
May 16, 2019
Johns Hopkins Medical School
Rebecca Li, PhD, Executive Director
Agenda

• Why share data?
• Sharing participant-level data using the Vivli Platform
• What are the requirements today? By journals and funders
• How can I benefit from using data in the Vivli platform?
• Q&A
Data Sharing in the News
Why should I share my data?

- Journal and funder mandates
- Increase citations
- Moral obligations (owe it to trial participants)
Evolution of Transparency in Clinical Trial Data

**Clinical trials registration**

ICMJE requirement for publication (2004)
FDAAA requirement for applicable trials (2007)

**Summary data shared**

FDAAA Final Rule (2016)
EU no. 536/2014 requires lay summaries

**Raw data (IPD) shared**

EMA Policy 0070 (2014), Policy 0043 (TBD)
PhRMA/EFPIA principles for data sharing (2014)
IOM Sharing Clinical Trial Data report (2015)
ICMJE IPD sharing statement (July 2018)
Why should I share my data?

- Journal and funder mandates
- Increase citations
- Moral obligations (owe it to trial participants)
Rewards and recognition for sharing

- Studies that made data available in a public repository received 9% more citations than similar studies that did not
- Sharing facilitates science
- Data availability was associated with a citation benefit and the number of reuse papers grows rapidly over years

Why Should I Share my Data?

Journal and funder mandates

Increase citations

Moral obligations (owe it to trial participants)
Patients demand data sharing and reuse

NEJM Aligning Incentives for Sharing Clinical Trial Data Summit, Boston, MA. April 2017
Barriers to IPD Sharing for Academics

- **For most academic trialists (Data Contributors)**
  - secure data hosting and sharing platforms not available or limited to within the institution
  - no standard data use and data sharing agreements
  - no independent review process available to adjudicate data requests
  - cost and difficulty of de-identifying IPD and making it available
  - **All this makes it difficult to meet data sharing requirements**

- **For Data Users**
  - difficult to discover what IPD is available for sharing
  - combining datasets from different platforms is resource- and time-intensive
  - different data standards, data requirements, security standards, policies
  - disease-specific data sharing platforms limit cross-disciplinary data discovery
  - limited range of analytic tools available
## Vivli Addresses Pain Points for Contributors and Requesters

<table>
<thead>
<tr>
<th>Data Contributors</th>
<th>IPD Sharing Requirements</th>
<th>Figshare</th>
<th>Dryad</th>
<th>CT.gov</th>
<th>Vivli</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IPD can be stored and securely hosted</td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td>Harmonized data contributor and data use agreements</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>IPD can be shared securely to anyone in the world</td>
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<tr>
<td></td>
<td>Independent review available</td>
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</table>
Introducing Vivli

**THE ENTITY**

- Non-profit organization
- Convening function
  - Biomedical industry (pharma, bio, device)
  - Academia
  - Non-profit funders and foundations
  - Government (funders and regulators)
  - Patient/patient advocates
- Governance and policy
  - Harmonizing language & agreements
  - Move culture of data sharing
- Advocacy
  - Lowering barriers
  - Promoting incentives
- Oversight of Implementation

**THE PLATFORM**

- A user-friendly, secure, state-of-the art data sharing and computing platform
- Serving the international community, including trials from any disease, country, sponsor, funder, or investigator
  - Open search
  - Robust security
  - Modern tools and technologies
Vivli By the Numbers

- 3,900+ Trials
- 1.9M Participants from 105 countries
- 19 Members
Founding Funders and Partners
Funders increasingly requiring data sharing

Draft NIH Data Sharing and Management Policy is requiring

- IPD sharing plan for all grants
- sharing and managing of data according to approved plan

Vivli provides an NIH-compliant data sharing plan template

Data sharing costs should be part of the budget proposal
https://vivli.org/resources/resources/
Journal Mandates as of July 1, 2018

• ICMJE includes

• Trial manuscripts must be submitted with a data sharing statement
  – how Individual participant-level data (IPD) will be shared - who, what, when, where, and why

• IPD sharing is not (yet) required but “editors may take into consideration data sharing statements when making editorial decisions”
At Trial Registration

• Data sharing plan is part of the ClinicalTrials.gov registration record
• Undecided is allowed in ClinicalTrials.gov but not by ICMJE
• As of January 1, 2019, ICMJE requires registration of your data sharing plan at time of trial registration
• This is a radical departure for most investigators to declare their sharing intentions upfront!

# Data Sharing Plan for ICMJE Journal Submission

<table>
<thead>
<tr>
<th>ICMJE Question</th>
<th>If using Vivli, proposed response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Will IPD (and data dictionaries) be made available?</td>
<td>Yes</td>
</tr>
<tr>
<td>What data in particular will be shared?</td>
<td>Final cleaned individual participant-level data, de-identified</td>
</tr>
<tr>
<td>What other documents will be made available?</td>
<td>Final protocol, statistical analysis plan, and the data dictionary. (Note: additional documents such as CRFs and analytic code may also be included.)</td>
</tr>
<tr>
<td>When will data be made available?</td>
<td>X months /years after study completion</td>
</tr>
<tr>
<td>With whom?</td>
<td>Anyone with the relevant skillsets to conduct the analysis and has submitted an approved proposal on Vivli. Proposals are submitted on <a href="http://vivli.org">vivli.org</a>.</td>
</tr>
<tr>
<td>For what types of analysis?</td>
<td>To achieve the aims and objectives in the scientific proposal as approved via Vivli.</td>
</tr>
<tr>
<td>By what mechanism will data be made available?</td>
<td>Following an approved request, a data use agreement must be signed. Data are made available via a secure research environment or download.</td>
</tr>
</tbody>
</table>
At Trial Completion

- JHMI is an institutional member of Vivli
  - Your membership covers the costs to store and share your study
- To host/archive your study on Vivli
  - Send us your NCT ID (Clinicaltrial.gov identifier)
  - Provide IPD Data Package to Vivli
- Vivli takes care of long-term data sharing even after your grant funds end
# Contents of the IPD Package*

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Required</strong></td>
<td></td>
</tr>
<tr>
<td>Study protocol</td>
<td>Final protocol with all amendments</td>
</tr>
<tr>
<td>Informed consent form</td>
<td>Final approved informed consent form</td>
</tr>
<tr>
<td>Data dictionary</td>
<td>Detailed descriptions of each variable in the dataset, including the definition, source, coding, etc. of the variable</td>
</tr>
<tr>
<td>Statistical Analysis Plan</td>
<td>Description of the principal features of the analyses described in the protocol</td>
</tr>
<tr>
<td>IPD dataset</td>
<td>Final cleaned individual participant-level data, de-identified</td>
</tr>
<tr>
<td><strong>Optional</strong></td>
<td></td>
</tr>
<tr>
<td>Analytic code</td>
<td>Software code used to carry out prespecified and additional analyses</td>
</tr>
<tr>
<td>Case report forms</td>
<td>Forms used to collect the data that is described in the protocol for each trial participant</td>
</tr>
<tr>
<td>Clinical Study Report (CSR)</td>
<td>Report that summarizes the efficacy and safety data from the study (after regulatory decision)</td>
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</table>

*NOTE: *this is a subset of the entire full data package and includes the data that underlies the publication findings (tables, figures)*
Data Sharing Timeline Summarized

- **Grant Submission**: Data sharing plan in proposal
- **Trial Registration**: Data sharing plan in registration
- **Trial Completion**: Archive IPD Data Package in Vivli
- **12 Months Later**: Summary results to CT.gov
- **Publication**: Data sharing statement to journal
- **Embargo Period**: Listed on Vivli
- **Requestable**: Available for requests
- **Shared**: IPD reused, tracked

Supported by Vivli
Providing IPD Data Package

**DE-IDENTIFY DATA**

Vivli accepts de-identified data from completed trials

**Confirm data package elements** for sharing (protocol, data dictionary, statistical analysis plan, and individual participant level data)

**SIGN AGREEMENT**

**Contact** support@vivli.org for the Data Contribution Agreement, which needs to be signed by the Principle Investigator.

Returned signed version.

**PROVIDE YOUR DATA**

Vivli will then provide access to its platform to upload your data. This is an easy drag and drop file-sharing process with support available every step of the way.

Data will be archived and a DOI assigned.
IPD must be transformed to reduce the risk of re-identification of study participants.

Vivli can connect you with our partner Privacy Analytics to de-identify/anonymize your data if necessary at a discount.
Data Standardization Approach

IPD is recommended to be in CDISC SDTM format

No requirements for using standardized data variables or common data elements (CDEs)
• Vivli manages the administration of data requests and makes the process easy for data contributors
• Approved requests are published on Vivli
  – title, lay summary, and name of requester
  – annual usage reports shared with your institution
• Under the Hopkins membership agreement, Hopkins IPD packages are downloadable by approved requesters
Why are DOIs important in data sharing?

• Digital Object Identifiers (DOIs) are persistent, citable and unique links on the internet. They help the community locate and cite data and objects.

• Vivli assigns a persistent identifier (DOI) to datasets and other objects (such as publications)

• DOIs facilitate subsequent attribution and data sharing

• They are ‘minted’ by several known entities
Repository & DOI updates

- All data shared on Vivli & approved data requests are provided a DOI minted by DataCite
- Vivli is presently listed on FAIR Sharing and by the BMJ
- Vivli is engaged in ongoing discussions to be added as a recommended repository for a number of journals and funders
Noninvasive Diagnosis of Renal Allograft Rejection by Urinary Cell mRNA Profiling

<table>
<thead>
<tr>
<th>Study Details</th>
<th>Administrative Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vivli DOI</td>
<td><a href="https://doi.org/10.25034/00003145">https://doi.org/10.25034/00003145</a></td>
</tr>
<tr>
<td></td>
<td>Vid ID</td>
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<tr>
<td></td>
<td>VIV00003145</td>
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<tr>
<td></td>
<td>Sponsor Protocol ID</td>
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<tr>
<td></td>
<td>DA1T CTOT-04</td>
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<tr>
<td></td>
<td>Acronym</td>
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| Primary Registry Name | ClinicalTrials.gov | Primary Registry ID | NCT00337220 | Primary Registry ID URL | https://clinicaltrials.gov/show/NCT00337220 |

<table>
<thead>
<tr>
<th>Lead Sponsor Agency</th>
<th>National Institute of Allergy and Infectious Diseases (NIAID)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data Contributor Organization Name</td>
<td>ImmPort (a data-sharing platform funded by the National Institutes of Health)</td>
</tr>
<tr>
<td>External Study URL</td>
<td><a href="http://www.immport.org/immport.org/public/study/displayStudyDetail/SDY479">http://www.immport.org/immport.org/public/study/displayStudyDetail/SDY479</a></td>
</tr>
</tbody>
</table>
Sample DOI, approved data request
Summary: Benefits of Sharing through Vivli

- **No cost** – Sharing de-identified data *covered* by membership in Vivli
- **Citation** – DOIs allow for citation and credit of your research data
- **Metrics** – Yearly metrics on number of data requests, resulting publications, etc.
- **Long-term archiving** – Archive your trials on Vivli (at least 25 years)
- **Post-grant data sharing** – IPD sharing solution that continues even after grant funds end
- **Funder and journal mandates** – Use Vivli to easily fulfill data sharing plan mandates
How to Access Data in Vivli?

3900+ Trials

1.9M Participants from 100 countries
Data Request and Access Process

SEARCH
Search Vivli platform for information about available studies.

REQUEST
Request IPD data package. Each Data Request reviewed according to contributor's publicly stated requirements.

ACCESS
Access data from approved requests in Vivli's secure research environment or downloaded with permission.

ANALYZE
Use robust analytical tools to combine and analyze multiple data sets.

DISSEMINATE
Completed research results assigned a DOI. Researchers may use the Vivli platform to meet their publication requirements.

Short video demo at https://vivli.org/resources/vivli-platform-demo/
Secure Environment Bridges Multiple Platforms
Data Contributors  Data Requesters

- Recognize value and opportunity -- but also burden -- of data contributors responding to data requesters and vice versa
  - communication and collaboration is entirely up to the parties involved
  - see Vivli webinar on how to prepare high quality data proposals

- Publications arising from use of Vivli data must
  - acknowledge use of the original data (by DOI citation)
  - be reported back to Vivli for tracking purposes
Summary: Benefits of Requesting Data through Vivli

- **One-stop search** – find individual-level participant data from more than 3,200 completed clinical trials
- **Harmonized request form** – use a single data request form for all studies
- **Bridges platforms** – can bring together data sets from Vivli and multiple other platforms
- **Secure yet customizable** – bring in your own data, tools and scripts to a secure research environment
Vivli Datathon

- Objective – balance data utility with privacy in small more identifiable trial datasets
- June 19th in Cambridge, MA
- No Prior Coding experience needed
- Mentors provided
- Hosted by Vivli and Microsoft
- [https://vivli.org/events/datathon/](https://vivli.org/events/datathon/)
- Prizes for student teams
Log on to Vivli.org

- Explore the thousands available via the Vivli platform
- Begin your search
- Contact support@vivli.org with questions
Questions?
Resources available from Vivli

• FAQs and promotional materials on submitting studies to Vivli
• How to guide to upload data on Vivli
• Coming soon: How to write data management plan using Vivli to cover your data sharing needs

• How else might we partner with you in your data sharing efforts?
# User fees

<table>
<thead>
<tr>
<th>Environment Type</th>
<th>Compute Charge (for 2018-2019)</th>
<th>Size of Compute Space and Tools</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard Research Environment</td>
<td>No charge, 365 days $12/day after 365 days, 2 concurrent logins and unlimited users can have access to the platform</td>
<td>(2CPUx7GB) size Office 365, Jupyter notebook, Python, STATA and R tools available</td>
</tr>
<tr>
<td>Premium Research Environment</td>
<td>No charge, 90 days $25/day after first 90 days, 2 concurrent logins and unlimited users can have access to the platform</td>
<td>(4CPUx14GB) size Office 365, Jupyter notebook, Python, R, STATA and SAS (academic license) tools are available</td>
</tr>
</tbody>
</table>
## Cost of sharing a single academic study on Vivli

<table>
<thead>
<tr>
<th>Study Metadata Curated and Listed on Vivli</th>
<th>Anonymized IPD Storage</th>
<th>Independent Review Panel</th>
<th>One-time Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study ready for sharing and needs storage</td>
<td>✓</td>
<td>✓</td>
<td>$2,000*</td>
</tr>
<tr>
<td>Study ready for sharing and needs Storage and Independent Review Panel</td>
<td>✓</td>
<td>✓</td>
<td>$4,500</td>
</tr>
<tr>
<td>Anonymization</td>
<td>✓</td>
<td>✓</td>
<td>Provided by Privacy Analytics (additional $2,000-$5000 / dataset)</td>
</tr>
</tbody>
</table>

*Anonymized data and documentation must be shared at the time of curating and listing the study and be available for download. Contributors must sign harmonized Data Contributor Agreement and Data Use Agreement. Does not include being named as a member for the institution or attendance at the Vivli Steering Committee.