

VA CSP-590

Lithium for Suicidal Behavior in  
Mood Disorders: A classic RCT  
addressing a real-world question

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# Background

- The hypothesis that lithium can prevent suicide in patients with bipolar disorder and major depression was proposed over two decades ago
- Meta-analyses of observational studies and RCTs conducted for other outcomes provide support
- A propensity-matching study of bipolar patients in the VA electronic health record gave equivocal findings
- At least two clinical trials were terminated early due to difficulties in recruitment
- There has never been an adequately powered clinical trial
- If this research can be done anywhere, it can be done in VA:
  - Large patient population in multiple sites in an integrated health care system
  - Successful program for cooperative studies
  - Infrastructure for suicide prevention

# Outcomes

- Question: Do the selection processes for a(n) RCT filter out patients at risk for suicidal behavior? If so, outcome rates (and statistical power) will be lower than expected.
- Answer: Probably, yes
  - The observed rates of repeated attempts in participants are very similar to estimates derived from the medical record
  - Comparable studies demonstrated higher rates
  - But the medical record may miss attempts

# Diagnoses

- Question: If the focus of the study is on suicide prevention rather than symptoms, is it still important to be rigorous about diagnoses? Should the inclusion criteria
  - Exclude comorbidities
  - Require “depression” or “major depressive disorder”
- Decision
  - Allow most comorbidities
  - Require “current or recurrent major depression” documented by a structured interview or the medical record

# Effect Size

- What is a meaningful reduction in rates of suicidal behavior? How should a study be powered?
- Decision: Surveying providers about what effect would lead them to modify their practice demonstrating that fairly low effects would be effective. Excluding them would require prohibitively large sample size. The study was powered on the basis of the effects demonstrated in the previous terminated trials, attenuated for estimates of non-adherence, 37%, a number needed to treat of 18.

# Monitoring

- What happens when the need for flexibility in caring for complex patients meets the need for rigorous monitoring of adherence to the protocol of a(n) RCT?
- Answer: Flexibility is difficult.