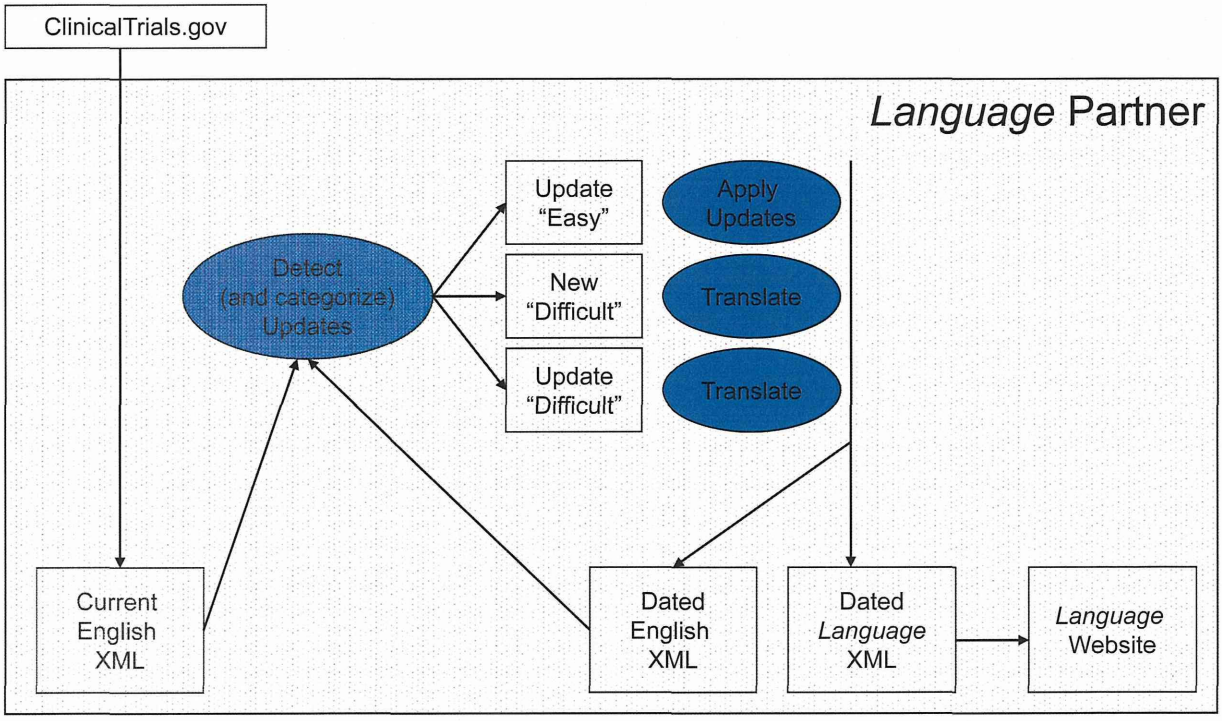
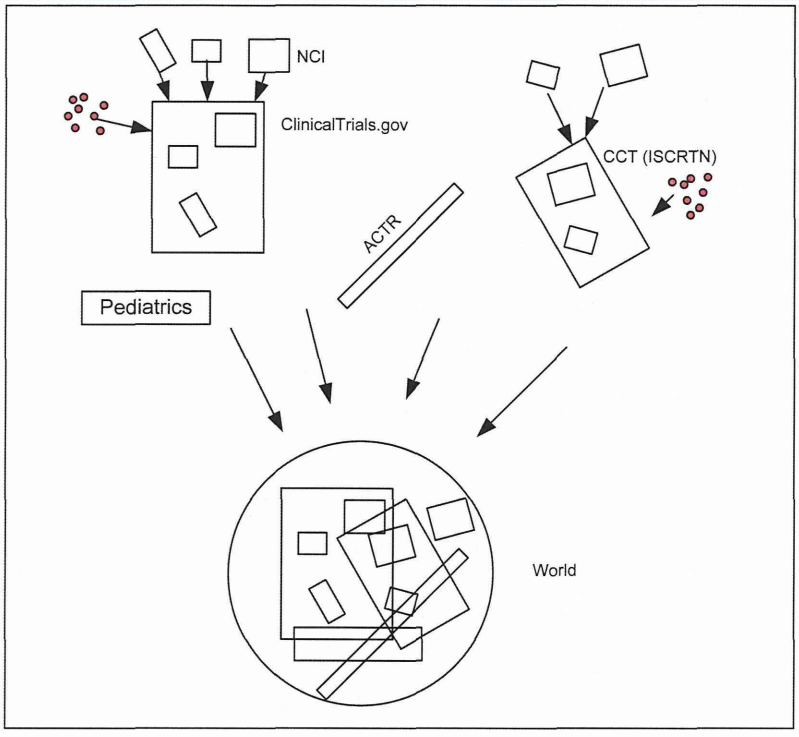
Content Dissemination



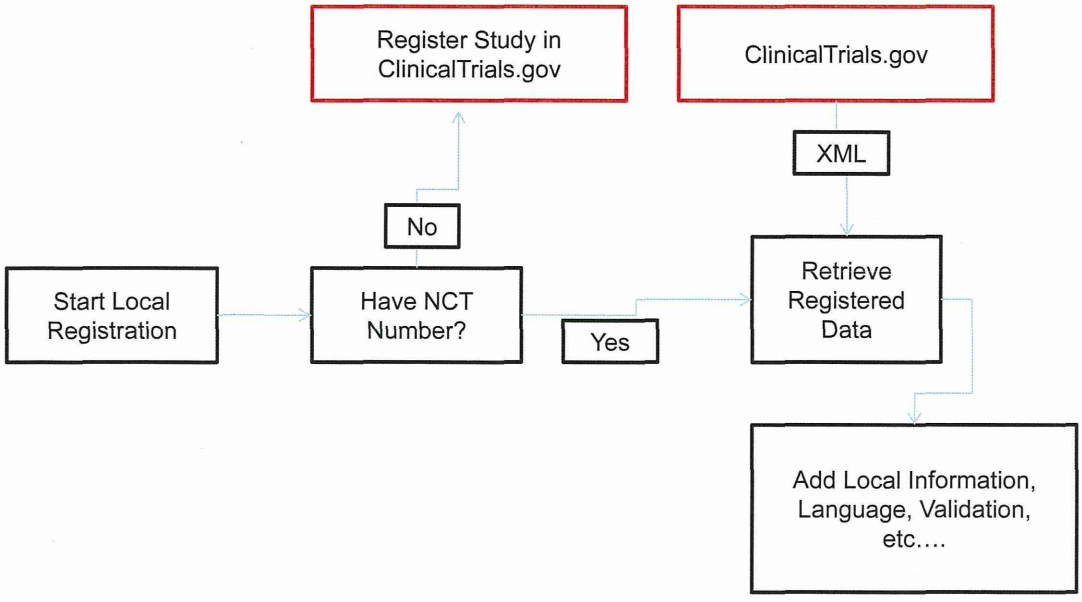
Global System of Trial Registration

1. Incentives – policies, legislation
2. Communication – outreach, guidelines
3. Data Collection – the database
4. Validation – correct and complete
5. Dissemination – available to constituents

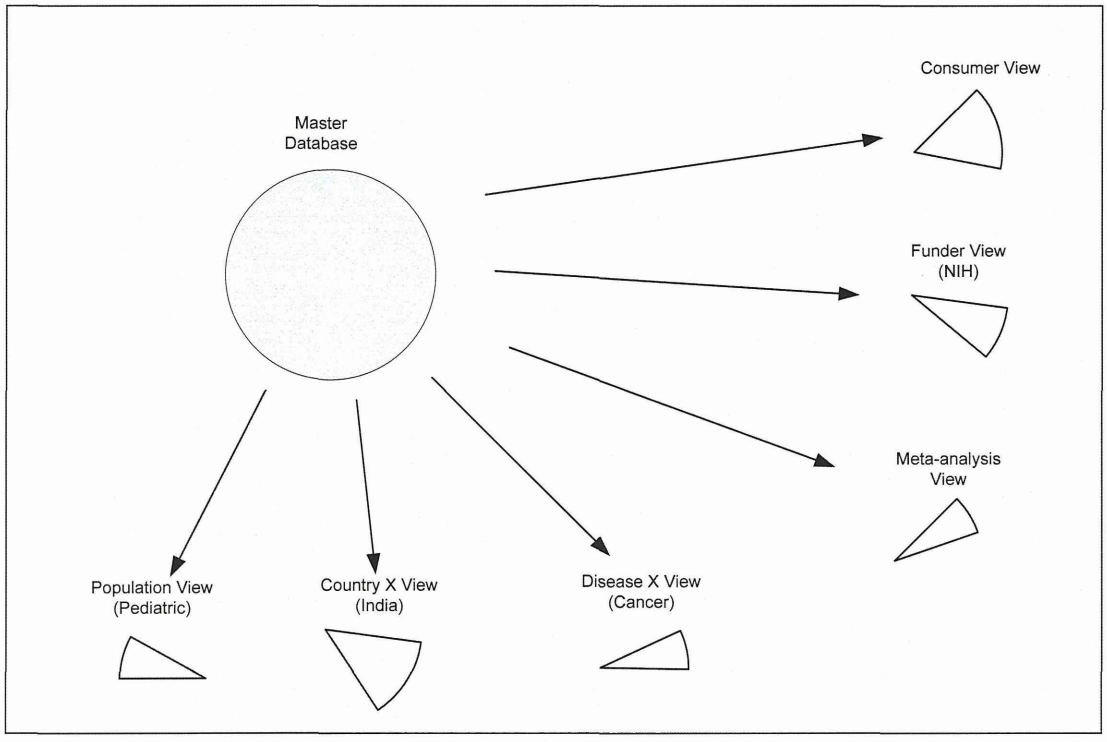
Uncoordinated Merging



Collaborative Data Collection



Collaborative Dissemination



Extra Slides

Sample Uses of ClinicalTrials.gov

http://ClinicalTrials.gov

Provides a Window Into the "Clinical Research Enterprise"

Characteristics of Clinical Trials Registered in ClinicalTrials.gov, 2007-2010

Robert M. Califf, MD
Deborah A. Zarin, MD
Judith M. Kramer, MD, MS
Rachel E. Sherman, MD, MPH
Laura H. Aberle, BSPH
Asba Tasneem, PhD

Context Recent reports highlight gaps between guidelines-based treatment recommendations and evidence from clinical trials that supports those recommendations. Strengthened reporting requirements for studies registered with ClinicalTrials.gov enable a comprehensive evaluation of the national trials portfolio.

Objective To examine fundamental characteristics of interventional clinical trials registered in the ClinicalTrials.gov database.

Methods A data set comprising 96 346 clinical studies from ClinicalTrials.gov was downloaded on September 27, 2010, and entered into a relational database to analyze aggregate data. Interventional trials were identified and analyses were focused on 3 clinical specialties—cardiovascular, mental health, and oncology—that together

CLINICAL TRIALS ARE THE CENtral means by which preventive,

Conclusion: "Clinical trials registered in ClinicalTrials.gov are dominated by small trials and contain significant heterogeneity in methodological approaches, including reported use of randomization, blinding, and DMCs."

137

JAMA. 2012;307(17):1838-1847

American Pain Society
RESEARCH
EDUCATION
TREATMENT
ADVOCACY
PUBLISHED BY ELSEVIER

The Journal of Pain, Vol 14, No 4 (April), 2013: pp 405-411
Available online at www.jpain.org and www.sciencedirect.com

Use of ClinicalTrials.gov to Estimate Condition-Specific Nocebo Effects and Other Factors Affecting Outcomes of Analgesic Trials

M. Soledad Cepeda, Victor Lobanov, and Jesse A. Berlin
Janssen Pharmaceutical Research & Development, LLC, Titusville, New Jersey.

Abstract: ClinicalTrials.gov is a registry and results database of federally and privately supported clinical trials conducted worldwide. We sought to answer: what are the characteristics of pain trials; how frequently are these trials stopped and why; what is the magnitude of attrition due to lack of

PERSPECTIVE: "ClinicalTrials.gov registry enables researchers to get a snapshot of a specific field and observe changes over time in trial design, including numbers of subjects accrued, and it can inform clinical trial design..."

Perspective: *ClinicalTrials.gov registry enables researchers to get a snapshot of a specific field and observe changes over time in trial design, including numbers of subjects accrued, and it can inform clinical trial design. We learned that recruitment challenges account for the largest proportion of noncompleted trials, attrition rates differed across pain conditions, and migraine studies had the lowest withdrawal rate.*

Key words: ClinicalTrials.gov, pain, trial design, placebo response, withdrawal rate, nocebo effect.

138

Helps to Identify Publication Bias & Supports Evidence-Based Medicine

Source: Ross et al. *BMJ* 2012;344:d7292.

BMJ

BMJ 2011;34

CONCLUSIONS: "Despite recent improvement in timely publication, fewer than half of trials funded by NIH are published in a peer reviewed biomedical journal indexed by MEDLINE within 30 months of trial completion. Moreover, after a median of 51 months after trial completion, a third of trials remained unpublished."

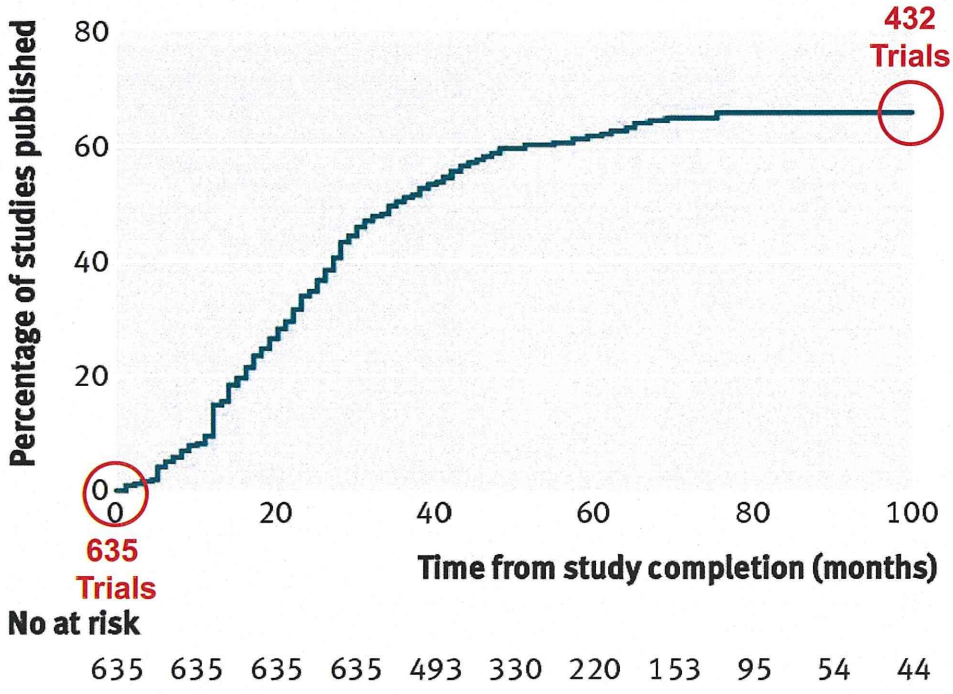
Publication of NIH funded trials registered in ClinicalTrials.gov: cross sectional analysis

OPEN ACCESS

Joseph S Ross *assistant professor of medicine*[1 2], Tony Tse *program analyst at ClinicalTrials.gov*[3], Deborah A Zarin *director of ClinicalTrials.gov*[3], Hui Xu *postgraduate house staff trainee*[4], Lei Zhou *postgraduate house staff trainee*[4], Harlan M Krumholz *Harold H Hines Jr professor of medicine and professor of investigative medicine and of public health*[2 5 6]

[1]Section of General Internal Medicine, Department of Medicine, Yale University School of Medicine, New Haven, CT, USA; [2]Center for Outcomes Research and Evaluation, Yale-New Haven Hospital, New Haven, CT; [3]Lister Hill National Center for Biomedical Communications, National Library of Medicine, National Institutes of Health, Bethesda, MD, USA; [4]Fuwai Hospital and Cardiovascular Institute, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [5]Robert Wood Johnson Clinical Scholars Program and Section of Cardiovascular Medicine, Department of Medicine, Yale University School of Medicine, New Haven, CT; [6]Section of Health Policy and Administration, Yale University School of Epidemiology and Public Health, New Haven, CT

Fig 2 Cumulative percentage of studies published in a peer reviewed biomedical journal indexed by MEDLINE during 100 months after trial completion among all NIH funded clinical trials registered within ClinicalTrials.gov



141

Ross et al. *BMJ* 2012;344:d7292.

Use of Trial Registries for Systematic Reviews

- "Sources of grey literature including regulatory data, clinical trial registries and conference abstracts should be searched in addition to bibliographic databases."
  - AHRQ *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*. Jan 2014 Update

AHRQ Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

- "Trials registers and trials results registers are an important source of ongoing and unpublished trials."
  - *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]

The Cochrane Collaboration
Trusted evidence. Informed decisions. Better health.

142

Encourages Disclosure of More Complete Data

143

OPEN ACCESS Freely available online

PLOS | MEDICINE

Timing and Completeness of Trial Results Posted at ClinicalTrials.gov and Published in Journals

Carolina Riveros[1,2,3], Agnes Dechartres[1,2,3]*, Elodie Perrodeau[1,3], Romana Haneef[1,3], Isabelle Boutron[1,2,3,4], Philippe Ravaud[1,2,3,4,5]

1 INSERM U738, Paris, France, 2 Université Paris Descartes—Sorbonne Paris Cité, Paris, France, 3 Centre d'Épidémiologie Clinique, Hôpital Hôtel-Dieu, Assistance Publique-Hôpitaux de Paris, Paris, France, 4 French Cochrane Centre, Paris, France, 5 Mailman School of Public Health, Columbia University, New York, New York, United States of America

Findings: "Reporting was significantly more complete at ClinicalTrials.gov than in the published article for the flow of participants (64% versus 48% of trials, p,0.001), efficacy results (79% versus 69%, p = 0.02), adverse events (73% versus 45%, p,0.001), and serious adverse events (99% versus 63%, p,0.001)."

Conclusions: "Our results highlight the need to search ClinicalTrials.gov for both unpublished and published trials. Trial results, especially serious adverse events, are more completely reported at ClinicalTrials.gov than in the published article."

144

Helps to Identify Discrepancies Across Sources of Results

145

Annals of Internal Medicine | Research and Reporting Methods

Reporting Discrepancies Between the ClinicalTrials.gov Results Database and Peer-Reviewed Publications

Daniel M. Hartung, PharmD, MPH; Deborah A. Zarin, MD; Jeanne-Marie Guise, MD, MPH; Marian McDonagh, PharmD; Robin Paynter, MLS; and Mark Helfand, MD, MS, MPH

Background: ClinicalTrials.gov requires reporting of result summaries for many drug and device trials.

Purpose: To evaluate the consistency of reporting of trials that are registered in the ClinicalTrials.gov results database and published in the literature.

Data Sources: ClinicalTrials.gov results database and matched publications identified through ClinicalTrials.gov and a manual search of 2 electronic databases.

Study Selection: 10% random sample of phase 3 or 4 trials with results in the ClinicalTrials.gov results database, completed before 1 January 2009, with 2 or more groups.

Data Extraction: One reviewer extracted data about trial design and results from the results database and matching publications. A subsample was independently verified.

Data Synthesis: Of 110 trials with results, most were industry-sponsored, parallel-design drug studies. The most common inconsistency was the number of secondary outcome measures reported (80%). Sixteen trials (15%) reported the primary outcome description inconsistently, and 22 (20%) reported the primary outcome value inconsistently. Thirty-eight trials inconsistently reported the number of individuals with a serious adverse event (SAE); of these, 33 (87%) reported more SAEs in ClinicalTrials.gov. Among the 84 trials that reported SAEs in ClinicalTrials.gov, 11 publications did not mention SAEs, 5 reported them as zero or not occurring, and 21 reported a different number of SAEs. Among 29 trials that reported deaths in ClinicalTrials.gov, 28% differed from the matched publication.

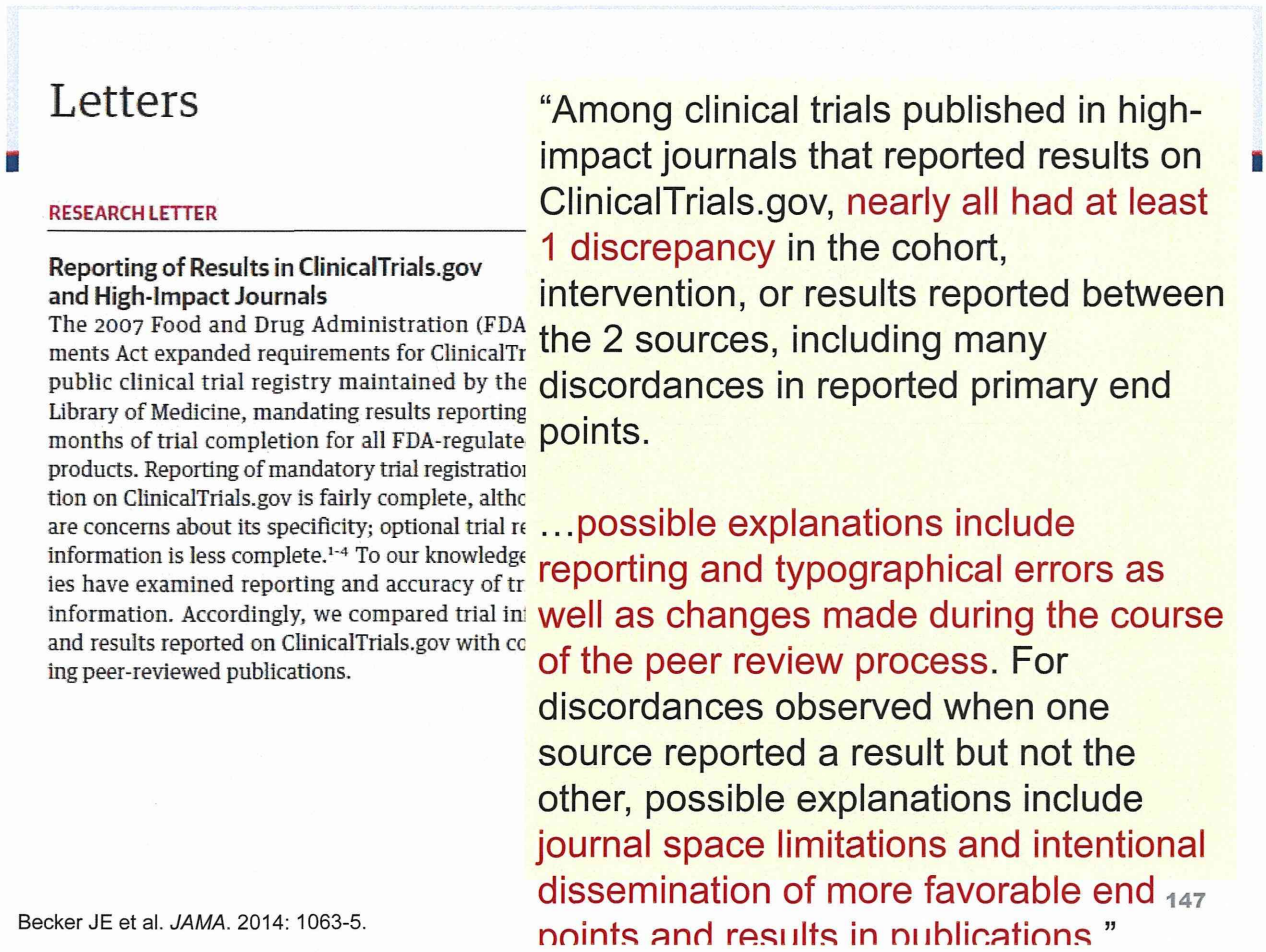
Limitation: Small sample that included earliest results posted to the database.

Conclusion: Reporting discrepancies between the ClinicalTrials.gov results database and matching publications are common. Which source contains the more accurate account of results is unclear, although ClinicalTrials.gov may provide a more comprehensive description of adverse events than the publication.

Primary Funding Source: Agency for Healthcare Research and Quality.

Ann Intern Med. 2014;160:477-483. www.annals.org
For author affiliations, see end of text.

146



Letters

RESEARCH LETTER

Reporting of Results in ClinicalTrials.gov and High-Impact Journals

The 2007 Food and Drug Administration (FDA ments Act expanded requirements for ClinicalTr public clinical trial registry maintained by the Library of Medicine, mandating results reporting months of trial completion for all FDA-regulate products. Reporting of mandatory trial registratio tion on ClinicalTrials.gov is fairly complete, althc are concerns about its specificity; optional trial re information is less complete.[1-4] To our knowledge ies have examined reporting and accuracy of tr information. Accordingly, we compared trial in and results reported on ClinicalTrials.gov with co ing peer-reviewed publications.

Becker JE et al. *JAMA*. 2014: 1063-5.

147

Reproducible Research on Discrepant Reporting of Results

	Hartung et al. (2014)	Becker et al. (2014)
Sample	Phase 3 & 4 trials with results on Clinicaltrials.gov & journal publication	Trials with results on ClinicalTrials.gov & high-impact journal publication
Key Discrepancies		
POM Descriptions	15%	15%
POM Values	20%	16%
SAEs	35% (Frequent underreporting or omissions in publication)	39% (Frequent underreporting or omissions in publication)
Other AEs	37% (Among ≥1 AE reported on ClinicalTrials.gov)	48% (Among all trials)

148

Becker & Ross. Unpublished manuscript; Hartung et al. Ann Intern Med. 2014:477-83; Becker et al. *JAMA*. 2014: 1063-5.