The YODA Project: A Use Case and Lessons Learned

Sharing Clinical Trial Data
NASEM Workshop
November 18, 2019
Potential Conflicts of Interest

• YODA Project funded by research grant through Yale from Johnson & Johnson, formerly funded by Medtronic, Inc.

• Research grant funding through Yale from:
  • Food and Drug Administration (FDA)
  • Centers for Medicare and Medicaid Services (CMS)
  • Blue Cross Blue Shield Association
  • NIH/NHLBI, AHRQ
  • Laura and John Arnold Foundation
Discovery consists of looking at the same thing as everyone else and thinking something different.

Albert Szent-Györgyi

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 Partners, 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 Partner must transfer full jurisdiction over data access to the YODA Project.

HOW IT WORKS

REQUEST DATA
Are you ready to request data? To date, 350 trials have been identified as available. The YODA Project and Data Partners continue to identify and add more.

GET STARTED
Overview and experience of the YODA Project with clinical trial data sharing after 5 years

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The Yale University Open Data Access (YODA) Project has facilitated access to clinical trial data since 2013. The purpose of this article is to provide an overview of the Project, describe key decisions that were made when establishing data sharing policies, and suggest how our experience and the experiences of our first two data generator partners, Medtronic, Inc. and Johnson & Johnson, can be used to enhance other ongoing or future initiatives.
Principles of the YODA Project

• Promote 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 by external investigators

• Protect rights of research participants
Johnson & Johnson Partnership

• Initiated in 2014 – effort focused on promoting and facilitating access to clinical trial data:
  • All pharmaceutical products (including legacy trials)
  • Device and diagnostic products as of 2015
  • Consumer products as of 2017
• Established data access policy and procedures, with input from Steering Committee, experts, stakeholders, and public comment
 Trials By Generic Name

A Randomized, Double-Blind Trial of Anti-TNF Chimeric Monoclonal Antibody (Infliximab) in Combination With Methotrexate for the Treatment of Patients With Polyarticular Juvenile Rheumatoid Arthritis

PRODUCT INFO

GENERIC NAME

INFliximab

PRODUCT CLASS

Antitumor Necrosis Factor (TNF) Receptor-Neutralizing Antibodies

Therapeutic Areas

Musculoskeletal, Immune, and Inflammatory Diseases

PID

123

Data Source

ClinicalTrials.gov

Data Partner

Johnson & Johnson

Condition Studied

Arthritis, Juvenile

Supporting Documentation

- Clinical study report
- Study protocol
- Data definitions and specifications
- Statistical analysis plan
- Additional data requests

APPROVED DATA REQUESTS ASSOCIATED WITH THIS TRIAL

Impact of the dose of Immunosuppressants on pharmacodynamics of Infliximab: report on meta-analysis of randomized controlled trials
Impact of Biological Therapy on the Risk of Arterial and Venous Thromboembolic Events in Chronic Autoimmune Diseases: A Post-hoc Analysis of RCTs
Requests Submitted Online

• Investigator names, affiliations, funding
• Narrative summary / public abstract
• Detailed research proposal, including:
  • Project background, clear objectives
  • Trials, sample eligibility criteria, variables
  • Primary and secondary endpoints
  • Statistical analysis plan
• Project purpose (meta-analysis, validation ...)
• Timeline and dissemination plan
• Data use agreement training

within 2 weeks
YODA Project Review

The YODA Project reviews proposals to ensure that each proposal has scientific merit, specifically verifying:

• Scientific purpose is clearly described

• Data requested will be used to create or materially enhance generalizable scientific and/or medical knowledge to inform science and public health

• Proposed research can be pursued using the requested data
Data Partner Review

Requests for data undergo a Due Diligence Assessment by the Data Partner to evaluate their ability to make the data available to be shared, including assessment of:

• Patient privacy

• Similar research studies

• Required variables

• Appropriateness of requested data (e.g. CSR vs IPD)
• Once approved, require signed DUA
• Investigators gain access to data maintained on secure platform, via VPN
• Prevents distribution, protects patient privacy
Number of Data Requests Submitted

- Median No. Trials Requested: 3 (IQR: 1-9)

*As of November 1, 2019*
YODA Project Data Requests

Purpose of Analysis
- New Question
- Meta-Analysis
- Clinical Prediction, Risk Prediction
- Validation
- Statistical Methods
- Clinical Trial Methods
- Pilot/Preliminary Research
- Other
- Comparision Group

Researcher Affiliation
- 90% Academia
- 5% Government
- 4% Industry
- 1% Other
Status of Data Requests

*As of November 1, 2019

<table>
<thead>
<tr>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
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<td>2015</td>
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</tbody>
</table>

- Manuscript Submitted for Publication
- Incomplete with Preliminary Results
- Incomplete without Results
- Data Access Enabled
- DUA/Data Preparation in Progress
- Under Review/Revisions Requested
- Withdrawn/Closed

*As of November 1, 2019"
# Approved Requests to Use Johnson and Johnson Data*

<table>
<thead>
<tr>
<th>YODA Project Protocol Number</th>
<th>PI and Affiliation</th>
<th>Research Proposal</th>
<th>Product(s) of Interest</th>
<th>YODA Project Review and Data Partner Due Diligence Assessment</th>
<th>Project Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014-0340</td>
<td>Heldt Storgard, MD, PhD. University of Copenhagen, Center for Diabetes Research</td>
<td><strong>The effects of SGLT-2 inhibitors in patients with type 2 diabetes: a systematic review with meta-analysis of randomized trials</strong></td>
<td>INVOKANA</td>
<td>YODA Project Review</td>
<td>Complete; Published in <em>PLosONE</em> November 11, 2016.</td>
</tr>
<tr>
<td>2014-0333</td>
<td>Guru Sonpavde, MD, University of Alabama, Birmingham (UAB) School of Medicine</td>
<td><strong>RECIST response as a surrogate endpoint in metastatic castration-resistant prostate cancer: Retrospective analysis of COU-AA-203 and COU-AA-301.</strong></td>
<td>ZYTIGA</td>
<td>YODA Project Review</td>
<td>Unknown; data access revoked, investigator has not reported results as requested.</td>
</tr>
<tr>
<td>2014-0324</td>
<td>Raymond Cross, MD, MS, University of Maryland,</td>
<td><strong>Gender differences in weight gain in patients with inflammatory bowel disease treated with Infliximab</strong></td>
<td>REMICADE</td>
<td>YODA Project Review</td>
<td>Complete; Published in <em>Inflamm Bowel Dis</em> July 2, 2019.</td>
</tr>
</tbody>
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*The YODA Project posts approved proposals once data access has been granted.

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# Submitted Data Requests Withdrawn/Not Approved*

The following data requests could not be fulfilled due to patient privacy concerns, data element availability, data security concerns, or lack of research proposal clarity.

<table>
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<tr>
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<tr>
<td>2014-0337</td>
<td>William J. Sandberg, MD, University of California, San Diego</td>
<td><strong>Post hoc analysis of the ACT-1 &amp; ACT-2 trials to simulate individualized dosing regimens using a predictive model</strong></td>
<td>REMICADE</td>
<td>YODA Project Review</td>
<td><em>Request originally approved but subsequently withdrawn: data could not be downloaded as requested.</em></td>
</tr>
<tr>
<td>2015-0406</td>
<td>Nicola Schianda, MD FRCP(C), University of Ottawa</td>
<td><strong>Is primary tumor in prostate cancer a reliable target lesion for measurable disease at contrast-enhanced CT (CE-CT)</strong></td>
<td>ZYTIGA</td>
<td>YODA Project Review</td>
<td><em>Request originally approved but subsequently withdrawn: CT scans not available due to patient privacy concerns.</em></td>
</tr>
<tr>
<td>2015-0501</td>
<td>Anthony Onley, MD, MSc</td>
<td><strong>Towards An Improved Pediatric Congenital Disease</strong></td>
<td>REMICADE</td>
<td>YODA Project Review</td>
<td><em>Request originally approved.</em></td>
</tr>
</tbody>
</table>

*The YODA Project posts withdrawn/unapproved proposals at the time the decision is made.
Experience so far …

• Of 350 trials currently listed on the site, 75% have thus far been requested (16 available only since July)

• Of 134 applications submitted, 117 (87%) approved, 4 (3%) remain under review; 13 (10%) withdrawn/closed
  • Usually because data not available/cannot be adequately de-identified

• Nearly all require some administrative revision, but 41 (31%) required scientific revision after review for clarity

• 31 manuscripts have been submitted for publication to peer-reviewed journals, 26 of which have been published
  • Thus far, 30% of projects with data access for ≥1 year published
Publications and Posters (includes multiple per project)

*As of November 1, 2019
Articles Using Data Shared Through YODA Project
Objective: Assess the benefits, harms and cost-effectiveness of two new biologic therapies, compared to existing therapies:

- certolizumab pegol (CZP; CIMZIA®, UCB Pharma, Brussels, Belgium)
- secukinumab (SEC; COSENTYX®, Novartis International AG, Basel, Switzerland)

Key Findings: Both CZP and SEC are effective therapies for improving the symptoms of PsA. These new biologics can be considered a cost-effective use of NHS resources.
Objective: Review new evidence on the use of bedaquiline to inform changes in the World Health Organization (WHO) interim policy guidance on the use of bedaquiline for the treatment of multidrug-resistant tuberculosis (MDR-TB).

Key Findings: Bedaquiline effective for treatment of MDR-TB.
Objective: Determine benefits and risks associated with SGLT2-i for patients with type 2 diabetes mellitus.

Key Findings: SGLT2-i reduced HbA1c when compared with placebo.
Strengthening Science through Data Sharing

• Numerous studies that might not otherwise have been feasible to pursue, some of which have impacted health policies and guidelines
• Facilitated direct collaborations with original investigators
• Developed efficiencies (J&J now conducts all trials intending to share)
• Replication studies have supported – not undermined – original study
• No instances of patient privacy breaches
• No publications of spurious safety findings that received unwarranted attention or disrupted patient care
• No data have been used for commercial or litigious purposes
Challenges Remain

• Broadening awareness of data availability
• Fostering expertise in using data from clinical trials (*it’s complicated*)
• Making older trial data available in a contemporary format
• Adopt data standards, across sponsors, to enable meta-analyses
• Sustainable model that covers the cost of data sharing
• Data Use Agreements …
• Establish standards: when should data be available, for how long, how to reward those who share data?
• Many large pharma sharing, what about other sponsors?
http://yoda.yale.edu

@YODAProject
We’ve Learned and Iterated with Experience ...

- Transparency
- Full authority and independence
- Independent Steering Committee
- Public list of available trials
- Supporting documentation
- Research proposal submission and public posting
- Blinded review of requests by the YODA Project and partnering company

- Opportunity for collaboration with partnering company
- Data Use Agreement
- Secure data access or transfer
- Results dissemination
- No data access fee
Benefits of Sharing Early Clinical Research Data

• Ensures all data can be used to inform clinical decisions
• Positions research as a public good
• Respects contributions of participants:
  • maximizing value of collected data, while
  • minimizing duplicative data collection
• Facilitates secondary studies of existing data
• Promotes transparency and reproducibility:
  • sample, design, and analysis