Veterans Health Administration
Research & Development
Improving Veterans' Lives — www.research.va.gov

VA Boston Healthcare System

MAVERIC
MASSACHUSETTS VETERANS EPIDEMIOLOGY RESEARCH AND INFORMATION CENTER

# A Novel User Survey to Determine a Clinically Meaningful Effect Size in the Planning of CSP 590 (Li+)

Kelly M. Harrington, Ph.D.
for the CSP 590 Study Group

Society for Clinical Trials Meeting
May 19, 2015

# Background

- Thoughtful pre–trial planning
  - determine the feasibility and costs
  - necessary to balance rigor, relevance, and resources available

- Estimation of an effect size is an important step in designing a clinical trial
  - adequately powered
  - feasible
  - potential to change clinical practice and improve patient outcomes

# Background (2)

- **VA Cooperative Study 590 (Li+):**
  "Double-Blind Placebo-Controlled Study of Lithium for Preventing Repeated Suicidal Self-Directed Violence in Patients with Depression or Bipolar Disorder"

- Primary Hypothesis: Lithium augmentation of enhanced usual care will reduce the rate of repeated suicide attempts in participants with bipolar disorder or depression who have survived a recent event

# Background (3)

- During planning phase of CSP 590, experts and consultants could not reach consensus on:
  - whether proposed study had field support
  - what effect size would be large enough to change prescribing behavior
- In response, we conducted a survey to address these concerns from potential users of trial results

# Goals of Survey

1. To understand current experience and practice with lithium among VA psychiatrists.
2. To see whether psychiatrists would endorse the study design and randomize their patients to lithium or placebo.
3. To determine what effect size would change prescribing behavior among practicing VA psychiatrists.

# Methods

- Develop provider survey
  - 12-item survey
  - Consultation with Boston IRB to confirm survey was a preparatory-to-research activity not requiring formal IRB review
  - Survey met VHA guidelines for “exempt research”
  - VA Central Office reviewed and approved the final survey

# Methods (2)

- Survey method: population study
- Assemble email distribution list using multiple Veterans Health Administration (VHA) databases
  1. VHA Outpatient Encounter file
  2. Decision Support System (DSS) – Providers' file
  3. VHA Corporate Data Warehouse (CDW) – Staff Table
- Manually trim provider list
  - Removed non-psychiatrists, duplicates, and those without VA email

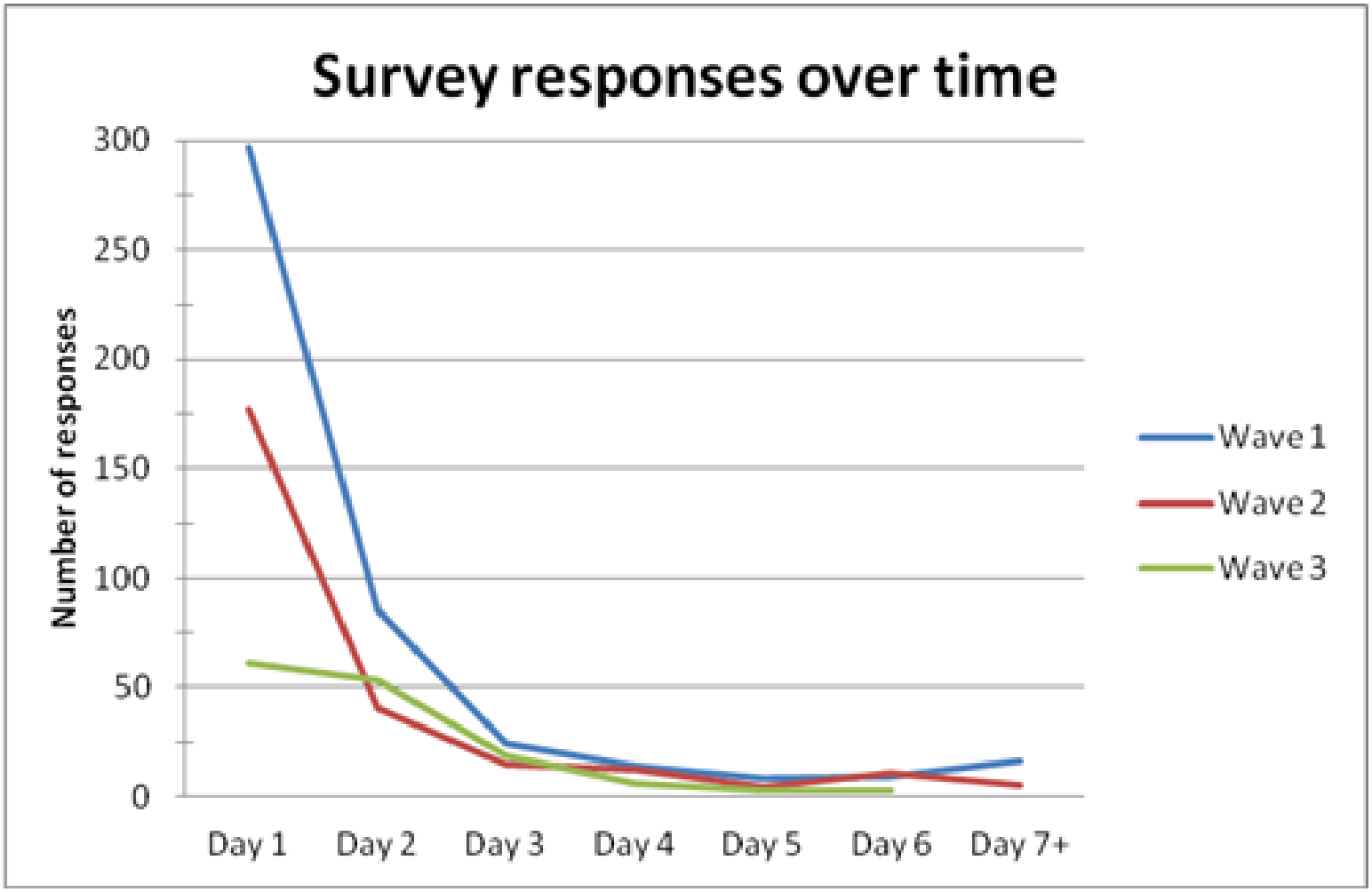
# Methods (3)

- Deploy provider survey
  - Hosted on SurveyMonkey©
  - 2,713 VA psychiatrists individually emailed (blind CC'ed) invitation to complete anonymous online survey
  - Survey conducted 4/16/12 to 5/16/12
  - Initial invitation letter and 2 reminders for non-responders
    - 3 waves, 9-14 days apart

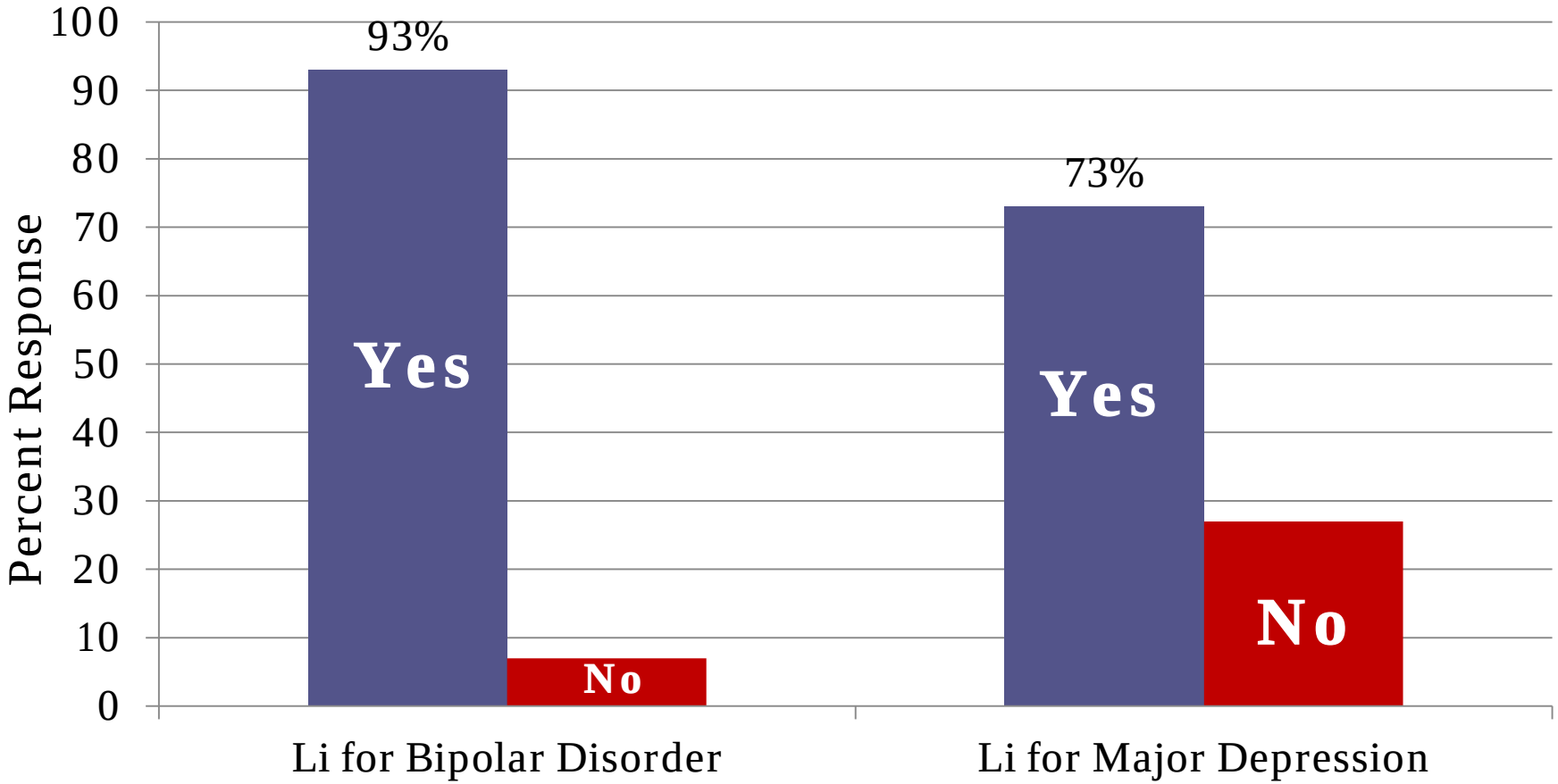
# Results

- Survey Response
  - Target population: 2,713 VA psychiatrists
  - Overall response rate = 32%
- Completeness of Response
  - Estimate of Denominator: N = 2,659 psychiatrists during pay period at the end of FY2013
    - Excludes trainees, non-VA paid staff
  - Response rate for other online surveys
    - Range: 20-47%; Average: 33% (Nulty, 2008)

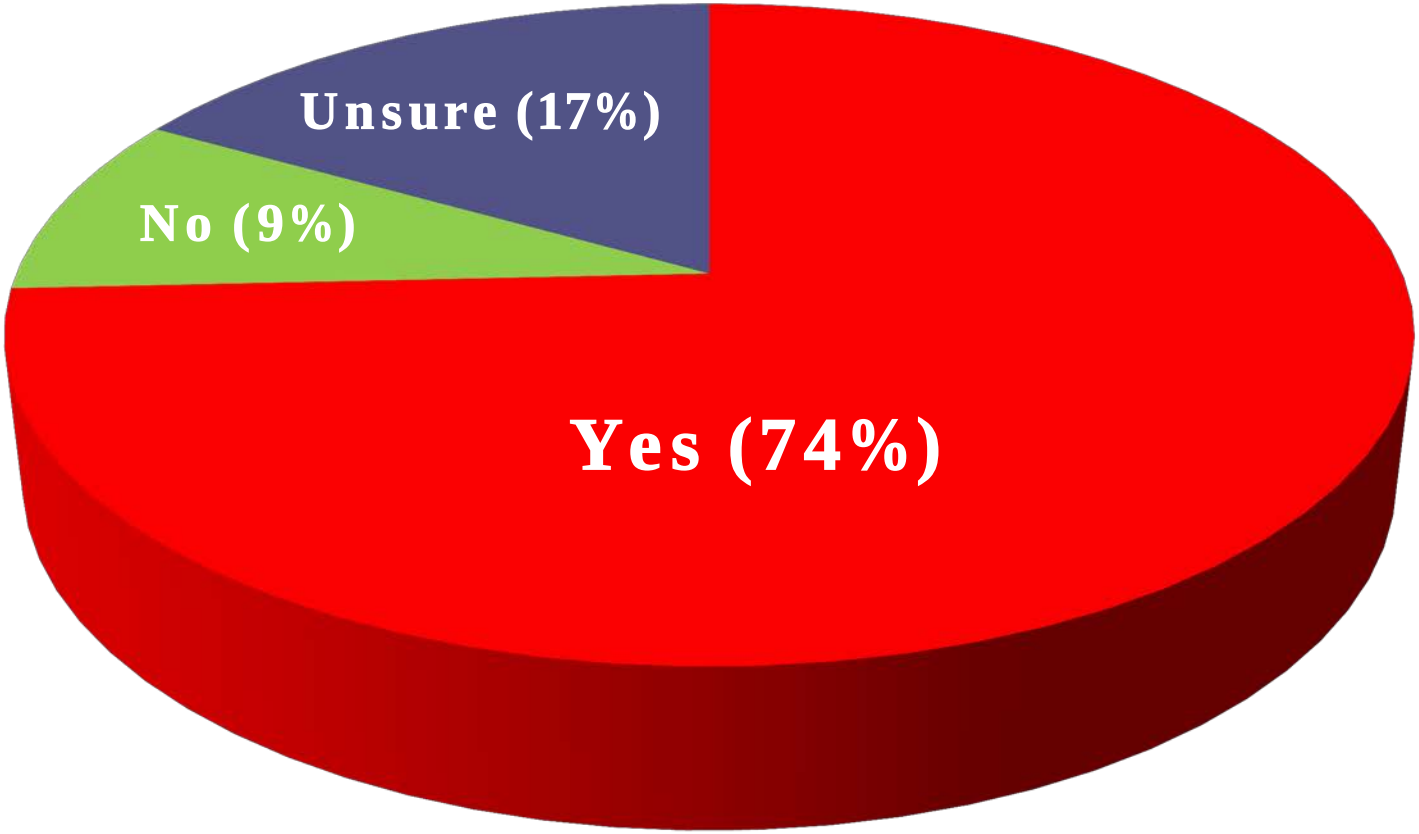
Nulty, D.D. Assessment & Evaluation in Higher Education. 2008: 33 ( 3), 301–314.


Survey responses over time
Number of responses
300
250
200
150
100
50
0
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Day 7+
Wave 1
Wave 2
Wave 3

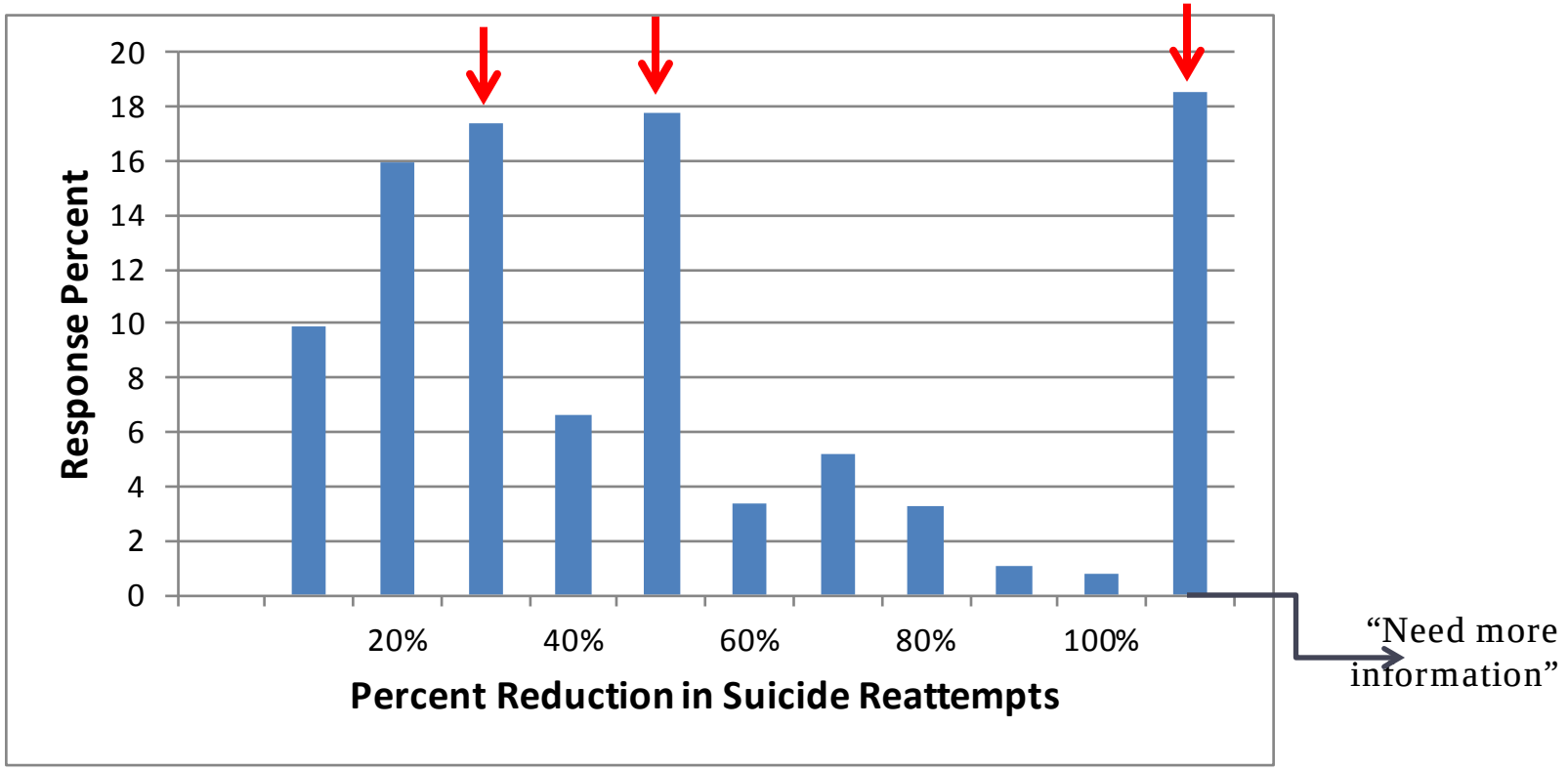
# Current lithium prescribing in the VA



# Willingness (%) to randomize patient to proposed trial



# Reduction in suicide reattempts needed to change practice



| Percent Reduction | Frequency | Cumulative Frequency | Cumulative Relative Frequency (%) |
|---|---|---|---|
| **10%** | 84 | 84 | 12.2 |
| **20%** | 135 | 219 | 31.8 |
| **30%** | 147 | 366 | 53.1 |
| **40%** | 56 | 422 | 61.2 |
| **50%** | 151 | 573 | 83.1 |
| **60%** | 29 | 602 | 87.3 |
| **70%** | 44 | 646 | 93.7 |
| **80%** | 28 | 674 | 97.7 |
| **90%** | 9 | 683 | 99.0 |
| **100%** | 7 | 690 | 100.0 |
| **TOTAL** | **690** | | |

# Summary of Results

- VA psychiatrists are experienced in use of Li
  - 93% prescribe lithium for bipolar disorder
  - 73% prescribe lithium for major depression patients not responding to antidepressants
- Good support for proposed trial
  - 74% would refer their patients to proposed RCT
- Confirmed effect size used for designing trial
  - 83% of respondents would change prescribing behavior with a 50% or less reduction in suicide attempts

# Implications for CSP 590

- Research question is clinically important and compelling
- A trial demonstrating the hypothesized effect would transform clinical management of suicidality
  - Hypothesized effect based on literature: 37% reduction in the rate of repeated suicidal self-directed violence
- A majority of potential end users would randomize their patients to RCT

# Caveats

- Responders may differ from non-responders
  - Anonymity precludes evaluating representativeness of survey responses
- Unknown reliability of survey responses on future prescribing behavior
- Preparation of distribution list is rate-limiting step
  - Estimated 50 person-hours
  - Alternatives: service distribution lists; lists maintained by boarding committees
- Guideline changes for conducting surveys in VA
- Generalizability outside of the VA system

# Conclusions

- Survey used to resolve two major concerns of the study sponsor
- Demonstrates the utility of user surveys in pre-trial planning
  - Instructive about current clinical practices
  - Help gauge interest of end users in trial
  - Estimate what effect size would change prescribing behavior among end-users
- Surveying potential users of a trial's results is a low-cost, convenient empirical method for determining meaningful, transformative effect sizes

# Co-authors from CSP 590 Study Team

- Matthew H. Liang, MD, MPH (Study Director)
- Keri Hannagan, MPH (Project Manager)
- Natalie Morgenstern, MPH (Project Manager)
- Soe Soe Thwin, PhD (Biostatistician)
- Ryan E. Ferguson, ScD, MPH (Acting Center Director, Boston CSPCC)
- Malcolm P. Rogers, MD (Study Psychiatrist)
- Tamara Y. Boney, MS (National Study Coordinator)
- Ira R. Katz, MD, PhD (Study Chair)

Thank you!

Contact: Kelly.Harrington@va.gov