Trial registration & reporting: academic medical centers & the “final rule”

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November 7, 2016
Reproducibility

Many results cannot be reproduced


- Methods reproducibility
- Results reproducibility
- Generalizability
- Inferential reproducibility

**PERSPECTIVE**

**SCIENTIFIC INTEGRITY**

What does research reproducibility mean?

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The language and conceptual framework of “research reproducibility” are nonstandard and unsettled across the sciences. In this Perspective, we review an array of explicit and implicit definitions of reproducibility and related terminology, and discuss how to avoid potential misunderstandings when these terms are used as a surrogate for “truth.”

Reporting biases

**Publication bias:** Selective publication based on the direction or strength of research findings (Dickersin, 1997)

**Selective outcome reporting:** Publication of outcomes from a trial based on the results (Chan, et al., 2004)
Food and Drugs Administration Amendments Act (FDAAA 2007)

- Applies to FDA regulated products
  - Drugs
  - Biologics
  - Devices

- Applicable clinical trials must registered shortly after beginning enrollment

- Applicable clinical trials must report their results within 12 months of the primary completion date
ClinicalTrials.gov

ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world. Learn more about clinical studies and about this site, including relevant history, policies, and laws.

ClinicalTrials.gov currently lists 169,991 studies with locations in all 50 states and in 187 countries.

Locations of Recruiting Studies
- Non-U.S. Only (51%)
- U.S. Only (43%)
- Both U.S. & Non-U.S. (6%)

Total N = 33,431 studies
Data as of June 30, 2014
- See more trends, charts, and maps

Search for Studies
Example: "Heart attack" AND "Los Angeles"

Advanced Search  See Studies by Topic  See Studies on a Map

Search Help
- How to search
- How to find results of studies
- How to read a study record

For Patients & Families
- How to find studies
- See studies by topic
- Learn about clinical studies
- Learn more...

For Researchers
- How to submit studies
- Download controls
- About the register
- Learn more...

ClinicalTrials.gov is a service of the U.S. National Institutes of Health

Find Studies  About Clinical Studies  Submit Studies  Resources  About This Site

Do you or someone you know want to participate in a clinical study? See information for patients and families.

Training Materials

Contents
- Online Presentations
  - Overview of ClinicalTrials.gov and Related Policies
  - Applying for a PRS Account and Registering a Clinical Study
  - Submitting Results Data
- Glossary
- How to Read Study Records
NIH will withhold clinical trial funding to grantees if the agency is unable to verify adequate registration and results reporting from all trials funded at that institution.

Clinical trials are the most publicly visible component of the biomedical research enterprise, from the potential human application of novel laboratory findings to the generation of robust evidence about treatments or preventive interventions in routine clinical care. These trials are also the point at which biomedical research most directly engages human participants—dedicated volunteers who trust investigators to uphold the highest standards of scientific rigor and ethical oversight. While clinical trials have evolved and improved over time—producing impressive advances in diagnosis, treatment, and prevention—there are still major challenges. Therefore, fundamental changes are needed to reflect...
What is new?

- Clarifies
  - Definition of a “clinical trial”
  - Which trials are “applicable”
  - Roles (e.g., “sponsor” and “responsible party”)
  - Required data elements

- Applies to approved and unapproved products
- Requires information about adverse events
- Analysis plan must be submitted with results
- Expands baseline reporting requirements
- NIH requirements extend beyond FDA regulated products
Elements of an outcome

Publication and reporting of clinical trial results: cross sectional analysis across academic medical centers

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ABSTRACT

OBJECTIVE
To determine rates of publication and reporting of results within two years for all completed clinical trials registered in ClinicalTrials.gov across leading academic medical centers in the United States.

DESIGN
Cross sectional analysis.

SETTING
Academic medical centers in the United States.

PARTICIPANTS
Academic medical centers with 40 or more completed interventional trials registered on ClinicalTrials.gov.

METHODS
Using the Aggregate Analysis of ClinicalTrials.gov database and manual review, we identified all interventional clinical trials registered on ClinicalTrials.gov. Disseminated results for 2892 (66%) trials, with 1560 (35.9%) achieving this within 24 months of study completion. The proportion of clinical trials with results disseminated within 24 months of study completion ranged from 16.2% (6/37) to 55.3% (57/103) across academic medical centers. The proportion of clinical trials published within 24 months of study completion ranged from 10.8% (4/37) to 40.3% (31/77) across academic medical centers, whereas results reporting on ClinicalTrials.gov ranged from 1.6% (2/122) to 40.7% (72/177).

CONCLUSIONS
Despite the ethical mandate and expressed values and mission of academic institutions, there is poor performance and noticeable variation in the dissemination of clinical trial results across leading academic medical centers.
Methods

- Downloaded registrations from ClinicalTrials.gov (Sept 2013)
  - Interventional Clinical trials
  - Primary completion Oct 2007 to Sept 2010

- Literature search to identify publications

- Results reporting on ClinicalTrials.gov
Results

- 4347 interventional trials
  - 50% phase II to phase IV
  - 9.8% NIH primary sponsor

- 67% published or reported results by July 2014
  - 27% reported on ClinicalTrials.gov

- No AMC published more than 40% or reported more than 41%
Limitations

- What proportion of trials are even registered (denominator unknown)
- AMCs contest these results
  - Not all trials were ACTs
  - Organization of CT.gov information is by account, not AMC
  - This report uses the PI’s affiliation (might not correspond to the responsible party)
Other reports reach similar conclusions

**Compliance with Results Reporting at ClinicalTrials.gov**

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**ABSTRACT**

The Food and Drug Administration Amendments Act (FDAAA) mandates timely reporting of results of applicable clinical trials to ClinicalTrials.gov. We characterized the proportion of applicable clinical trials with publicly available results and determined independent factors associated with the reporting of results.

Stanford University, Memorial Sloan Kettering Cancer Center, and prestigious medical research institutions have flagged the federal law requiring public reporting of study results, depriving patients and doctors of complete data to gauge the safety and benefits of treatments, a STAT investigation has found.