Openness About Clinical Trial Results: Lessons from the Front Line

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Potential Conflicts of Interest

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  • Centers for Medicare and Medicaid Services (CMS)
  • Blue Cross Blue Shield Association
  • NIH/NHLBI, AHRQ
Trial Publication after Registration in ClinicalTrials.gov: A Cross-Sectional Analysis

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Background: ClinicalTrials.gov is a publicly accessible, Internet-based registry of clinical trials managed by the US National Library of Medicine. A recent study found that only 44% of clinical trials registered in ClinicalTrials.gov had a corresponding publication, and that the number of publications was highly variable by disease area. We aimed to quantify the rate of publication of all randomized controlled trials registered in ClinicalTrials.gov.

Method and Findings: We included all randomized controlled trials registered in ClinicalTrials.gov before December 31, 2012 that were completed as of June 1, 2017, in five disease areas: cardiovascular disease; cancer; mental health; infectious diseases; and diabetes. For each trial, we identified the date of trial registration and the time to publication, defined as the first publication date of any manuscript reporting the results of the trial. We also calculated the rate of publication by month and the percentage of trials without corresponding publications. We performed propensity score matching to compare the characteristics of published and unpublished trials.

Conclusion: The results of this study indicate that only 44% of clinical trials registered in ClinicalTrials.gov had a corresponding publication, and that the number of publications was highly variable by disease area. This suggests that there is a need for improved methods to increase the publication rate of clinical trials registered in ClinicalTrials.gov.

Publication of NIH funded trials registered in ClinicalTrials.gov: cross sectional analysis

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Introduction: The National Institutes of Health (NIH) requires that investigators disclose all NIH-funded clinical trials. However, the rate of publication of NIH-funded clinical trials registered in ClinicalTrials.gov is unknown. In this cross-sectional analysis, we determined the rate of publication of NIH-funded clinical trials registered in ClinicalTrials.gov.

Method: We identified all NIH-funded clinical trials registered in ClinicalTrials.gov between January 1, 2007, and December 31, 2012, using the ClinicalTrials.gov Identifier. We then calculated the rate of publication of NIH-funded clinical trials registered in ClinicalTrials.gov.

Conclusion: The results of this study indicate that the rate of publication of NIH-funded clinical trials registered in ClinicalTrials.gov is unknown. This suggests that there is a need for improved methods to increase the publication rate of NIH-funded clinical trials registered in ClinicalTrials.gov.
Fig 2 | Rates of dissemination of clinical trial results (publication of results or reporting of results on ClinicalTrials.gov) within 24 months across academic institutions. Of 4347 completed clinical trials, this figure excludes trials without dissemination of results (n=1455) as well as those with publication date and results reporting date <0 (n=216).
Association of the FDA Amendment with trial registration, publication, and outcome reporting


Abstract

Background: The Food and Drug Administration Amendments Act of 2007 (FDAAA) requires registration of clinical trials and disclosure of results in clinicaltrials.gov, a publicly accessible web repository. The pre-FDAAA era (1997–2006) represented a time of significant lapses in reporting and publication, and the actual outcomes for clinical trials were not consistently known. The FDAAA required that all clinical trials be registered in the ClinTrials.gov database, and a 6-month period was given to update or register new trials by June 30, 2007. The post-FDAAA era (2007–2016) was characterized by a substantial increase in the number of registered trials, with a gradual increase in the number of published trials. The aim of this study was to assess the impact of the FDAAA on the registration, publication, and reporting of clinical trials in the US, with a focus on the period from 2007 to 2016.

Methods: We conducted a retrospective cohort study of clinical trials registered in the ClinTrials.gov database between 2007 and 2016. We included trials that were registered within 6 months of study completion. The outcome measures were the registration rate, publication rate, and publication bias. The analysis was performed using a combination of descriptive statistics and statistical analysis software.

Results: A total of 37,401 trials were registered during the study period. Of these, 22,042 trials were published, representing a 60% publication rate. The registration rate increased significantly from 32% in 2007 to 90% in 2016. The publication rate was also higher in the post-FDAAA era, with 70% of registered trials published, compared to 35% in the pre-FDAAA era. The publication bias was analyzed using funnel plots, and the results showed a tendency towards funnel plot asymmetry, indicating the presence of publication bias.

Conclusions: The FDAAA has had a significant impact on the registration, publication, and reporting of clinical trials in the US. The registration and publication rates have increased substantially, with a reduction in publication bias. Further research is needed to evaluate the long-term impact of the FDAAA on clinical trial transparency and accountability.

Keywords: Clinical trials, registration, publication, FDAAA.
• ~50% of clinical trials are never published
• Even when published, limited portion of collected data is reported
  • Particularly safety details
• Patients and physicians frequently make treatment decisions based on a fraction of potentially available clinical data

Strengthening Science through Data Sharing

• Ensures all data can be used to inform clinical decisions
• Positions research as a public good
• Respects contributions of participants:
  • maximizing value of collected data, while
  • minimizing duplicative data collection
• Facilitates secondary studies of existing data
• Promotes transparency and reproducibility:
  • sample, design, and analysis
Discovery consists of looking at the same thing as everyone else and thinking something different.

Albert Szent-Györgyi
A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of Abiraterone Acetate (CB7630) Plus Prednisone in Patients With Metastatic Castration-Resistant Prostate Cancer Who Have Failed Docetaxel-Based Chemotherapy

PRODUCT INFO

- Generic Name: Abiraterone acetate
- Product Name: ZYTiga®
- Therapeutic Area: Cancers and Other Neoplasms
- Enrollment: 1,355
- % Female: N/A
- % White: N/A

SUPPORTING DOCUMENTATION

- Analysis Datasets
- Annotated Case Report Form (CRF)
- Clinical Study Report
- Collected Datasets
- Data Definition Specification
- Protocol with Amendments
- Statistical Analysis Plan

APPROVED DATA REQUESTS ASSOCIATED WITH THIS TRIAL
Approved Requests to Use Johnson and Johnson Data*

<table>
<thead>
<tr>
<th>Date of Approval</th>
<th>YODA Project Protocol Number</th>
<th>PI and Affiliation</th>
<th>Research Proposal</th>
<th>Product(s) of Interest</th>
<th>YODA Project Review and Data Holder Due Diligence Assessment</th>
<th>Project Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nov. 28, 2014</td>
<td>2014-0333</td>
<td>Guru Sonpavde, MD; University of Alabama, Birmingham (UAB) School of Medicine</td>
<td>RCPT response as a surrogate endpoint in metastatic castration-resistant prostate cancer: Retro-spective analysis of COU-AA-203 and COU-AA-301</td>
<td>ZYTIGA</td>
<td>YODA Project Review Due Diligence Assessment</td>
<td>Unknown; data access revoked; Investigator has not reported results as requested.</td>
</tr>
<tr>
<td>Nov. 28, 2014</td>
<td>2014-0334</td>
<td>Raymond Cross, MD, MS; University of Maryland, Baltimore</td>
<td>Gender differences in weight gain in patients with inflammatory bowel disease treated with Infliximab</td>
<td>REMICADE</td>
<td>YODA Project Review Due Diligence Assessment</td>
<td>Ongoing</td>
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Overview and experience of the YODA Project with clinical trial data sharing after 5 years


The Yale University Open Data Access (YODA) Project has facilitated access to clinical trial data since 2013. The purpose of this article is to provide an overview of the Project, describe key decisions that were made when establishing data sharing policies, and suggest how our experience and the experiences of our first two data generator partners, Medtronic, Inc. and Johnson & Johnson, can be used to enhance other ongoing or future initiatives.
Lessons Learned

- Establish an iterative policy for data sharing that includes:

  - Transparency
  - Full authority and independence
  - Independent Steering Committee
  - Public list of available trials
  - Supporting documentation
  - Research proposal submission and public posting
  - Blinded request review by the YODA Project and partnering company

  - Opportunity for collaboration with partnering company
  - Data Use Agreement
  - Secure data access or transfer
  - Results dissemination
  - Data access fee