Clinical Trial Data Sharing

NPA FDA Taskforce Meeting
December 15, 2014

Joseph S. Ross, MD, MHS
Section of General Internal Medicine, School of Medicine
Center for Outcomes Research and Evaluation, Yale-New Haven Hospital
A substantial number of clinical trials are conducted, but never published (~33%-50%)
Selective Publication of Antidepressant Trials and Its Influence on Apparent Efficacy

Table 1. Overall Publication Status of FDA-Registered Antidepressant Studies.

<table>
<thead>
<tr>
<th>Publication Status</th>
<th>No. of Studies (%)</th>
<th>No. of Patients in Studies (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Published results agree with FDA decision</td>
<td>40 (54)</td>
<td>7,272 (58)</td>
</tr>
<tr>
<td>Published results conflict with FDA decision (published as positive)</td>
<td>11 (15)</td>
<td>1,843 (15)</td>
</tr>
<tr>
<td>Results not published</td>
<td>23 (31)</td>
<td>3,449 (27)</td>
</tr>
<tr>
<td>Total</td>
<td>74 (100)</td>
<td>12,564 (100)</td>
</tr>
</tbody>
</table>

Source: Turner et al., NEJM 2008;358:252-60.
Selective Publication of Antidepressant Trials and Its Influence on Apparent Efficacy

Table 1. Overall Publication Status of FDA-Registered Antidepressant Studies.

<table>
<thead>
<tr>
<th>Publication Status</th>
<th>No. of Studies (%)</th>
<th>No. of Patients in Studies (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Published results agree with FDA decision</td>
<td>40 (54)</td>
<td>7,272 (58)</td>
</tr>
<tr>
<td>Published results conflict with FDA decision (published as</td>
<td>11 (15)</td>
<td>1,843 (15)</td>
</tr>
<tr>
<td>positive)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Results not published</td>
<td>23 (31)</td>
<td>3,449 (27)</td>
</tr>
<tr>
<td>Total</td>
<td>74 (100)</td>
<td>12,564 (100)</td>
</tr>
</tbody>
</table>

Source: Turner et al., NEJM 2008;358:252-60.
Trial Publication after Registration in ClinicalTrials.Gov: A Cross-Sectional Analysis

• 46% of trials published
• Least likely to be published
  • Industry-sponsored studies
  • Single arm trials

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

Source: Ross et al., BMJ 2012;344:d7292.
A substantial number of clinical trials are conducted, but never published (~33%-50%).

Even among published clinical trials, a limited portion of the collected data is reported on.
  • Particularly relevant for safety information

Thus, patients and physicians frequently make treatment decisions with access to only a fraction of clinical research data.
Why Share Data?

• Facilitates follow-up studies of secondary research questions using existing data
• Promotes transparency, allowing multiple examinations of research data
• Minimizes duplicative data collection
• Respects contributions of participants, maximizing value of collected data
• Positions research as a public good
Focus on Industry

• Issues relevant to clinical trials conducted both publicly and privately, but are particularly important among industry trials
  • Industry funds majority of clinical trial research about drugs, devices and other products, both pre-market and post-market
  • Industry research is proprietary, no requirement for publication or dissemination
  • Public perception: industry has a financial interest in promoting “supportive” research, not publishing rest
Somewhere, something incredible is waiting to be known. - Carl Sagan

OUR MISSION
The Yale University Open Data Access (YODA) Project's mission is to advocate for the responsible sharing of clinical research data, open science, and research transparency. The Project is committed to supporting research focused on improving the health of patients and informing science and public health. The YODA Project can only improve with your feedback. Please share your comments and ideas.

CONTACT US

OUR MODEL
The YODA Project seeks mutually beneficial partnerships with Data Holders, promoting independence, responsible conduct of research, good stewardship of data, and the generation of knowledge in the best interest of society. To participate, each Data Holder must transfer full jurisdiction over data access to the YODA Project.

LEARN MORE

REQUEST DATA
Are you ready to request data? 80 trials are currently available to request as of November 10, 2014.

GET STARTED
Objectives of the YODA Project

• Project’s goal is to facilitate greater access to clinical trial data, increasing transparency and accelerating generation of new knowledge, while promoting responsible conduct of research

• Better inform patients, clinicians, and industry
  • Facilitate independent assessment and dissemination of data relevant to benefits and harms of medical therapies

• Physicians and patients can base their decisions on the most comprehensive and contemporary evidence available
Principles of the YODA Project

• Promote the sharing of clinical research data to advance science and improve public health and healthcare
• Promote responsible conduct of research
• Ensure good stewardship of clinical research data
• Protect the rights of research participants
This section of the site provides information on study sponsor's criteria for listing studies and other relevant sponsor specific information.

Select the sponsor's logo to view this information.
How YODA Project is Different

• Independent, academic, third party without interest in the data, removing perception of influence over access
• Data sharing partners have given YODA Project full jurisdiction to make decisions regarding data access
• YODA Project established policies and procedures that are in the best interests of:
  • Scientific profession and investigators
  • Patients and research subjects
  • Data Holders
Brief Summary of Progress/Process

• Current partnerships
  • Johnson & Johnson: pharmaceuticals (all products, historical) and devices (2014 onward)
  • Medtronic, Inc.: 1 product, 17 trials

• Nearly 100 trials available, ~37,000 participants

• Submit requests via website, including investigator info, COI forms, research proposal – all of which are publicly posted
  • Requests reviewed by YODA Project, others if needed

• Data made available through secure data sharing platform created by SAS

• Findings posted on YODA Project website (like CT.gov) and dissemination via peer-reviewed journals
A Historic Moment for Open Science: The Yale University Open Data Access Project and Medtronic

Closing in on the Truth About Recombinant Human Bone Morphogenetic Protein-2: Evidence Synthesis, Data Sharing, Peer Review, and Reproducible Research

The Changing Structure of Industry-Sponsored Clinical Research: Pioneering Data Sharing and Transparency

Partnership with Medtronic

• 1\textsuperscript{st} company to contract with the YODA Project to allow access to its clinical trial data for independent reanalysis

• Patient-level data for 17 rhBMP-2 clinical trials

• Large effort devoted to 2 independent reviews

• Data access policy established with Steering Cmte, experts, stakeholders, public comment input

• Requires registration, public reporting, publication

• Designed to facilitate the release of data, ensure high quality reviews of the evidence, and provide the public with the scrutiny of independent review
Partnership with Johnson & Johnson

- Current and historical clinical trial data for all pharmaceutical products
- Clinical trial data for device and diagnostic products from 2014-present
- Plan to expand to consumer clinical trial data in 2015
- The YODA Project has full jurisdiction to grant or deny access to data
Editor's Perspective

Sea Change in Open Science and Data Sharing
Leadership by Industry

Harlan M. Krumholz, MD, SM; Cary P. Gross, MD; Katrina L. Blount, PhD;
Jessica D. Ritchie, MPH; Beth Hodshon, JD, MPH, RN; Richard Lehman, MRCGP;
Joseph S. Ross, MD, MHS

• Share upon request from qualified scientific and medical researchers patient-level clinical trial data, study-level clinical trial data, and protocols from clinical trials in patients for medicines and indications approved in the US and the EU as necessary for conducting legitimate research

• Make publicly available, at a minimum, the synopses of clinical study reports (CSRs) for clinical trials in patients submitted to the FDA, EMA, or national competent authorities of EU Member States

• Work with regulators to adopt mechanisms for providing a factual summary of clinical trial results and make the summaries available to research participants

• Certify on a publicly available web site that they have established policies and procedures to implement these data sharing commitments

• All company-sponsored clinical trials should be considered for publication in the scientific literature irrespective of whether the results of the sponsors’ clinical trials are positive or negative

Data should be made as widely and freely available as possible while safeguarding the privacy of participants, and protecting confidential and proprietary data.

Investigators submitting a research application requesting $500,000 or more of direct costs in any single year to NIH are expected to include a plan for sharing final research data for research purposes, or state why data sharing is not possible.

All trials must be registered and report results within 1 year of completion.

Publications are discoverable and accessible online immediately.

Publication will be on “Open Access” terms.

Foundation will pay necessary fees.

Data underlying published results will be accessible to others immediately.
Sharing of clinical trial data among trialists: a cross sectional survey

- Shared for reasons related to promoting open science (n=248)
- Shared for reasons related to academic benefit or recognition (n=133)
- Shared for reasons related to administrative requirements (n=55)

Sharing of clinical trial data among trialists: a cross sectional survey

Data Sharing Supports NPA Guiding Principles

• Facilitates fair and objective assessment of trial data, as opposed to speculative analysis based on incomplete data
• Promotes transparency
• Compete on science, not marketing
• Untenable to withhold information about product effectiveness and safety
• Reinforcement of open scientific inquiry
• Verification, refutation, or refinement
• Promotion of new research on existing data
• Encourages multiple perspectives
• Reduces duplicative data collection
• Respects efforts of volunteers/subjects
• Informs patient decisions and influence clinical practice
References for more information

• http://yoda.yale.edu
• https://clinicalstudydatarequest.com/
• http://www.phrma.org/sites/default/files/pdf/PhRMAPrinicplesForResponsibleClinicalTrialDataSharing.pdf
• http://grants.nih.gov/grants/policy/data_sharing/data_sharing_guidance.htm
• http://www.gatesfoundation.org/How-We-Work/General-Information/Open-Access-Policy
ClinicalStudyDataRequest.com

• 11 sponsors
• Over 1500 trials available for request
• 36 approved requests as of May 2014, 13 of which have received access to data