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Characteristics of mental health trials registered in ClinicalTrials.gov

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ABSTRACT

The ClinicalTrials.gov registry was established in 2000 to address concerns about publication bias and public access to information about clinical trials. We aimed to evaluate differences between for-profit and non-profit sponsors of efficacy mental health trials registered in ClinicalTrials.gov on key trial characteristics that relate to data integrity. We also sought to evaluate whether the registry is fulfilling its purpose as a means of promoting transparency between researchers and the public by providing complete and quality information about the trials it contains. We found that trials tend to be small, use a placebo instead of an active comparator, and employ randomization and blinding. We discuss the implications of these design characteristics and the limitations of the registry.

1. Introduction

The ClinicalTrials.gov registry was created by the National Institutes of Health following the Food and Drug Administration Modernization Act of 1997, in response to concerns about public access to information on clinical research. Published research can provide a misleading picture of findings: studies with positive findings are more likely to be published than studies with nonsignificant findings and it can be difficult to track or find information on unpublished research (Dickersin, 1990; Dickersin and Min, 1993; Sterling, 1959). Further, selective outcome reporting can distort the results of trials (Chan et al., 2004; Dwan et al., 2008).

Randomized, double-blinded, controlled clinical trials, considered the "gold standard" of research studies, are thought to be the most rigorous research design for assessing safety and efficacy, and thus any bias generated in such trials may be particularly insidious (Kaptchuk, 2001). The overestimation of treatment effects that may result from biased publications endangers patients (Chalmers, 1990) and, particularly if published in a high-impact journal, may persist in influencing clinical practice even after the publication of conflicting evidence (Begg and Berlin, 1988). Additionally, selective outcome reporting and publication bias pose threats to meta-analyses where researchers depend on published research (Egger et al., 1997; Thornton and Lee, 2000).

Evidence suggests that publication bias, known as the "file drawer problem" in psychology (Rosenthal, 1979), is characteristic of antidepressant medication research and the mental health field more broadly (Turner, 2013). An analysis of all published and unpublished studies related to 12 FDA-approved antidepressants found that 31% were unpublished; among published papers, 94% had positive results (Turner et al., 2008). Reviews that include unpublished research have indicated that both psychotherapy and medication for depression are less efficacious than suggested by previous published literature (Cuijpers et al., 2010; Driessen et al., 2015). Conflict of interest has also been found to be associated with a greater likelihood of reporting positive results in psychiatric clinical trials (Perlis et al., 2005). In addition, because mental health trials often involve clinician-judged or self-report data, there may be a greater tendency toward additional forms of bias than in trials that rely on lab or radiographic data. With an estimated 18.1% of adults in the United States living with a clinically-diagnosed mental illness (Hedden et al., 2014) and lifetime mental illness prevalence of 46.3% in 13–18 year olds (Merikangas et al., 2010), the impact that biased publications can have on treatment in this population is of particular concern.

In the 15 years that the registry has been accessible, a number of researchers have studied the information available in the registry and its effectiveness in fostering transparency between study investigators and the public. Studies have shown that publication of registered trial

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results is low (Jones et al., 2013; Ross et al., 2012) and that many trials remain unpublished two or more years after study completion (Bourgeois et al., 2010; Ross et al., 2012). Moreover, studies with null findings are published more slowly than studies with significant results (Reyes et al., 2011).

In addition, differences between sponsor categories have emerged. Industry- and government-funded researches are dissimilar in conditions studied, trial type, results, and missing data. For example, Roumiantseva et al. (2013) found that compared with government-funded research, industry-funded studies that appear in the registry are more likely to test drugs, less likely to study mental health, and less likely to omit study design and intervention data. Additionally, compared with government-funded research, studies with industry funding have higher rates of non-publication, and the majority of these studies do not post results in the registry (Jones et al., 2013). Moreover, Bourgeois et al. (2010) found that industry-funded studies reported positive findings in 85% of studies vs 50% in government-funded research.

The current investigation sought to evaluate differences in mental health efficacy trial design between sponsors (e.g., industry, U.S. government, university/hospital), particularly characteristics that relate to trial quality and trends over time. We also aimed to evaluate whether the clinical trials registry is conveying key information to the public about mental health study design and characteristics.

2. Method

2.1. Data source

We used the database for Aggregate Analysis of ClinicalTrials.gov (AACT), publicly available through the Clinical Trials Transformation Initiative (http://www.ctti-clinicaltrials.org/what-we-do/analysis-dissemination/state-clinical-trials/aact-database) (Clinical Trials Transformation Initiative, n.d.). This dataset included all study records on the ClinicalTrials.gov website that were registered and released before September 25, 2014, a total of 175,538 studies. Data for this analysis were downloaded in pipe-delimited format.

2.2. Data preparation

Text cleaning in preparation for importing the data into Stata, such as the removal of embedded soft returns, was performed using a Python script. Subsequent data cleaning and analysis were completed with Stata 14 (Stata Statistical Software: Release 14, 2015).

2.3. Sponsorship

For each registered trial, the AACT dataset includes every sponsor and sponsor category. Sponsor categories in the downloaded dataset include industry, United States government, and "other". Within the "other" category, we followed (Roumiantseva et al., 2013) method to create a hospital or university sponsorship category by searching for variations on related terms, such as hospital, university, school, college, and clinic. Subsequently, the "other" sponsorship category was reduced to funders that did not fall into the industry, U.S. government, or university/hospital categories. We then further divided sponsorship into exclusive and joint categories.

2.4. Inclusion criteria

We selected mental health trials that studied conditions reported in the National Comorbidity Survey, a National Institute of Mental Health funded representative survey of U.S. households that uses the World Health Organization World Mental Health Survey, because they are commonly experienced in the United States and represent a range of types of mental health conditions (Hudson et al., 2007; Kessler et al., 2005a,b). These conditions included anxiety (panic disorder, generalized anxiety disorder, agoraphobia, specific phobia, post-traumatic stress disorder, obsessive-compulsive disorder, separation anxiety disorder), mood (major depressive disorder, dysthymia, bipolar I and II disorders), impulse control (oppositional-defiant disorder, conduct disorder, attention-deficit/hyperactivity disorder, intermittent explosive disorder), substance abuse (drug and alcohol abuse and dependence), eating (anorexia nervosa, bulimia nervosa, binge-eating disorder), or non-affective psychosis disorders (schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, psychosis not otherwise specified).

We identified relevant mental health studies by two methods. The dataset downloaded from AACT included both a "condition" field, in which researchers input the disease or condition studied in the trial, and a Medical Subject Heading (MeSH) term generated based on the condition field using a National Library of Medicine (NLM) algorithm. In method one, we searched for terms relevant to these disorders in the condition field and trial title. In method two, one author (K.A.) reviewed MeSH terms for relevant mental health trials. Discordant trials were manually reviewed on the ClinicalTrials.gov website and individually classified. Over 10% of trials do not include a MeSH term (Tasneem et al., 2012), and thus the majority of discordant trials were produced by method one, which identified trials based on the condition field.

2.5. Analysis

Frequencies and percentages of trial design characteristics and reporting practices are displayed by sponsor category. We performed regression analyses to examine differences between sponsor groups: logistic with binary trial characteristics and multinomial logistic with categorical trial characteristics, controlling for trial phase. To test whether sponsors differ in their use of active comparators over time, we calculated a logistic regression model exploring the interaction between funder and registration year, controlling for mental health condition and trial phase.

3. Results

3.1. Trial inclusion

We identified 9772 trials that met our mental health inclusion criteria (8855 identified by both methods, 917 added after review). We restricted analyses to trials that indicated an efficacy or efficacy/safety endpoint and either phase 2, 3, or phase N/A, in order to focus on trials that may in particular influence clinical care (4784 trials). Phase 2 and 3 trials are associated with efficacy/safety and efficacy endpoints, and we included phase N/A trials with efficacy/safety and efficacy endpoints to capture behavioral trials. Due to changes in reporting requirements, we included only trials recorded in the ClinicalTrials.gov registry on or after October 1, 2007 (3258 trials).

3.2. Sponsorship

The majority of trials included a university or hospital sponsor (64.0%), and a plurality reported exclusive university/hospital sponsorship (42.9%) (Table 1). Government was the second most common sponsor (25.6%), followed by industry (21.5%) and "other" funders (14.9%). Joint sponsorship with industry was less common (4.9%) than without industry (19.8%).

3.3. Trial characteristics

The majority of included trials were conducted for the purpose of treatment and employed a parallel assignment design (Table 2). A plurality of trials included a behavioral or drug intervention. Industry

Table 1
Sponsorship.

Sponsorship	Total trials sponsored, *n*(%) *N* = 3258	Exclusive sponsor, *n*(%) *N* = 2453	Joint sponsorship with industry, *n*(%) *N* = 159	Joint sponsorship without industry, *n*(%) *N* = 646
Industry	703(21.58)	544(16.70)		
Government	835(25.63)	160(4.91)	29(0.89)	646(19.83)
University/Hospital	2086(64.03)	1398(42.91)	112(3.44)	576(17.68)
Other	486(14.92)	351(10.77)	35(1.07)	100(3.07)

Note: trials with joint sponsorship are counted in each relevant sponsor category.

tended to sponsor trials of treatments that could be patented, typically drugs (95.2%), as opposed to behavioral trials (0.9%). Industry-sponsored trials were less likely to include a behavioral intervention (0.9% vs. 60.6%, $p < .0001$) than were government-sponsored trials. Government trials, in contrast to industry, tended to sponsor behavioral trials (60.6%) more frequently than drug trials (25.6%).

Mood disorders were overall the most commonly studied condition (40.0%). Industry tended to sponsor more mood disorder trials than the government (42.8% vs. 26.2%, $p < .01$). Industry was less likely than government to study substance abuse (5.1% vs 25.0%, $p < .0001$) or anxiety (9.3% vs. 51.8%, $p < .0001$) disorders, and more likely to study impulse control disorders (11.5% vs 1.8%, $p < .01$) and psychosis (32.3% vs. 15.6%, $p < .0001$).

Key trial characteristics in relation to data integrity are presented in Table 3. The majority of trials both anticipated and actually enrolled 100 or fewer participants, were randomized, and employed some form of masking. Industry sponsored a greater proportion of trials with 101–1000 participants relative to trials with 100 or fewer participants (74.2% vs. 36.2%, $p < .0001$), and smaller proportions of data committee (DMC) - monitored trials (24.2% vs. 45.0%, $p < .0001$), and open label (17.4% vs. 40.0%, $p < .0001$) or single blind (1.2% vs. 28.7%, $p < .0001$) relative to double blind trials, than did government.

Regression results comparing sponsor categories with respect to the use of an active comparator over time are displayed in Fig. 1. Industry sponsorship of trials with an active comparator decreased steadily over the time period explored in this analysis (2007–2014) in comparison to other funders (OR 0.22, 95% CI 0.05–0.86 in 2014; OR 1.16, 95% CI 0.42–3.17 in 2008).

4. Discussion

4.1. Overall trial design and enrollment trends

Our examination of efficacy and efficacy/safety mental health trials in the registry reveals that the majority include university or hospital sponsorship, enroll 100 or fewer participants, and are focused on treatment evaluation, most often of a mood disorder. Study design characteristics and data entry practices varied by sponsor category, particularly industry in comparison to nonprofit organizations. In general, industry-sponsored trials tend to be larger and test a drug

Table 2
Unadjusted trial characteristics.

	All *n*(%)	Exclusively government *n*(%)	Exclusively university or hospital *n*(%)	Exclusively industry *n*(%)	Exclusively other *n* (%)	Joint with industry *n*(%)	Joint without industry *n*(%)
Primary purpose							
Treatment (base)	2648(81.28)	124(77.50)	1107(79.18)	531(97.61)	276(78.63)	139(87.42)	471(72.91)
Prevention	245(7.52)	5(3.12)	122(8.73)*	2(0.37)**	36(10.26)*	2(1.26)	78(12.07)**
Diagnostic	22(0.68)	3(1.88)	11(0.79)	2(0.37)*	3(0.85)	2(1.26)	1(0.15)*
Supportive care	108(3.31)	4(2.50)	55(3.93)	3(0.55)*	13(3.70)	5(3.14)	28(4.33)
Screening	14(0.43)	0(0.00)	10(0.72)	0(0.00)	1(0.28)	1(0.63)	2(0.31)
Health Services	105(3.22)	14(8.75)	45(3.22)**	0(0.00)	7(1.99)**	5(3.14)*	34(5.26)
Basic Science	50(1.53)	4(2.50)	27(1.93)*	1(0.18)	6(1.71)	3(1.89)	9(1.39)
Missing	66(2.03)	6(3.75)	21(1.50)*	5(0.92)*	9(2.56)	2(1.26)	23(3.56)
Intervention							
Behavioral	1418(43.52)	97(60.62)	727(52.00)*	5(0.92)***	138(39.32)***	26(16.35)***	425(65.79)
Drug	1369(42.02)	41(25.62)	391(27.97)	518(95.22)***	127(36.18)*	105(66.04)***	187(28.95)
Device	246(7.55)	10(6.25)	133(9.51)	21(3.86)	43(12.25)*	17(10.69)	22(3.41)
Procedure	94(2.89)	5(3.12)	57(4.08)	0(0.00)	10(2.85)	3(1.89)	19(2.94)
Dietary supplement	84(2.58)	1(0.62)	52(3.72)	2(0.37)	17(4.84)*	5(3.14)	7(1.08)
Radiation	2(0.06)	0(0.00)	1(0.07)	0(0.00)	0(0.00)	0(0.00)	1(0.15)
Biological	7(0.21)	0(0.00)	3(0.21)	1(0.18)	2(0.57)	1(0.63)	0(0.00)
Genetic	1(0.03)	0(0.00)	0(0.00)	1(0.18)	0(0.00)	0(0.00)	0(0.00)
Other	428(13.14)	25(15.62)	226(16.17)	15(2.76)***	50(14.25)	18(11.32)	94(14.55)
Condition							
Mood	1306(40.09)	42(26.25)	624(44.64)***	233(42.83)***	142(40.46)**	64(40.25)**	201(31.11)
Substance abuse	654(20.07)	40(25.00)	226(16.17)**	28(5.15)***	67(19.09)	30(18.87)	263(40.71)***
Anxiety	808(24.80)	83(51.88)	381(27.25)***	51(9.38)***	97(27.64)***	21(13.21)***	175(27.09)***
Impulse control	222(6.81)	3(1.88)	88(6.29)*	63(11.58)**	20(5.70)	23(14.47)***	25(3.87)
Psychosis	549(16.85)	25(15.62)	195(13.95)	176(32.35)***	73(20.80)	24(15.09)	56(8.67)*
Eating	103(3.16)	2(1.25)	50(3.58)	11(2.02)	10(2.85)	6(3.77)	24(3.72)
Assignment							
Single	447(13.72)	17(10.62)	209(14.95)	75(13.79)	56(15.95)	33(20.75)*	57(8.82)
Parallel (base)	2518(77.29)	121(75.62)	1048(74.96)	446(81.99)	266(75.78)	113(71.07)	524(81.11)
Crossover	167(5.13)	12(7.50)	81(5.79)	21(3.86)*	18(5.13)	12(7.55)	23(3.56)*
Factorial	121(3.71)	10(6.25)	58(4.15)	1(0.18)**	10(2.85)	12(7.55)*	23(3.56)
Missing	5(0.15)	0(0.00)	2(0.14)	1(0.18)	1(0.28)	0(0.00)	1(0.15)

***$p < .0001$, **$p < .01$, *$p < .05$, ref. group = exclusively-government sponsored trials.

Table 3
Unadjusted key trial characteristics.

	All *n*(%)	Exclusively government *n*(%)	Exclusively university or hospital *n*(%)	Exclusively industry *n* (%)	Exclusively other *n* (%)	Joint with industry *n*(%)	Joint without industry *n*(%)
Anticipated enrollment							
≤100 (base)	969(52.78)	51(50.00)	519(59.52)	47(29.19)	138(59.48)	45(64.29)	169(42.36)
101–1000	817(44.50)	49(48.04)	331(37.96)	104(64.6)**	91(39.22)	24(34.29))	218(54.64)
>1000	50(2.72)	2(1.96)	22(2.52)	10(6.21)*	3(1.29)	1(1.43)	12(3.01)
Actual enrollment							
≤100 (base)	793(55.92)	35(60.34)	399(76.00)	86(22.63)	77(64.71)	66(74.16)	130(52.63)
101–1000	588(41.47)	21(36.21)	119(22.67)*	282(74.21)***	36(30.25)	23(25.84)	107(43.32)
>1000	37(2.61)	2(3.45)	7(1.33)	12(3.16)	6(5.04)	0(0.00)	10(4.05)
Randomized							
Yes	2815(86.40)	144(90.00)	1190(85.12)	471(86.58)	289(82.34)	122(76.73)	599(92.72)
No	161(4.94)	6(3.75)	80(5.72)	27(4.96)	18(5.13)	10(6.29)	20(3.10)
Missing	282(8.66)	10(6.25)	128(9.16)	46(8.46)	44(12.54)*	27(16.98)**	27(4.18)
Masking							
Open Label	1066(32.72)	64(40.00)	518(37.05)	95(17.46)***	121(34.47)*	47(29.56)***	221(34.21)
Single Blind	705(21.64)	46(28.75)	370(26.47)	7(1.29)***	75(21.37)**	13(8.18)***	194(30.03)
Double Blind (base)	1484(45.55)	49(30.63)	508(36.34)	442(81.25)	155(44.16)	99(62.26)	231(35.76)
Missing	3(0.09)	1(0.62)	2(0.14)	0(0.00)	0(0.00)	0(0.00)	0(0.00)
Has DMC							
Yes	1411(43.31)	72(45.00)	590(42.20)	132(24.26)***	137(39.03)*	81(50.94)	399(61.76)**
No	1668(51.20)	72(45.00)	737(52.72)	343(63.05)	207(58.97)	76(47.80)	233(36.07)
Missing	179 (5.49)	16(10.00)	71(5.08)*	69(12.68)	7(1.99)***	2(1.26)**	14(2.17)***

***$p < .0001$, **$p < .01$, *$p < .05$, ref. group = exclusively-government sponsored trials.

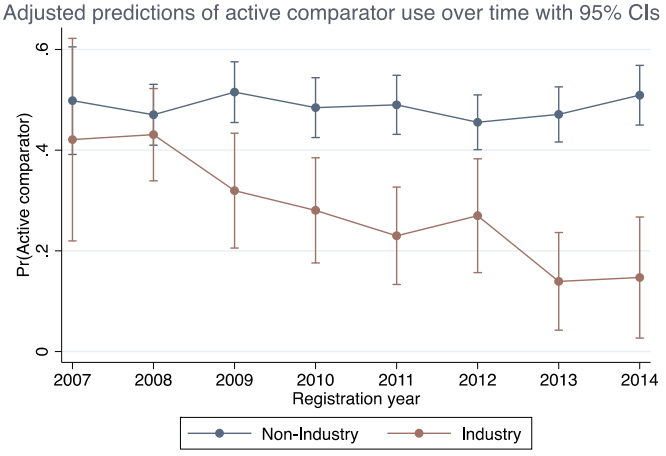

Fig. 1. Adjusted predictions of active comparator use over time with 95% CIs.

intervention, which is unsurprising given their financial interests and ability to seek patent protection. Government- or university/hospital-sponsored studies, meanwhile, tend to be smaller and test a behavioral intervention.

4.2. Data integrity

4.2.1. Trial comparator

We found that from 2007 to 2014, industry sponsored trials using active comparators steadily decreased compared to non-industry funders. Use of less stringent placebo, rather than active, comparators in efficacy trials is controversial. Some experts recommend that placebo comparators be used only when no effective treatment yet exists (World Medical Association, 2018); others argue that placebo comparators are necessary, particularly in psychiatry, because given the heterogeneity of patient response, some established drugs do not consistently outperform placebo comparators (Temple and Ellenberg, 2000) and because if a new drug has fewer or less serious side effects, it could have clinical utility even if it is less effective than an existing treatment (Miller, 2000). However, pharmaceutical companies have been criticized for using placebo comparators as a way to reduce costs, as such trials typically entail a smaller sample size and may be more likely to result in positive findings than trials with active comparators (Miller, 2000). In addition, trials that compare drugs patented by different companies have been found to be rare, suggesting that pharmaceutical companies may be reluctant to initiate trials that may promote a competitor's product (Lathyris et al., 2010). The consistent decrease in use of active comparators over time by industry in comparison to other funders merits further investigation because it could raise questions about impartiality. In light of the increased scientific rigor and 'real world' relevance of using active comparators, U.S. government funding agencies can help through more actively promoting active comparators when possible in government- and co-sponsored trials.

4.2.2. Enrollment

Universities or hospitals were listed as a sponsor in the majority of trials and tended to enroll 100 or fewer participants. While small trials can provide useful information and are sometimes the only option if the condition under study is rare, making patient recruitment difficult (Cornu et al., 2013), they typically do not provide sufficient statistical power for treatment trials with an efficacy endpoint. Large trials may be of better methodological quality and therefore more likely to be published even if the results are not significant, while small trials that show null effects may remain unpublished (Sterne et al., 2001).

4.2.3. Other design characteristics

Randomization, blinding, and data monitoring committee use have been identified as trial design practices that minimize bias and uphold data integrity (Califf et al., 2012; Moher et al., 2010). While the majority of trials across sponsor categories included randomization, differences between sponsors emerged with the use of blinding and data monitoring committees. The majority of industry-, government-, or university/hospital- sponsored trials reported use of some form of blinding, although industry reported significantly greater double blind over single blind trials than did government. In addition, across sponsor categories a substantial portion of trials were reported as "open label", i.e. providers and patients were not blinded to treatment assignment.

The open label design of many government and university/hospital sponsors may be due to the frequency of behavioral trials that they sponsor. The nature of psychotherapy typically precludes patient or

provider blinding. However, outcome assessor blinding in non-pharmacological trials is frequently possible (Boutron et al., 2007) and given the subjectivity of many behavioral trial outcomes, is particularly important. Failure to use outcome assessor blinding may bias study results (Hróbjartsson et al., 2012, 2013, 2014) and subsequently publication, as blinded trials are more likely to have null findings and thus remain unpublished (Huhn et al., 2014).

Across sponsor categories, less than half of registered trials indicated use of a data monitoring committee. Non-industry—government, university/hospital, or other—used a data monitoring committee in a greater proportion of trials than did industry, which indicated use of a data monitoring committee in less than 25% of trials. While all trials must have some form of monitoring for safety, the FDA requires sponsors to formally monitor only trials of new drugs, biologics, and devices (Clinical Trials Registration and Results Information Submission, 2016). The NIH imposes its own requirements for trials that it sponsors and requires a DSMB for multi-site interventional trials that involve possible risk (NIH policy for data and safety monitoring, 1998). DSMBs are composed of experts that review study design and progress for patient safety and quality assurance. As independent advisors, they are meant to provide unbiased recommendations to principal investigators. The consensus in publications about data safety monitoring in clinical trials is that DSMBs are recommended for trials involving vulnerable populations, for which most psychiatric trials qualify (Lin and Lu, 2014). Thus, we might have expected a greater proportion of trials to voluntarily convene a DSMB.

4.3. Implications for the ClinicalTrials.gov registry

Enrollment, Data Safety Monitoring Board, use of placebo comparators, and masking trends provide a few clues as to potential sources of bias or imprecision in psychiatric research. Small trials with inconsistent records of masking and DSMB use, and industry-sponsored trials with a placebo comparator, were common. However, the information available in the registry allows for only limited assessment of bias. Only a subset of trials in the registry are required to post results and of those that must report, compliance is low (Anderson et al., 2015; Law et al., 2011; Zarin et al., 2011). Without results reporting, if a trial is unpublished in a medical journal, it remains unknown if the trial had null or negative findings.

Enforcement of penalties for noncompliance may help to improve reporting practices but to date have not occurred (Anderson et al., 2015; Meister, 2014), and the extent to which these penalties might be used for registered but poorly reported trials is unknown (Viergever et al., 2014). In addition, it is unclear in the registry which trials are subject to particular reporting requirements and may be failing in their duty to report. More complete reporting and additional information on eligibility for reporting requirements would enhance the registry as both a service to the public and a research tool.

The FDA clarified and expanded reporting requirements, effective early 2017. It now requires results submission for any applicable trial, regardless of drug or device approval status. It also requires more specific information on outcome data collection and measurement, as well as a copy of the full study protocol and analysis plan (Zarin et al., 2016). In addition, the NIH released a new requirement in 2016 that NIH-funded trials must register and post results at ClinicalTrials.gov, regardless of subjectivity to FDA reporting requirements (National Institutes of Health, Department of Health and Human Services, 2016). While it is too early to gauge the impact of these changes, they are meant to improve the quality and utility of trial reporting. Greater oversight and enforcement may aid in the effort to reach this goal.

4.4. Limitations

Trials were identified for inclusion through registry fields that rely on researcher-entered terms. Thus, any error that a researcher may have made in inputting study information, or their choice in wording, would affect that trial's inclusion or exclusion in this analysis. We used two methods to categorize and identify mental health trials. These methods agreed in the vast majority of cases, and discordant trials were reviewed by one author (K.A.) prior to inclusion.

Additionally, not all trials are required by U.S. law to be registered with ClinicalTrials.gov. In particular, behavioral interventions may be underrepresented because they are not regulated by the FDA. Although the International Committee of Medical Journal Editors requires that all interventional studies be registered in a recommended database, and ClinicalTrials.gov is one of only two such registries, not all psychiatric or general medical journals require study registration. However, many high impact factor journals do have such a requirement.

4.5. Conclusion

The ClinicalTrials.gov registry, the most comprehensive resource in the United States on clinical trials, provides several clues about sources of bias or imprecision in psychiatry efficacy trials, such as small enrollment, frequent use of an open label (unblinded) design, and use of placebo comparators. However, despite widespread concern about bias in clinical trials, particularly in psychiatry, researchers are required to enter limited information that might help the public assess the quality of these trials. A lack of clarity regarding trial subjectivity to reporting requirements—for example, which trials are required to report results—further limit the utility of the registry. Although the FDA and NIH have issued additional reporting requirements, given historically low compliance with reporting, they may have limited success.

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Declaration of Competing Interest

None.

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