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who benefits the most?

Clinical Features Indicating Future Response to ECT

NACT - Gjøvik 22-24.05.2019

Conflict of interest

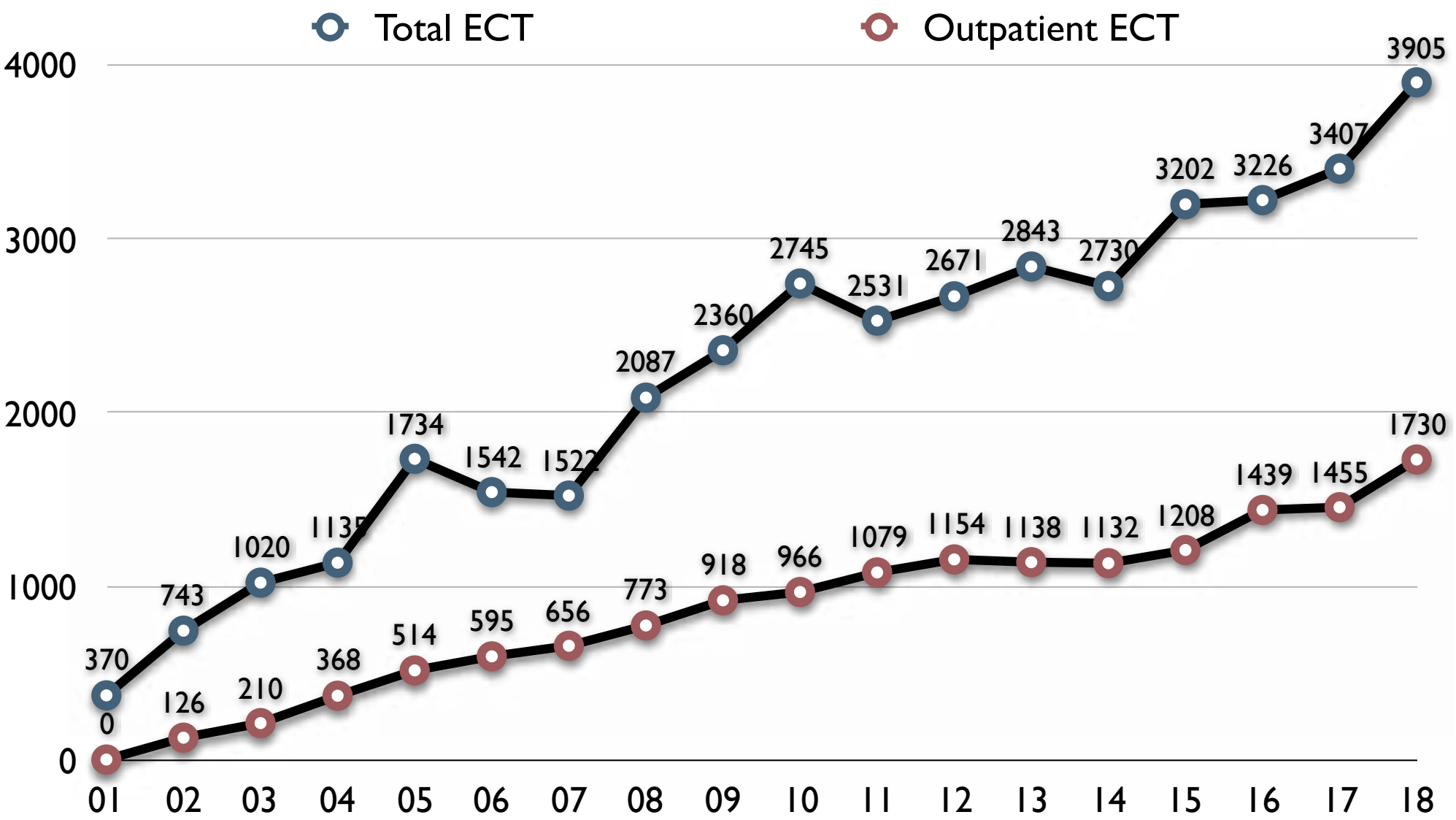
LIVANOVA
Honorarium and travel expenses
Livanova Campus Düsseldorf, 2019
LivaNova Symposium ECNP, Paris, 2017

MECTA
Honorarium and travel expenses
International Course on ECT, Barcelona, 2017

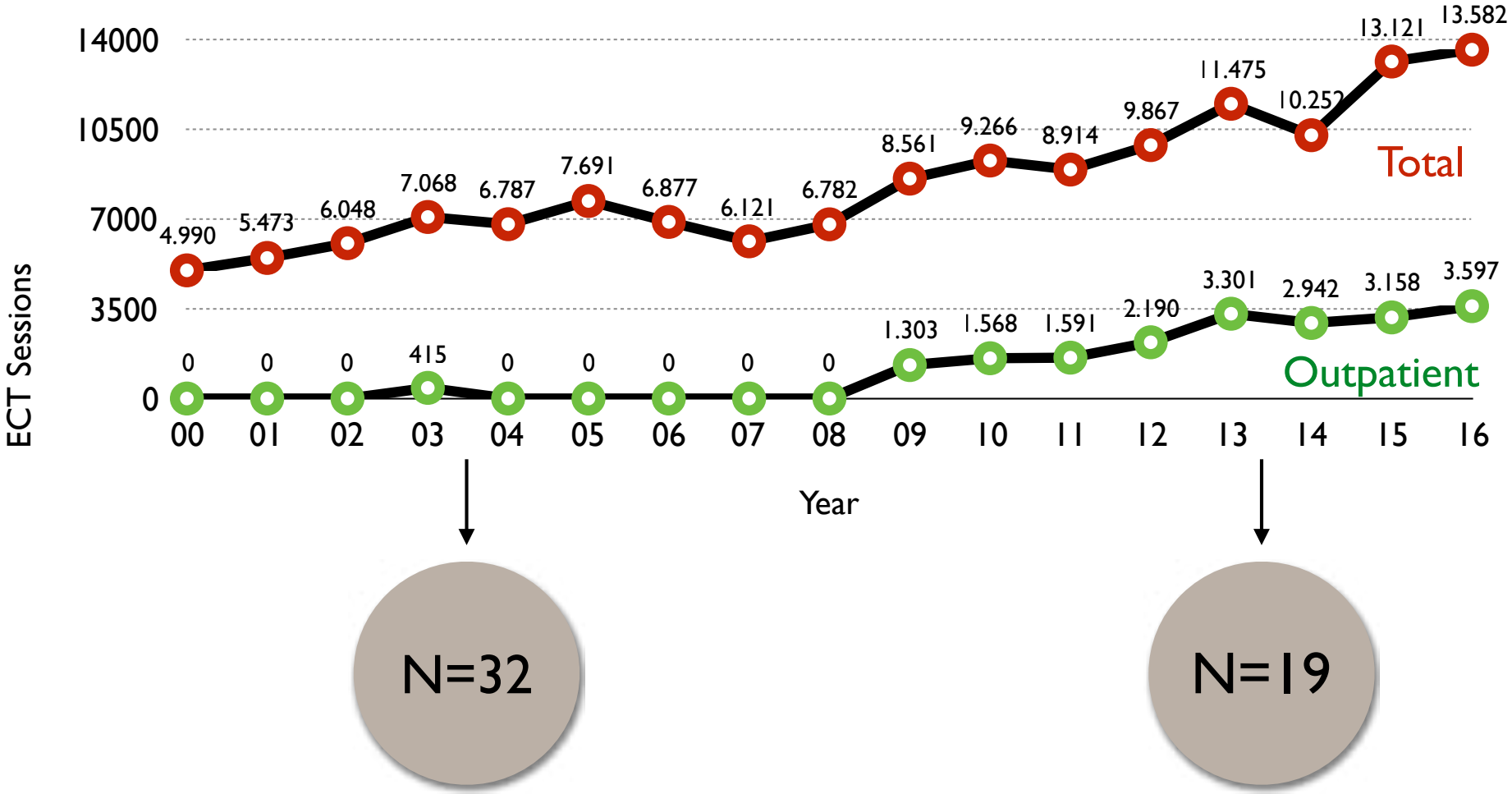
JOURNAL OF ECT
associate editor

- 51 consultant psychiatrists
- capacity 572
  - 487 beds
  - 85 chairs
- 4.047 admissions / year
- 40.000 outpatient consultations / year
- 3905 ECT-sessions 2018

ECT *UPC KU Leuven*

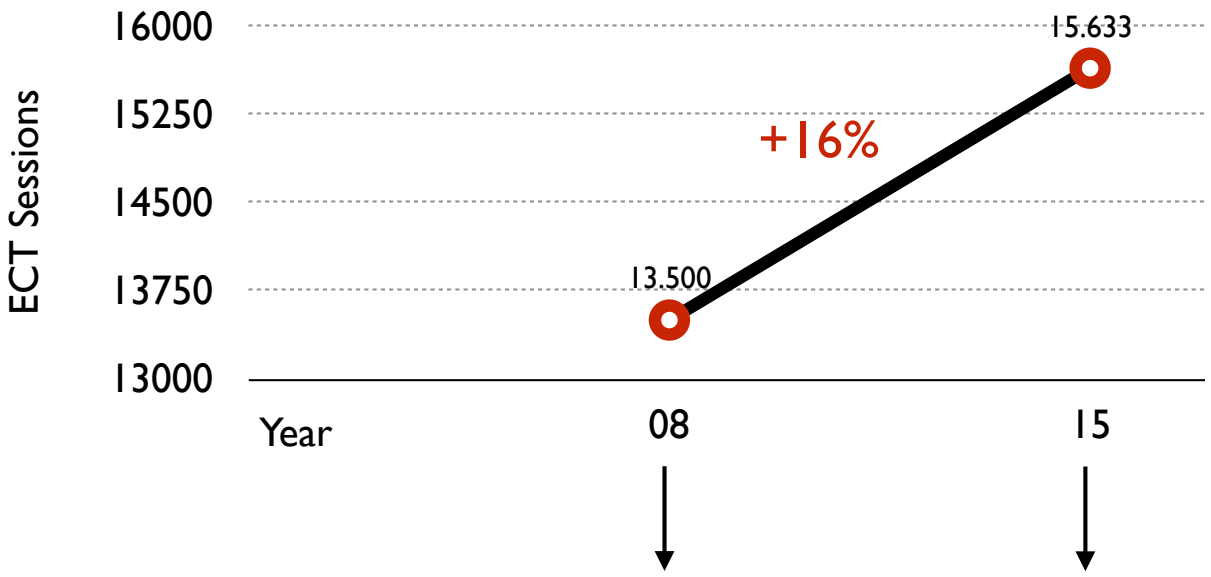


ECT Belgium *2000-2016*



P. Sienaert - RIZIV-INAMI, *personal communication*

Increase ECT-rate



35 units

33 units

2008>17

x2

183 units

Verwey et al. ECT in the Netherlands: the practice in 2015 compared to that in 2008. Tijdschr Psychiatr. 2017;59:775

Range of Action

ECT

	AD	AAP	Li	AC	BDZ	APar	ECT
Anti-Depressive	+	+	+	+			+
Anti-Manic		+	+	+			+
Anti-Catatonic					+		+
Anti-Psychotic		+				-	+
Anti-Parkinson		-				+	+
Anti-Convulsive	-	-		+	+		+
Anti-Obsessive	+						+
Anti-Anxiety	+				+		-

- Depression
- Mania
- Psychosis
- Catatonia
- Delirium

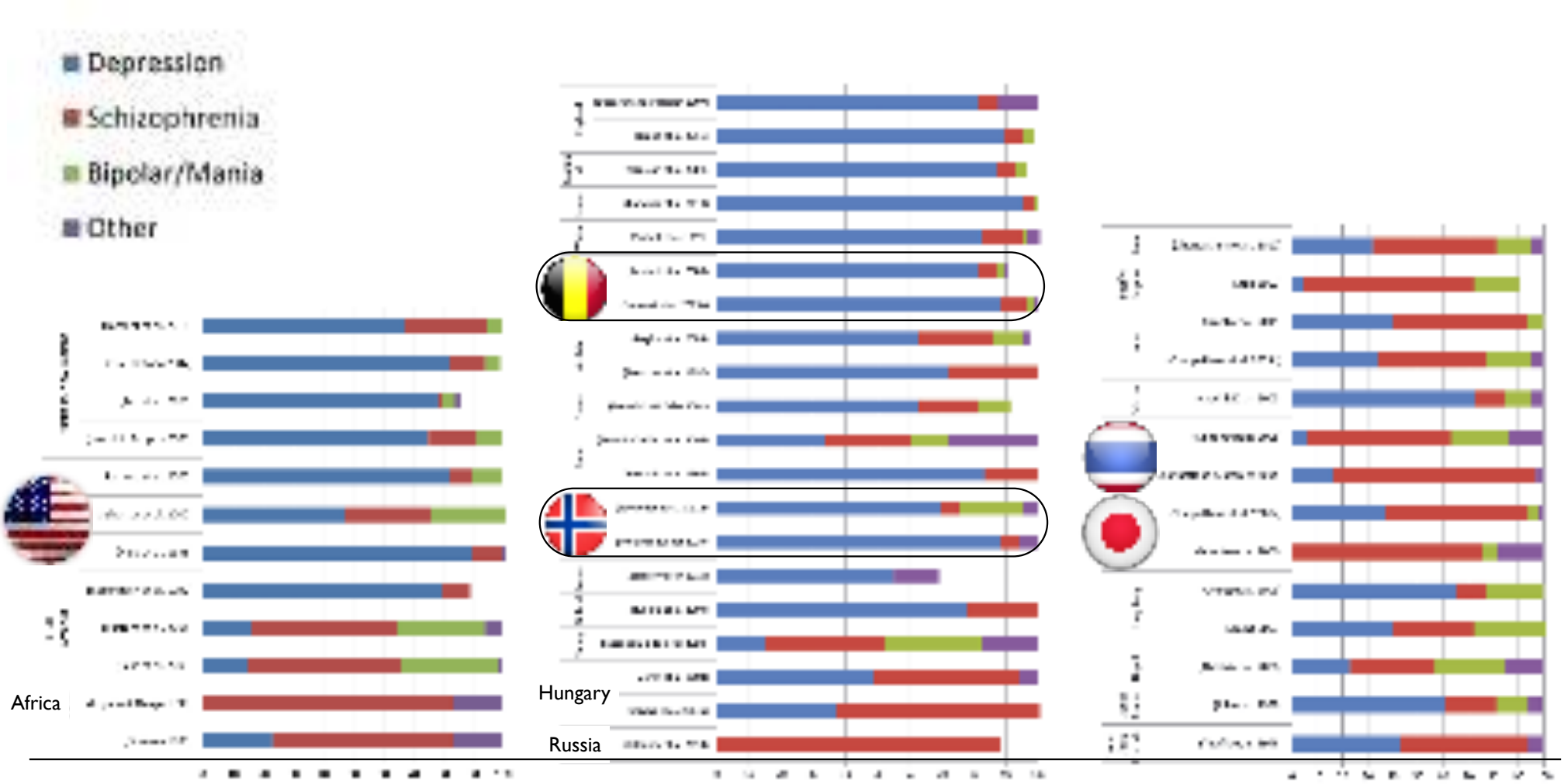
- *Parkinson's*
- *Epilepsy*

- Dementia
- Anxiety disorders
- Conduct disorders
- Personality disorders
- Eating disorders
- Sleep disorders
- Substance related
- Negative symptoms

- OCD

Why is ECT used?

worldwide



US, Africa, Australia *Europe* *Asia*

Leiknes et al (2012). Contemporary use and practice of ECT worldwide. *Brain and behavior* 2, 283-344

Efficacy & safety of ECT in depressive disorders

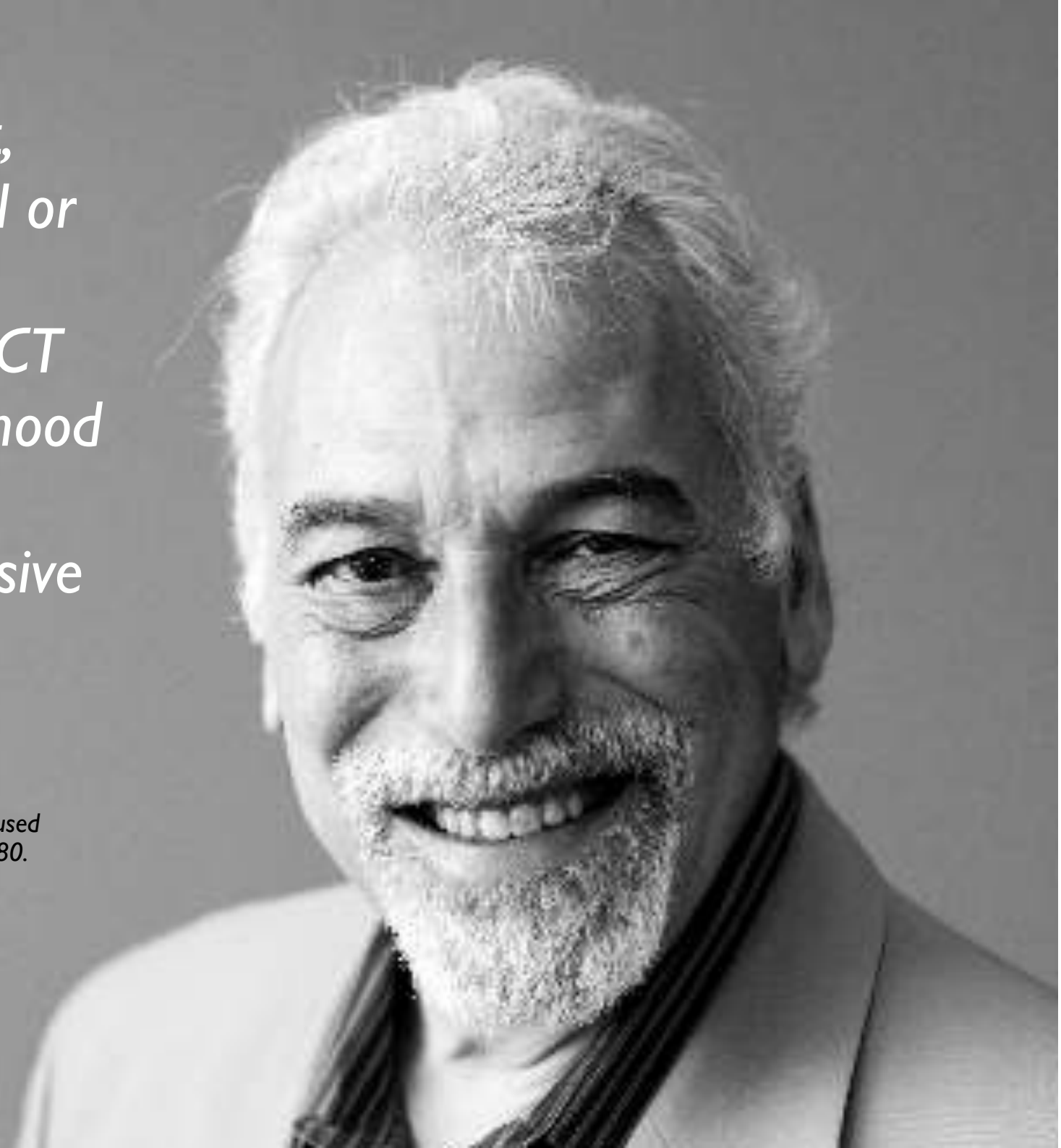
systematic review & meta-analysis

	RCT	N		HDRS
ECT vs SHAM	7	256	ECT > SHAM	9.7
ECT vs AD	18	1144	ECT > AD	5.2

UK ECT review group, Lancet 2003, 361, 799-808

no treatment,
pharmacological or
otherwise,
has matched ECT
in speed or likelihood
of remission
of major depressive
episodes

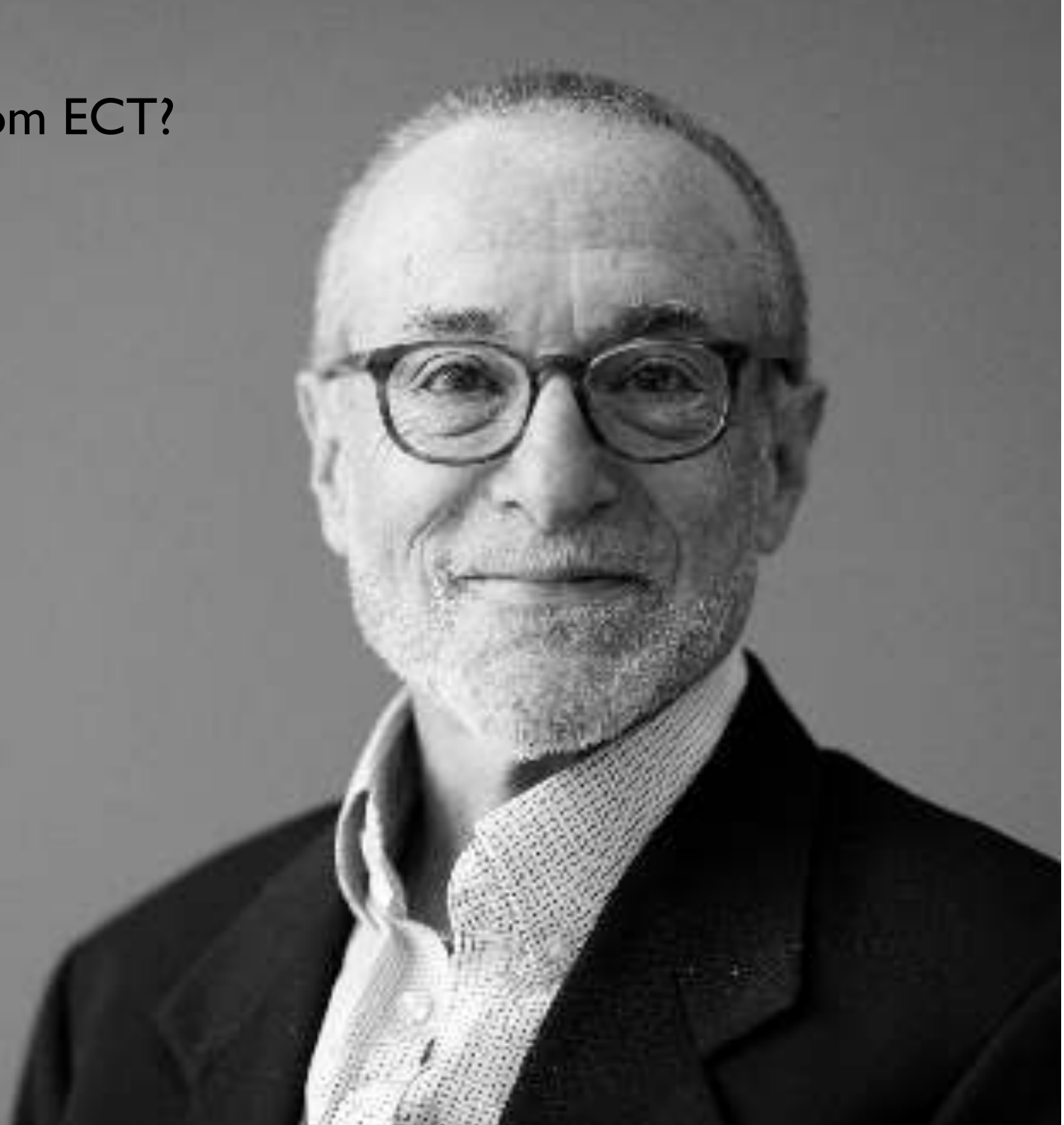
Harold A. Sackeim
Modern ECT
Vastly Improved Yet Greatly Underused
JAMA Psychiatry 2017;74:779-780.



Who benefits from ECT?

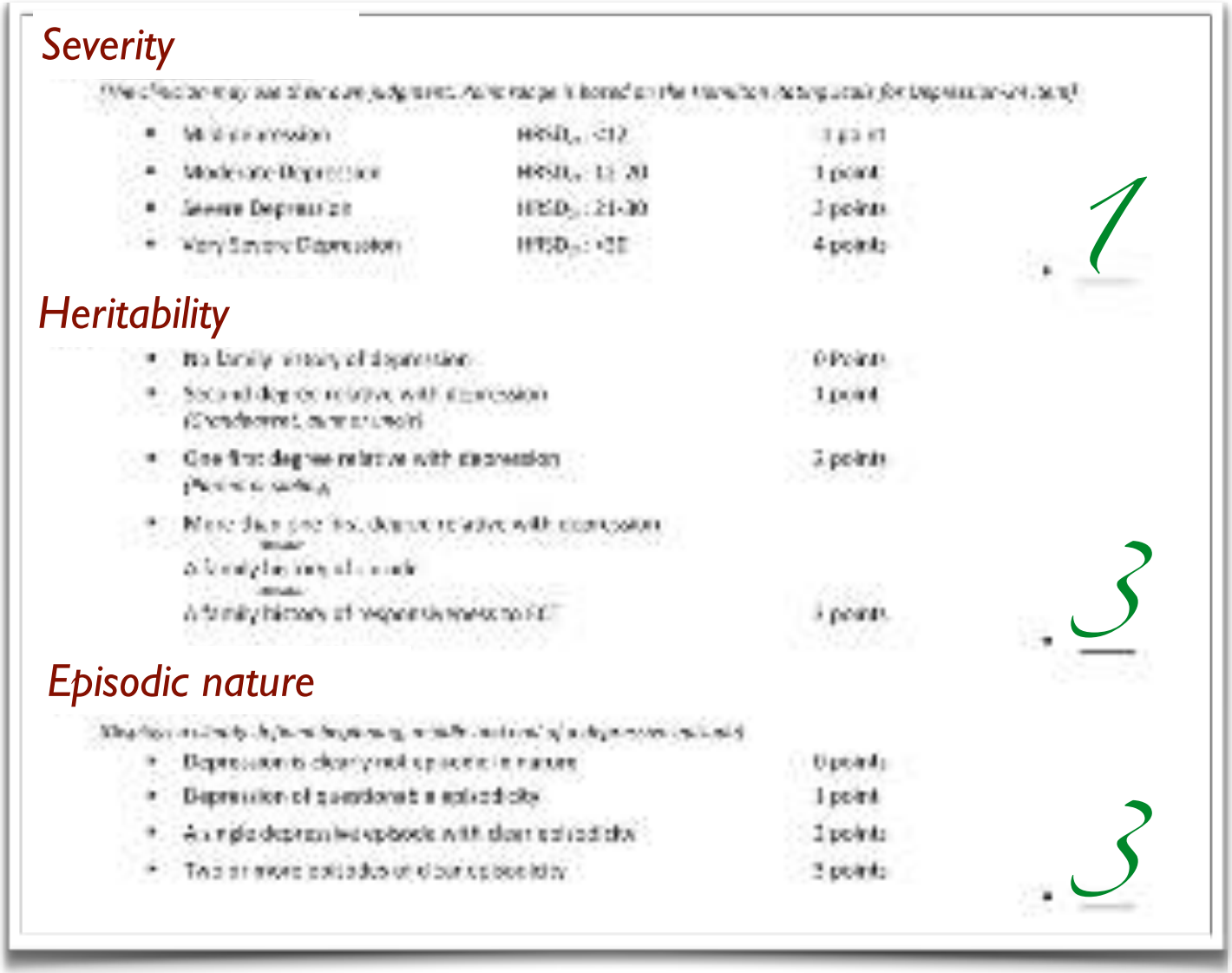
mood disorders

- Severe
- Heritable
- Episodic



Kellner et al.
Appropriateness for ECT can be assessed on a 3-item scale.
Med Hypotheses 2012
79:204-206

ECT Appropriateness Scale



Kellner et al. Appropriateness for ECT can be assessed on a 3-item scale. Med Hypotheses 2012;79:204-206

Expert Opinion

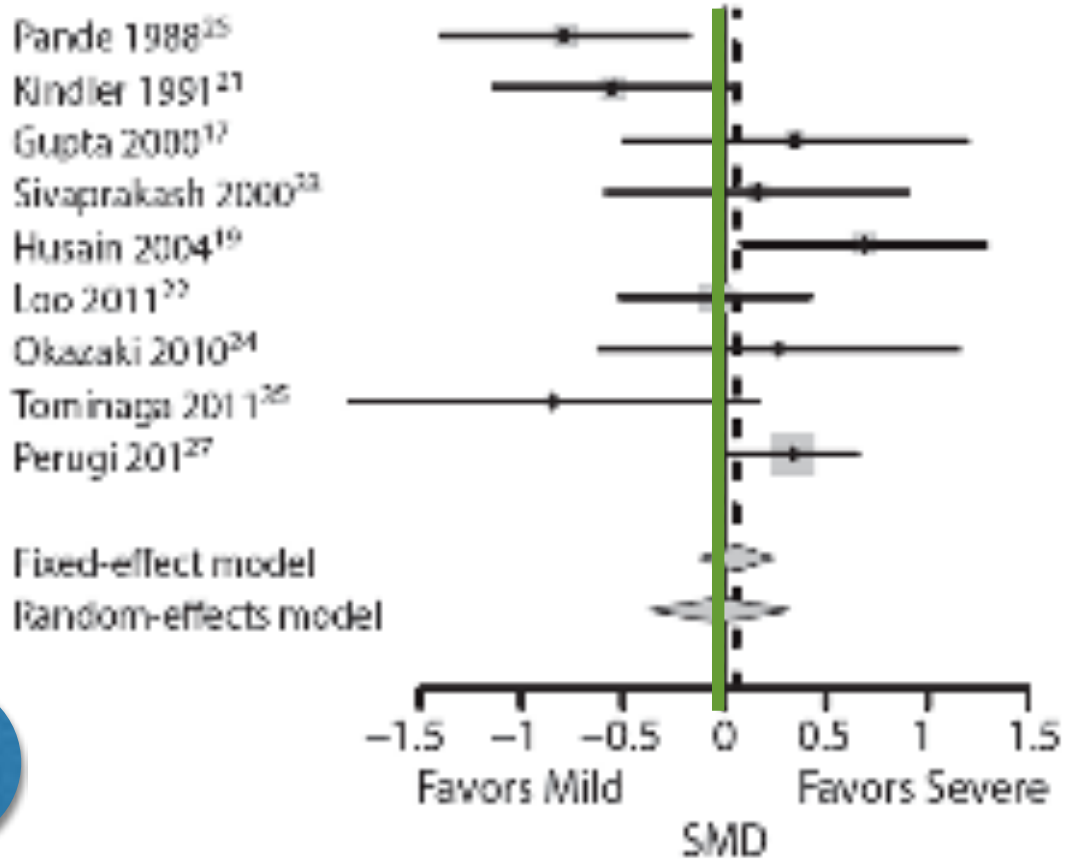
score ≥6: *patient may be appropriate candidate for ECT*

Expert Opinion

- More *severe*
- More *acute*
- *Older*

Severity

does (not) predict outcome



N=9

Haq et al. Response of depression to ECT - a meta-analysis of clinical predictors. J Clin Psychiatry 2015, 76, 1374-1384.

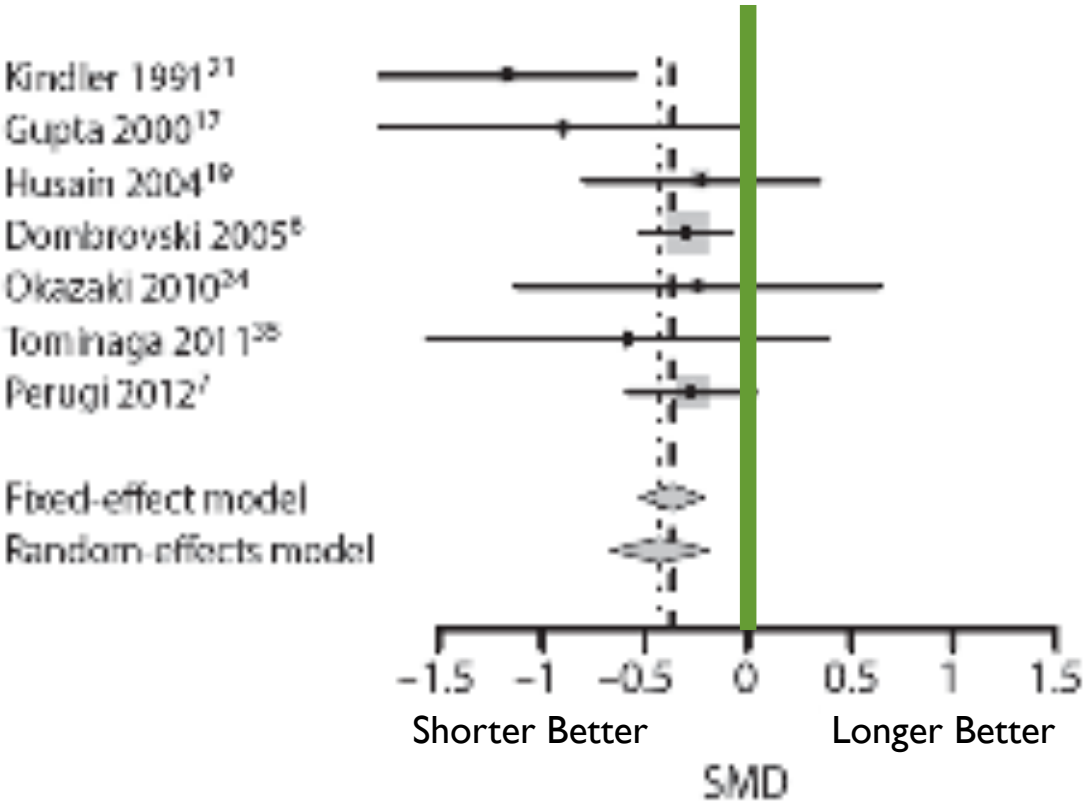
N=24

more severe
more likely
to respond
(remission NS)

Van Diermen et al. Prediction of ECT response and remission in major depression - a meta-analysis. Br J Psychiatry 2018;212:71-80

Episode duration

outcome predictor



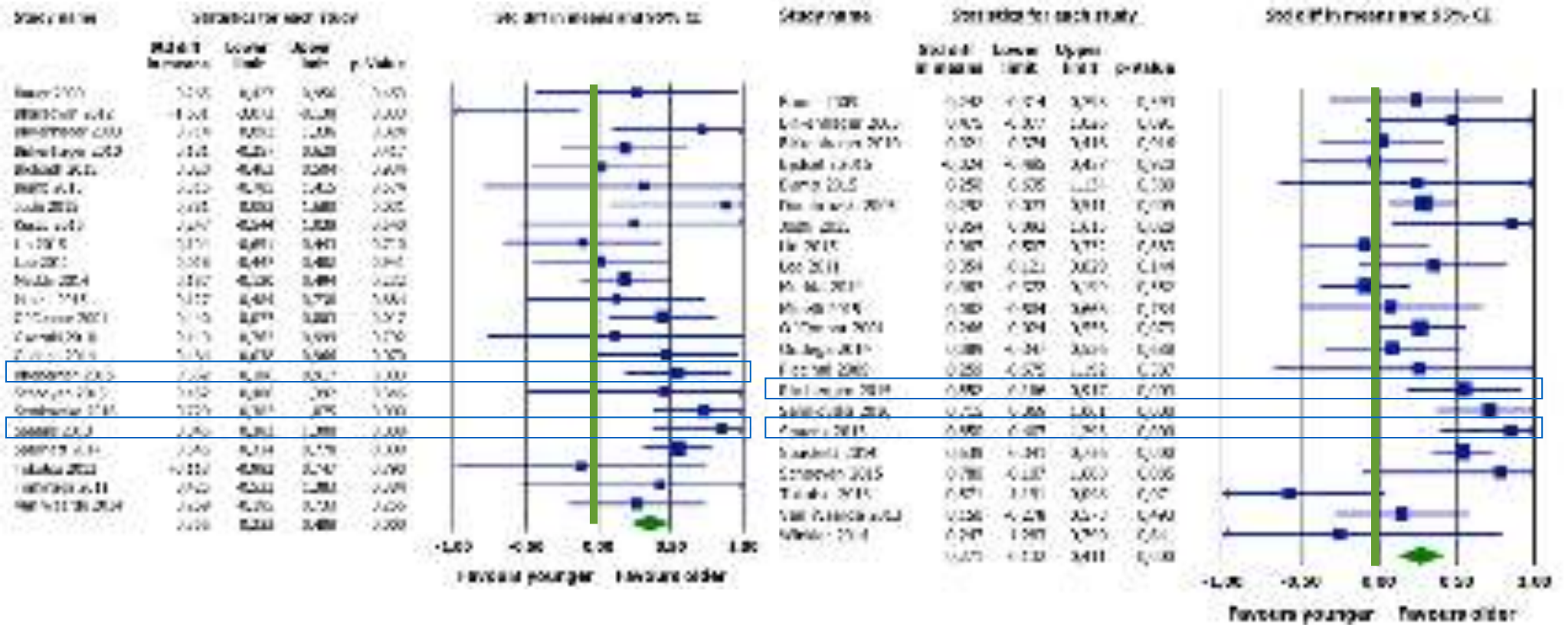
N=7

Haq et al. Response of depression to ECT - a meta-analysis of clinical predictors.
J Clin Psychiatry 2015, 76, 1374-1384.

Older Age

predicts response & remission

N=23



Van Diermen et al. Prediction of ECT response and remission in major depression - a meta-analysis. Br J Psychiatry 2018;212:71-80

	Total (n = 402) Mean (sd)	18–45 years Young (n = 137) Mean (sd)	46–64 years Middle age (n = 173) Mean (sd)	65–85 years Old (n = 92) Mean (sd)	Analysis F/χ^2	P
Age (years)	52.1 (13.9)	36.6 (6.4)	54.6 (5.3)	70.5 (4.2)	1067.855	.000
Gender (Female), n (%)	263 (65.4)	74 (54)	116 (67.1)	73 (79.3)	15.971	.000
Age of onset (years)	30.4 (14.5)	21.3 (6)	32.7 (13.3)	39.5 (17.8)	62.661	.000
Duration of current episode (months)	9.6 (10.8)	9.6 (12.4)	11.2 (11.2)	6.8 (6.4)	4.841	.008
Number of previous episodes	5.7 (3)	5.2 (2.5)	5.9 (3.3)	6.1 (3.2)	3.494	.031
Number of previous hospitalizations	3.5 (2.6)	2.8 (2)	4.1 (3.2)	3.4 (1.8)	9.219	.000
Suicide attempts, n (%)	121 (30.1)	50 (36.5)	48 (27.7)	23 (25)	4.257	.119
Current episode, diagnosis	N (%)	N (%)	N (%)	N (%)		
Unipolar Depression	43 (10.7)	10 (7.3)	20 (11.6)	13 (14.1)	2.926	.232
Bipolar II Depression	198 (49.3)	62 (45.3)	90 (52)	46 (50)	1.428	.490
Bipolar I Depression	161 (40)	65 (47.4)	63 (36.4)	33 (35.9)	4.742	.093
Psychotic features	136 (33.8)	55 (40.1)	49 (28.3)	32 (34.8)	4.822	.090
HAM-D-17						
	N (%)	N (%)	N (%)	N (%)		
Responders (relative decrease > 50%)	247 (61.4)	87 (63.5)	96 (55.5)	64 (69.6)	5.394	.067
Remitters (final score ≤ 7)	118 (29.4)	43 (31.4)	48 (27.7)	27 (29.3)	.489	.783

Socci et al. Electroconvulsive therapy and age: Age-related clinical features and effectiveness in treatment resistant major depressive episode. J Affect Disord 2017;227:627-632.

Attributes of responsive syndromes

	Mood	*Motor*	*Vegetative*
Melancholia	depression	retarded, agitated	abnormal
Catatonia	depressed, manic	2+ CRS signs, 24 hrs	often abnormal
Delirium	depressed, manic	agitated	usually abnormal
Mania	excited	agitated	usually abnormal

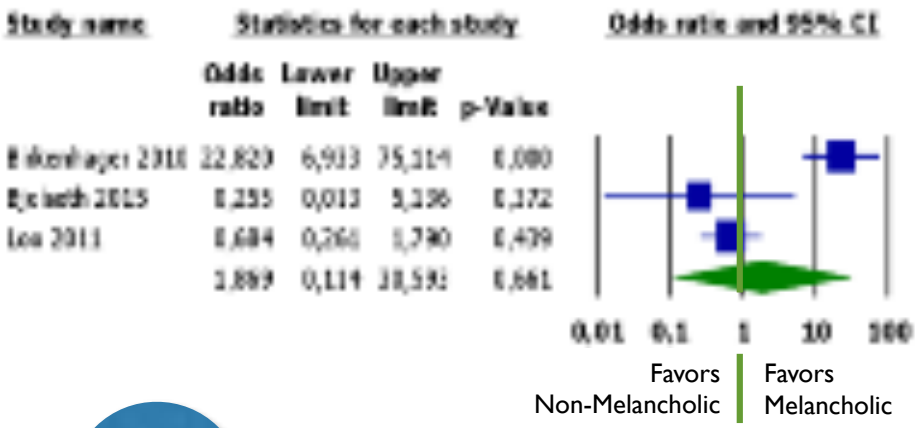
Courtesy of Max Fink

Expert Opinion

Melancholic features

do not predict outcome

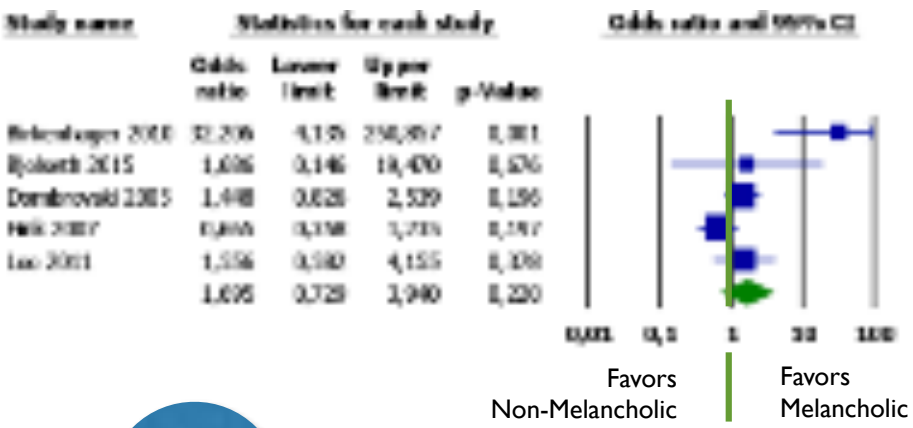
Response



N=3

Response-rate
Melancholia 70.8%
Non-melancholia 49.1%
(NS)

Remission



N=5

Remission-rate
Melancholia 64.1%
Non-melancholia 65.5%
(NS)

Van Diermen et al. Prediction of ECT response and remission in major depression - a meta-analysis. Br J Psychiatry 2018;212:71-80

ECT treats only illness that is *observable*

Expert Opinion

Conrad M Swartz
Patient selection and electroconvulsive therapy indications. 2009

Melancholia

- *observable* psychomotor retardation or agitation
- delusional thoughts
- unchanging abnormal mood
- vegetative signs

≠ DSM criteria of melancholic features

Fink et al. DSM melancholic features are unreliable predictors of ECT response: a CORE publication. J ECT. 2007;23:139–146.

Who benefits from ECT?

British Journal of Psychiatry (1992), 160, 355–359

Who Benefits from Electroconvulsive Therapy?
Combined Results of the Leicester and Northwick Park Trials

HEATHER BUCHAN, EVE JOHNSTONE, K. McPHERSON, R. L. PALMER, T. J. CROW and S. BRANDON

This paper describes the results obtained by combining data from the Northwick Park and Leicester randomised controlled trials of ECT. Patients who suffered from depression in which ***retardation*** **and** ***delusions*** were features and who received real ECT had a significantly improved outcome at the end of four weeks of treatment (as measured by improvement in the HRSD) in comparison with those who received simulated ECT. However, this treatment effect was not detectable at six-month follow-up. Patients who were neither retarded nor deluded did not benefit significantly from real as opposed to simulated ECT.

1980

1985

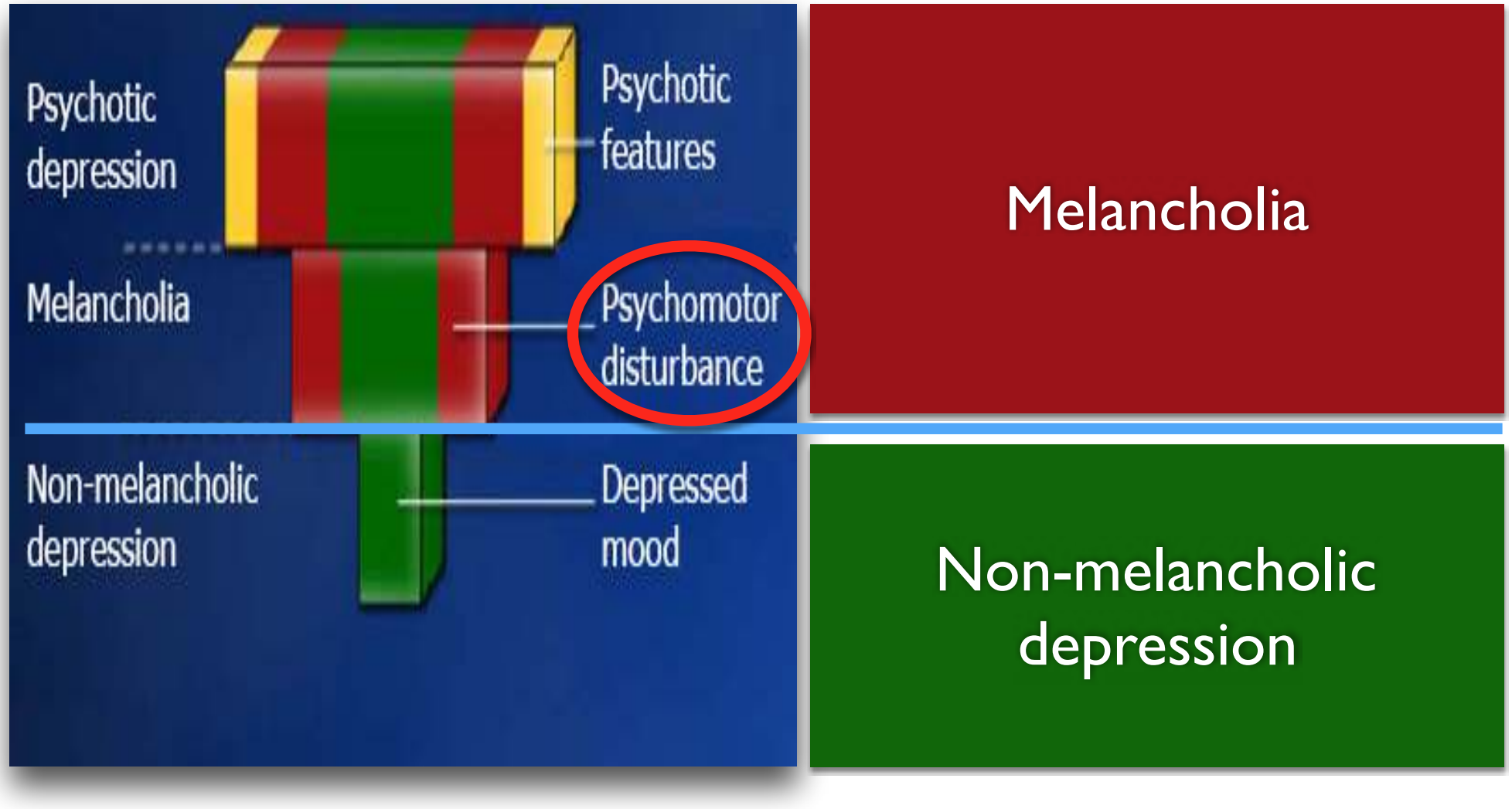
N=165

SHAM

Electroconvulsive therapy (ECT) has been a frequently used treatment for depressive illness for nearly 50 years. During this time there has been considerable debate about whether the electrically induced convulsion plays a critical role in producing therapeutic benefit or, alternatively, whether this is due to an elaborate placebo response. This question was investigated in two randomised controlled trials of ECT carried out in Leicester and Northwick Park Hospital, London. This paper gives the results of a combined analysis of the data from these two trials with the aim of clarifying the effects of real ECT compared with simulated therapy.

Method

Melancholia



Parker & Manicavasagar (2005)

Taylor & Fink (2006)

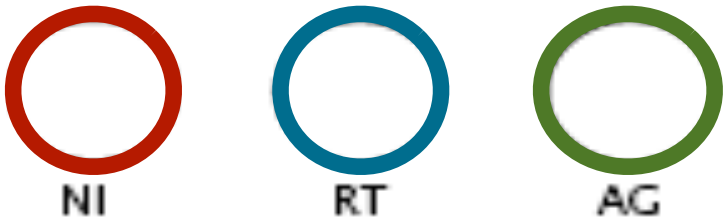
CORE

assessment of psychomotor change

- 18 items
- score after 20' interview
- *observable* signs
- 4-point-scale

7. Length of verbal responses
8. Inattentiveness
9. Facial agitation
10. Body immobility (amount, not speed)
11. Motor agitation
12. Poverty of associations
13. Slowed movement (speed, not amount)
14. Verbal stereotypy
15. Delay in motor activity
16. Impaired spontaneity of talk
17. Slowing of speech rate
18. Stereotyped movements

NI = Non-interactiveness
RT = Retardation
AG = Agitation



Total CORE score = NI + RT + AG = ≥8 melancholic depression

Melancholia,
as defined by CORE,
predicts ECT
response!

Hickie et al. Prediction of ECT response: validation of a refined sign-based (CORE) system for defining melancholia. Br J Psychiatry 1996;169(1):68-74.

Prediction of ECT response

Hickie et al. Br J Psychiatry 1996;169(1):68-74

- N=81 - elderly*67.2 y* - severe depression*HRSD 28.8* - marked psychomotor symptoms*CORE 24.*
- outcome predictors
  - *total CORE score*
  - *subscale CORE scores* *retardation / non-interactiveness > agitation*
  - *psychotic features*

- *high CORE + psychotic features = best outcome*

Prediction of ECT response

MODECT

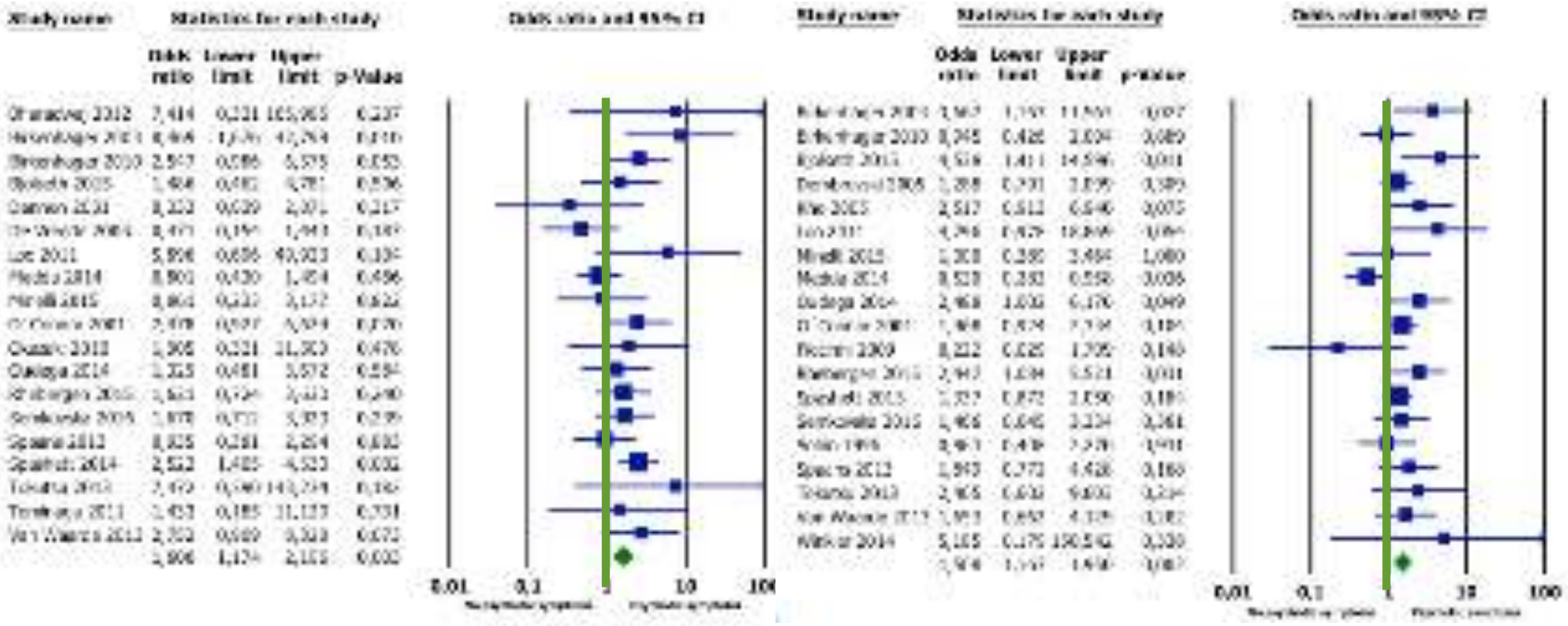
- depressed older inpatients N=89 / Melancholic (CORE≥8) N=75
- melancholic depression[CORE 16]
  - higher depression severity[$p<0.001$]
  - lower cognitive functioning[$p=0.04$]
  - lower overall functioning[$p<0.05$]
  - no significant relation CORE - remission/response
    - *selection bias - rather homogeneous sample of severely depressed in-patients, in which the CORE may lack power to differentiate*
  - in non-psychotic patients - correlation 'neared significance' - $p=0.057$
- psychotic symptoms significantly higher response/remission

Veltman EM, de Boer A, Dols A, van Exel E, Stek ML, Sienaert P, Bouckaert F, van der Mast R, Rhebergen D (2019). Melancholia as Predictor of Electroconvulsive Therapy Outcome in Later Life. J ECT

Psychotic Symptoms

predict response & remission

N=19



Van Diermen et al. Prediction of ECT response and remission in major depression - a meta-analysis. Br J Psychiatry 2018;212:71-80

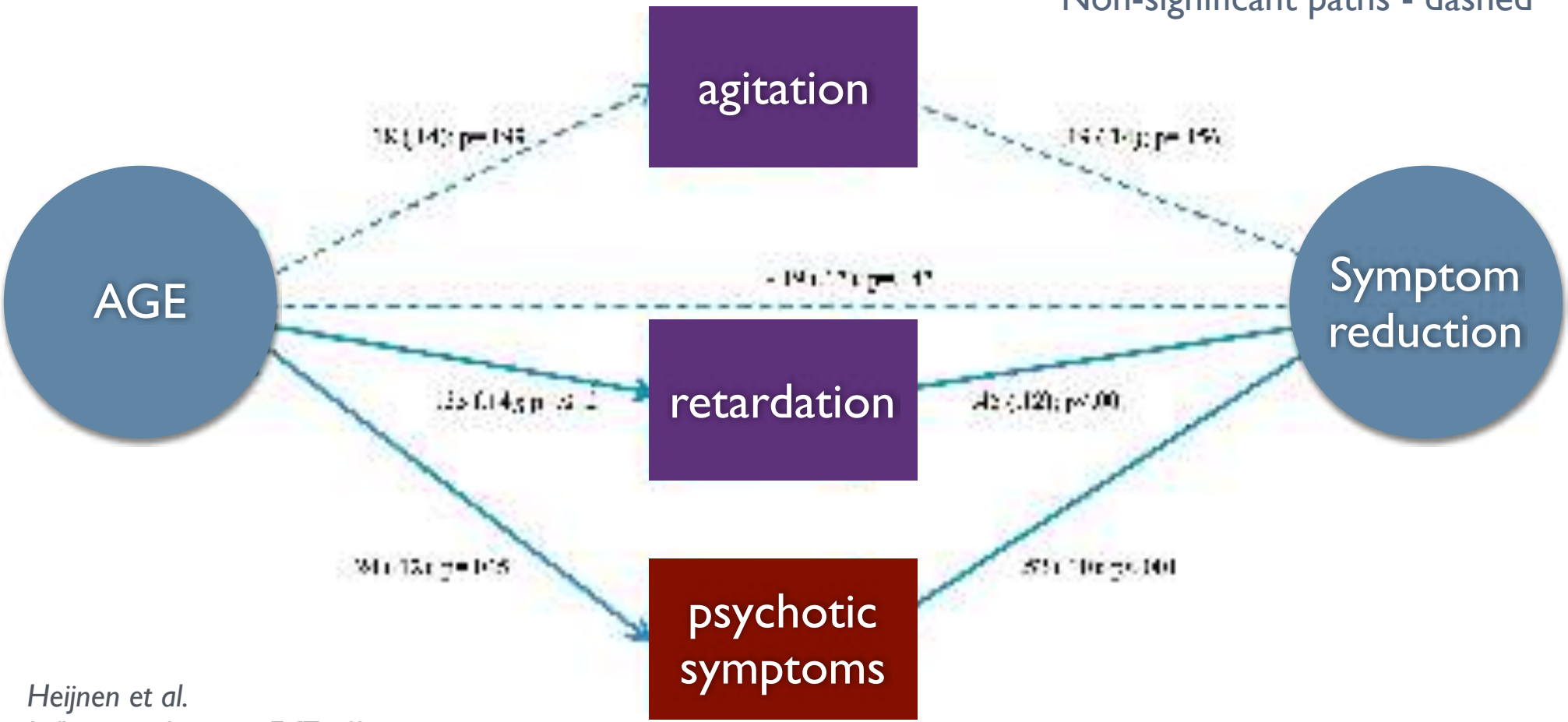
ECT in Psychotic Depression

"harder, better, faster, stronger"

Wijkstra et al (2010). Treatment of unipolar psychotic depression: RCT comparing imipramine, venlafaxine, and venlafaxine plus quetiapine. Acta Psychiatr Scand 121,190.

Petrides et al (2001). ECT remission rates in psychotic versus nonpsychotic depressed patients. J ECT17, 244.

Path model of the relationship between age, clinical features and ECT efficacy on depressive symptoms.
Significant paths - bold
Non-significant paths - dashed



Heijnen et al.
Influence of age on ECT efficacy in depression and the mediating role of psychomotor retardation and psychotic features.
J Psychiatr Res. 2019;109:41-47.

N=96

MDD

BT 2/W

older patients respond better to ECT

because older patients have
more psychomotor symptoms
and psychotic symptoms

Who benefits most?

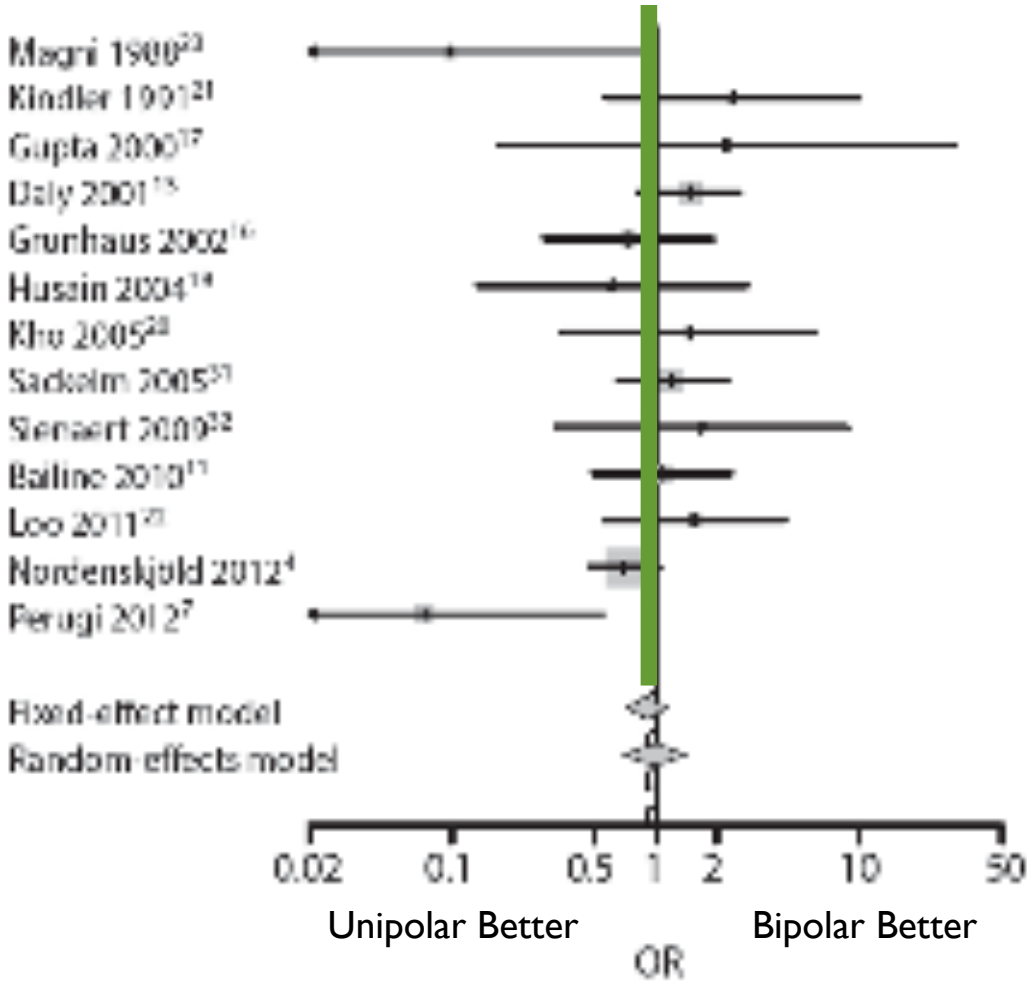
- more acute
- older
- psychomotor changes
- psychotic symptoms

Factors affecting efficacy

- bipolarity
- medication-resistance
- suicidality
- personality disorders
- age-related brain changes

ECT is equally effective

in unipolar and bipolar depression



Haq et al. Response of depression to ECT - a meta-analysis of clinical predictors. J Clin Psychiatry 2015, 76, 1374-1384.

ECT is equally effective

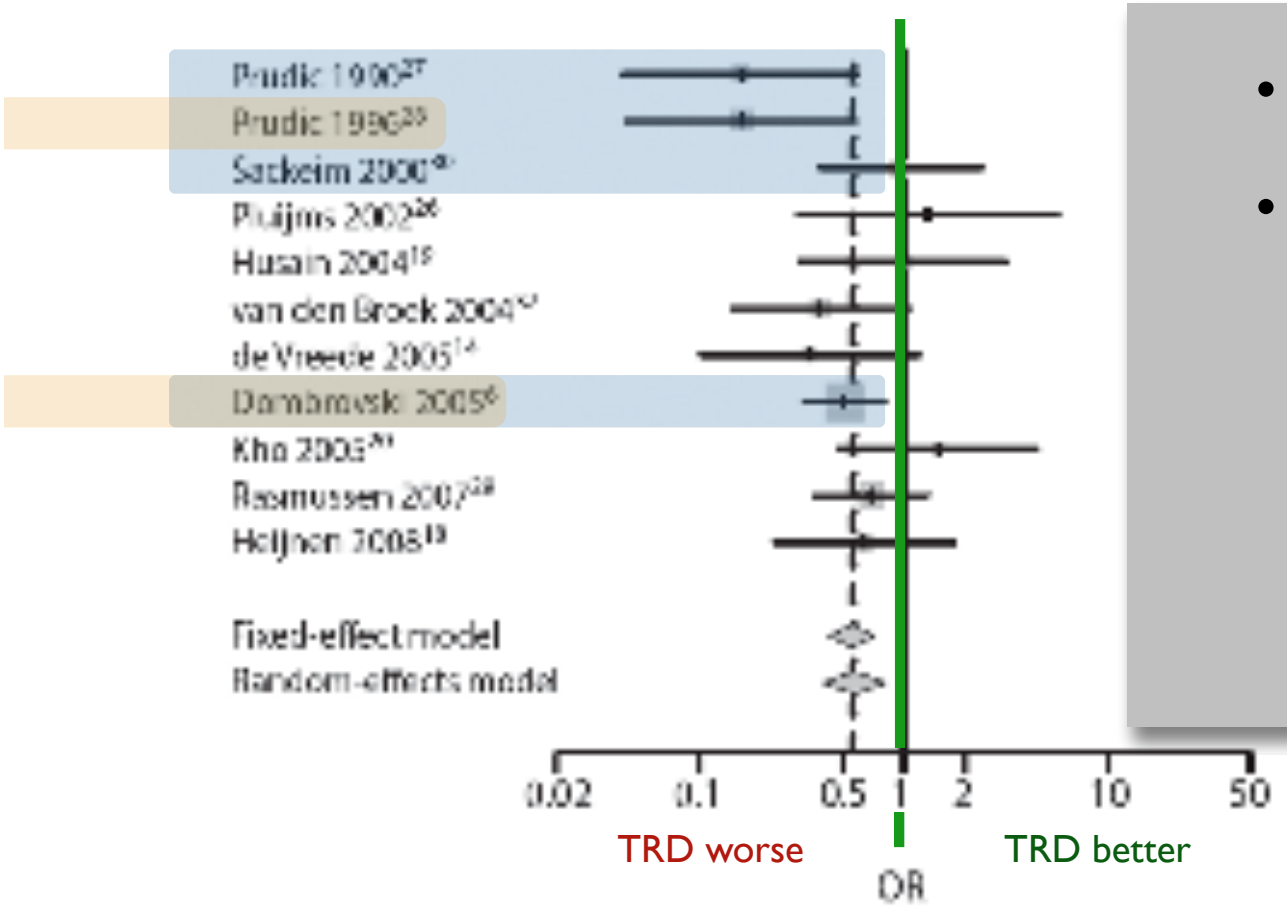
in unipolar and bipolar depression

	N UP/BP	Efficacy	Speed
Stromgren, 73	26/26	BP=UP	
Daly et al, 01*	162/66	BP=UP	BP>UP
Grunhaus et al, 02	111/20	BP=UP	
Medda et al, 09	17/113	BP<UP	
Sienaert et al, 09	51/13	BP=UP	BP>UP
Bailine et al, 10	170/50	BP=UP	BP=UP
Spaans et al, 13*	74/13	BP=UP	BP=UP

**pooled data - 3 RCT *unpublished analysis*

Medication Resistance

and response to subsequent ECT



- 11 studies - N=1175
- overall response rate
  - previous pharmacotherapy failure - 58.0%
  - no medication resistance - 70%
  - OR = 0.56

Columbia Group - Moderate dose RUL - Lorazepam

Prudic 96 = subsample of Dombrovski 2005

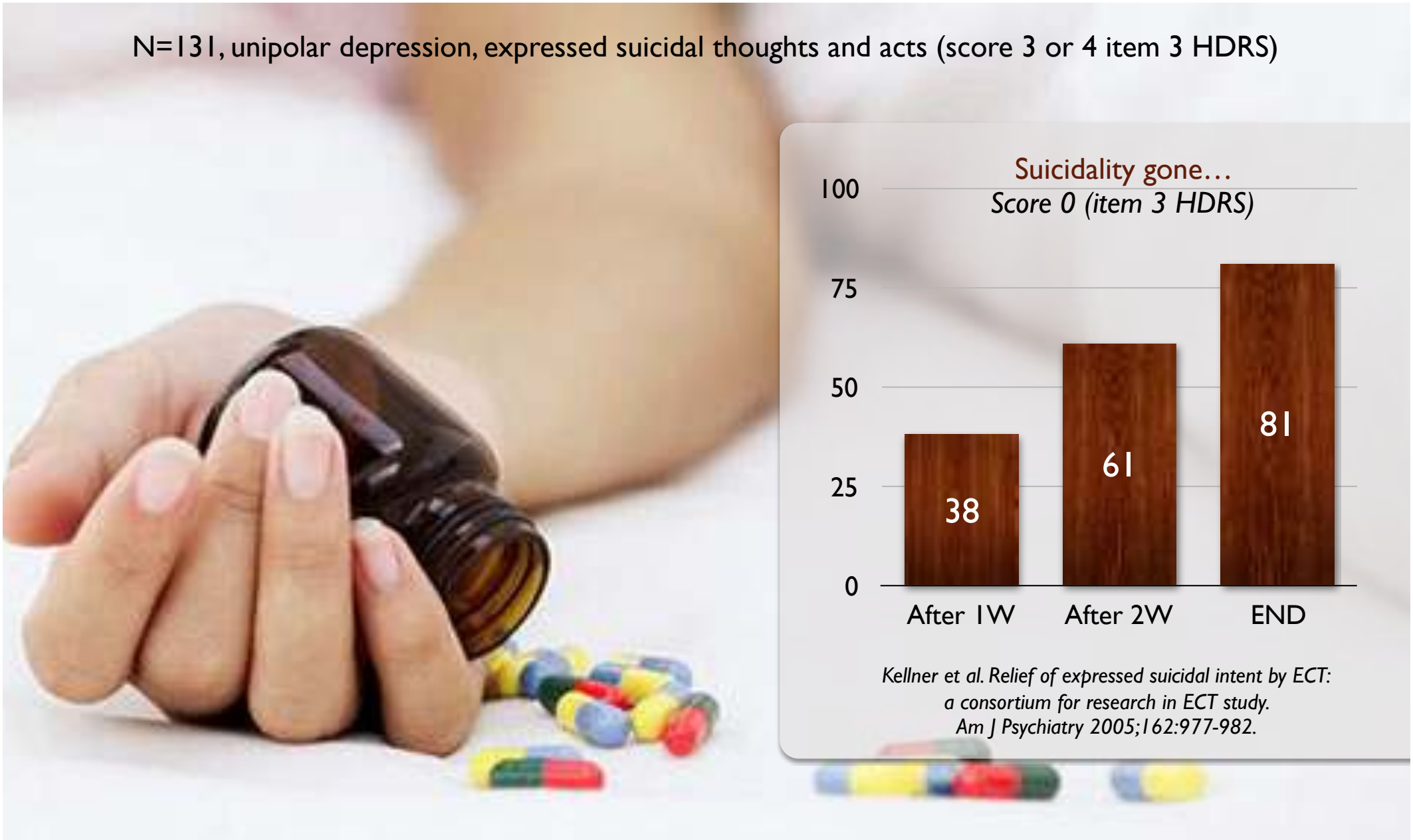
Haq et al. Response of depression to ECT - a meta-analysis of clinical predictors. J Clin Psychiatry 2015;76:1374-1384.

AD treatment failure should *not discourage* the clinician from prescribing ECT

Sienaert. What We Have Learned About Electroconvulsive Therapy and its Relevance for the Practicing Psychiatrist. *Can J Psychiatry* 2011

ECT is *antisuicidal*

N=131, unipolar depression, expressed suicidal thoughts and acts (score 3 or 4 item 3 HDRS)



Kellner et al. Relief of expressed suicidal intent by ECT: a consortium for research in ECT study. Am J Psychiatry 2005;162:977-982.

Negative predictive features

early research - Hobson 53 - Roberts 59 - Hamilton & White 60 - Carney et al 65 - Mendels 67

- emotional lability
- neurotic traits
- hysterical attitude
- fluctuating course of depressive symptoms
- inadequate personality
- hypochondriasis

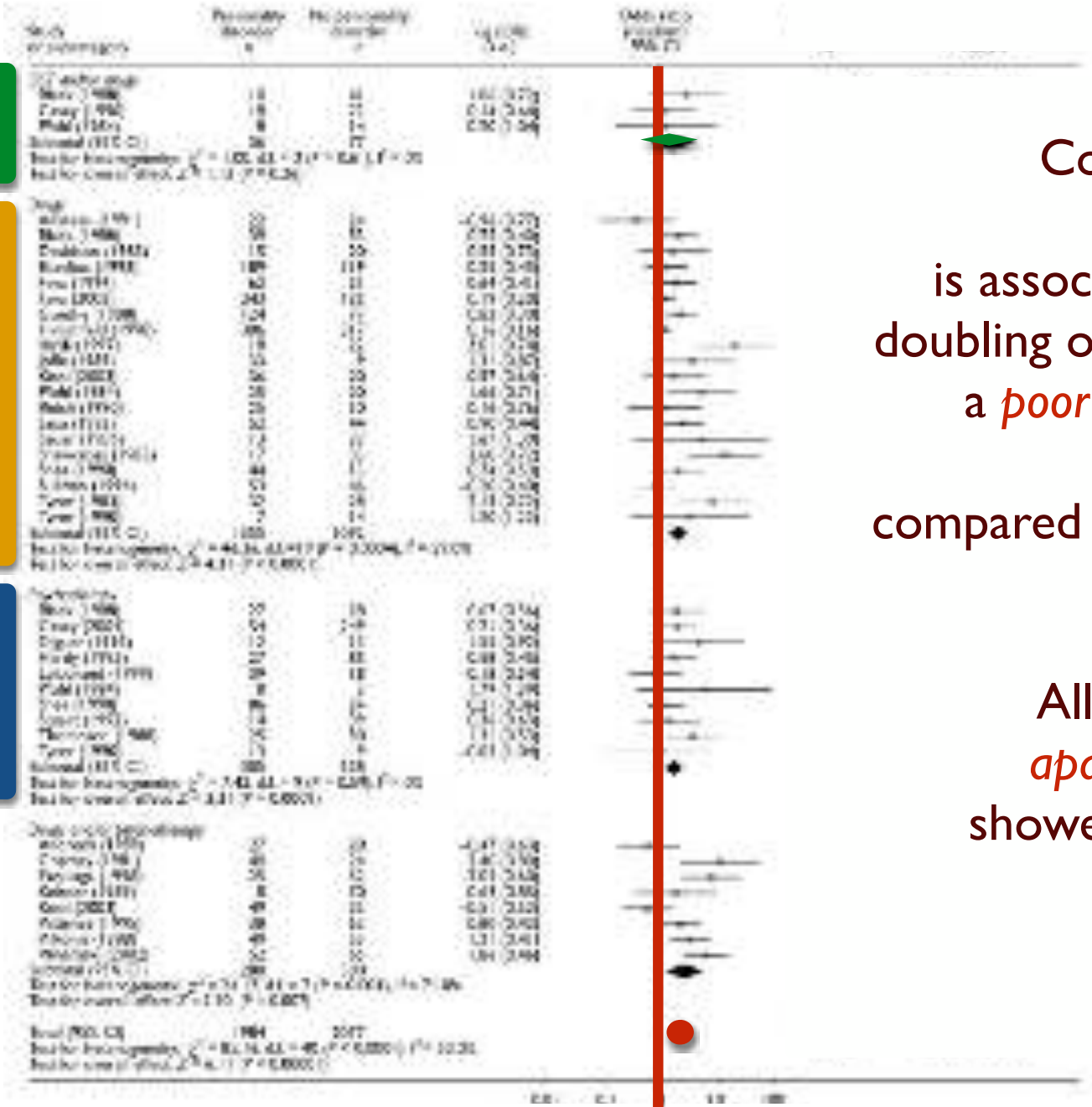
It is likely that many of the patients described by the early investigators as having traits predicting negative ECT outcomes would now be diagnosed as having personality disorders.

Rasmussen (2014)
Do Patients With Personality Disorders Respond Differentially to ECT? A Review of the Literature and Consideration of Conceptual Issues. *J ECT*

ECT

Drugs

Psychotherapy



Poor Outcome No PD | Poor Outcome PD

Newton-Howes et al. Personality disorder and the outcome of depression: meta-analysis of published studies. *BJP* 2006.

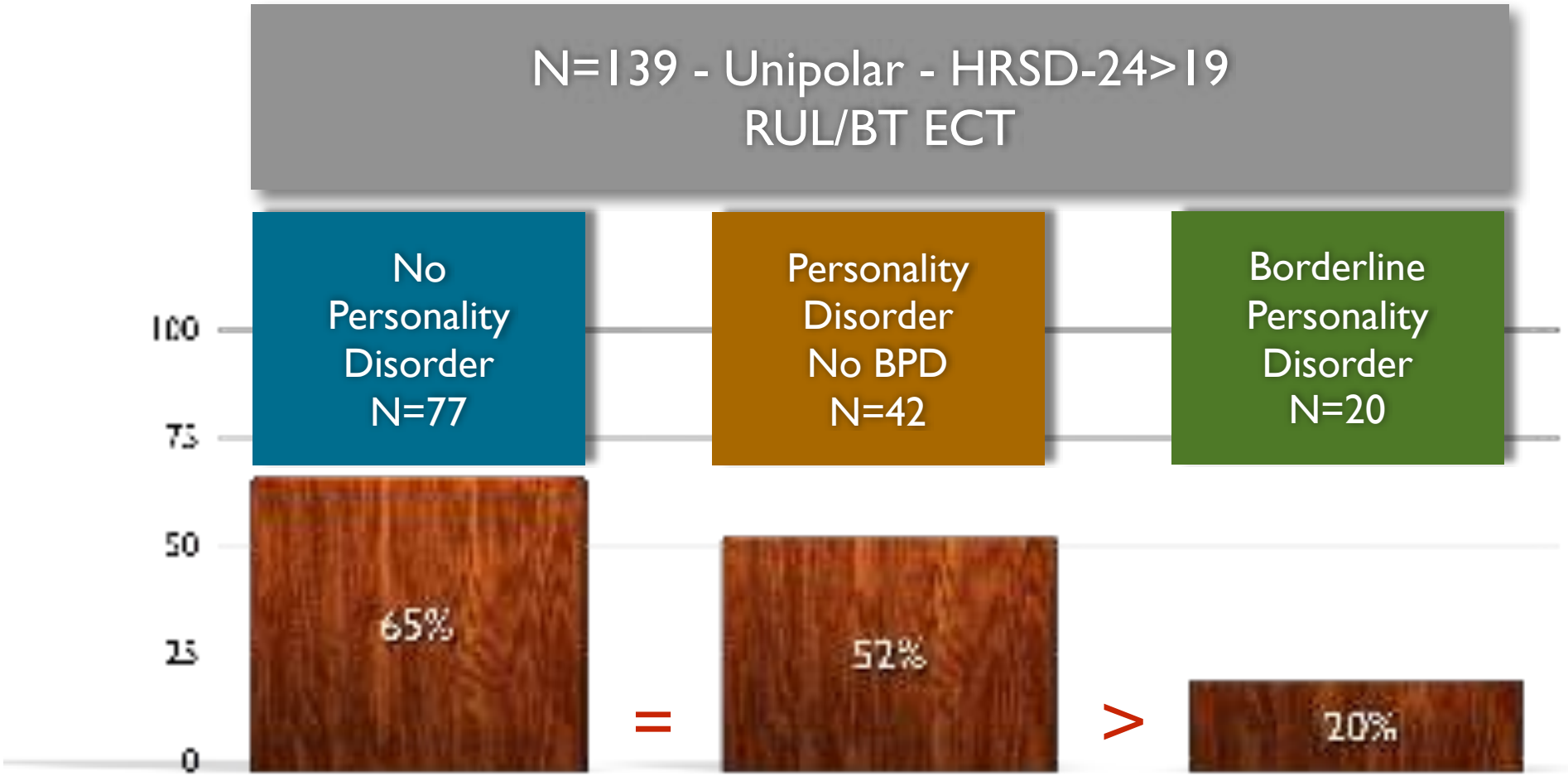
Comorbid PD

is associated with a doubling of the risk of a *poor outcome for depression* compared with no PD *(OR.2.18)*

All treatments *apart from ECT* showed this poor outcome

Comorbid BPDS

lowers the chance of achieving remission



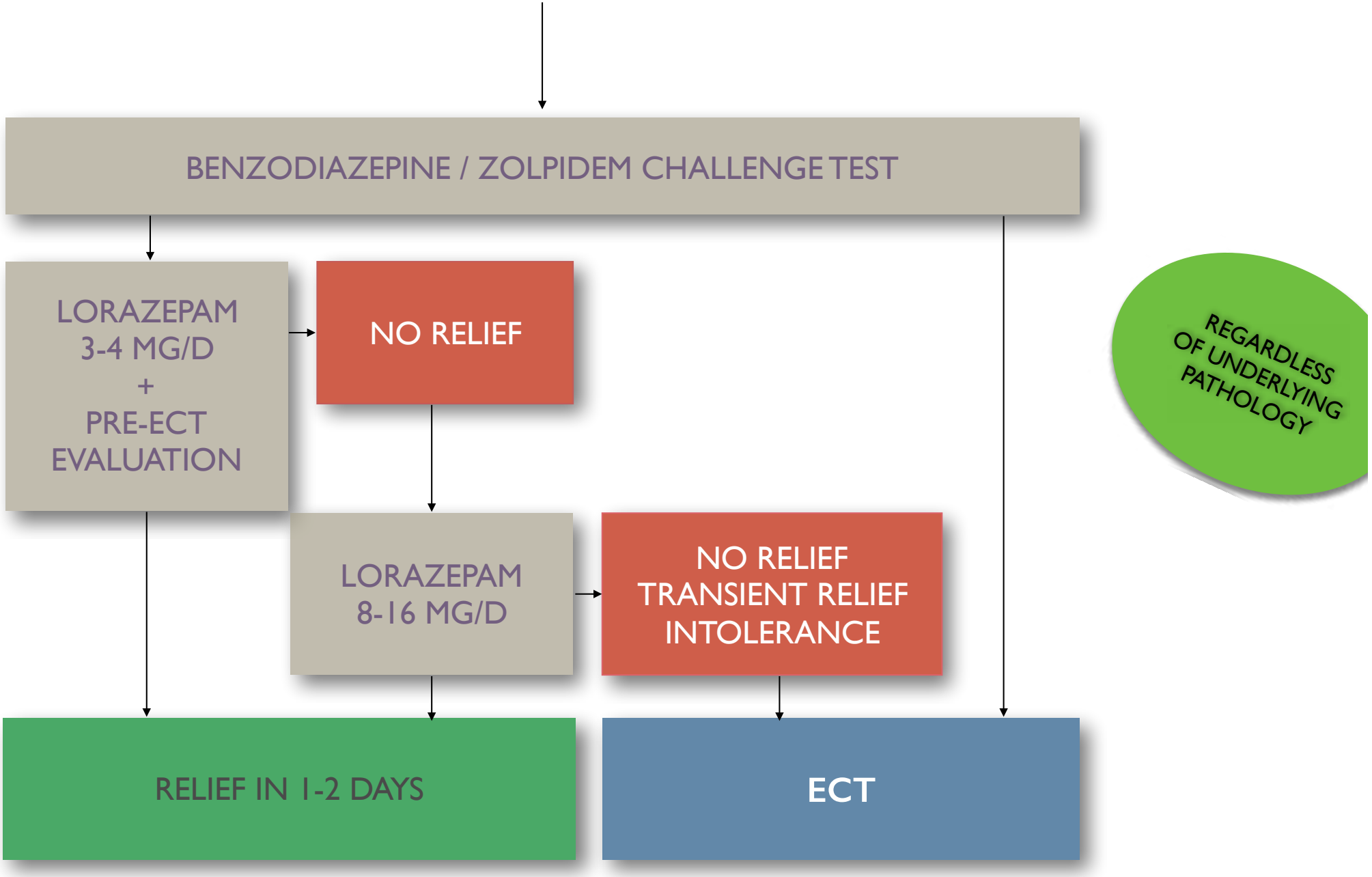
Feske et al (2004). Clinical outcome of ECT in patients with major depression and comorbid borderline personality disorder. *Am J Psychiatry* 161, 2073-80.

Vascular burden does not predict unfavorable outcome

MODECT

- brain aging
  - lower volume hippocampus
  - more white matter hyperintensities
  - higher amyloid load
- indication on clinical grounds regardless of age-related brain pathology

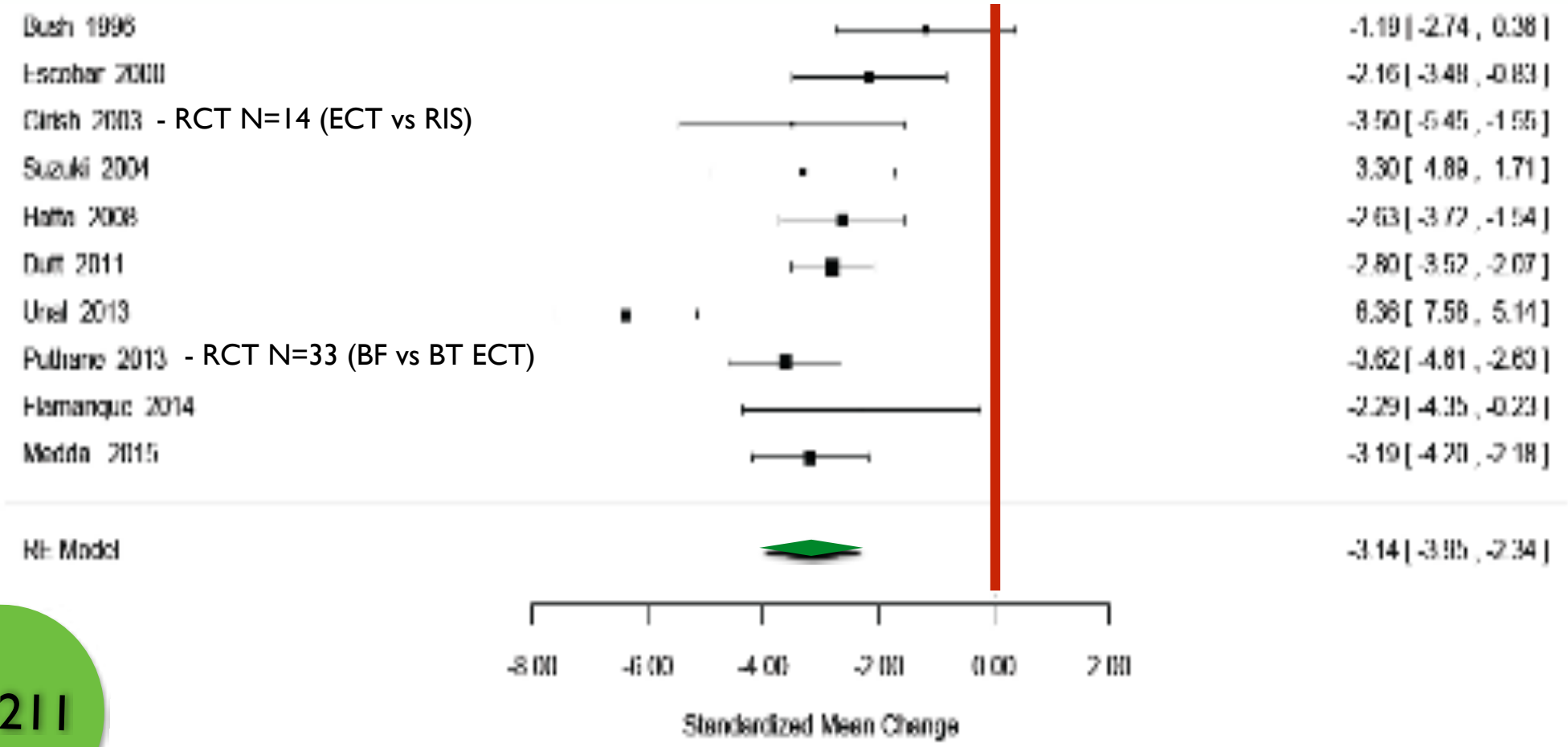
Bouckaert e.a. Relationship Between Hippocampal Volume, Serum BDNF, and Depression Severity Following ECT in Late-Life Depression. Neuropsychopharmacology 2016; 41(11): 2741-8.



Sienaert et al. In: Handbook of Neurology 2019 (In Press)

ECT in Catatonia

meta-analysis

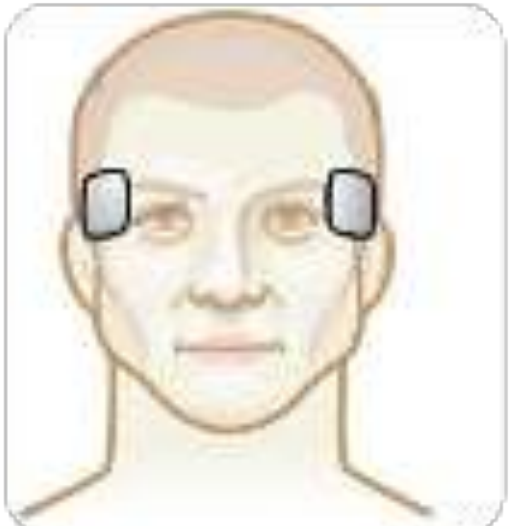


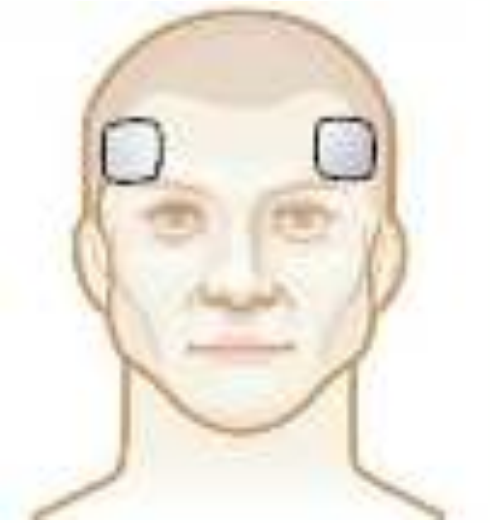
N=211

Forest plot for pre-post-differences in severity after ECT.

Leroy et al. Is electroconvulsive therapy an evidence-based treatment for catatonia? A systematic review and meta-analysis. Eur Arch Psychiatry Clin Neurosci 2018;268:675-687.

ECT





- consider *daily* ECT
- substantially *above* threshold
- if response to BDZ *do not stop abruptly*
  - *flumazenil before anesthetic*
- number of ECT unpredictable
  - *response after one / few ECT >< high number* *Ozgen 12; de Silva 13*

Sienaert et al. A clinical review of the treatment of catatonia. Frontiers in Psychiatry 2014;5(163).

ECT in schizophrenia

High quality evidence

- Meta-review *ECT N=2; rTMS N=3*
- 9 RCT high quality
- Improvement in global symptom severity
  - *Short term*
  - *Small but signficant*
  - *+/- AP*

Matheson et al. 2010. Quality assessment and comparison of evidence for ECT and rTMS for schizophrenia: A systematic meta-review. *Schizophr Res* 118, 201-210.

Clozapine + ECT

resistant schizophrenia

2 RCT

Petrides et al, 2015
Single blind - Crossover

Masoudzadeh & Khalilian, 2007
Unblinded

N=39

N=18

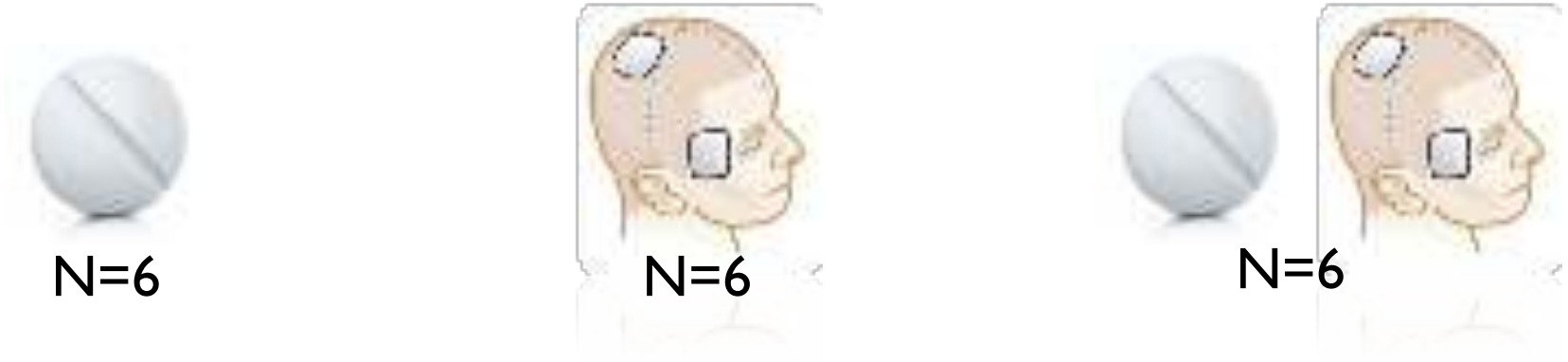
resistance to CLOZ

resistance to NON-CLOZ AP

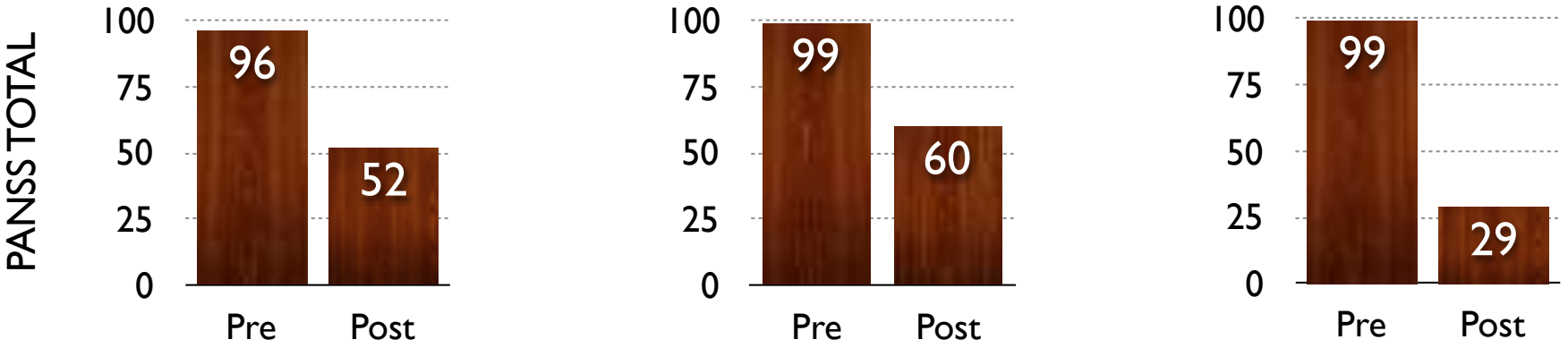
Clozapine + ECT

non-clozapine ap resistant schizophrenia

RCT, unblinded - N=18 - no response definition



N=6 N=6 N=6



F = 189.15, df = 4,63, p=0.0001)

Masoudzadeh & Khalilian, 2007. Comparative study of clozapine, ECT and the combination of ECT with clozapine in TRS patients. Pakistan Journal of Biological Sciences 10 (23), 4287–4290.

Clozapine + ECT

RCT - clozapine resistant schizophrenia

N=39

8W

ECT + CLOZ
N=20
Completers N=17

- *N=10 - 50%*
- *N=10 - 50%*

continue CLOZ
N=19
Completers N=16

- *N=0 - 0%*
- *N=19 - 100%*

ECT + CLOZ
N=19

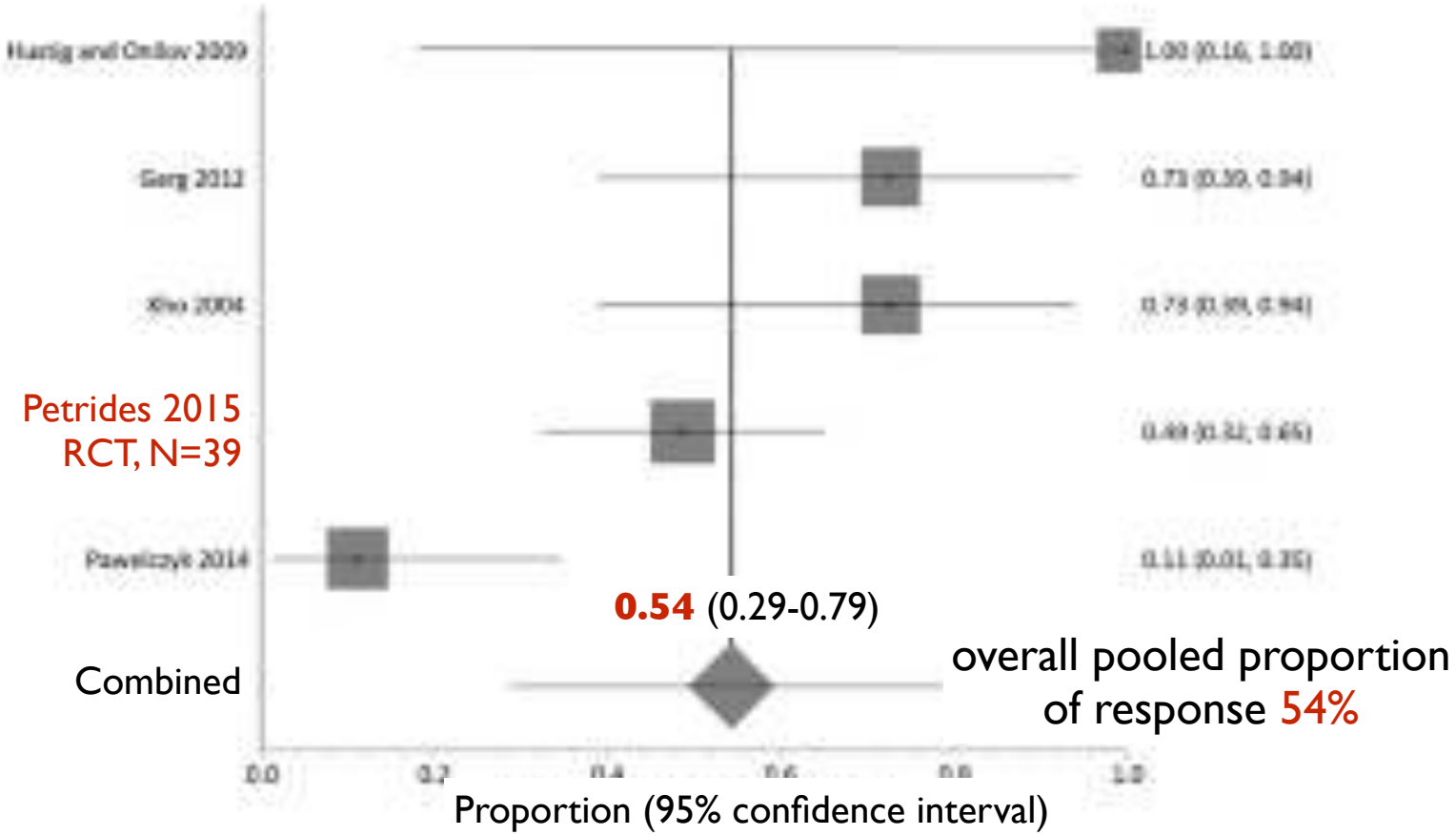
- *N=9*
  47%
- *N=10*
  53%

Petrides et al. ECT augmentation in clozapine-resistant schizophrenia: a prospective, randomized study. *Am J Psychiatry* 2015;172(1):52-8.

Response - *Non-response*

Clozapine + ECT

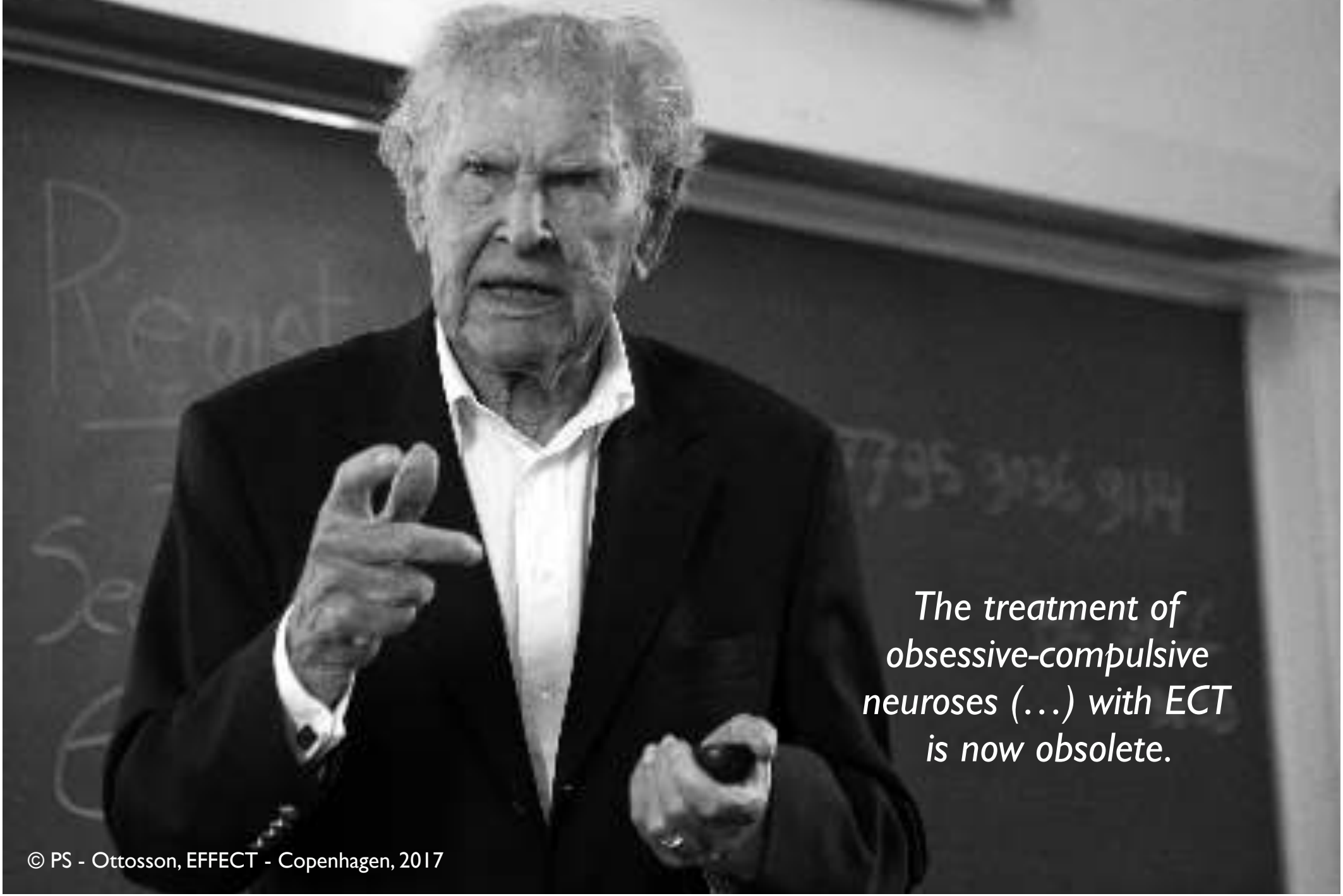
meta-analysis - proportion of responders



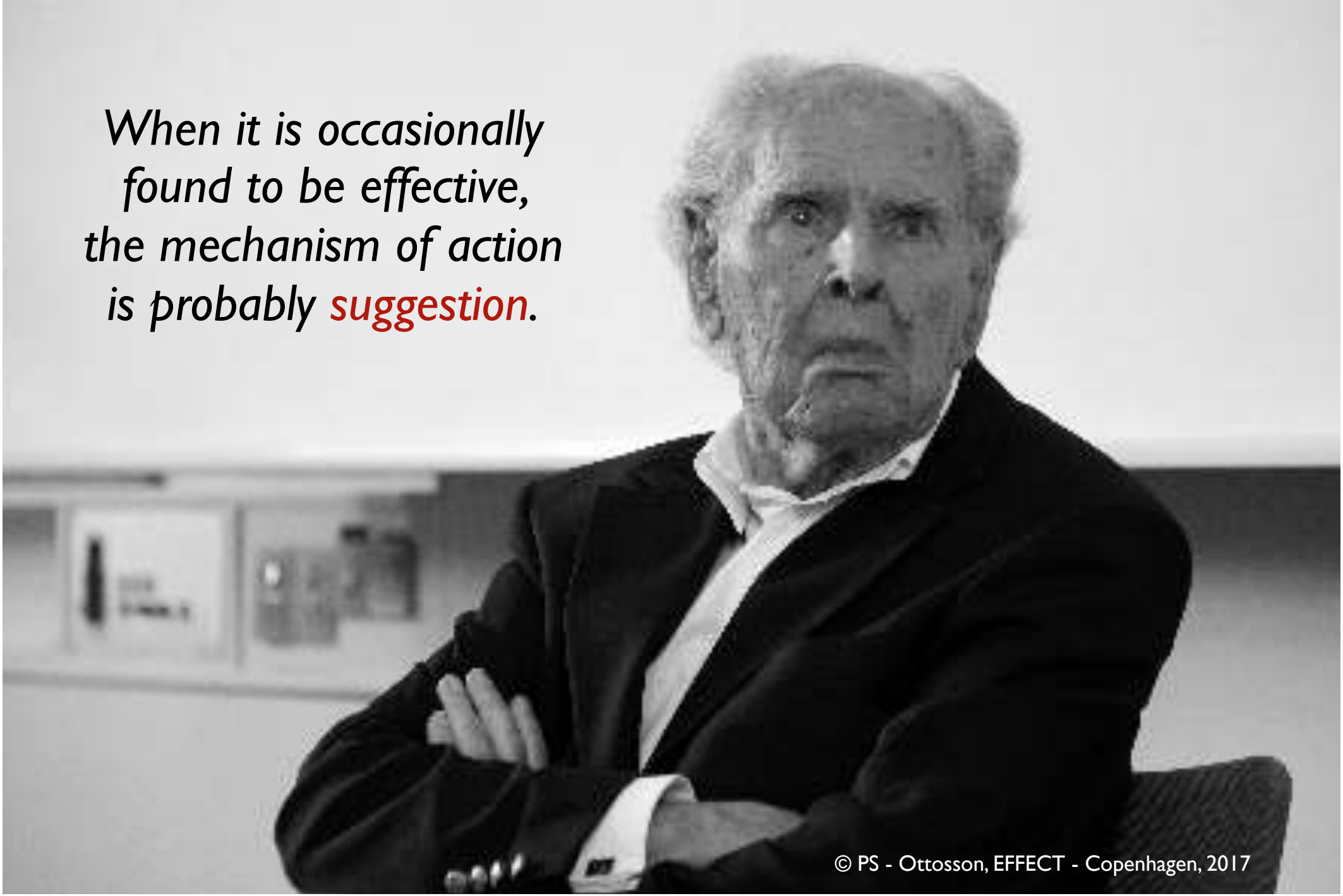
Trials
N=5

Patients
N=71

Lally et al. Augmentation of clozapine with ECT in treatment resistant schizophrenia: A systematic review and meta-analysis. Schizophr Res. 2016;171:215-224.



Jan-Otto Ottosson (1985). Use and misuse of electroconvulsive treatment. *Biol Psychiatry* 20, 933



Jan-Otto Ottosson (1985). Use and misuse of electroconvulsive treatment. *Biol Psychiatry* 20, 933

1988

Convulsive Therapy
4(4):314–320 © 1988 Raven Press, Ltd., New York

Electroconvulsive Therapy in Obsessive-Compulsive Disorder

Sumant Khanna, B. N. Gangadhar, Vinod Sinha, P. N. Rajendra, and S. M. Channabasavanna

- N=9, Non-response *<30% improvement with TCA + CBT*
  - RUL / BT ECT
  - *Subjects with depression were included provided the depression started ≥2 months after onset of OCD symptoms*

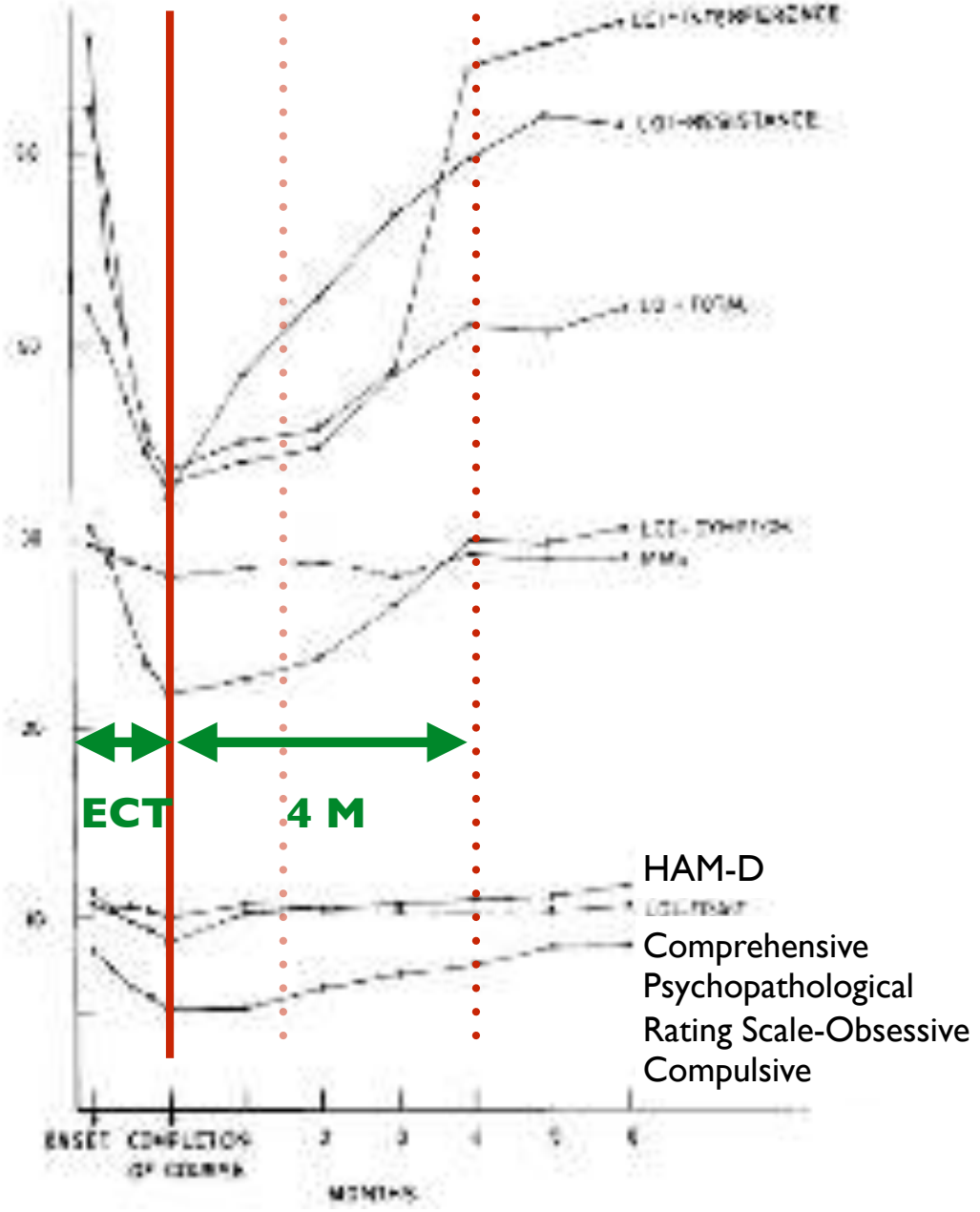
>20% ↓
global OCD ratings

initial *improvement*

maintained short-term
1-4 months

Khanna et al (1988). ECT in Obsessive-Compulsive Disorder
Convuls Ther 4(4), 314-20

Leyton's Obsessional Inventory



ECT in OCD

case reports/series

- positive response in 60.4%
- ECT responders
  - *later onset of OCD*
  - *more frequently non-depressed*
  - *more commonly being treated with ECT for severe OCD*
  - *received a fewer number of ECT sessions*
  - *less frequently previously treated with adequate trials of SSRI/CBT*

Fontenelle et al. Electroconvulsive therapy for obsessive-compulsive disorder: a systematic review. *J Clin Psychiatry* 2015;76(7):949-57.

need to reevaluate the role of ECT in the treatment of OCD

substantial acute effect, but high relapse potential

option in severe refractory cases

www.theeffect.eu