What Is The YODA Project?

Lessons Learned and How to Operationalize Academic Data Sharing

University College London & Yale University
Facilitating Data Access to Non-Industry Funded Research
Strategy Development Meeting
London
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Somewhere, something incredible is waiting to be known. - Carl Sagan
Objectives of the YODA Project

• 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 so that decisions can be based on the most comprehensive and contemporary evidence available relevant to benefits and harms of therapies
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
- Designed to facilitate the release of data, ensure high quality reviews of the evidence, and provide the public with the scrutiny of independent review
**YODA Project**

**A Model for Dissemination and Independent Analysis of Industry Data**

Source: Krumholz and Ross, JAMA 2011;306:1593-4.
YODA Project 1.0 Model

- Began with Data Holder data release to YODA Project
- YODA Project assembled independent steering committee for expertise, input
- Advantages: External “oversight”, internal jurisdiction

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

- YODA Project competitively funded two research groups to independently systematically review and synthesize all available clinical trial data
  - Industry and non-industry research
  - Used individual-level data, in addition to trial summary-level data
- Advantages:
  - Distance between Data Holder & Reviewers
  - Reproducibility and validity

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

• YODA Project made Data Holder’s individual-level data available to other external researchers
  • Via a Web site, requiring public registration and proposal, commitment to results reporting
• Data access policy established with Steering Cmte, experts, stakeholders, public comment input
• Advantages:
  • Complete transparency
  • Allows replication, scrutiny, further independent research

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

- Scope includes clinical trial data for:
  - All pharmaceutical products (including historical)
  - Device and diagnostic products from 2014 onward

- YODA Project website provides info on trial and supporting documentation
YODA Receives All J&J Clinical Trial Data Requests via Portal

Request Made for either
• Redacted CSRs
• De-identified Patient Level Data

YODA Project
Standard Review
• Completed registration information
• Conflict of Interest forms
• Description of data requested
• Is proposal for a scientific purpose?
YODA Receives All J&J Clinical Trial Data Requests via Portal

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Request Made for either
- Redacted CSRs
- De-identified Patient Level Data

Request is for a scientific purpose

Scientific purpose is unclear
Requestor submits additional info

Request is NOT for a scientific purpose

Requestor disagrees with YODA decision
To External Review

Requestor agrees with YODA decision

Request Denied - Decision Posted - END
Data Request & Review Process

YODA Project
  Standard Review
  • Completed registration information
  • Conflict of Interest forms
  • Description of data requested
  • Is proposal for a scientific purpose?

Request is for a scientific purpose

Data in Safe Harbor

Data not in Safe Harbor

Request Fulfilled
  - Decision Posted -

To Janssen
  Resource Estimation

END
Janssen Performs Resource Estimation
- Estimate of resources needed to redact CSR(s) or De-identify IPD(s)
- Partnering considerations

YODA Reviews Janssen’s Resource Estimation
Review materials posted

Resources Required are Reasonable

Resources Required Exceed Reasonable

External Review
- YODA Project solicits Two independent peer reviews
- Steering Cmte Member(s) Review

External Review
- YODA and one Steering Committee member discuss reviews

YODA Approves

J&J Redacts CSR(s) and/or De-Identifies IPD

YODA Rejects

Request Fulfilled - Decision Posted - END

Request Denied - Decision Posted - END
After the “thumbs up” from YODA, J&J

- All approved requests sign a Data Use Agreement, includes restrictions of use
- Data made available through secure data sharing platform created by SAS
- Dissemination via peer-reviewed journals
  - If not published, findings posted on YODA (~CT.gov)
Experience thus far

- Launched October 2014, ~100 trials listed as available for sharing
YODA Website Traffic

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<td><strong># sessions</strong></td>
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Data requests thus far

- 22 requests
  - For 4, part of work is to validate previously published studies
  - Most requests to address secondary research questions or to combine data as part of larger meta-analysis
YODA Project Data Requests

22 Data Requests Received

18 Data Requests Approved by YODA
- 14 Data Requests Approved with no changes needed by the investigator
- 2 Data Requests Closed (out of scope)

4 Data Requests Under Review by the YODA Project
- 4 Data Requests Approved after changes were requested and made by the investigator

10 Data Requests with Data Access
Try not.

Do or do not.
There is no try.

- Yoda
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.

• Engaging research community to use data

• 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

• Data Use Agreements
Considerations – lessons learned

• Can a trial’s data be shared? Is it even feasible
  • Ownership/authority
    • Identifying trials and authority to share them. A Due Diligence Assessment (DDA) is the process by which partnering Data Holders provide an assessment of its ability as an organization to make the data available to be shared externally, including whether Data Holders have legal and ethical rights to make the data available to external investigators for scientific purposes.
  • Patient Consent

• Among the trials that could be shared:
  • Ensuring Patient privacy
    • The amount of time, effort, and expense required for appropriate data de-identification
  • Review process: Third-party review
  • commercial/litigious interests?

• DUA – disseminate via peer review

• Cost – who will pay?
Operationalizing for academic sharing ...

- Same platform?
- Who pays? Role of public funding ...
- Need for independent review?
- What about Due Diligence Assessments?
- What about Data Use Agreements?
Restoring Study 329: efficacy and harms of paroxetine and imipramine in treatment of major depression in adolescence

Joanna Le Noury, John M Nardo, David Healy, Jon Jureidini, Melissa Raven, Catalin Tufanaru, Elia Abi-Jaoude

ABSTRACT

OBJECTIVES

To reanalyse SmithKline Beecham’s Study 329 (published by Keller and colleagues in 2001), the primary objective of which was to compare the efficacy and safety of paroxetine and imipramine with placebo in the treatment of adolescent depression. The reanalysis used and abandoned trials (RIAT) to determine whether access to and reanalysis of the controlled trial relevant implications for evidence.

DESIGN

Double-blind randomised placebo controlled trial

SETTING

275 adolescents with major depressive disorder, each for 8 weeks in duration. Exclusion criteria included:

HAM-D score ≤ 8 or ≥ 25% reduction in baseline HAM-D score at acute endpoint. Prespecified secondary outcome were changes from baseline to endpoint in depressive symptoms in K-SADS-L, clinical global impression, autonomous function, checklist, self-perception profile, and sickness impact scale; predictors of response to treatment.

RIAT

Paroxetine
Imipramine
Placebo

SKB

Paroxetine
Imipramine
Placebo

KELLER

Paroxetine
Imipramine
Placebo

*Correspondence to: Jureidini Jon.Jureidini@adelaide.edu.au

Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/bmj.j877).

End of acute study
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
## Summary of Available Trials (N=106)

<table>
<thead>
<tr>
<th>Therapeutic Area</th>
<th>Product Name</th>
<th>Generic Name</th>
<th># Trials Available</th>
<th># Times Requested</th>
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<td>Urinary Tract, Sexual Organs, and Pregnancy Conditions</td>
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<th># Times Requested</th>
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