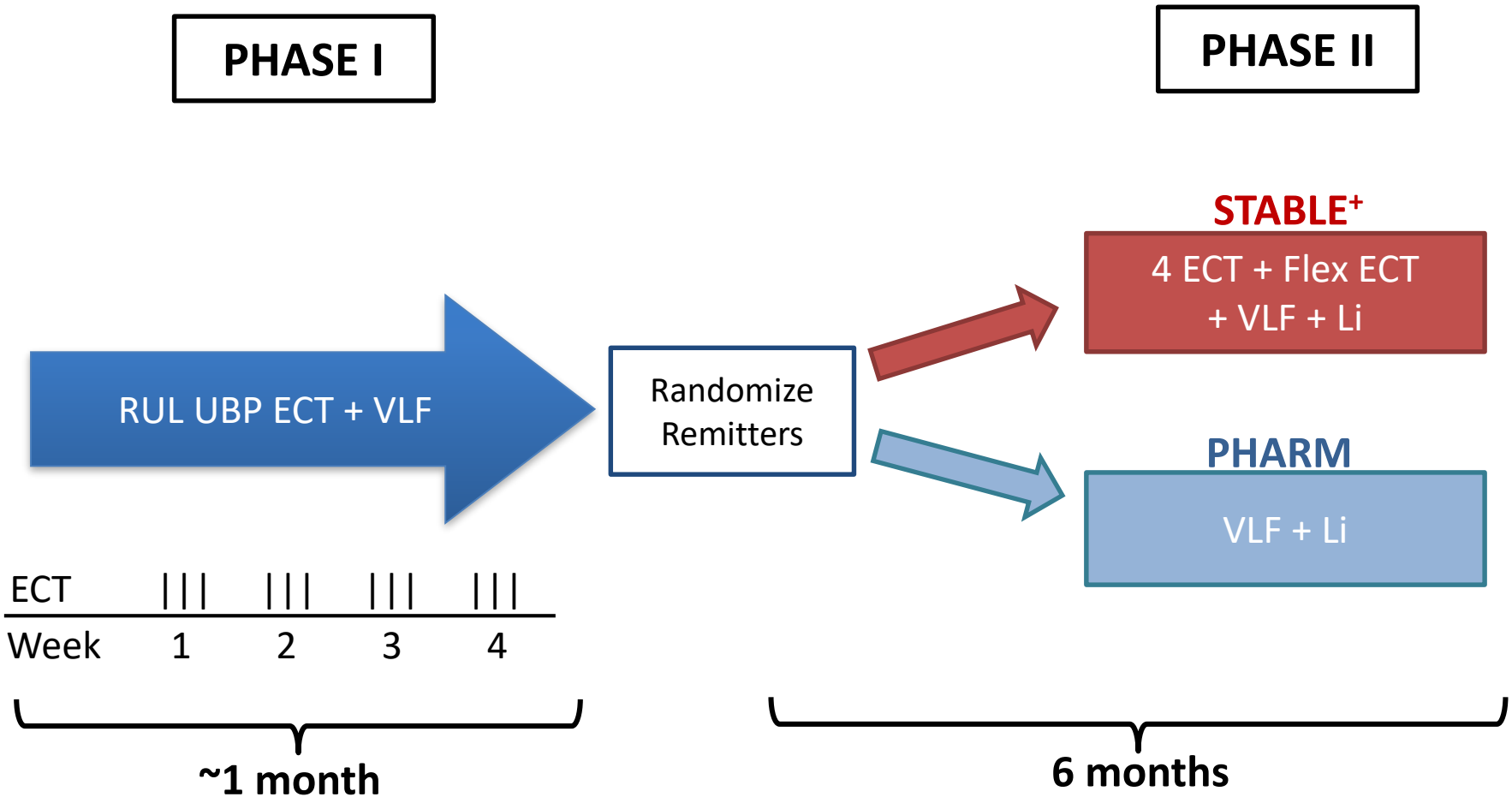
Patient Populations

- Mood disorders
    - Geriatric
- Schizophrenia
- Parkinson's Disease
- OCD
- PTSD
- Autism with SIB

CORE PRIDE Sites



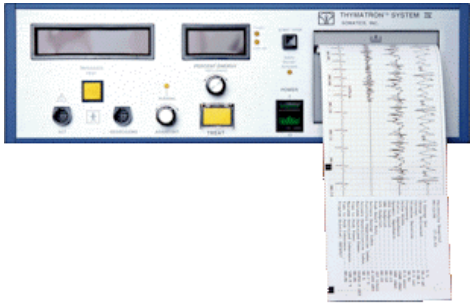
Prolonging Remission in Depressed Elderly (PRIDE)



PRIDE Selection Criteria

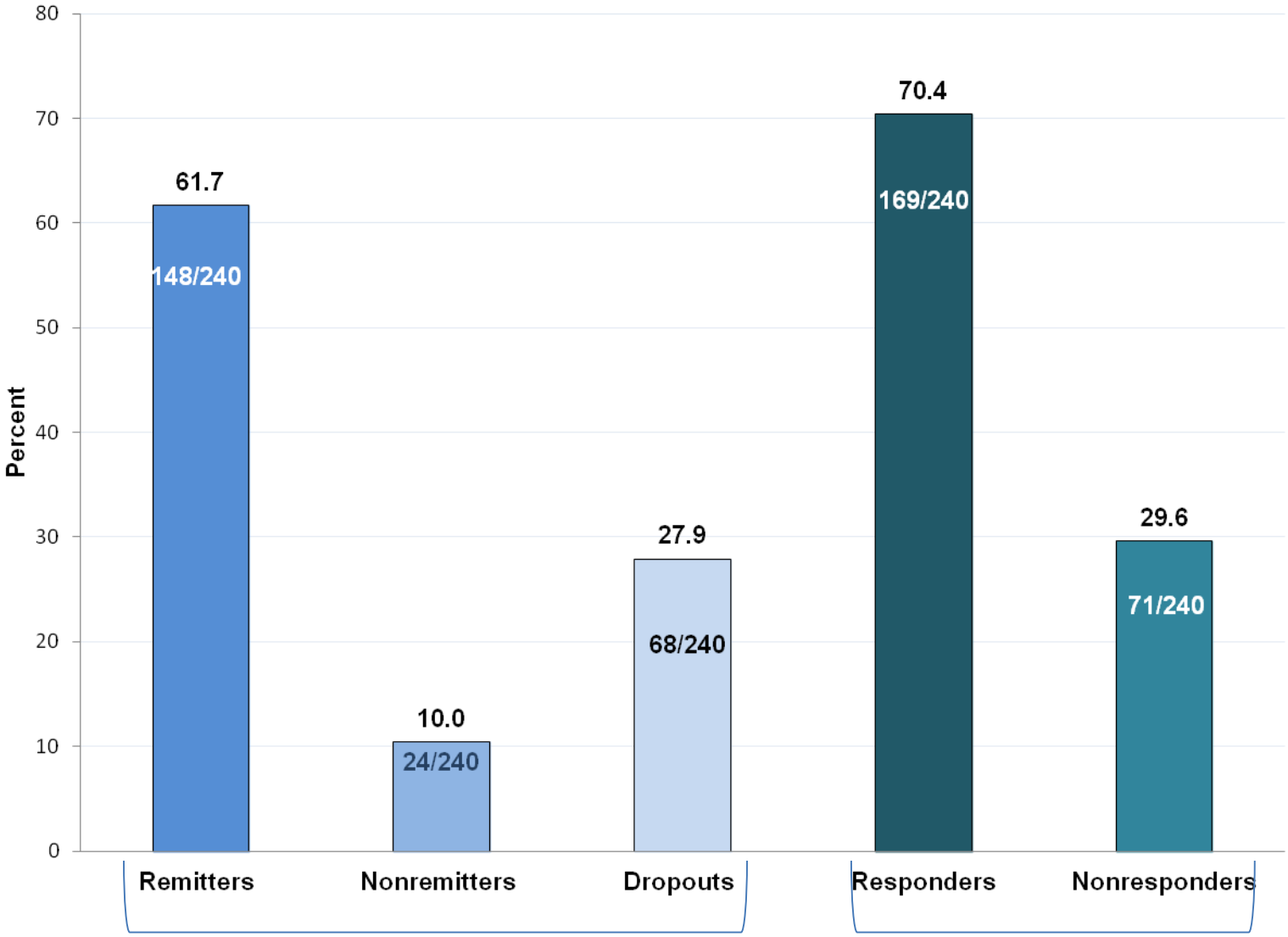
- **Inclusion**
  - ≥60 yr, MDE, Unipolar (MINI)
  - Baseline HRSD≥21 (24-item)
  - ECT clinically indicated, competent to give consent
- **Exclusion**
  - bipolar disorder, schizophrenia, schizoaffective disorder, mental retardation
  - delirium, dementia, or substance abuse/dependence in past 6 months
  - general medical condition or CNS disease that may affect cognition or response to treatment.
  - medical condition contraindicating Li or VLF
  - Failure to respond to adequate trial of Li + VLF, or ECT, in the current episode, or history of intolerance to Li or VLF.

PRIDE ECT Procedures



- Dose Titration (5, 10, 15, 20 %)
- 6x Seizure Threshold RUL (0.25 ms) ECT 3/wk
- Anesthesia
  - Glycopyrrolate (0.2 mg IV) (first procedure only)
  - Methohexital (0.75 mg/kg)
  - Succinylcholine (0.75 mg/kg)
- Adequate seizure ≥15s motor
- Midcourse dose increase if response plateaus

PRIDE Phase I Remission[1] and Response Proportions[2]



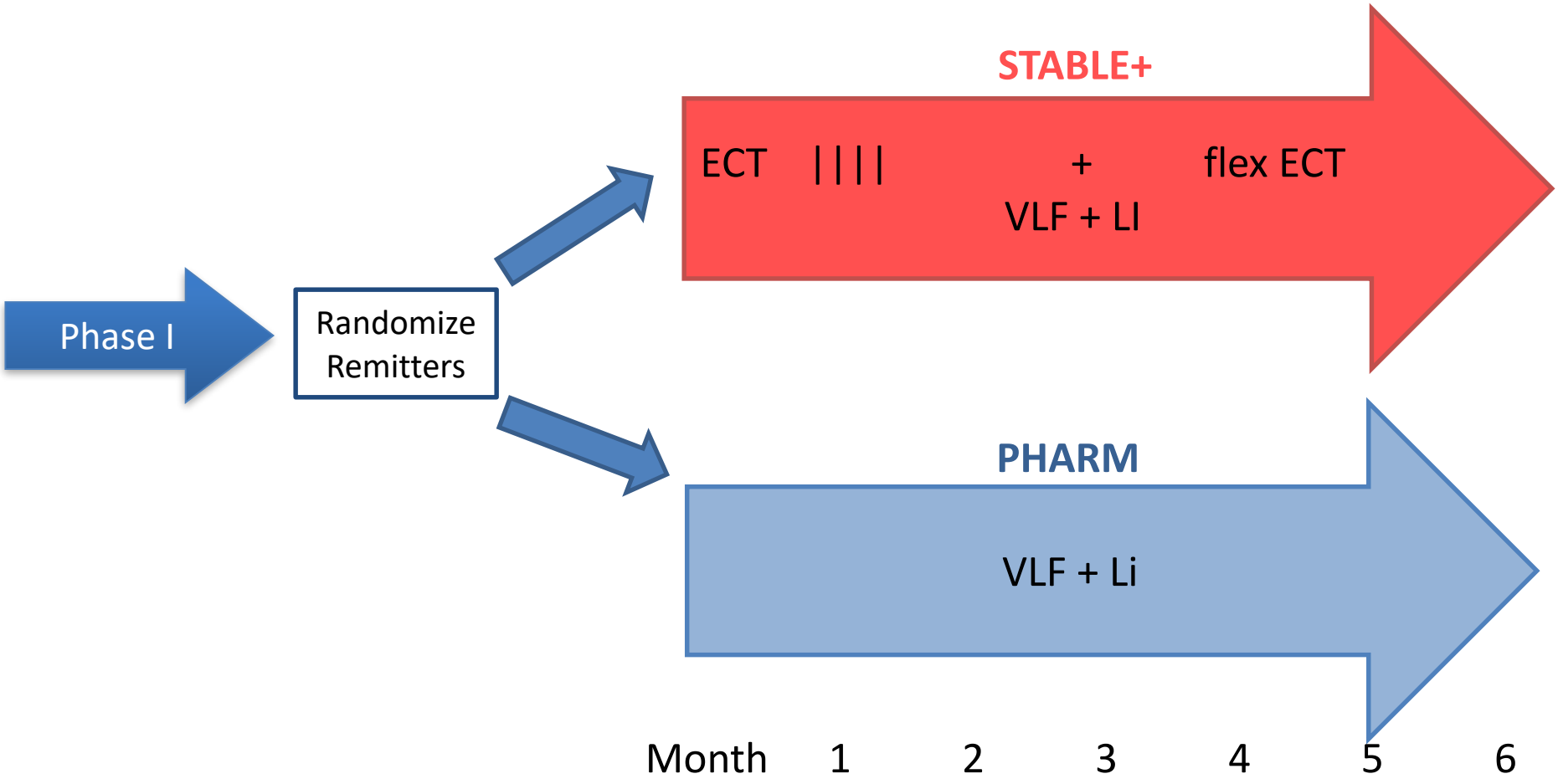
[1]Remission: Last two $HRSD_{24} \leq 10$

[2]Response: ≥ 50% decrease $HRSD_{24}$ (Baseline - Last)

PRIDE Phase I Conclusions

- RUL-UBP ECT is a viable treatment technique for geriatric depression
- RUL-UBP is rapidly acting (including on suicidality)
- RUL-UBP is generally well-tolerated

PRIDE Phase II



Symptom-**T**itrated **A**lgorithm-**B**ased **L**ongitudinal **E**CT

STABLE

STABLE Algorithm

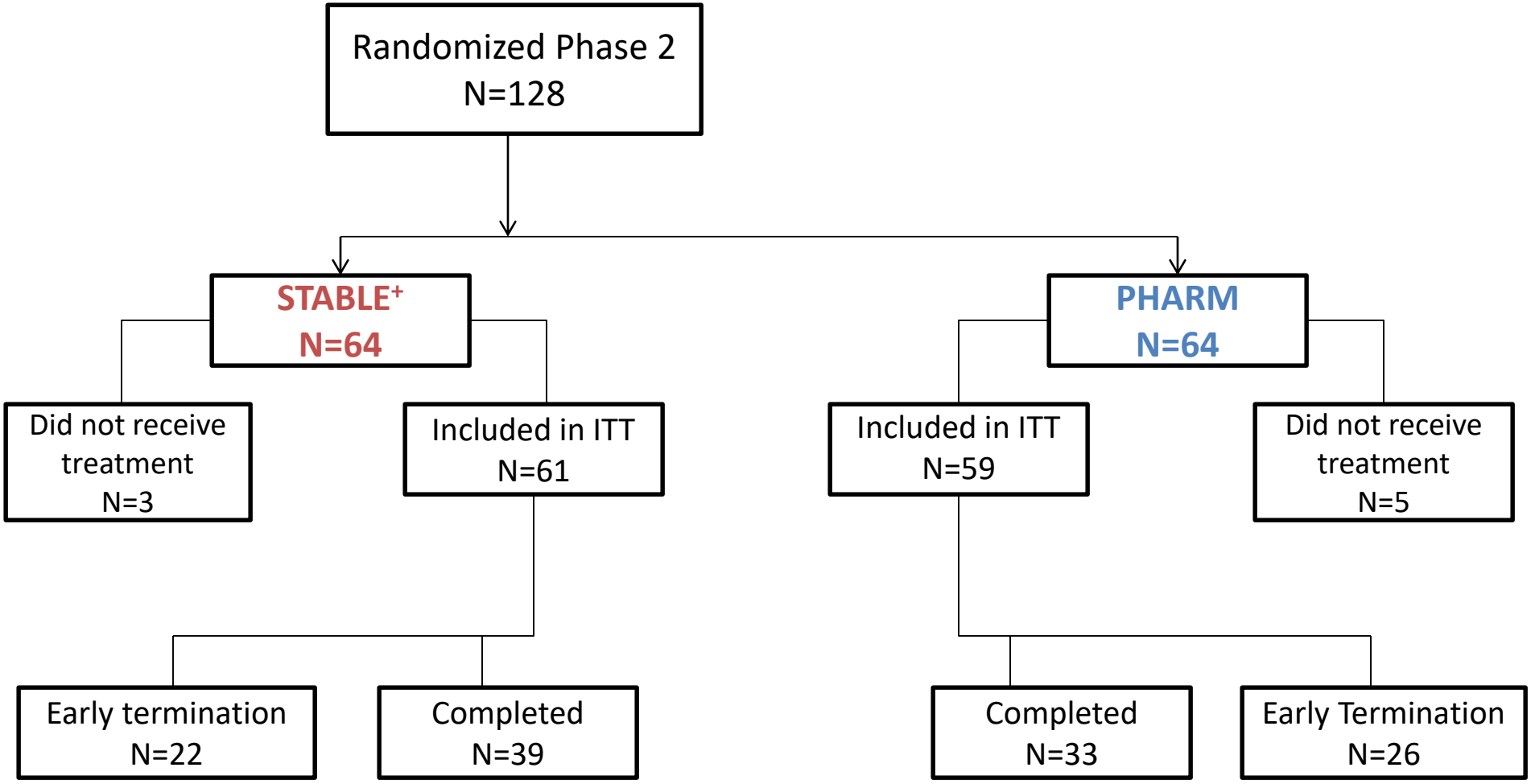
Phase 2: Weeks 1-4: Fixed ECT Schedule: 1 ECT 2-5 days after randomization, 1 ECT 7-12 days after randomization, 1 ECT 14-19 days after randomization, 1 ECT 23- 28 after randomization (Total = 4 ECT in one month

Phase 2: Weeks 5-24: Symptom Titrated Schedule

Number ECT per week	Description	Corresponding HAM-D Condition	Relapse potential
0	**Current symptomology level very low**, *or*	HAM-$D_C \leq 6$, *or*	Low
	Current symptomology level low to moderate, with only small drift from baseline level, *or*	$7 \leq$ HAM-$D_C \leq 12$ *and* HAM-D_C-HAM-$D_B \leq 2$, *or*	Low
	Last 2 HAM-D in remitted range with flat trajectory (remission stable with less than 2 point change from previous)	$7 \leq$HAM-$D_C \leq 10$ *and* $5 \leq$HAM-$D_P \leq 10$ *and* (HAM-D_C-HAM-D_P) ≤ 2	Low
2	**Current symptomology level very high**, *or*	HAM-$D_C \geq 16$, *or*	High
	Current symptomology level moderate to high, with trajectory increasing rapidly and large drift from baseline	$11 \leq$ HAM-$D_C \leq 15$, *and* (HAM-D_C-HAM-D_P) ≥ 3, *and* (HRSD_C-HRSD_B) ≥ 8	High
1	**Patients not requiring 0 or 2 received 1 ECT**	HAM-D_C intermediate between criteria for "low" or "high" relapse potential	Moderate
Discontinue study	HAM-D_C *and* HAM-$D_P \geq 21$, or patient suicidal, or patient requires psychiatric hospitalization		

[a]HAM-D_B= baseline HAM-D; HAM-D_C=current visit HAM-D; HAM-D_P= previous visit HAM-D (visit preceding current visit)

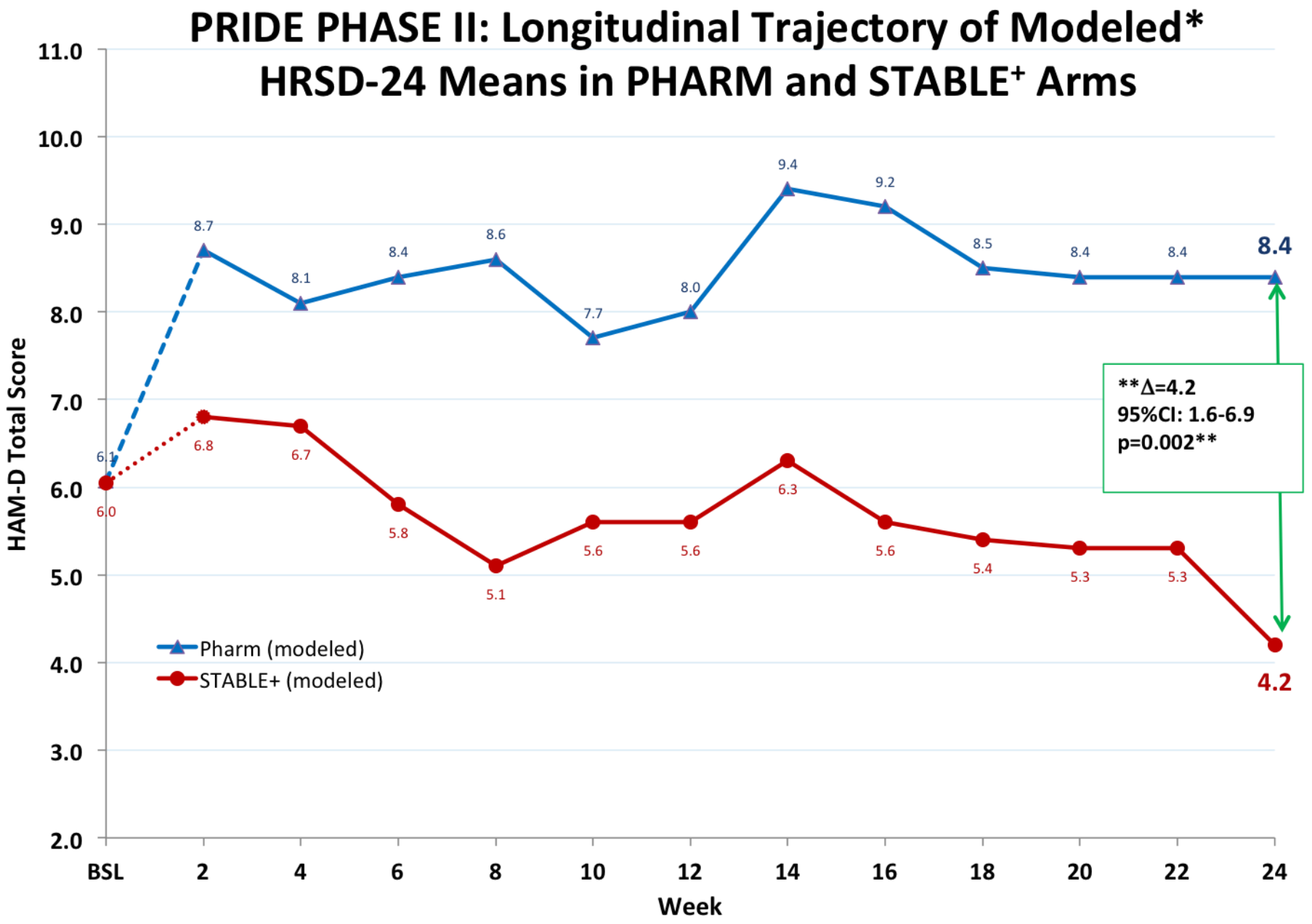
PRIDE Phase II Consort Chart



Li and VLF in Phase II

- VLF dose (mean): 192 mg (no difference between arms)

- Li level (mean): 0.53 mEq/l (PHARM)
- Li Level (mean): 0.36 mEq/l (STABLE^{+})



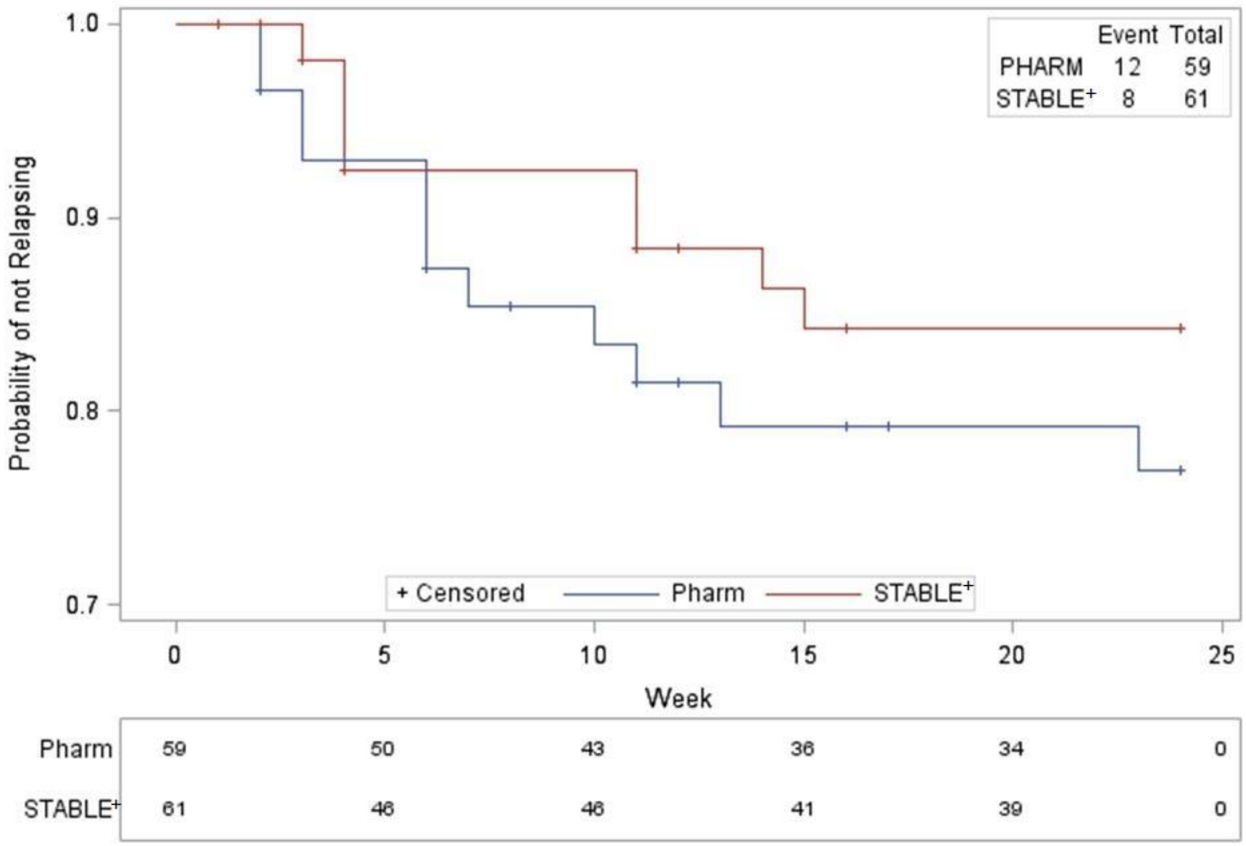
*Model contains treatment, time, treatment-by-time with HRSD baseline, site, psychosis as adjustment covariables

** Δ=4.2 is difference in baseline, site, psychosis adjusted least squares means for STABLE+ vs PHARM

PRIDE Phase II Results

- At 6 month study endpoint, mean HRSD-24 score for STABLE^{+} = 4.2 vs PHARM = 8.4 (p=0.002)
- CGI-S: odds of being rated “not at all ill” were 5.2 times greater for STABLE^{+} vs PHARM
- Odds of relapsing 1.7 times higher for PHARM vs STABLE^{+}
- 34.4% (21/61) of STABLE^{+} patients received at least one additional ECT in weeks 5-24

PRIDE PHASE II: Time to relapse for patients in STABLE^{+} and PHARM treatment arms



Relapse* by Treatment Group

- Overall Relapse Rate: 16.7%

- PHARM Relapse Rate: 20.3%
- STABLE+ Relapse Rate: 13.1%

*Relapse defined as when a patient was removed from the study for safety because of worsening of MDD requiring alternative treatment (2 consecutive $HRSD_{24} \geq 21$, or patient required psychiatric hospitalization, or patient became suicidal).

PRIDE PHASE II Conclusions

- STABLE^{+} was superior to PHARM in maintaining low depression symptom severity for 6 months after remission
- RUL UBP was safe and well tolerated
- Practitioners should be liberal in prescribing additional ECT past the acute course (taper, continuation/maintenance)
- Aim is to prevent full syndromic relapse and its attendant catastrophic consequences

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Review article

Maintenance ECT in schizophrenia: A systematic review

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ABSTRACT

Relapse after discontinuation of ECT is significant in patients with schizophrenia. The purpose of this systematic review was to examine use of M-ECT in schizophrenia to guide clinical decision making for relapse prevention in schizophrenia. We reviewed studies examining the role of continuation (C-ECT) and maintenance electroconvulsive therapy (M-ECT) in schizophrenia. Following PRISMA guidelines, we included randomized controlled trials, open label trials, retrospective chart reviews, case reports, and case series in this review. We evaluated adjunctive pharmacological regimens; ECT treatment parameters, including frequency, duration of continued treatment, electrode placement; clinical outcomes including cognitive side effects and relapse rates from included studies. Our findings suggest M-ECT could provide an effective form of relapse prevention in these patients and persistent cognitive side effects are minimal.

A Case of Long-Term Maintenance ECT in a 78-Year-Old with Depression and Possible Parkinson's Disease

To the Editor: ***February 21, 2007***

Electroconvulsive therapy (ECT) is a well-established treatment modality in psychiatry. However, much concern has been raised about the possible cognitive effects of long-term ECT.

This case report concerns a 78-year-old woman with depression and Parkinson's-like symptoms who has continued to receive maintenance ECT for 6 years with intact cognitive status.

ECT is an efficacious treatment option for major depression, especially with melancholic features, cases that are medication resistant or are acutely suicidal, and those with associated psychotic features. There is also sufficient data[1] to suggest that ECT helps in movement disorders, especially Parkinson's disease.

Here we report a case of Ms. J, a 78-year-old single black woman with a long-standing history of major depression, recurrent with psychotic features. Ms. J has been receiving long-term maintenance ECT (6 years duration), initially monthly, but in order to maintain complete remission and euthymia, she has required biweekly treatments for over 1.5 years.

Ms. J has a past psychiatric history significant for several psychiatric hospitalizations and suicide attempts by overdose. Up until early 2000, she had been relatively stable on a combination of fluoxetine 20 mg/day and thiothixene 8 mg/day without significant extrapyramidal symptoms. She developed medication resistance in late 2000 and received an acute course of ECT, followed by continuation and maintenance ECT. She continues to receive such treatments to date. When euthymic, Ms. J is usually neatly dressed, has no gross psychomotor abnormality, is bright, cheerful, and interactive with a fairly preserved cognitive status. Her Mini-Mental Status Exam scores usually range between 25/30 and 28/30. However, in the rare instance that she does not receive ECT at the requisite frequency, she shows a rapid decline not only in terms of mood and appearance of psychotic symptoms, but also in her gait, cognition, and appearance of pseudoparkinsonian symptoms, such as rigidity, mask-like faces, and tremors. Over the years, successful maintenance ECT has not only helped her to continue to live independently, it has preserved her mental status as well.

This case highlights several points. First, it reiterates that for some resistant cases long-term maintenance ECT may be the only successful treatment option.

Second, cognitive impairment is not necessarily a consequence of long-term maintenance ECT.[2] In this case, maintenance ECT has improved the patient's cognition throughout acute episodes of depression, and has enabled her to live independently as opposed to being committed to a state hospital or group home for the rest of her life.

Lastly, we suggest that this might be a case of long-term maintenance ECT not only for depression but also for parkinsonism. It has been difficult to clearly delineate whether or not this patient's motor symptoms are a state related feature or symptoms of true Parkinson's disease, as mood and neurologi-

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Editorial

ECT for Parkinson's disease

ARTICLE INFO

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SUMMARY

Parkinson's disease (PD) is a chronic, progressive, degenerative disorder that affects over five million people worldwide. Pharmacotherapy with dopamine enhancing medications is the mainstay of treatment. Neurosurgical techniques, ranging from pallidotomy to deep brain stimulation (DBS) are used in refractory patients. Another treatment, electroconvulsive therapy (ECT), has repeatedly been shown to have beneficial effects in PD, but has never gained acceptance as a clinical treatment option. We review the literature on the use of ECT in PD, pointing out that ECT has beneficial effects on both the core motor symptoms of PD as well as the commonly occurring psychiatric co-morbidities. ECT is hypothesized to act in PD by enhancing dopamine neurotransmission, including increasing sensitivity of dopamine receptors. The beneficial effects of ECT in PD persist for variable periods. Maintenance ECT has been used to increase the length of benefit. The stigma surrounding ECT has likely been responsible for its lack of use in PD. We suggest that ECT has a role in the treatment of PD, both in patients with PD alone, or PD with co-occurring depression.

ECT for Parkinson's Disease

- May need to decrease dopamineric drugs
- RUL electrode placement preferred
- Ultrabrief pulsewidth stimuli may be preferred

J Clin Psychiatry. 2015 Jul;76(7):949-57. doi: 10.4088/JCP.14r09129.

Electroconvulsive therapy for obsessive-compulsive disorder: a systematic review.

Fontenelle LF[1], Coutinho ES, Lins-Martins NM, Fitzgerald PB, Fujiwara H, Yücel M.

Author information

Abstract

OBJECTIVE: Surgical therapies for treatment-refractory obsessive-compulsive disorder (OCD), such as deep brain stimulation or psychosurgery, remain unattainable for many patients. Despite the long-held view that electroconvulsive therapy (ECT) is an ineffective treatment for OCD, there is no systematic review to support or refute this claim, which is the basis of the current review.

DATA SOURCES: A systematic search of MEDLINE, Web of Science, Scopus, and LILACS databases was conducted on December 22, 2013, using the terms obsessive-compulsive disorder and electroconvulsive therapy. Reference lists, specific journals, and clinical trial registries were also scrutinized. No date or language limitation was imposed on the search.

STUDY SELECTION: After irrelevant and redundant records from the 500 identified titles were excluded, the 50 articles reporting the acute treatment effects of ECT in OCD and related constructs (involving a total of 279 patients) were analyzed for this study.

DATA EXTRACTION: The relevant sociodemographic, clinical, and outcome data of individual cases were extracted. Data from individual cases were used to compare the characteristics of responders versus nonresponders to ECT.

RESULTS: Most selected records were case reports/series; there were no randomized controlled trials. A positive response was reported in 60.4% of the 265 cases in which individual responses to ECT were available. ECT responders exhibited a significantly later onset of OCD symptoms (P = .003), were more frequently nondepressed (P = .009), more commonly reported being treated with ECT for severe OCD (P = .01), and received a fewer number of ECT sessions (P = .03). ECT responders were also less frequently previously treated with adequate trials of serotonin reuptake inhibitors (P = .05) and cognitive-behavioral therapy (P = .005).

CONCLUSIONS: Although 60% of the reported cases reviewed exhibited some form of a positive response to ECT, it cannot be stated that this provides evidence that ECT is indeed effective for OCD.

Prim Care Companion CNS Disord. 2018 Oct 18;20(5). pii: 18r02342. doi: 10.4088/PCC.18r02342.

A Systematic Review of the Utility of Electroconvulsive Therapy in Broadly Defined Obsessive-Compulsive-Related Disorders.

Dos Santos-Ribeiro S[1], de Salles Andrade JB[2], Quintas JN[1], Baptista KB[1], Moreira-de-Oliveira ME[1], Yücel M[3], Fontenelle LF[4,1,2,3].

Author information

Abstract

OBJECTIVE: To assess the efficacy of electroconvulsive therapy (ECT) in DSM-5 obsessive-compulsive-related disorders (OCRDs) and conditions subsumed under an "extended" OCD spectrum, including tic disorders and self-injurious behaviors.

DATA SOURCES: A systematic search of the MEDLINE, Web of Science, Scopus, and LILACS databases and other sources was performed between June 6 and July 2, 2017. Search terms included (Autis*) AND (ECT OR electroconvulsive), (Self-injur*) AND (ECT OR electroconvulsive), (Tic* OR Tourette) AND (ECT OR electroconvulsive), (Body Dysmorphic Disorder OR Dysmorphophobi*) AND (ECT OR electroconvulsive), (Hoard*) AND (ECT OR electroconvulsive), (Trichotillomani*) AND (ECT OR electroconvulsive), (Skin Picking OR Excoriation) AND (ECT OR electroconvulsive), (Grooming) AND (ECT OR electroconvulsive), (Kleptomani*) AND (ECT OR electroconvulsive), and (Pyromani*) AND (ECT OR electroconvulsive). No search restrictions (ie, date, language, or document type) were used.

STUDY SELECTION: Fifty-two records that described the individual responses of OCRDs to ECT (involving 69 patients) were selected.

DATA EXTRACTION: Clinical data and responses of individual cases were recorded. Data from responders were compared to nonresponders.

RESULTS: All records were case reports or case series; there were no randomized controlled trials. Of the 69 OCRD participants who had undergone ECT, a positive response was reported in 73.4% of the cases (including 44.0% of the BDD, 74.1% of the tic disorder, and 85.7% of the self-injurious behavior patients). At follow-up, the majority of responders who had abstained from further ECT had experienced relapse. However, a positive response was obtained in all participants who received a new course of ECT. Patients who responded positively to ECT were likely to report previous unsuccessful treatment with antipsychotics ($P < .001$) and antidepressants ($P = .007$).

CONCLUSIONS: The finding that more than 70% of the reviewed cases showed some response to ECT should not be considered unequivocal evidence of its efficacy in OCRDs. The available evidence suggests that a randomized controlled trial of ECT in OCRDs may be warranted, particularly in severe tic disorders and self-injurious behaviors.

PMID: 30407758 DOI: 10.4088/PCC.18r02342

Depress Anxiety. 2016 Jul;33(7):640-7. doi: 10.1002/da.22451. Epub 2015 Nov 10.

EFFICACY AND LONG-TERM CLINICAL OUTCOME OF COMORBID POSTTRAUMATIC STRESS DISORDER AND MAJOR DEPRESSIVE DISORDER AFTER ELECTROCONVULSIVE THERAPY.

Ahmadi N[1,2], Moss L[1], Simon E[1], Nemeroff CB[3], Atre-Vaidya N[1].

Author information

Abstract

BACKGROUND: Many patients fulfill criteria for both posttraumatic stress disorder (PTSD) and major depressive disorder (MDD). Electroconvulsive therapy (ECT) is generally acknowledged to be the most-effective treatment for refractory MDD. This study investigated the efficacy of ECT on long-term clinical outcome of comorbid PTSD and MDD.

METHODS: This retrospective nested matched case-control study is inclusive of 22,164 subjects [3,485 with comorbid MDD and PTSD (92 with ECT and 3,393 without ECT) and 18,679 without MDD and PTSD].

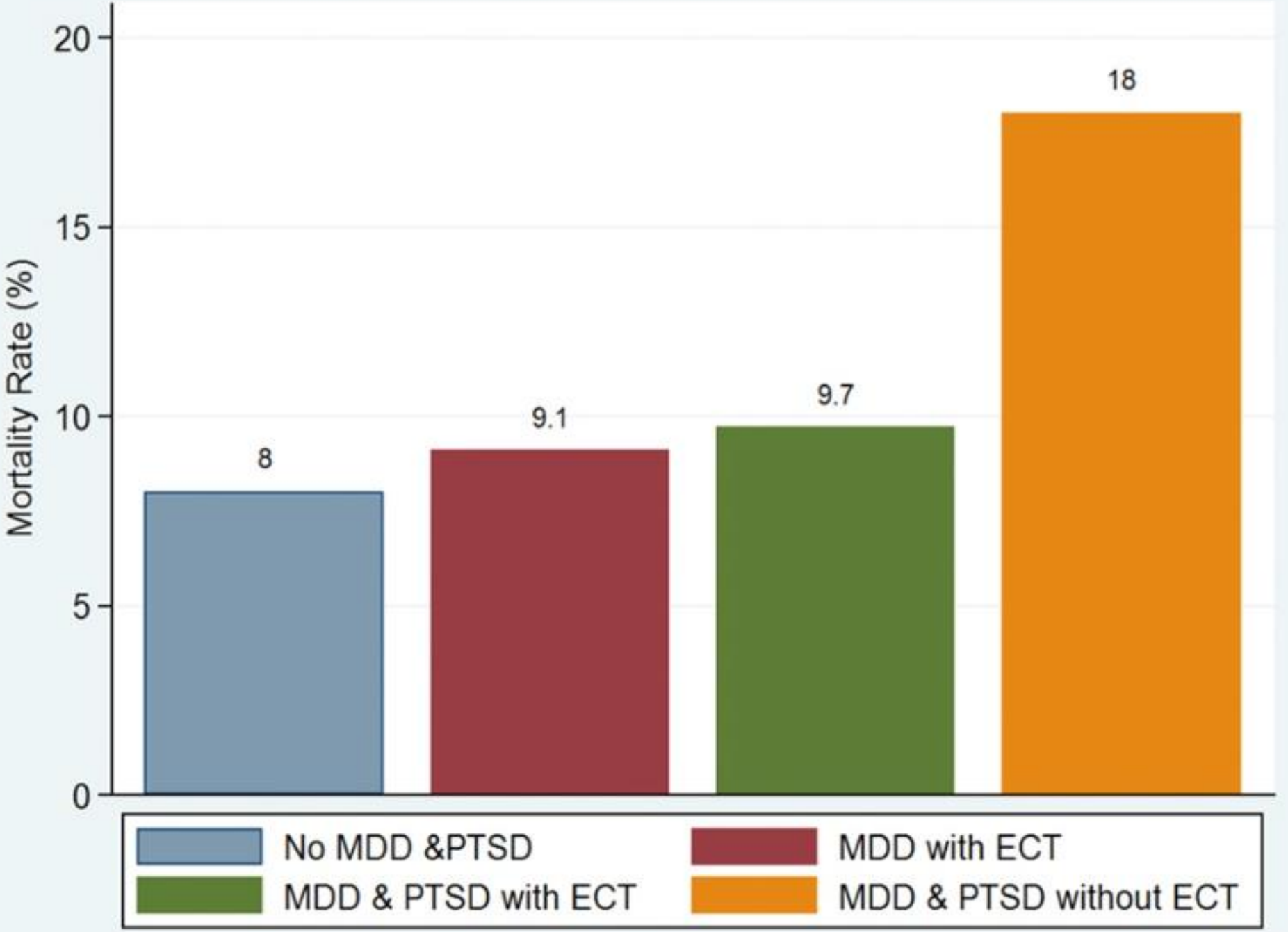
RESULTS: Using the clinical global impression scale (CGI) to assess efficacy, more-robust improvement of PTSD and MDD symptoms was observed with ECT (90%), compared to antidepressant-treatment alone(50%) ($P = 0.001$). During the median of 8 years of follow-up, the death-rate was 8% in subjects without PTSD and MDD, 9.7% in PTSD and MDD treated with ECT and 18% in PTSD and MDD without ECT ($P < 0.05$). The suicide-rate was 2.2 and 5.9% in PTSD and MDD with and without ECT-treatment, respectively ($P < 0.05$). Survival-analyses revealed that the relative-risk of cardiovascular and all-cause mortality is not significantly different in patients with comorbid MDD and PTSD treated with ECT, compared to a matched-cohort without PTSD and MDD ($P > 0.05$). The relative risk of suicidality, all-cause, and cardiovascular mortality was reduced 64, 65, and 46% in MDD and PTSD patients treated with ECT, compared to those without ECT ($P < 0.05$).

CONCLUSION: ECT is associated with a significant reduction of symptoms of PTSD and MDD, as well as reduction in risk of suicidality, cardiovascular, and all-cause mortality in MDD and PTSD, an effect more robust than antidepressant-therapy alone.

KEYWORDS: electroconvulsive therapy; major depressive disorder; mortality; outcome; posttraumatic stress disorder; suicide

PMID: 26555786 DOI: 10.1002/da.22451

[Indexed for MEDLINE]


20
15
10
5
0
Mortality Rate (%)
8
9.1
9.7
18
No MDD &PTSD
MDD with ECT
MDD & PTSD with ECT
MDD & PTSD without ECT

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Clinical outcome of maintenance electroconvulsive therapy in comorbid Posttraumatic Stress Disorder and major depressive disorder

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Keywords:
Major depressive disorder
Posttraumatic stress disorder
Electroconvulsive therapy
Heart rate variability
Clinical global impression severity scale
Suicide

ABSTRACT

Background: Post-traumatic stress disorder (PTSD) and major depressive disorder (MDD) are prevalent and frequently comorbid. Approximately 42–48% of patients with PTSD also meet diagnostic criteria for MDD. Maintenance electroconvulsive therapy (mECT) has been found to be efficacious for the prevention of recurrence of MDD. This study investigated the efficacy of mECT in the treatment of MDD with and without comorbid syndromal PTSD.

Methods: This retrospective study includes 36 patients, 26 with MDD and 10 with comorbid MDD & PTSD receiving monthly mECT for a mean of 1.5 years. The mean age was 52 ± 14 years and 25% were female. The change in PTSD and MDD symptoms in response to mECT was assessed using Clinical Global Impression - Severity Scale (CGI-S). Heart rate variability (HRV), 12-month hospitalization rate, suicide rate and all-cause mortality in response to mECT were assessed and compared between groups using repeated generalized linear regression (GLM) analysis.

Results: At mECT baseline, there were no statistically significant differences in CGI-S scores, HRV between patients with MDD alone and those with comorbid MDD and PTSD ($P > 0.05$). After 12-months of mECT, a significant increase in HRV (mean difference: 10.9 95%CI 4.8–20.3, $p = 0.001$) and decrease in CGI-S overall (mean difference: 3.5, 95% CI 3.3–3.6, $p = 0.001$)], PTSD (mean difference: 3.4, 95% CI 3.2–3.6, $p = 0.001$)], and MDD (mean difference: 3.8, 95% CI 3.5–3.9, $p = 0.001$)] symptoms in both groups were noted ($p < 0.05$). No psychiatric hospitalization or suicide occurred in any of the patients.

Conclusions: Maintenance ECT is associated with improved HRV, reduction of both major depression and PTSD symptoms, and a favorable clinical outcome.

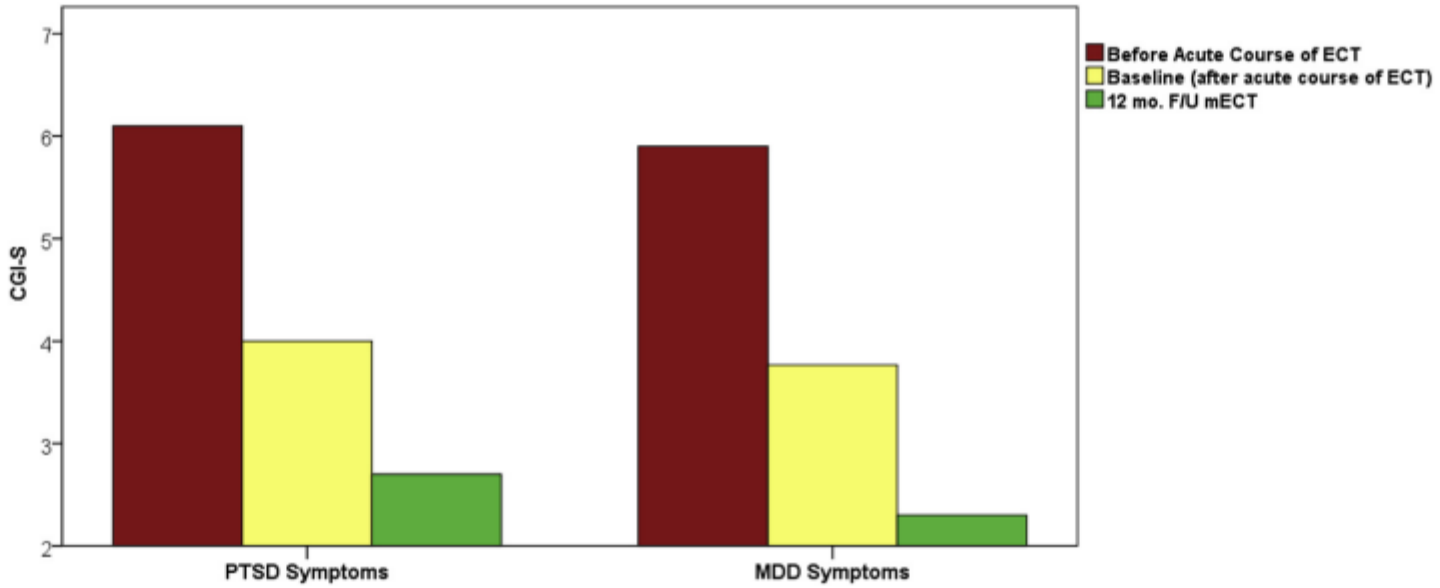

Fig. 1. The Change in MDD and PTSD symptoms in response to mECT, compared to baseline (before and after acute course of ECT).

ECT for SIB in Autism

- Theory that SIB is form of catatonia
- ECT works well to clam these behaviors in most cases
- C/M ECT always needed to maintain benefit
- Typically start with 3 X/week BL ECT, then taper, then maintenance
- Evidence base in the literature small, but increasing

ORIGINAL CONTRIBUTION

The multiple faces of catatonia in autism spectrum disorders: descriptive clinical experience of 22 patients over 12 years

Lee Elizabeth Wachtel[1]

Received: 30 April 2018 / Accepted: 24 July 2018 / Published online: 1 August 2018

Abstract

A retrospective review was conducted from the inpatient and outpatient records of twenty-two autistic youth presenting to a neurobehavioral service over a twelve-year period for combined psychiatric and behavioral pathology who also met DSM5 criteria for catatonia. Six autistic girls and 16 autistic boys ranging from ages eight to 26 years old were identified, and their variegated symptoms evaluated. Stereotypy, posturing, negativism, mutism and stupor were the most common catatonic symptoms, each present in more than half of the study patients. One patient had abnormal vital signs indicative of malignant catatonia. Twenty patients had concomitant repetitive self-injurious behaviors that had led to significant tissue injury and were refractory to psychotropic and behavioral interventions. The sample was weighted towards patients with severe self-injurious behavior, which often was the reason for admission. The many "faces" of catatonia in autism spectrum disorders are seen in this sample, and the novel recognition of repetitive self-injury as an under-recognized motor symptom of catatonia is highlighted. The preliminary findings in this study open many important future vistas for ongoing research regarding catatonia in ASDs.

Case #1

- 19 year old male with first episode psychosis (some mood features, not clear if bipolar disorder or schizophrenia)
- Failed 3 neuroleptic trials
- Remitted after acute course of 8 bilateral ECT
- Acute ECT course tapered for 2 weeks, then stopped

Case #2

- 69 year old male, unusual “neuropsychiatric” presentation with tremor, delirium, severe depression, visual hallucinations, and catatonic features
- Remitted after acute course of 12 high-dose bilateral ECT
- Relapsed quickly with catatonia
- Maintenance ECT scheduled Q 3 weeks (he and wife would want Q 2 weeks, but schedule does not allow)

Case #3

- 45 year old male with moderate intellectual disability and autism, atypical bipolar disorder
- Failed medication trials too numerous to count
- When depressed, is regressed and incontinent
- When manic, is violent and unmanageable
- Maintenance ECT scheduled either weekly or Q 2 weeks, indefinitely

Case #4

- 72 year old female, with > 10 severe episodes of psychotic depression, 6 lifetime hospitalizations, 2 serious suicide attempts
- Well interval between current presentation and prior episode = 4 months
- Remitted after acute course of 12 RUL UBP ECT
- Acute ECT course tapered, maintenance ECT scheduled starting at Q 2 weeks, extended to monthly after 2 months

Conclusions

- C/M ECT works
- Schedule/frequency should be tailored to patient's history of illness
- C/M ECT should be combined with medication(s)
- Lithium has a special place
- Long term M-ECT is typically safe and well tolerated

The Final order

- Federal Register/Vol. 83, No.246/Wednesday, December 26, 2018
- 21 CFR Part 882 [Docket No. FDA-2014-N-1210]
- 22 pages (mostly response to public comments)

Fed Regist. 2018 Dec 26;83(246):66103-24.

Neurological Devices; Reclassification of Electroconvulsive Therapy Devices; Effective Date of Requirement for Premarket Approval for Electroconvulsive Therapy Devices for Certain Specified Intended Uses. Final order.

Food and Drug Administration, HHS.

Abstract

The Food and Drug Administration (FDA) is issuing a final order to reclassify the electroconvulsive therapy (ECT) device for use in treating catatonia or a severe major depressive episode (MDE) associated with major depressive disorder (MDD) or bipolar disorder (BPD) in patients age 13 years and older who are treatment-resistant or who require a rapid response due to the severity of their psychiatric or medical condition, which is a preamendments class III device, into class II (special controls). FDA is also issuing this final order to require the filing of a premarket approval application (PMA) or a notice of completion of a product development protocol (PDP) for the preamendments class III ECT devices for all other uses that are not being reclassified to class II (product code GXC).

PMID: 30596410

[Indexed for MEDLINE]

[Docket No. FDA–2014–N–1210]

Neurological Devices; Reclassification of Electroconvulsive Therapy Devices; Effective Date of Requirement for Premarket Approval for Electroconvulsive Therapy Devices for Certain Specified Intended Uses

AGENCY: Food and Drug Administration, HHS.

ACTION: Final order.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final order to reclassify the electroconvulsive therapy (ECT) device for use in treating catatonia or a severe major depressive episode (MDE) associated with major depressive disorder (MDD) or bipolar disorder (BPD) in patients age 13 years and older who are treatment-resistant or who require a rapid response due to the severity of their psychiatric or medical condition, which is a preamendments class III device, into class II (special controls). FDA is also issuing this final order to require the filing of a premarket approval application (PMA) or a notice of completion of a product development protocol (PDP) for the preamendments class III ECT devices for all other uses that are not being reclassified to class II (product code GXC).

I. Table of Abbreviations/Commonly Used Acronyms in This Document

TABLE OF ABBREVIATIONS AND ACRONYMS

Abbreviation or acronym	What it means
510(k)	Premarket Notification.
2011 Panel	2011 Neurological Devices Panel Meeting.
AACAP	American Academy of Child and Adolescent Psychiatry.
APA	American Psychiatric Association.
BPD	Bipolar Disorder.
CANTAB	Cambridge Neuropsychological Test Automated Battery.
CFR	Code of Federal Regulations.
CGI–I	Clinical Global Impressions-Improvement scale.
ECT	Electroconvulsive Therapy Device.
FDA	Food and Drug Administration.
FDARA	FDA Reauthorization Act of 2017.
FDASIA	Food and Drug Administration Safety and Innovation Act.
FD&C Act	Federal Food, Drug, and Cosmetic Act.
FR	Federal Register.
IDE	Investigational Device Exemption.
MAUDE	Manufacturer and User Facility Device Experience.
MDD	Major Depressive Disorder.
MDE	Major Depressive Episode.
MDR	Medical Device Reporting.
M–ECT	Maintenance ECT.
MMSE	Mini Mental State Exam.

Received a recommendation from a device classification panel (an FDA advisory committee); (2) published the panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) published a final regulation classifying the device. FDA has classified most preamendments devices under these procedures.

Devices that were not in commercial distribution prior to May 28, 1976 (generally referred to as postamendments devices) [1] are automatically classified by section 513(f) of the FD&C Act into class III without any FDA rulemaking process. Those devices remain in class III and require premarket approval unless, and until, the device is reclassified into class I or II or FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the FD&C Act, to a predicate device that does not require premarket approval. The Agency determines whether new devices are substantially equivalent to predicate devices by means of premarket notification procedures in section 510(k) of the FD&C Act (21

[1] ECT devices with intended uses outside the scope of those listed in paragraphs 21 CFR

FDA ECT Final Order

Abstract

The Food and Drug Administration (FDA) is issuing a final order to reclassify the electroconvulsive therapy (ECT) device for use in treating **catatonia or a severe major depressive episode (MDE) associated with major depressive disorder (MDD) or bipolar disorder (BPD) in patients age 13 years and older who are treatment-resistant or who require a rapid response due to the severity of their psychiatric or medical condition**, which is a preamendments class III device, into class II (special controls). FDA is also issuing this final order to require the filing of a premarket approval application (PMA) or a notice of completion of a product development protocol (PDP) for the preamendments class III ECT devices for all other uses that are not being reclassified to class II (product code GXC).

SafetyandEffectiveness

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SUPPLEMENTARY INFORMATION:

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of acronym	
RWD	Real-World Data.
RWE	Real-World Evidence.
SE	Safety and Effectiveness.
U.S.C.	United States Code.
WFSBP	World Federation of Societies of Biological Psychiatry.

II. Background

The Federal Food, Drug, and Cosmetic Act (FD&C Act), establishes a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the FD&C Act (21 U.S.C. 360c) established three categories (classes) of devices, reflecting the regulatory controls needed to provide reasonable assurance of their safety and effectiveness (SE). The three categories of devices are class I (general controls), class II (special controls), and class III (premarket approval).

Under section 513(d) of the FD&C Act, devices that were in commercial

FDA "Cleared Indications for Use" ECT Devices, 1975-2018

1. Depression (unipolar and bipolar)
2. Schizophrenia
3. Bipolar manic (and mixed) states
4. Schizoaffective disorder
5. Schizophreniform disorder
6. Catatonia

FDA “Cleared Indications for Use” ECT Devices, 2019

1. Depression (unipolar and bipolar)
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5. Schizophreniform disorder
6. Catatonia

% ECT Use by Indication*

- Depression 60%
- Catatonia 5%
- (Adolescents 13-18 years <1%)

- Schizoaffective 15%
- Mania/mixed 10%
- Schizophrenia 10%

*(estimated)

Re: “Off-Label” Treatment

“FDA does not regulate the practice of medicine. Diagnosis and treatment of patients are clinical decisions that fall within the practice of medicine…FDA does not regulate off-label use of ECT by physicians,”

Re: “Off-Label” Treatment

“While the treatment of patients falls under the practice of medicine, health care professionals should carefully consider all ECT device labeling, including potential adverse events, warnings, and medical conditions that can increase patient risk when deciding if ECT is appropriate for their patients, including those with comorbid conditions.”

Re: “Off-Label” Treatment

“FDA is not permitted to limit or interfere with the authority of a healthcare professional to administer any legally marketed device to a patient for any condition or disease within a legitimate clinician-patient relationship.”

Special Controls

- Technical parameters of the device
- “Device” labeling
- “Patient” labeling

Device labeling

- Generic ECT adverse events
- Pre-ECT medical/psychiatric evaluation
- Patient monitoring during the procedure
- Use of general anesthesia/muscle relaxation
- Mouth/dental protection
- EEG monitoring until seizure end
- Instructions electrode placement, skin prep
- Cognitive status monitoring
- Clinical training of users
- 2 warnings, “Prominently placed”

Patient Labeling I

- Contradictions, warnings, precautions
- “Summation of the clinical testing,” (includes clinical outcomes, summary of adverse events and complications)
- How device operates, typical course
- Potential benefits
- Alternative treatments
- 2 warnings, “Prominently placed”

Patient Labeling II

- **Repeated** memory loss statement (paragraph)
- Risk of manic symptoms or worsening psychiatric condition
- Physical risks:
  - Pain, skin burns, physical trauma, prolonged or delayed onset seizures, pulmonary complications, cardiovascular complications, death

“Prominently Placed (Both “Device” AND “Patient” Labeling)

“Warning: ECT device use may be associated with: disorientation, confusion, and memory problems”

“Prominently Placed (Both “Device” AND “Patient” Labeling)

“Warning: When used as intended, this device provides short-term relief of symptoms. The long-term safety and effectiveness of ECT treatment has not been demonstrated.”

An Even Playing Field?

- Is penicillin called a treatment for the “short-term relief” of symptoms of pneumonia?

- Is cardiac stenting called a treatment for the “short-term relief” of symptoms of coronary artery disease?

Maintenance ECT

"Based upon all available evidence and FDA's own analysis of the published scientific literature, FDA concluded that the long-term SE of ECT has not been demonstrated. However, FDA recognizes that ECT healthcare professionals often conduct longer term treatment strategies with ECT.

The reclassification of ECT does not specifically address the issue of maintenance or continual[sic]ECT, which would be at the discretion of the healthcare professional. However, as described in the special controls, results from longer term performance data should be considered for inclusion in the healthcare professional and patient labeling, if warranted."

Informed Consent

The new labeling requirements do not specifically mandate changes to the informed consent process or documents, provided all the required elements are present, which they likely already are, in most practices. FDA clarifies that the specific content of informed consent documents is left to local hospital, or other, authority.

Cognitive Status Monitoring I

- “Cognitive status monitoring prior to beginning ECT and during the course of treatment via formal neuropsychological assessment for evaluating specific cognitive functions (e.g., orientation, attention, memory, executive function).”

Cognitive Status Monitoring II

The requirement for “formal neurological assessment” does not mean that a full neuropsychological test battery needs to be administered. Rather, commonly used instruments such as the MOCA or MMSE, both of which cover cognitive domains suggested in the order, administered at appropriate time points, are acceptable.

Conclusions

- “Off-Label” use not an impediment to practice
- New labeling suggests review of informed consent process/documents for completeness
- Cognitive testing now mandated part of ECT procedure

Thank you
Takk