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CENTER FOR GLOBAL CLINICAL RESEARCH DATA

Vivli Clinical Research Data Sharing: Share. Discover. Innovate.

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

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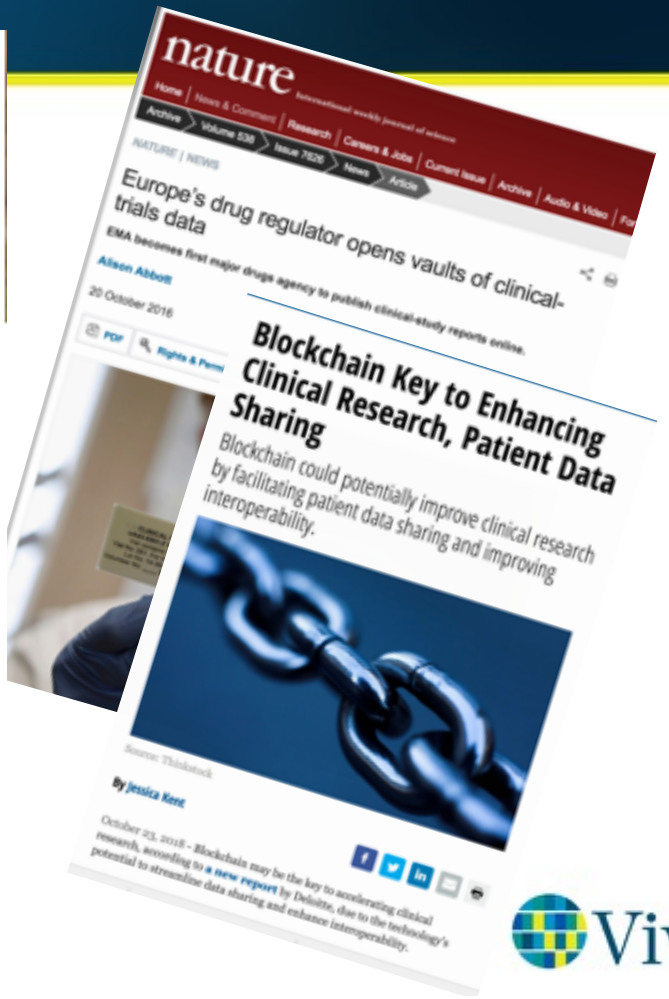
Data Sharing in the News



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Why should I share my data?

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

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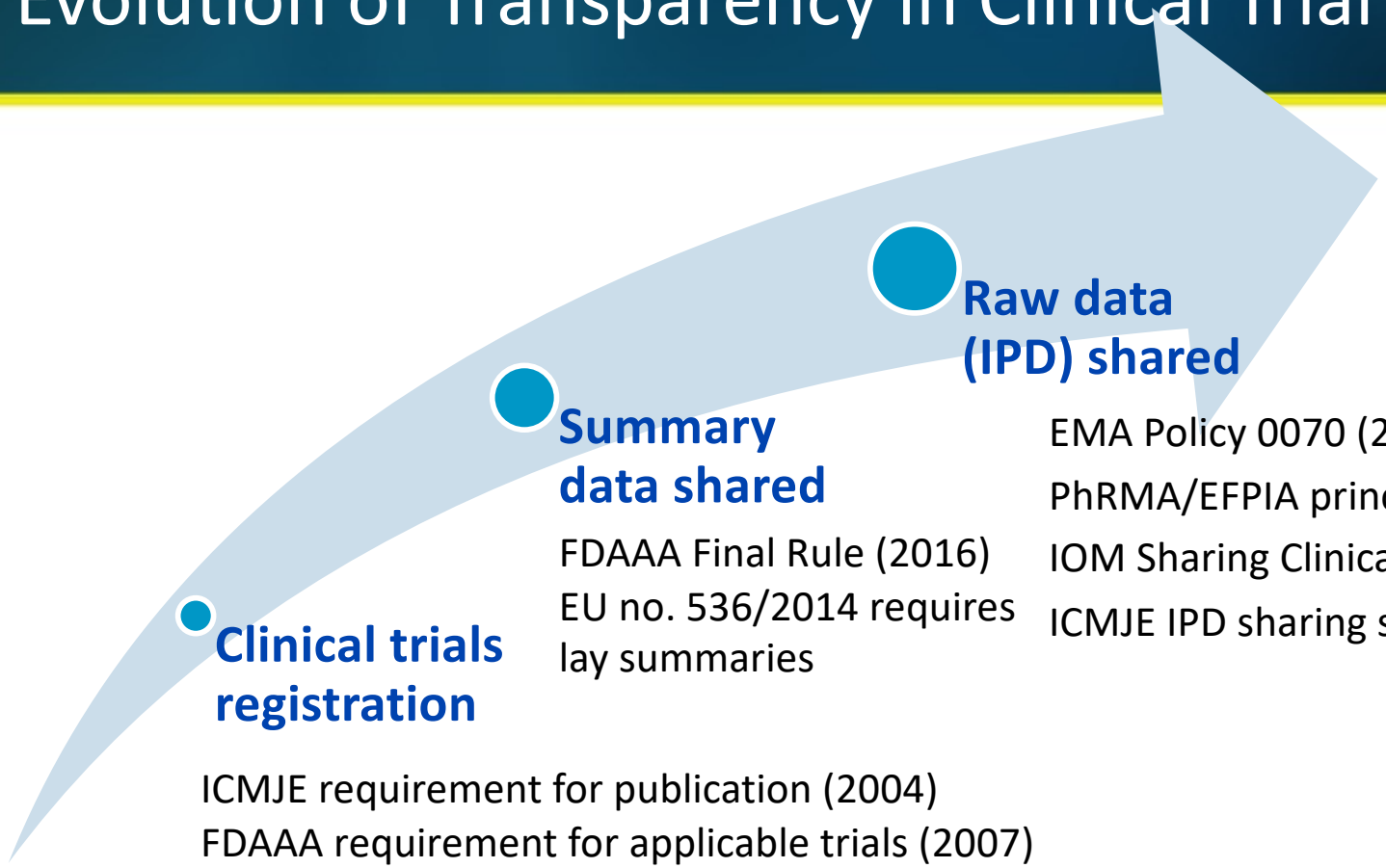
Evolution of Transparency in Clinical Trial Data



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)

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Why should I share my data?

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

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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

Piwowar, Heather A., and Todd J. Vision. "Data reuse and the open data citation advantage." *PeerJ* 1 (2013): e175.

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Why Should I Share my Data?

Journal and funder mandates

Increase citations

Moral obligations (owe it to trial participants)

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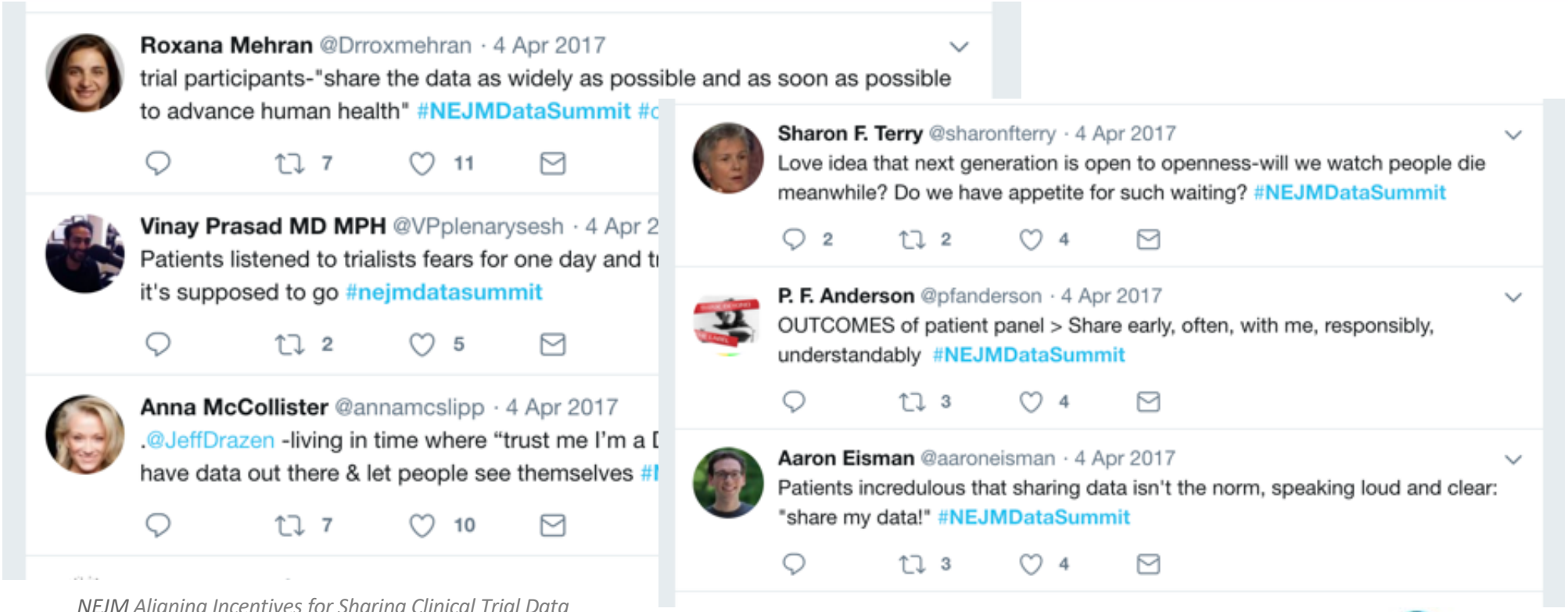
Patients demand data sharing and reuse



Roxana Mehran @Drroxmehran · 4 Apr 2017
trial participants-"share the data as widely as possible and as soon as possible to advance human health" #NEJMDataSummit #c
7 11

Vinay Prasad MD MPH @VPplenarysesh · 4 Apr 2
Patients listened to trialists fears for one day and t
it's supposed to go #nejmdatasummit
2 5

Anna McCollister @annamcslipp · 4 Apr 2017
.@JeffDrazen -living in time where "trust me I'm a D
have data out there & let people see themselves #
7 10

Sharon F. Terry @sharonfterry · 4 Apr 2017
Love idea that next generation is open to openness-will we watch people die meanwhile? Do we have appetite for such waiting? #NEJMDataSummit
2 2 4

P. F. Anderson @pfanderson · 4 Apr 2017
OUTCOMES of patient panel > Share early, often, with me, responsibly, understandably #NEJMDataSummit
3 4

Aaron Eisman @aaroneisman · 4 Apr 2017
Patients incredulous that sharing data isn't the norm, speaking loud and clear: "share my data!" #NEJMDataSummit
3 4

NEJM Aligning Incentives for Sharing Clinical Trial Data Summit, Boston, MA. April 2017

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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

	IPD Sharing Requirements	Figshare	Dryad	CT.gov	Vivli
Data Contributors	IPD can be stored and securely hosted				
	Harmonized data contributor and data use agreements				
	IPD can be shared securely to anyone in the world				
	Independent review available				

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

Vivli Members

Founding Funders and Partners

For Grant Submission

Funders increasingly requiring data sharing

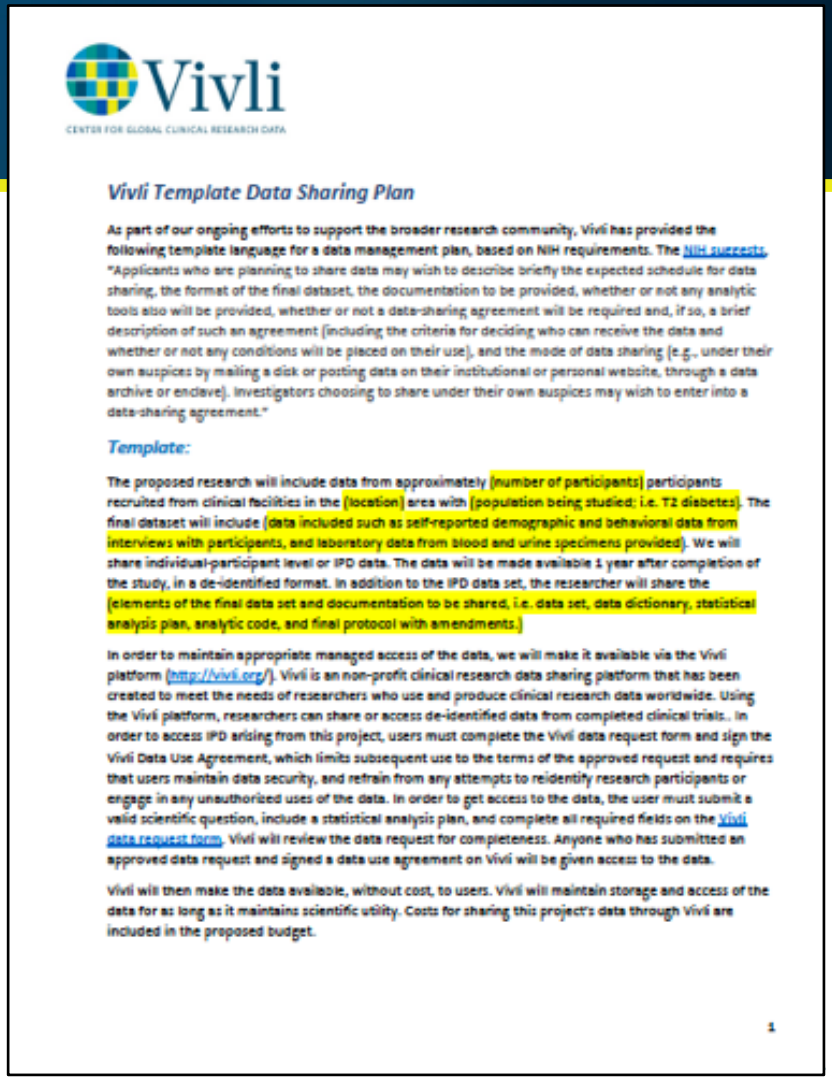
Draft NIH Data Sharing and Management Policy is requiring

- 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/



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Vivli Template Data Sharing Plan

As part of our ongoing efforts to support the broader research community, Vivli has provided the following template language for a data management plan, based on NIH requirements. The NIH suggests, "Applicants who are planning to share data may wish to describe briefly the expected schedule for data sharing, the format of the final dataset, the documentation to be provided, whether or not any analytic tools also will be provided, whether or not a data-sharing agreement will be required and, if so, a brief description of such an agreement (including the criteria for deciding who can receive the data and whether or not any conditions will be placed on their use), and the mode of data sharing (e.g., under their own auspices by mailing a disk or posting data on their institutional or personal website, through a data archive or enclave). Investigators choosing to share under their own auspices may wish to enter into a data-sharing agreement."

Template:

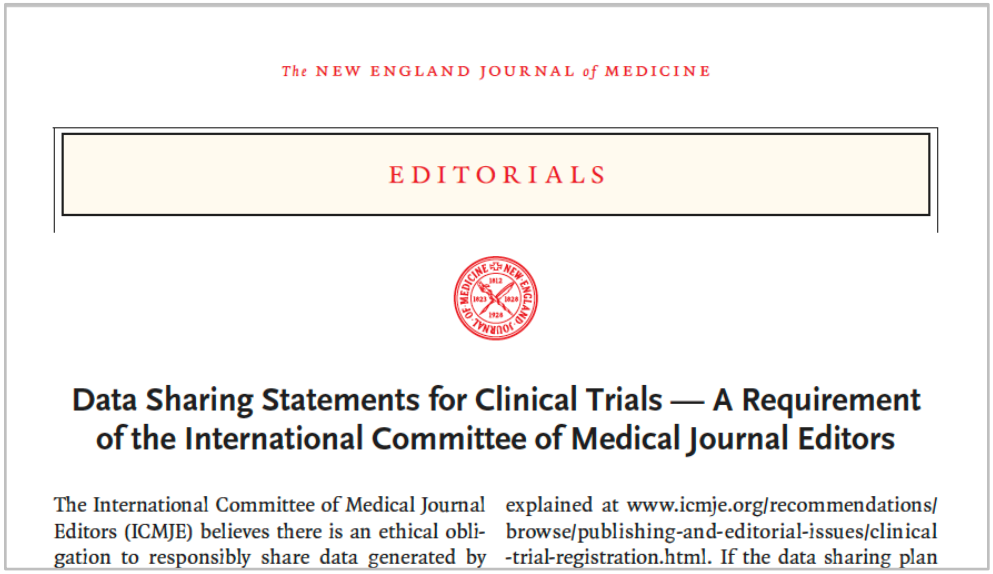
The proposed research will include data from approximately [number of participants] participants recruited from clinical facilities in the [location] area with [population being studied; i.e. T2 diabetes]. The final dataset will include [data included such as self-reported demographic and behavioral data from interviews with participants, and laboratory data from blood and urine specimens provided]. We will share individual-participant level or IPD data. The data will be made available 1 year after completion of the study, in a de-identified format. In addition to the IPD data set, the researcher will share the [elements of the final data set and documentation to be shared, i.e. data set, data dictionary, statistical analysis plan, analytic code, and final protocol with amendments.]

In order to maintain appropriate managed access of the data, we will make it available via the Vivli platform (http://vivli.org/). Vivli is an non-profit clinical research data sharing platform that has been created to meet the needs of researchers who use and produce clinical research data worldwide. Using the Vivli platform, researchers can share or access de-identified data from completed clinical trials.. In order to access IPD arising from this project, users must complete the Vivli data request form and sign the Vivli Data Use Agreement, which limits subsequent use to the terms of the approved request and requires that users maintain data security, and refrain from any attempts to reidentify research participants or engage in any unauthorized uses of the data. In order to get access to the data, the user must submit a valid scientific question, include a statistical analysis plan, and complete all required fields on the Vivli data request form. Vivli will review the data request for completeness. Anyone who has submitted an approved data request and signed a data use agreement on Vivli will be given access to the data.

Vivli will then make the data available, without cost, to users. Vivli will maintain storage and access of the data for as long as it maintains scientific utility. Costs for sharing this project's data through Vivli are included in the proposed budget.

1

Journal Mandates as of July 1, 2018



The NEW ENGLAND JOURNAL of MEDICINE

EDITORIALS

Data Sharing Statements for Clinical Trials — A Requirement of the International Committee of Medical Journal Editors

The International Committee of Medical Journal Editors (ICMJE) believes there is an ethical obligation to responsibly share data generated by

explained at www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html. If the data sharing plan

Taichman DB, et al. N Engl J Med 2017; 376:2277-2279

- ICMJE includes
  - NEJM, JAMA, The Lancet, BMJ, Annals of Internal Med, PLoS Medicine, others
- 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"

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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** !

12. IPD Sharing Statement

Plan to Share IPD
Definition: Indicate whether there is a plan to make individual participant data (IPD) collected in this study, including data dictionaries, available to other researchers (typically after the end of the study). Select one.

- Yes: There is a plan to make IPD and related data dictionaries available.
- No: There is not a plan to make IPD available.
- Undecided: It is not yet known if there will be a plan to make IPD available.

IPD Sharing Plan Description
Definition: If Plan to Share IPD is "Yes," briefly describe what specific individual participant data sets are to be shared (for example, all

http://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html

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Data Sharing Plan for ICMJE Journal Submission

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

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

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Contents of the IPD Package*

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

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

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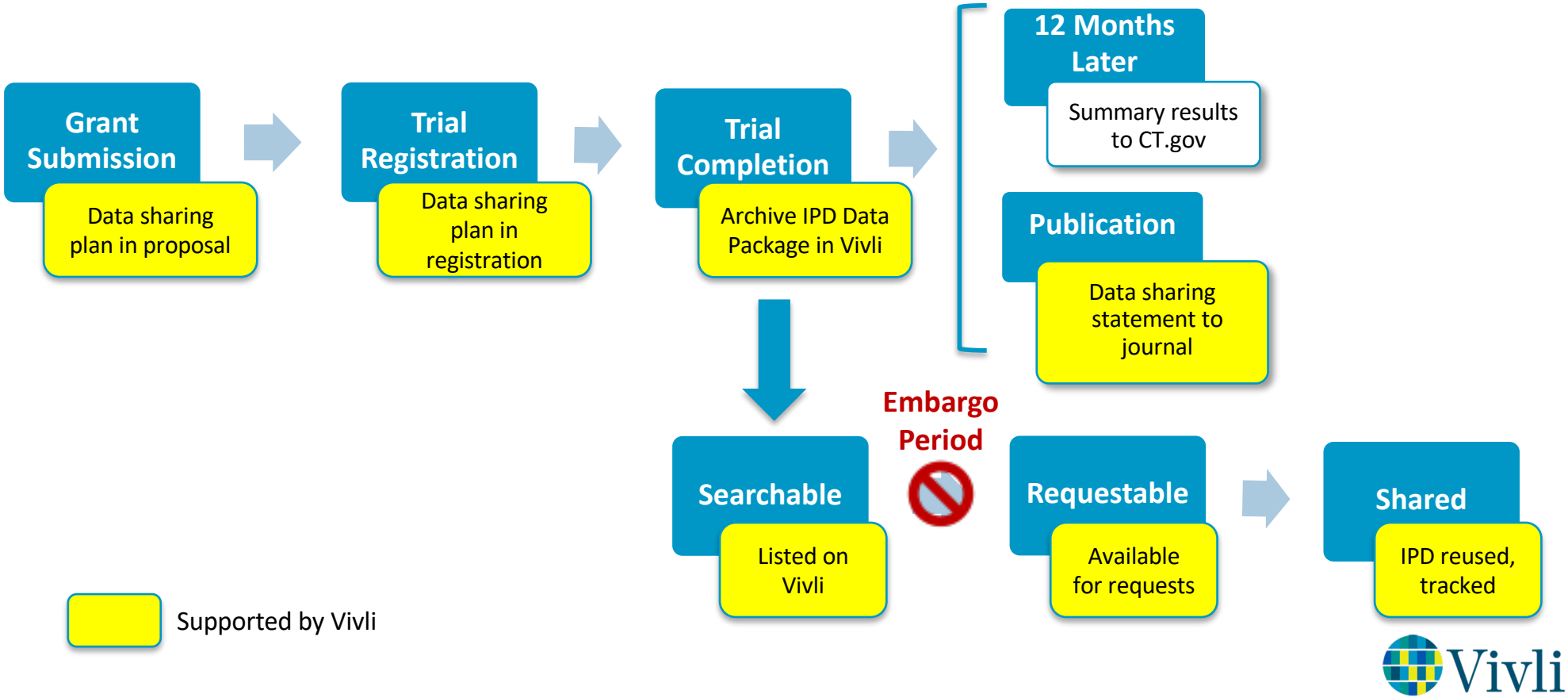
Data Sharing Timeline Summarized



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)

1

SIGN AGREEMENT

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

Returned signed version.

2

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.

3

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De-identification/Anonymization

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

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Data Standardization Approach

IPD is recommended to be in CDISC SDTM format

No requirements for using standardized data variables or common data elements (CDEs)

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When a Data Request is made

- 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

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Why are DOIs important in data sharing?

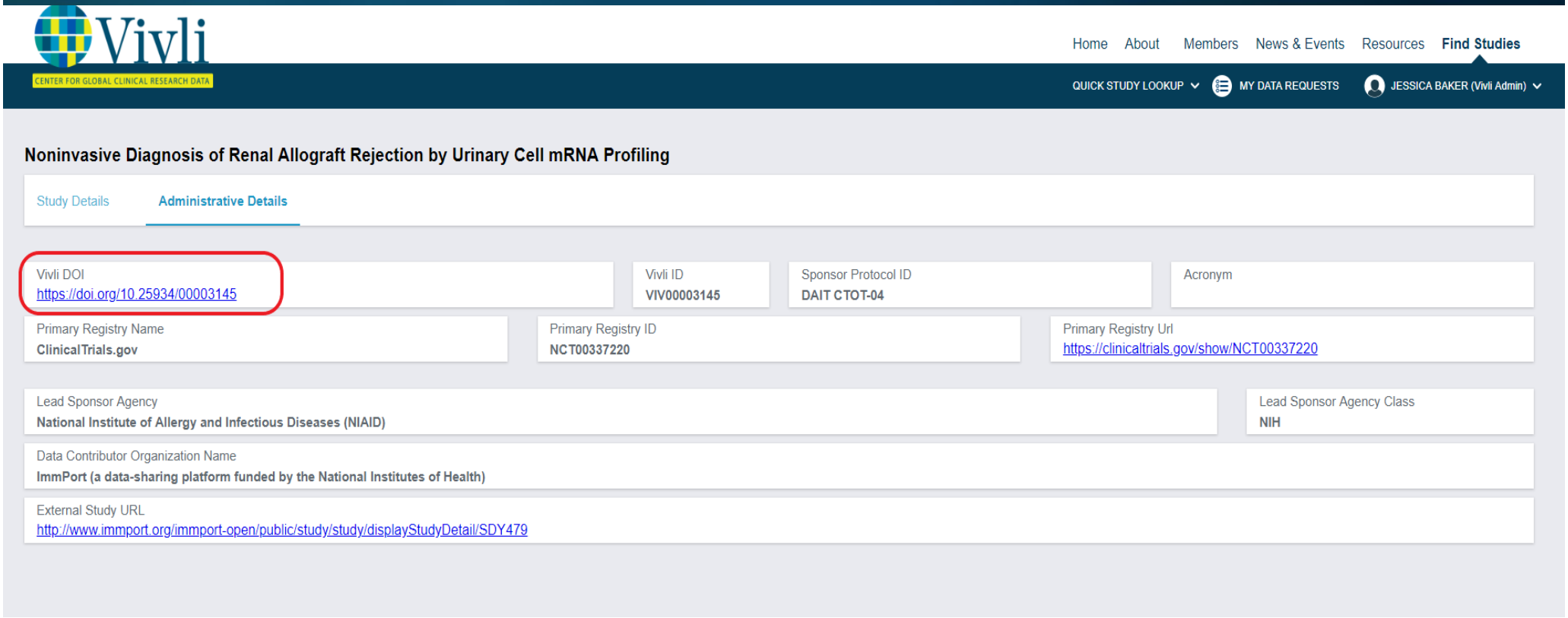
- Digital Object Identifiers (DOIs) are persistent, citable and unique links on the internet. They help the community locate and cite data and objects.
- Vivli assigns a persistent identifier (DOI) to datasets and other objects (such as publications)
- DOIs facilitate subsequent attribution and data 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

DataCite
FIND, ACCESS, AND REUSE DATA

DOI, study listed on Vivli



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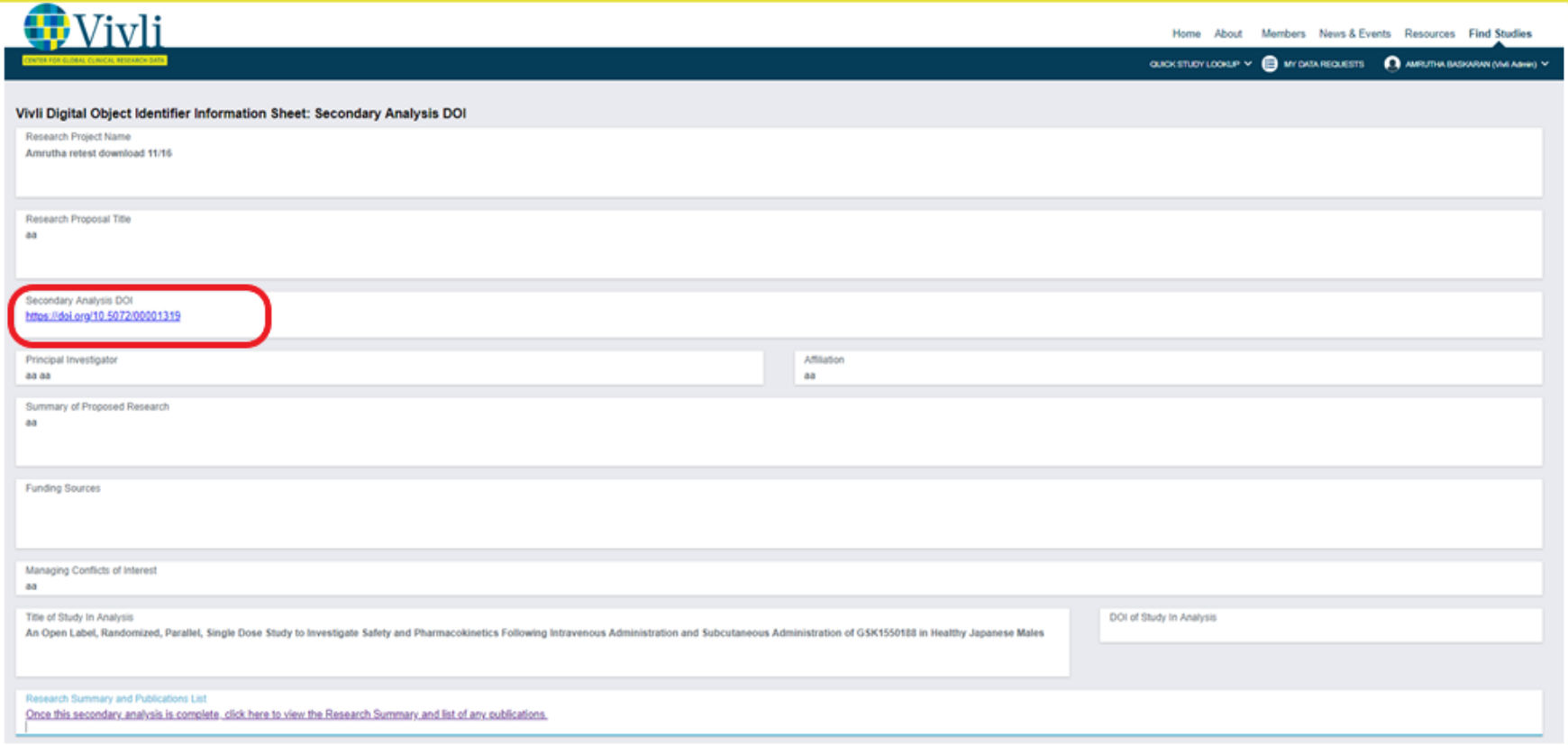
Sample DOI, approved data request



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QUICK STUDY LOOKUP MY DATA REQUESTS AMRUTHA BASKARAN (Vivli Admin)

Vivli Digital Object Identifier Information Sheet: Secondary Analysis DOI

Research Project Name
Amrutha retest download 11/16

Research Proposal Title
aa

Secondary Analysis DOI
https://doi.org/10.5072/00201319

Principal Investigator
aa aa

Affiliation
aa

Summary of Proposed Research
aa

Funding Sources

Managing Conflicts of Interest
aa

Title of Study In Analysis
An Open Label, Randomized, Parallel, Single Dose Study to Investigate Safety and Pharmacokinetics Following Intravenous Administration and Subcutaneous Administration of GSK1550188 in Healthy Japanese Males

DOI of Study In Analysis

Research Summary and Publications List
Once this secondary analysis is complete, click here to view the Research Summary and list of any publications.

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

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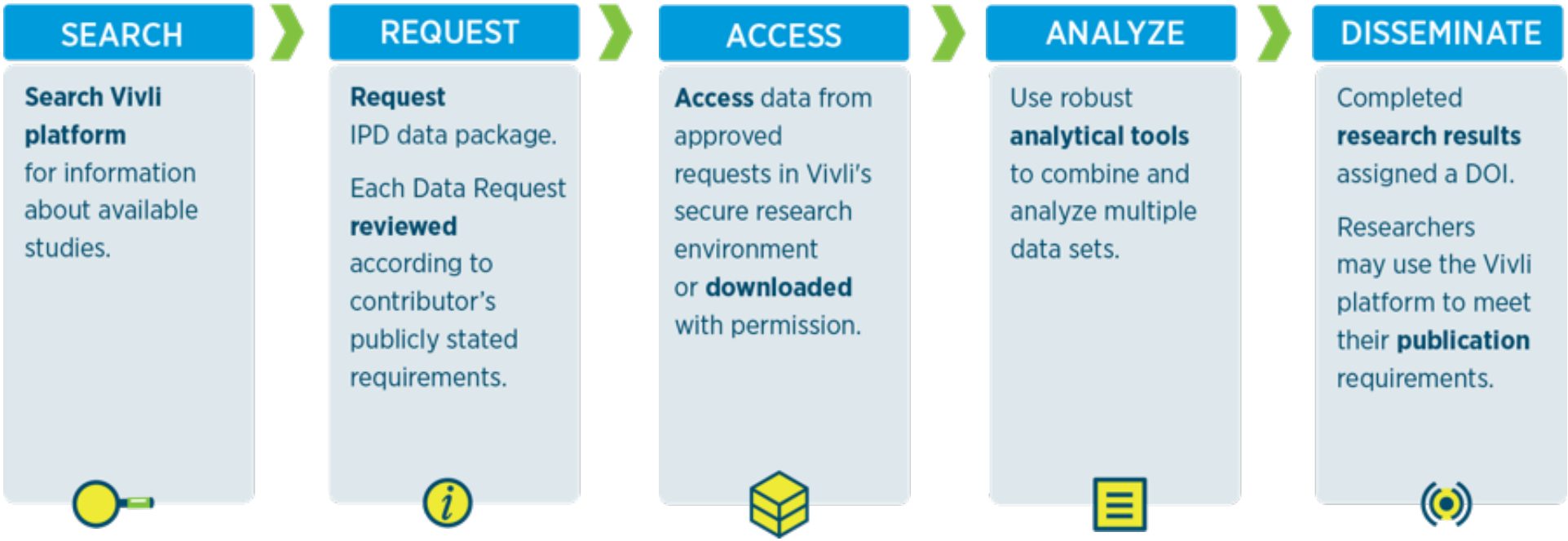
How to Access Data in Vivli?

Data Request and Access Process



Short video demo at https://vivli.org/resources/vivli-platform-demo/

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Secure Environment Bridges Multiple Platforms

BioLINCC
Biologic Specimen and Data Repository Information Coordinating Center

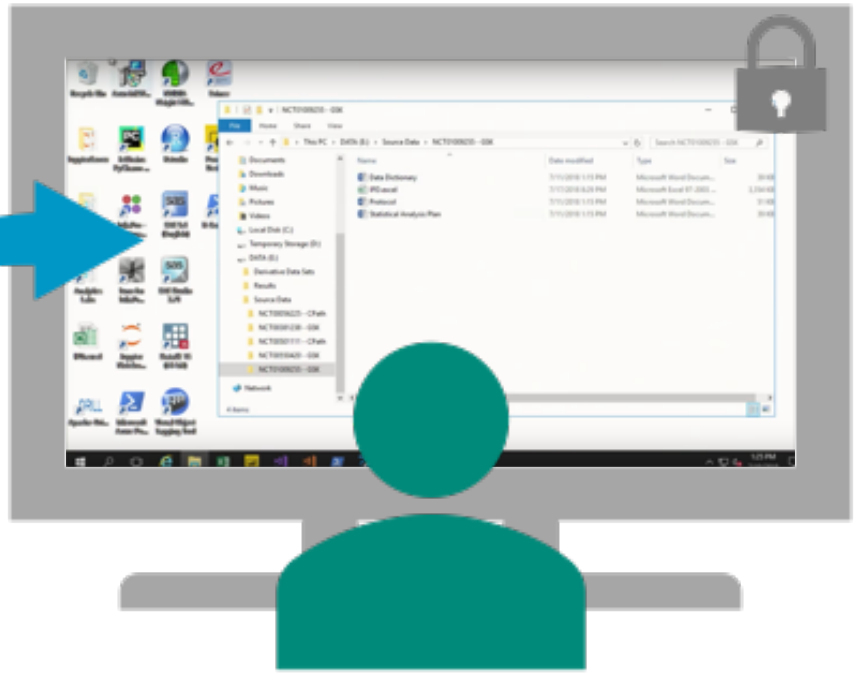
Pfizer

ImmPort
Bioinformatics For The Future Of Immunology

Project Data Sphere

gsk
do more
feel better
live longer

Vivli Secure Environment



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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

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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

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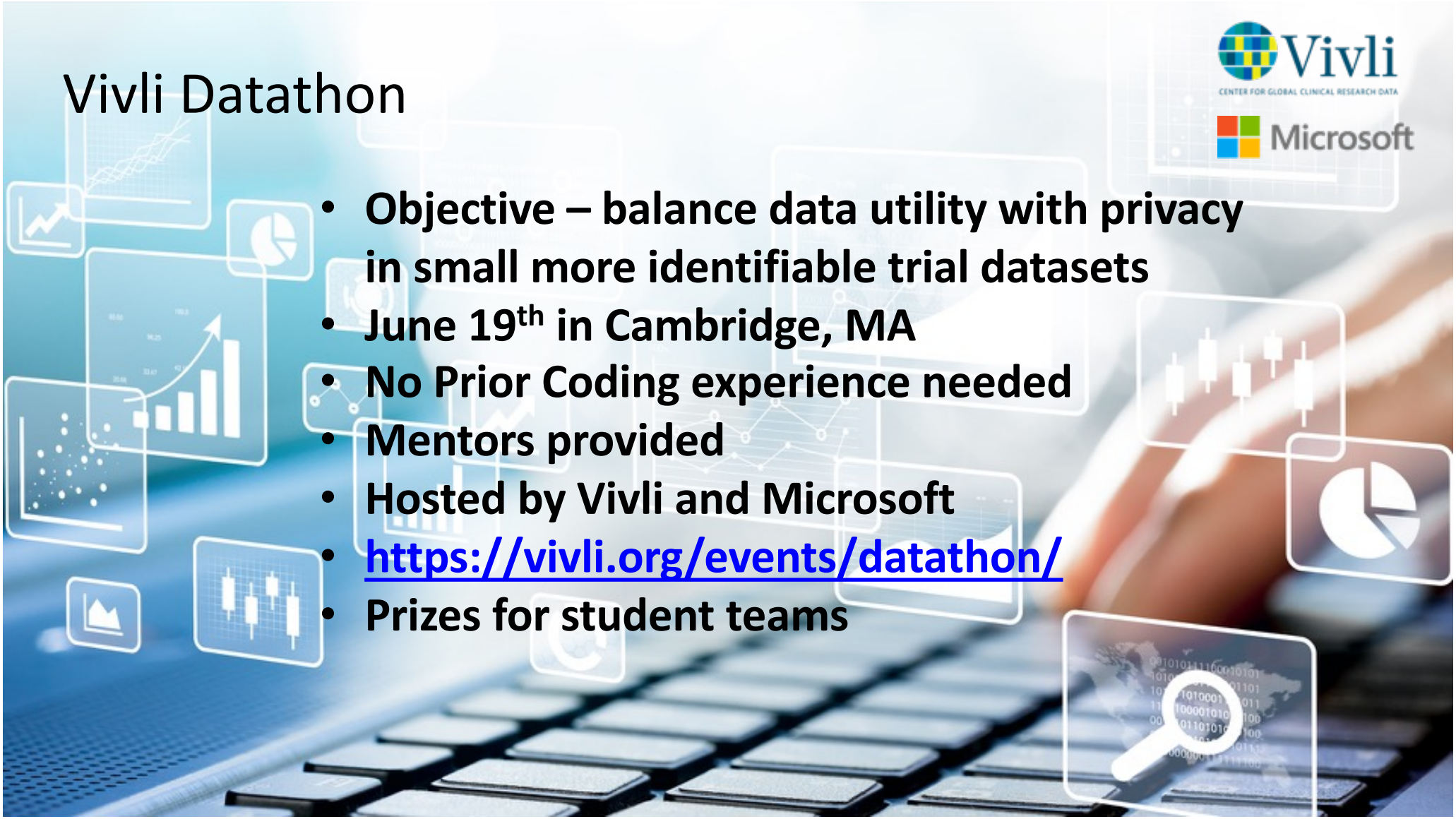
Vivli Datathon



- **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/**
- **Prizes for student teams**

Log on to

Vivli.org

- Explore the thousansavailable via the Vivli platform
- Begin your search
- Contact support@vivli.org with questions

Questions?

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A GLOBAL CLINICAL RESEARCH DATA SHARING PLATFORM
Take part in the first Vivli Data Challenge
Submit your data request today
FIND OUT MORE

User fees

Environment Type	Compute Charge (for 2018-2019)	Size of Compute Space and Tools
Standard Research Environment	No charge, 365 days $12/day after 365 days, 2 concurrent logins and unlimited users can have access to the platform	(2CPUx7GB) size Office 365, Jupyter notebook, Python, STATA and R tools available
Premium Research Environment	No charge, 90 days $25/day after first 90 days, 2 concurrent logins and unlimited users can have access to the platform	(4CPUx14GB) size Office 365, Jupyter notebook, Python, R, STATA and SAS (academic license) tools are available

Cost of sharing a single academic study on Vivli

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

*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.