Data Sharing: Perspectives from a Third Party, Independent Academic Process (YODA)

CBI Conference on Clinical Data Disclosure and Transparency
January 29, 2015

Joseph S. Ross, MD, MHS
Section of General Internal Medicine, School of Medicine
Center for Outcomes Research and Evaluation, Yale-New Haven Hospital
Where did the YODA Project (Yale Open Data Access) Come From?
Trial Publication after Registration in ClinicalTrials.Gov: A Cross-Sectional Analysis

- 46% of trials published
- Lowest rates: Industry-sponsored studies

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
Recommendations

1. “Stakeholders should foster a culture in which data sharing is the expected norm, and should commit to responsible strategies aimed at maximizing benefits, minimizing risks, and overcoming challenges of sharing trial data”

2. Clarified specific points in time by which various types of data are reported/shared

3. Data Holder strategies:
   1. Data Use Agreement
   2. Independent panels, including lay public
   3. Transparency
   4. Monitor “outcomes”

4. More work to be done, need to address key infrastructure, technological, sustainability, and workforce challenges ahead
How to 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
Somewhere, something incredible is waiting to be known. - Carl Sagan

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

• This is not our data
• 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
Partnership with Medtronic

• 1st company to contract with the YODA Project to allow access to its clinical trial data for independent reanalysis (2011)
• 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
• Required 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
Dissemination of findings

Conferences to discuss issues associated with promoting access to individual clinical product data:
1. Creating standardized protocol for permitting access to product clinical data
2. Issues in conducting systematic review and meta-analysis of product data, including clinical trial and post-market surveillance data
3. Other issues: importance, strategies, gaps in statistical practice, practical concerns

Company releases to Coordinating Organization all clinical trial data (published/unpublished); post-market surveillance data; and spontaneous adverse events

Coordinating Organization

Development and Refinement of Approach for Disseminating Data

Conferences to discuss issues associated with promoting access to individual clinical product data:
1. Creating standardized protocol for permitting access to product clinical data
2. Issues in conducting systematic review and meta-analysis of product data, including clinical trial and post-market surveillance data
3. Other issues: importance, strategies, gaps in statistical practice, practical concerns

Dissemination of conference proceedings via peer-reviewed journals and project Web site

Development of Web site for project communications and facilitation of data distribution

Communication of description of data files that will be made available to researchers

Acceptance of requests for data using standardized protocol; review of proposals

Processing of requests for data access; request and application posted on Web site

Distribution of data

Requirement to submit results within 6 months of completion

Dissemination of findings

Solicitation of proposals to conduct independent reviews

Selection of 2 research groups

Review Organizations conduct independent evaluations in parallel

Dissemination of findings

Source: Krumholz and Ross, JAMA 2011;306:1593-4.
YODA Project Model

• Begins with company release of data to coordinating organization
• Coordinating organization assembles independent steering committee for oversight

Product identified, including areas of concern

Company releases to coordinating organization all clinical trial data (published/unpublished), postmarket surveillance data, and spontaneous adverse events

Source: Krumholz and Ross, JAMA 2011;306:1593-4.
Formal Independent Analysis

- Coordinating organization (YODA Project) contracts with two research groups that independently systematically review and synthesize all available clinical trial data
  - Industry and non-industry research
  - Uses individual-level data, in addition to trial summary-level data
- Advantages:
  - Distance btw company & reviewers
  - Reproducibility and validity

Source: Krumholz and Ross, JAMA 2011;306:1593-4.
Data Dissemination

• Coordinating organization (YODA Project) makes industry’s individual-level data available to other external researchers
  • Via a Web site, requiring a registration process, commitment to results reporting

• Advantages:
  • Complete transparency

Source: Krumholz and Ross, JAMA 2011;306:1593-4.
# YODA Project 1.0: rhBMP-2 Review

<table>
<thead>
<tr>
<th>Group</th>
<th>Role</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Coordinating Center (YODA Project)</strong></td>
<td>• Assembled and informed the SC</td>
</tr>
<tr>
<td></td>
<td>• Designed policies and procedures</td>
</tr>
<tr>
<td></td>
<td>• Solicited and selected subcontractors</td>
</tr>
<tr>
<td></td>
<td>• Coordinated data dissemination</td>
</tr>
<tr>
<td><strong>Medtronic, Inc.</strong></td>
<td>• Provided Yale all data on product</td>
</tr>
<tr>
<td></td>
<td>• Answered data related questions</td>
</tr>
<tr>
<td></td>
<td>• Feedback on P&amp;P, reports, manuscripts</td>
</tr>
<tr>
<td><strong>Subcontractors (OHSU and University of York)</strong></td>
<td>• Independently analyzed Medtronic data</td>
</tr>
<tr>
<td></td>
<td>• Prepared a comprehensive report</td>
</tr>
<tr>
<td></td>
<td>• Prepared a manuscript</td>
</tr>
<tr>
<td><strong>Steering Committee</strong></td>
<td>• Participated in data sharing discussions</td>
</tr>
<tr>
<td></td>
<td>• Provided substantive feedback on all project related issues</td>
</tr>
</tbody>
</table>
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

YODA Project 2.0: More ‘open’ data

• Facilitate wider access to clinical trial data assets
• No need for formal independent reviews by independent research groups
• Protections for data privacy and scientific rigor even more important
• Continued importance of
  • Steering committee
  • Public input
  • Transparency
Partnership with Johnson & Johnson

• Current and historical clinical trial data for:
  • All pharmaceutical products (including historical)
  • Device and diagnostic products from 2014 onward

• Requests submitted via website, including investigator info, COI forms, research proposal – all publicly posted
  • Requests reviewed by YODA Project, others if needed; does project advance scientific and medical knowledge with goal of improving public health and healthcare delivery
  • (Blinded) request reviewed by J&J: Due Diligence Assessment; is data available and can it be shared?

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

• Findings posted on YODA Project website (like CT.gov) and dissemination via peer-reviewed journals
Challenging Issues We’ve Faced ...

- Creating a platform that facilitates research
  - What trials are or can be made available?
  - What meta-data are needed: CRFs, study protocol, SAPs.
- Resources are not unlimited – should there be a fee?
- Patient privacy, secure data analytic platform – how easy can it be?
- Maintaining public input, transparency
- Scope and intensity of YODA project review and J&J’s Due Diligence Assessment
Experience thus far ... “outcomes”?

• Established policies and procedures after soliciting feedback from stakeholders, experts, public

• Launched October 2014, more than 80 trials cleared for sharing

• Many inquiries, 8 submitted requests, DUAs signed/pending, requestors just getting access to data via secure platform
  • No requests (yet) to validate previously published studies
  • Most requests to address secondary research questions or to combine data as part of larger meta-analysis
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 Hodson, JD, MPH, RN; Richard Lehman, MRCGP; Joseph S. Ross, MD, MHS

References for more information

• http://yoda.yale.edu
• https://clinicalstudydatarequest.com/
• http://www.phrma.org/sites/default/files/pdf/PhRMAPrinciplesForResponsibleClinicalTrialDataSharing.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
• 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