NACT Nordic Association for Convulsive Therapy

Lithium for post-ECT depressive relapse prevention

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Disclosure

No disclosures to report

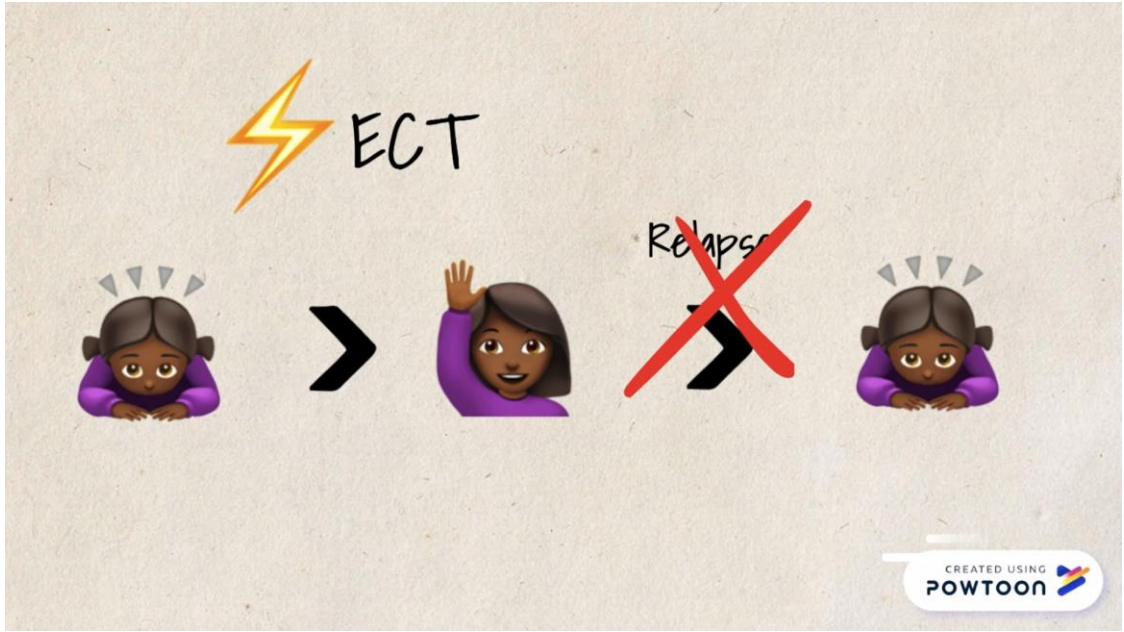
Relapse after ECT

- ECT
  - Safe and effective
  - Major depression

- 1-year relapse rate: 50% *Jelovac et al. (2013), Neuropsychopharmacology*

Relapse prevention strategies

- ECT
- CBT
- Pharmacotherapy

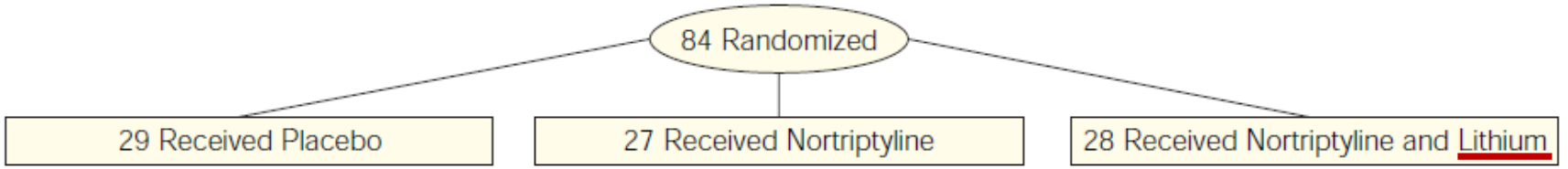


Lithium entering the ECT field

Continuation Pharmacotherapy in the Prevention of Relapse Following Electroconvulsive Therapy

A Randomized Controlled Trial

Harold A. Sackeim, PhD
Roger F. Haskett, MD
Benoit H. Mulsant, MD
Michael E. Thase, MD
J. John Mann, MD
Helen M. Pettinati, PhD
Robert M. Greenberg, MD
Raymond R. Crowe, MD
Thomas B. Cooper, MA
Joan Prudic, MD



84% relapse

60% relapse

39% relapse

Sackeim et al. (2001), Jama

Does lithium prevent relapse following successful electroconvulsive therapy for major depression? A systematic review and meta-analysis

Simon Lambrichts[1] | Johan Detraux[2] | Kristof Vansteelandt[1] | Axel Nordenskjöld[3] | Jasmien Obbels[1] | Didier Schrijvers[4] | Pascal Sienaert[1]

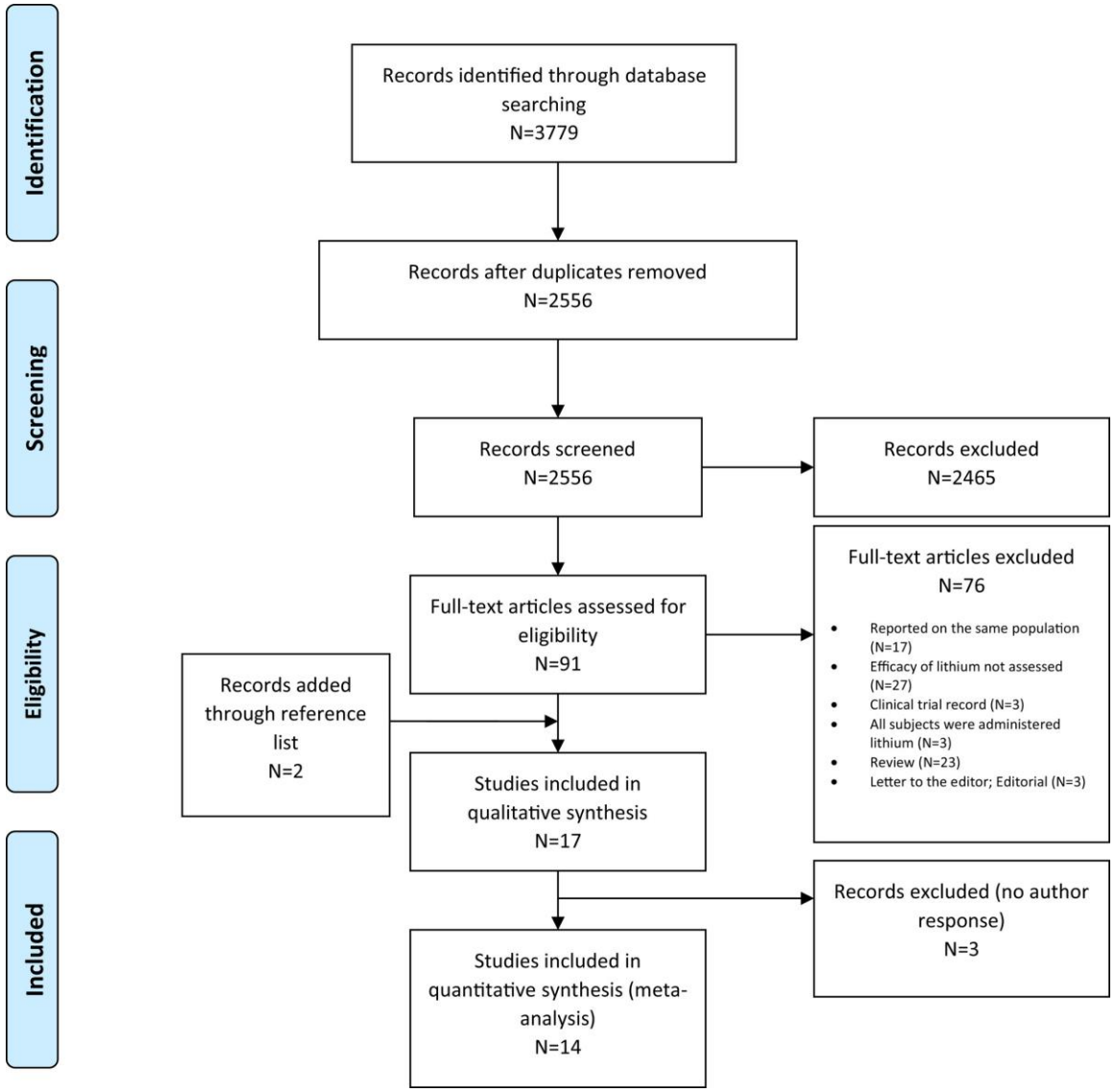
Lambrichts et al. (2021), Acta Psychiatr Scand

Methods

- Systematic search
- Risk of bias
- Meta-analysis (OR)
- Subgroup and meta-regression analyses
- Publication bias
- GRADE (high, moderate, low or very low)

Study selection

- 14 articles
- 9748 participants
  - With lithium: N=1571
  - Without lithium: N=8177



Study characteristics

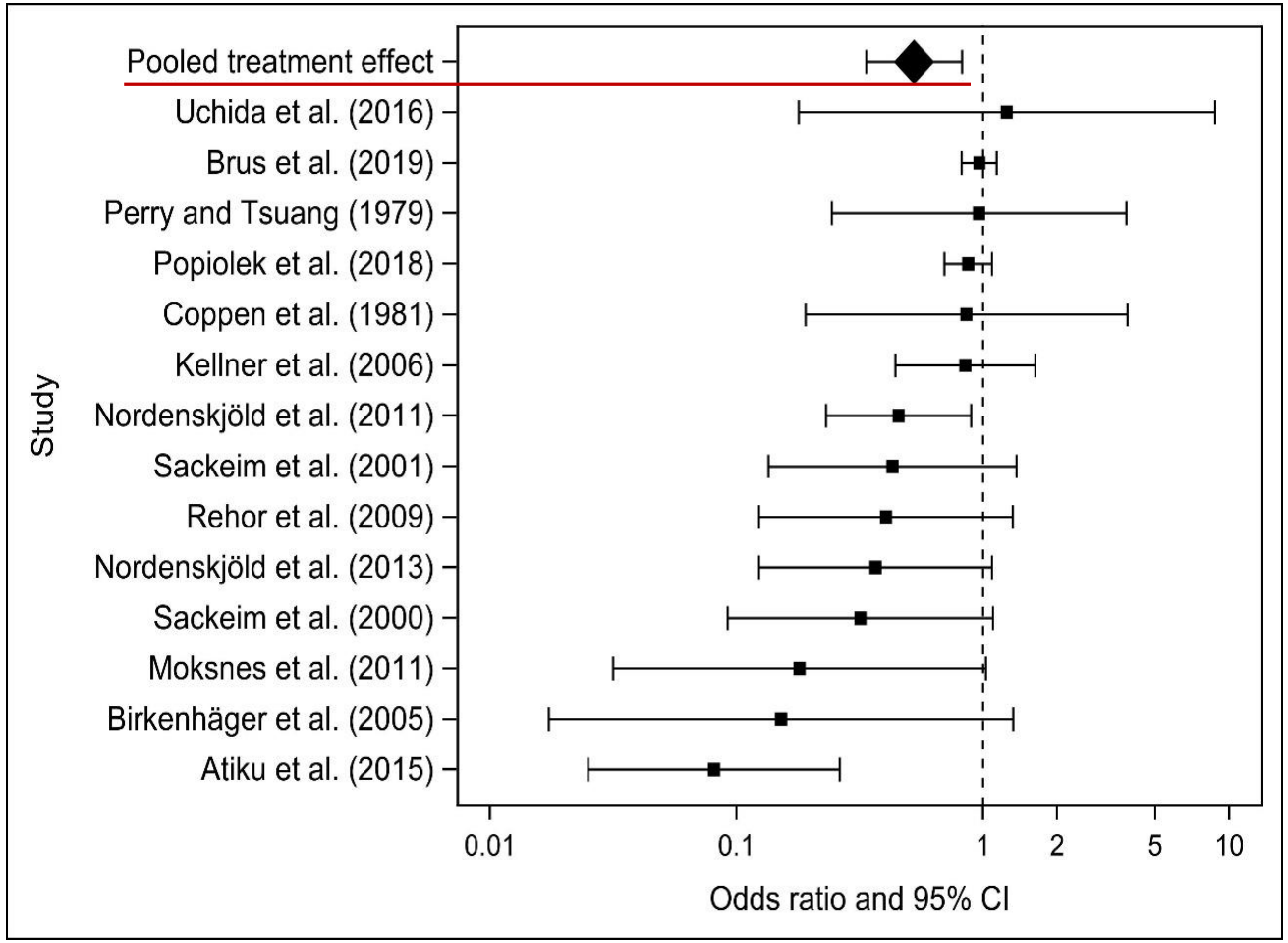
- Participants: 27-7350 (median=88)
- Mean age: 51-70 years
- Psychotic features: 23% (18-49%)
- Follow-up duration: 15-58 weeks (median=26)
- Observational (11/14)
- Low risk of bias (10/14)

Study characteristics

- Diagnosis
  - Unipolar only: 7
  - Unipolar or bipolar: 6
  - Bipolar only: 1

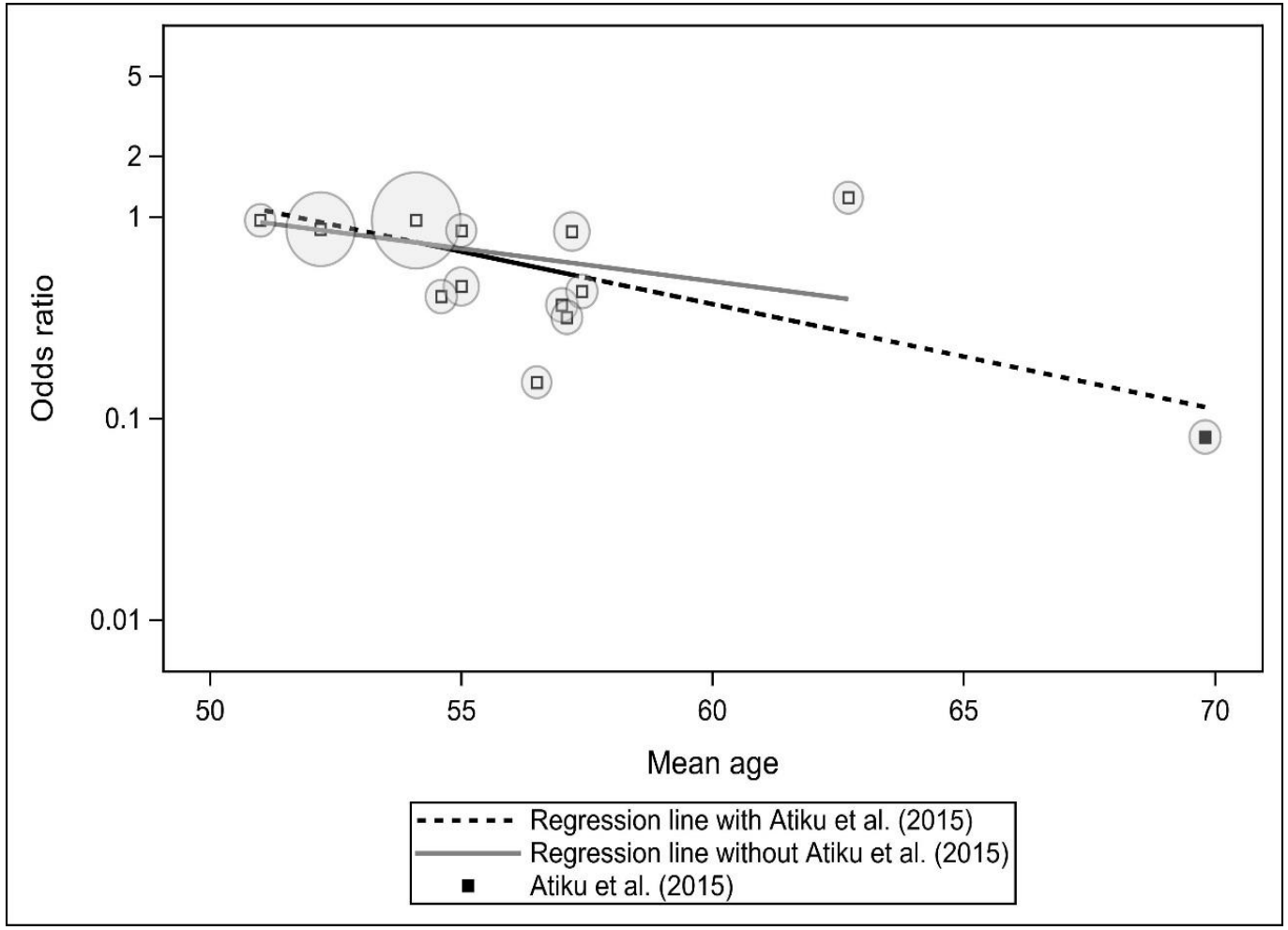
- Lithium
  - Monotherapy: 2
  - + TCA: 3
  - + Antidepressant: 1
  - Monotherapy / + Antidepressant(s) and/or antipsychotic(s) and/or mood stabilizer(s) and/or continuation ECT: 8

Patients receiving lithium less likely to relapse

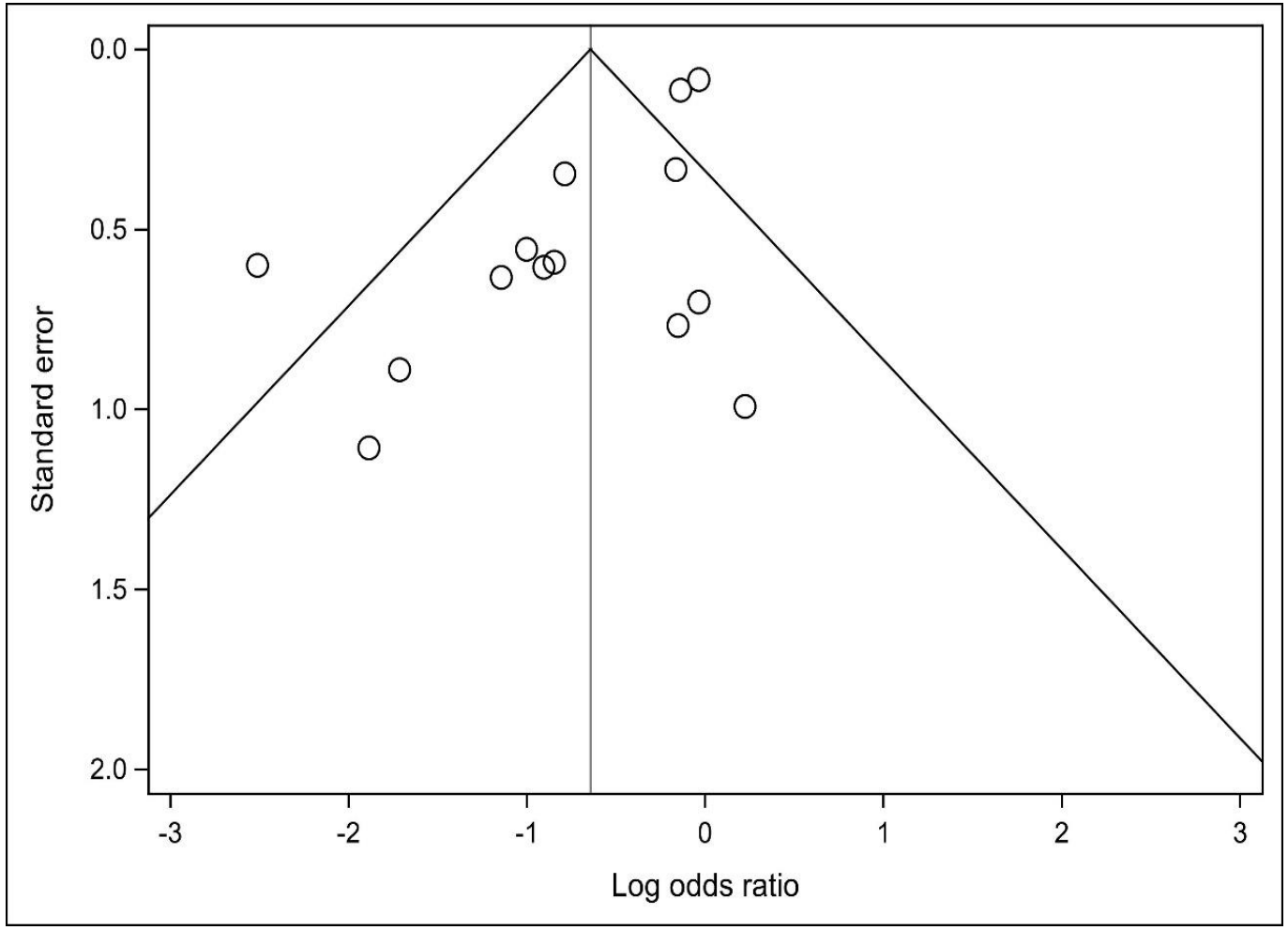


OR=0.53 (95% CI=0.34-0.82)

Stronger protective effect of lithium in studies with patients with a higher mean age



Indications for publication bias



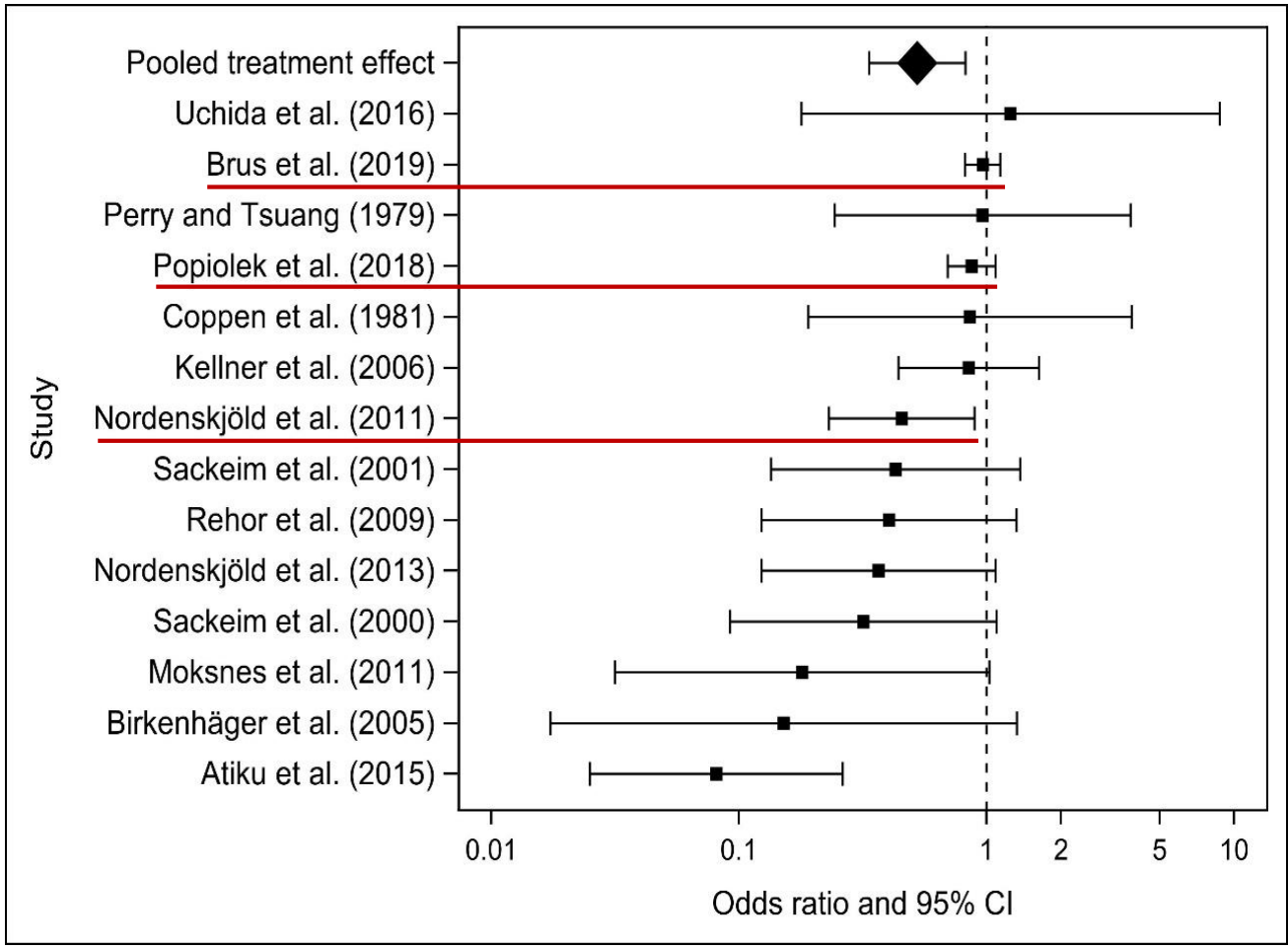
Quality of evidence (GRADE)

Quality level	Current definition
High	We are very confident that the true effect lies close to that of the estimate of the effect
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Guyatt et al. (2011), Journal of Clinical Epidemiology

Discussion

- Small to medium effect
- Very low quality of evidence (GRADE)
- Specific effect of lithium addition?



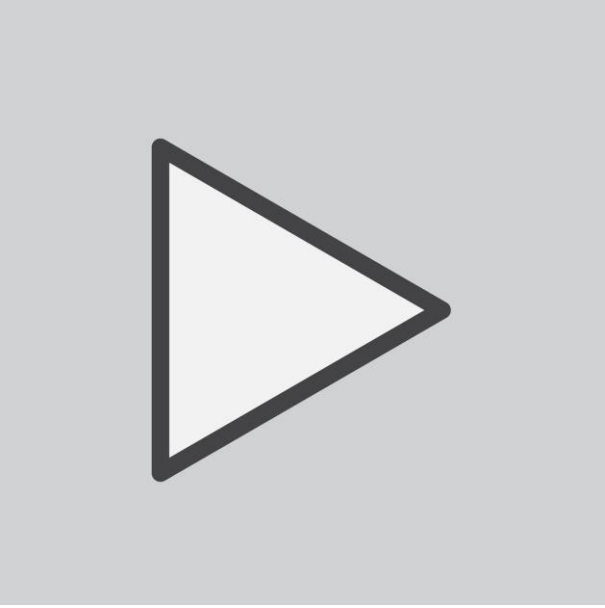
Conclusion

Research

- Lithium may have superior efficacy
- High-quality studies

Clinical practice

- Risks versus benefits
- Case by case

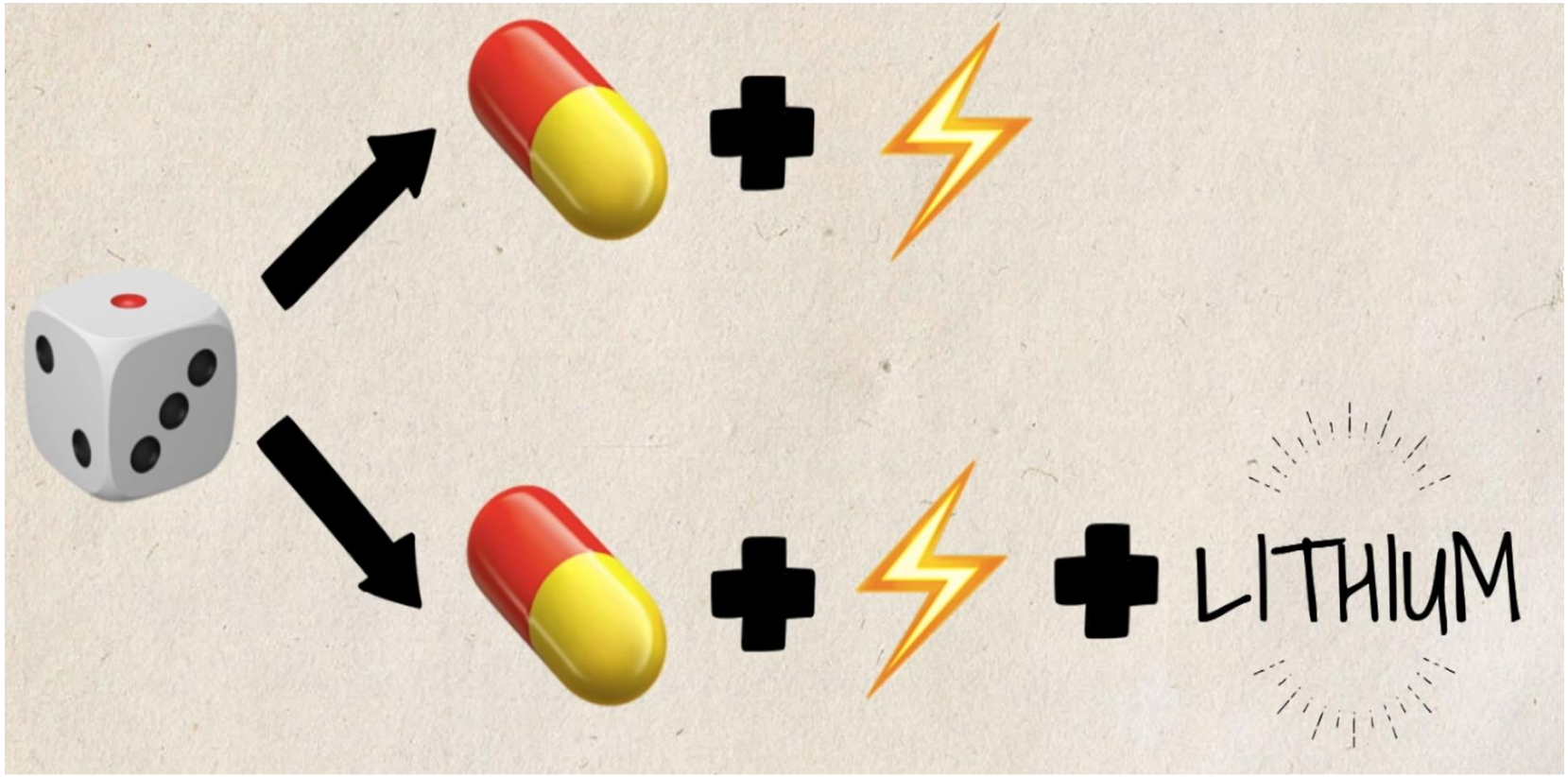


How to proceed?

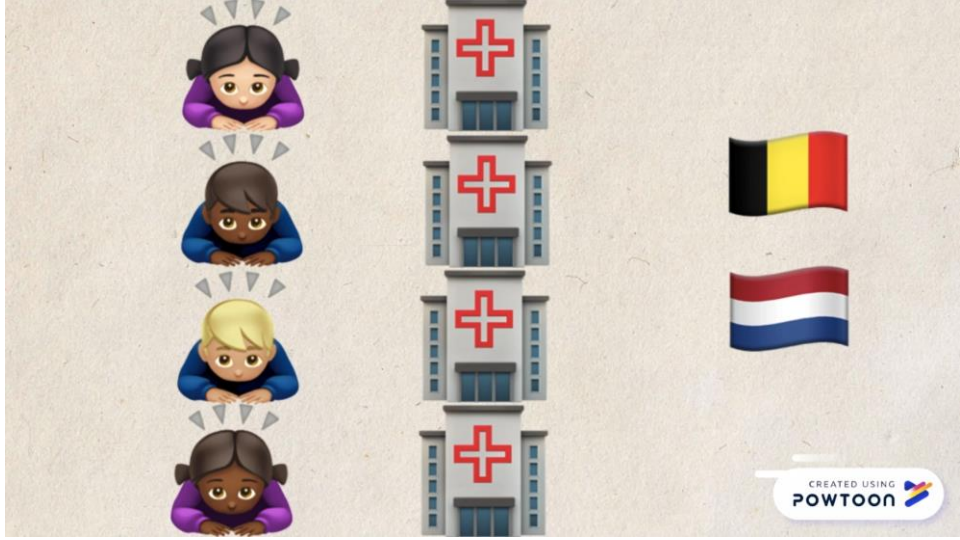
PRASED study

Preventing **R**elapse **A**fter **S**uccessful **E**CT for **D**epression

Design

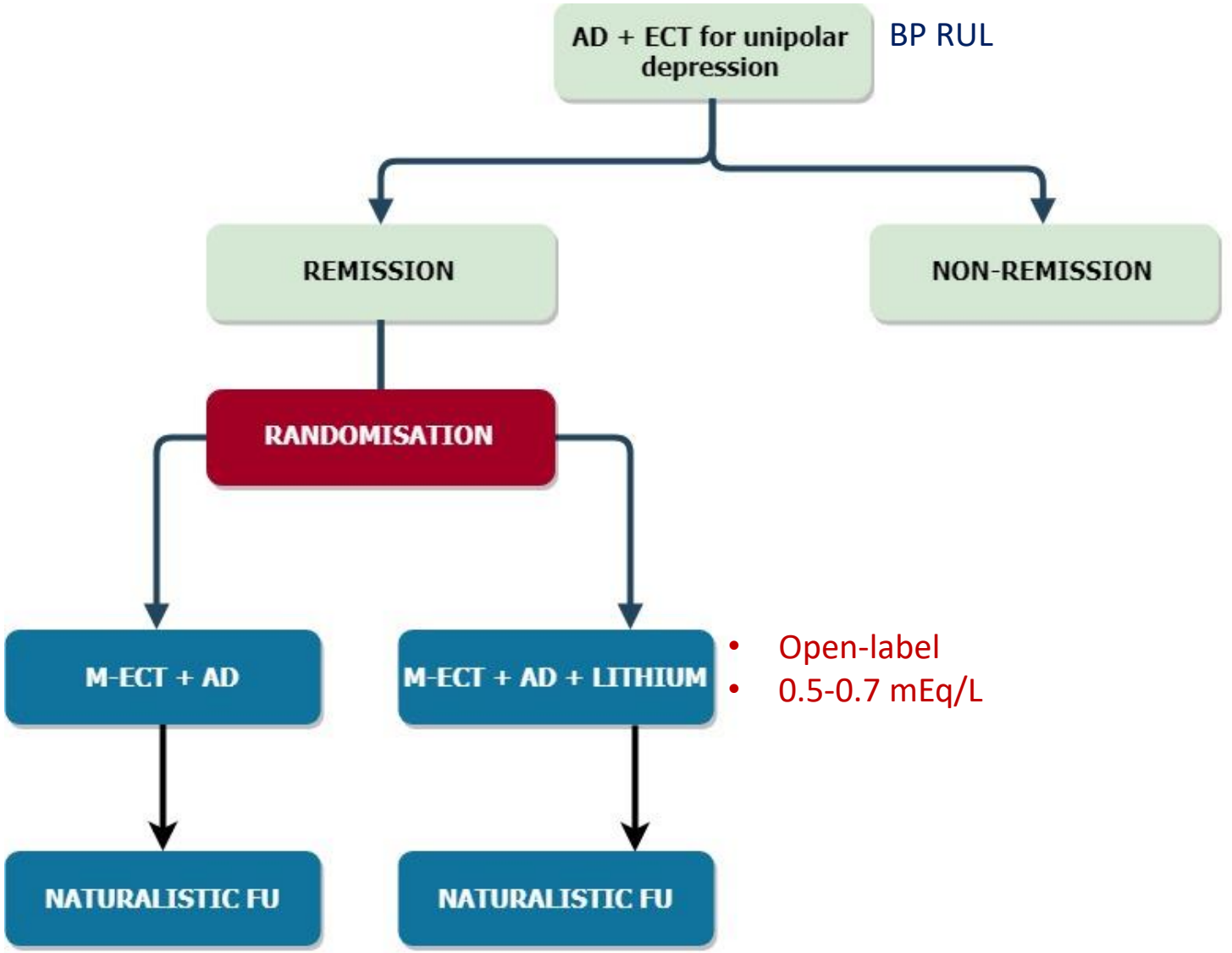


PRASED study



- Inclusion criteria
  - ≥18 years old
  - MDD diagnosis
  - Pre-treatment IDS-C score ≥29
  - Remission after acute ECT course (IDS-C score ≤12 on 2 consecutive ratings)

- Exclusion criteria
  - Diagnosis: bipolar disorder, schizoaffective disorder or schizophrenia; dementia or intellectual disability; substance abuse or dependence in the past 6 months
  - Current lithium therapy or contraindications for lithium therapy
  - ECT within the past 3 months


AD + ECT for unipolar depression
BP RUL
REMISSION
NON-REMISSION
RANDOMISATION
M-ECT + AD
M-ECT + AD + LITHIUM
NATURALISTIC FU
NATURALISTIC FU
Open-label
0.5-0.7 mEq/L
Regular Care
Phase 1
(0-6 months)
Phase 2
(6-12 months)

Symptom-titrated algorithm-based longitudinal ECT (STABLE)

Week 1–4: Fixed ECT schedule		
One treatment 2–5 days after randomization, one treatment 7–12 days after randomization, one treatment 14–19 days after randomization and one treatment 23–28 days after randomization (a total of four ECT treatments in 1 month)		
Week 5–26: Symptom-driven ECT schedule		
Number of additional ECT treatments	IDS-C conditions	Relapse potential
0	Current IDS-C score ≤ 9 Current IDS-C score 10-13 and previous score was 7-13 and current score is ≤ 2 points higher than previous score Current IDS-C score 10-17 and ≤ 2 points higher than baseline score	Low
1	Current IDS-C score intermediate between criteria for low and high relapse potential	Moderate
2	Current IDS-C score ≥ 22 Current IDS-C score 14-21 and current score is ≥ 3 points higher than previous score and current score is ≥ 9 points higher than baseline score	High

Lisanby et al. (2008), J ect

Outcome measures

Primary

- 6-month relapse* rate

**Relapse*

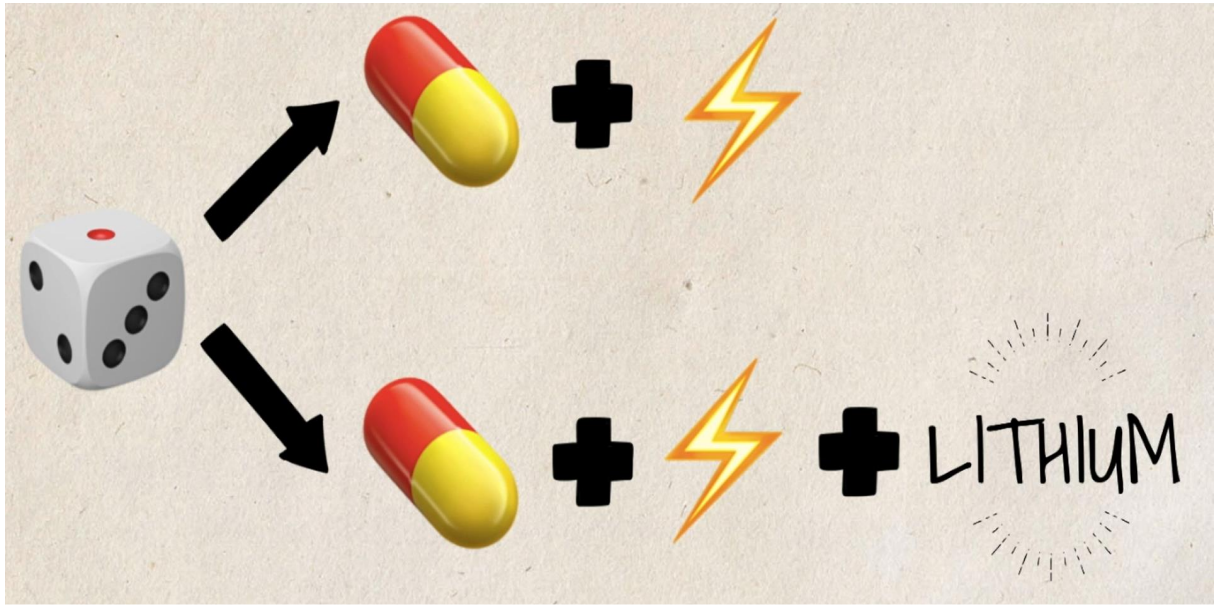
- *2 consecutive IDS-C scores ≥29*
- *Psychiatric hospitalization*
- *IDS-C score 3 on the suicide item*

Secondary

- Time to relapse
- Time to first additional ECT treatment
- IDS-C score at 6-month follow-up
- Total number of additional ECT treatments at 6-month follow-up
- Cognitive function

Randomized participants per site

- Kortenberg: 25
- Duffel: 23
- Bruges: 27
- Rotterdam: 4
- Total: 79



Clinical practice

Rasmussen (2015), J ect

How much?

- Target steady-state level
  - Sackeim et al. (2001): 0.5-0.9 mEq/L
  - Kellner et al. (2006): 0.7 mEq/L
  - Kellner et al. (2016): 0.4-0.6 mEq/L
  - PRASED: 0.5-0.7 mEq/L

- Level at final study visit
  - Sackeim et al. (2001): 0.59 (0.2) mEq/L
  - Kellner et al. (2006): 0.53 (0.38) mEq/L
  - Kellner et al. (2016): 0.53 (0.27) mEq/L (medication only); 0.36 (0.23) mEq/L (medication plus ECT)

How long?

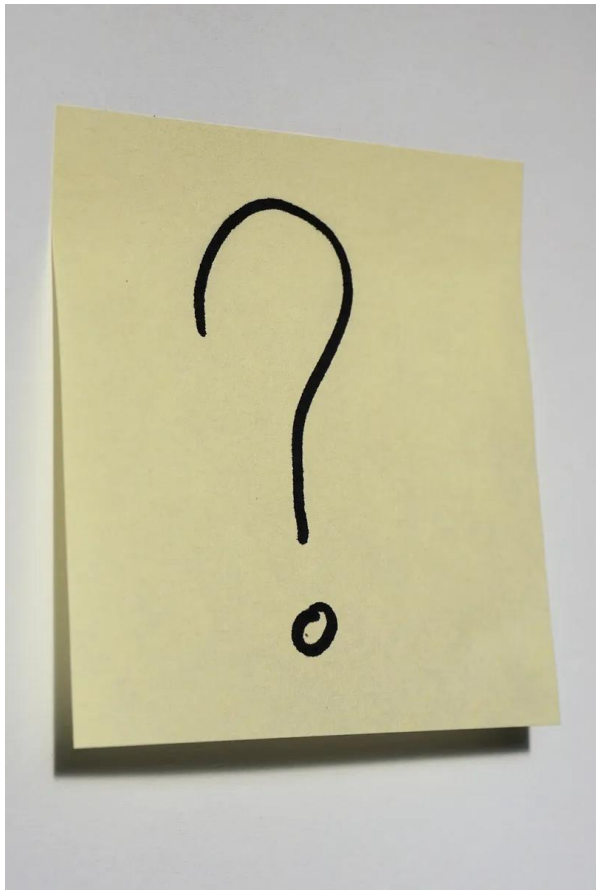
- At least 6 months
- Longer if highly recurrent

Monotherapy or in combination?

- Nortriptyline
- Venlafaxine

When to start?

- *After* the acute course?
- *Toward the end* of the acute course?



Lithium plus ECT

- Close monitoring
- Hold for at least 24 hours

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

Charles H. Kellner, M.D., Mustafa M. Husain, M.D., Rebecca G. Knapp, Ph.D., W. Vaughn McCall, M.D., M.S., Georgios Petrides, M.D., Matthew V. Rudorfer, M.D., Robert C. Young, M.D., Shirlene Sampson, M.D., Shawn M. McClintock, Ph.D., Martina Mueller, Ph.D., Joan Prudic, M.D., Robert M. Greenberg, M.D., Richard D. Weiner, M.D., Ph.D., Samuel H. Bailine, M.D., Peter B. Rosenquist, M.D., Ahmad Raza, M.D., Ph.D., Styliani Kaliora, M.D., Vassilios Latoussakis, M.D., Kristen G. Tobias, M.A., Mimi C. Briggs, B.A., Lauren S. Liebman, B.A., Emma T. Geduldig, B.A., Abeba A. Teklehaimanot, M.S., Mary Dooley, M.S., Sarah H. Lisanby, M.D., the CORE/PRIDE Work Group

Kellner et al. (2016), Am J Psychiatry

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