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Design and conduct of a provider survey to determine a clinically persuasive effect size in planning VA Cooperative Study #590 (Li+)

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ABSTRACT

Background: The estimation of an effect size is an important step in designing an adequately powered, feasible clinical trial intended to change clinical practice. During the planning phase of VA Cooperative Study #590, "Double-Blind Placebo-Controlled Study of Lithium for Preventing Repeated Suicidal Self-Directed Violence in Patients with Depression or Bipolar Disorder (Li+)," it was not clear what effect size would be considered large enough to influence prescribing behavior among practicing clinicians.
Methods: We conducted an online survey of VA psychiatrists to assess their interest in the study question, their clinical experience with lithium, and their opinion about what suicide reduction rate would change their prescribing habits. The 9-item survey was hosted on SurveyMonkey© and VA psychiatrists were individually emailed an invitation to complete an anonymous online survey. Three email waves were sent over three weeks.
Results: Overall, 862 of 2713 VA psychiatrists (response rate = 31.8%) responded to the anonymous survey. 74% of the respondents would refer a patient to the proposed trial, 9% would not, and 17% were unsure. Presented with suicide reduction rates in 10% increments ranging from 10 to 100%, 61% of respondents indicated that they would use lithium if suicide attempts were reduced by at least 40%; 83% would use lithium if it reduced attempts by at least 50%.
Conclusions: Even with the limitations of response bias and the reliability of responses on future prescribing behavior, a survey of potential users of a clinical trial's results offers a convenient, empirical method for determining and justifying clinically relevant effect sizes.

1. Introduction

Randomized controlled trials face numerous challenges to complete successfully [1,2]. Thoughtful pre–trial planning is necessary to determine the feasibility and to balance rigor, relevance, and the resources available. The estimation of an effect size is an important step in designing an adequately powered, feasible clinical trial that has the potential to change clinical practice and to improve patient outcomes.

The Veterans Affairs Cooperative Studies Program (CSP) has unique characteristics that make investigator-initiated multicenter studies possible: an integrated healthcare system, a large stable patient population, national databases, the oldest functioning universal electronic medical record, core infrastructure with statistical, epidemiological, pharmaceutical, and health economics expertise, and resources for planning studies [3]. During the planning phase of CSP #590, "Double-Blind Placebo-Controlled Study of Lithium for Preventing Repeated Suicidal Self-Directed Violence in Patients with Depression or Bipolar Disorder (Li+)," a multi-center study that has since been funded by the Veterans Affairs Cooperative Studies Program, there was a lack of agreement among experts and outside consultants on whether there was sufficient support for the proposed study in the field. In addition, it was not clear what effect size would be considered large enough to

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influence prescribing behavior among practicing clinicians. In response, we designed a provider survey to address these concerns from the largest number of potential users of the trial results. CSP#590 would be the first adequately powered randomized clinical trial to evaluate the effectiveness of lithium in preventing episodes of suicidal self-directed violence.

The survey was intended to address three primary goals. The first was to understand current experience and practice with regards to lithium; the second was to see whether psychiatrists would be supportive of randomizing their patients to lithium or placebo and endorse the study design; and the third goal was to determine what effect size would be considered large enough to influence prescribing behavior among practicing psychiatrists.

2. Methods

2.1. Overview of survey design

The study team developed a nine-item survey to address the three major goals outlined above (see Appendix A for survey questions). Before conducting the survey, we had extensive consultation with our Quality Assurance department and the Institutional Review Board (IRB) at VA Boston Healthcare System. We were advised that IRB approval was not necessary as the survey was a preparatory to research activity and meant to facilitate the planning of a study. After completion of the survey, we realized that the methods and results may be of interest to the scientific community and we again sought guidance from the local VA IRB. The VA Boston Healthcare System IRB Committee certified that the provider survey met all published guidelines for “exempt research” as defined in 38 CFR §16.101 and Veterans Health Administration (VHA) Handbook 1200.05 [4,5]. The VA Boston Healthcare System Research and Development Committee subsequently approved this research study (i.e., publication of the survey results).

The survey was aimed at the entire population of VA psychiatrists. Specifically, we used an informatics-based approach to identify all actively prescribing psychiatrists in the VA system. Information from several VHA databases were merged and compiled to assemble an email distribution list for all survey recipients. Prescribing psychiatrists were surveyed from approximately 129 VA medical centers and VA healthcare systems across the 50 United States as well as Puerto Rico. The final survey was hosted on SurveyMonkey©. The online survey took approximately 5 minutes to complete. The CSP Study Director (MHL) emailed 2713 individual VA psychiatrists inviting them to complete an anonymous online survey that would help with the planning of a VA Cooperative Study. The survey was conducted between April 16th and May 16th of 2012. After the initial email was deployed, two additional reminder emails were sent to encourage individuals to complete the survey (see Appendix A for invitational email letter). Therefore, there were three waves of data collection occurring 9 to 14 days apart.

2.2. Identifying study population and creating the distribution list

The assembly of 2713 active VA email addresses was the most labor intensive and time consuming aspect of implementing the survey. In brief, the VHA Outpatient Encounter file was used to identify all physicians who completed encounter forms for outpatient visits to VA Mental Health clinics during Fiscal Year (FY) 2011. Next, this list was narrowed to the most relevant Provider Type in the database: Allopathic and Osteopathic Physicians; Psychiatry and Neurology; Psychiatry providers. Scrambled Social Security Numbers (SSNs), VA station codes, and names of the selected providers were retrieved from the Decision Support System (DSS) Providers file. This list of providers was then merged with the Staff Table of the Corporate Data Warehouse (CDW) database and the automated Lightweight Directory Access Protocol (LDAP) lookup system was used to retrieve email addresses for all providers.

Finally, duplicates were manually checked and records that had missing or obviously wrong position titles (e.g., incorrect provider type, non-MDs) and/or non-VA addresses were excluded from the final list. Psychiatry Residents and Fellows were included in the final list of providers. The total number of psychiatry providers identified using the VHA databases was validated against the number identified by the VA Office of Mental Health. The resultant list was inserted into the blind CC portion of email so that each individual got a personal letter without disclosing the addressees of other recipients.

2.3. Data collection

The final survey was hosted on SurveyMonkey© (https://www.surveymonkey.com/). This platform records all survey responses as well as the precise time (EST) that the online survey was completed. SurveyMonkey© has the capability of analyzing data online in real time as responses are accumulating. It is also possible to export the data file to analyze the responses using statistical software of one's choice.

3. Results

A total of 2713 email invitation letters were sent and online survey responses were received from 862 psychiatrists at VA medical centers across the United States. Overall, the response rate after three waves each 9 to 14 days apart was 31.8%. Among respondents, the response rate for individual items ranged from 98.0 to 99.9% with one exception: only 34.3% of respondents provided their three digit VA station code. Fig. 1 shows the frequency of survey response over time. The best response rate occurred on the first day the survey opened (n = 297). The response after the first email reminder (Wave 2, Day 1) was also very strong (n = 177). However, by the third email reminder (Wave 3, Day 1), the responses tapered off considerably (n = 61).

The first goal of the survey was to understand current experience and practice with respect to lithium usage (see Appendix A, Questions 2 and 3). As shown in Table 1, 93.3% of the responders currently prescribed lithium for patients with bipolar disorder and 72.7% for patients with major depression who did not respond to antidepressants. Among respondents who reported currently prescribing lithium for bipolar disorder, approximately three-quarters (73.9%) prescribed lithium for 10 to 50% of their patients with bipolar disorder. Among respondents who endorsed currently

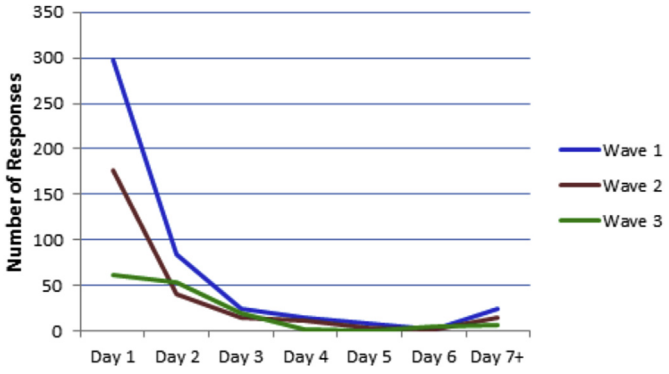

Fig. 1. Provider survey response rate over time.