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CENTER FOR GLOBAL CLINICAL RESEARCH DATA

Implementation of Data Sharing platforms and How Researchers are Utilizing these Platforms to Further their Research and Share Data

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Agenda

- Overview of clinical trial data sharing
- Why share data in a platform or repository ?
- What type of data is available from data sharing platforms?
- How can researchers request data from data sharing platforms?
- Examples of outputs from data sharing platforms
- Demo of searching for studies of interest
- Q & A

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1. Why Should We Share Our Clinical Research Data

- Funder requirements
- Journal requirements
- Publicly stated commitments for industry (EFPIA/PhRMA)
- Drive new science (integrate data to drive new insights faster)
- Ethical obligations to trial participants
- Enhance and advance your career

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What Do Surveys Show Regarding Patient and Participant Preference Regarding Data Sharing?

- High levels of support for data sharing; however, patients are reluctant to have their data “commodified” purely for commercial gain [1]
- If adequate safeguards were in place, trial participants are willing to share their data[2]

[1] Davidson S, McLean C, Treanor S, Aitken M, Cunningham-Burley S, Laurie G, et al. Public acceptability of data sharing between the public, private and third sectors for research purposes. Edinburgh: Scottish Government Social Research; 2013.Google Scholar

[2] Mello, Michelle M., Van Lieou, and Steven N. Goodman. "Clinical trial participants’ views of the risks and benefits of data sharing." *New England Journal of Medicine* 378.23 (2018): 2202-2211.

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Perhaps most importantly for participants if the data is not shared…

It is used only one time to answer one question (the primary endpoint) rather than leveraging participants' contributions to answer multiple scientific lines of inquiry thereby advancing science

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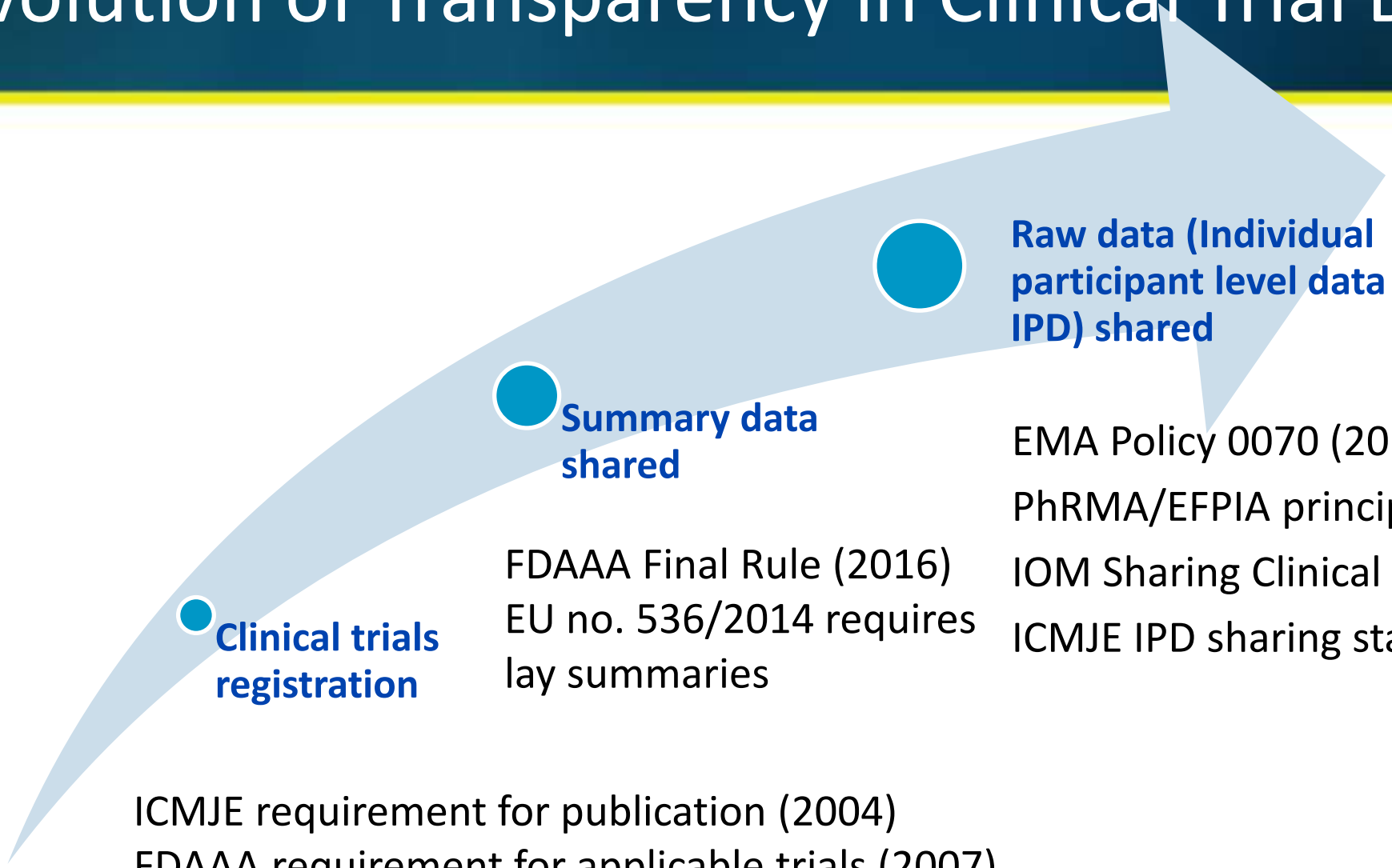
Evolution of Transparency in Clinical Trial Data



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 (Individual participant level 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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Major Journals Have Required A Data Sharing Statement Since July 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

- Major journals including NEJM, JAMA, The Lancet, BMJ, Annals of Internal Med, PLoS Medicine, and hundreds of others (ICMJE)
- Trial manuscripts must be submitted with a data sharing statement
  - Must describe how you will share your Individual participant-level data (IPD), including 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"

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

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Declaring Your Data Re-use Plans as part of the Trial Registration Record… before the 1st patient is enrolled

- Data sharing plan is part of the ClinicalTrials.gov registration record
- **As of 1 January 2019, ICMJE requires registration of your data sharing plan at time of trial registration.**

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.

Note: Undecided is not allowed as a choice for the ICMJE but is a choice in CT.gov

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We Probed the Intent to Share Individual Patient level data (IPD) in a Pandemic

What is the “upper bound” of COVID trialist interest in sharing their IPD?

Methods:

- Data sharing declarations in ClinicalTrials.gov
  - interventional trials on COVID-19 (and related terms) before 6/30/20:

    924 COVID interventional trials
  - reviewed data sharing fields
- Data sharing statements in publications
  - Searched PubMed in May 2020 for COVID-related interventional trials in humans: **28 COVID publications**
  - reviewed data sharing statements

*Li, R., et al. Trials **22,** 153 (2021). https://doi.org/10.1186/s13063-021-05104-z*

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COVID-19 Trial Registrations: Data Sharing Intent

Intend to share?	
Yes	**145 (16%)**
Undecided	131 (14%)
No	440 (48%)
No response	208 (22%)
TOTAL	924

Li, R., *et al. Trials* **22,** 153 (2021). https://doi.org/10.1186/s13063-021-05104-z

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COVID-19 Trial Registrations: Data Sharing Intent

Intend to share?	
Yes	**145 (16%)**
Undecided	131 (14%)
No	440 (48%)
No response	208 (22%)
TOTAL	924

Timing of intended sharing	
Immediately	56 (39%)
1 to < 6 months	14 (10%)
6-12 months	22 (15%)
12-24 months	16 (11%)
No timing given	37 (25%)
TOTAL NUMBER	145

Li, R., *et al. Trials* **22,** 153 (2021). https://doi.org/10.1186/s13063-021-05104-z

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COVID-19 Trial Publications: Data Sharing Intent

Intend to share? (Publication)	
Yes	6 (21.4%)
Undecided	0 (0%)
No	1 (3.5%)
No response	21 (75%)
TOTAL	28

Li, R., *et al. Trials* **22,** 153 (2021). https://doi.org/10.1186/s13063-021-05104-z

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Summary of COVID-19 Trial Data Sharing Intent

- Prior surveys showed an intent to share in the 5-10% range (all trials)
- 16% sharing is an increase and moving directionally in the right direction for COVID trials
- **However, only 7.6% agreed to share their data (70/924) within the first 6 months an alarming statistic in a time of pandemic!**
- What are some promising signs in 2021?

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2021 and Beyond

- Funders (Gates Foundation, Wellcome Trust) and NIH have begun to institute data sharing requirements and recommend specific repositories for data
- Industry and some academic institutions have voluntarily been sharing data for some time in repositories and platforms
- Let's look at Vivli, the largest data sharing platform for clinical trial data

https://gatesopenresearch.org/for-authors/data-guidelines
https://wellcomeopenresearch.org/for-authors/data-guidelines
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-013.html
https://www.nlm.nih.gov/NIHbmic/generalist_repositories.html

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Gates Funded Trials

- As of 2021, Gates Open Research requires source data underlying the results to be made available as soon as an article is published.
- Authors also are required to include the location of where data are stored
- Vivli is the approved repository listed for clinical trial data

https://gatesopenresearch.org/for-authors/data-guidelines

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Approaches to Sharing Human Data

Type	Key Features	Examples
Open access	Anyone can access, simple account creation, simple on-line data use agreement (DUA)	Health CAN, EMA, Project Datasphere
Managed access	• for scientific purposes only (standard request form) • (independent) review process • secure environment for data access • clear legal framework	**Vivli, CSDR, SOAR, VISTA**
Restricted access	Invitation only, access only to those who provide data	DataCelerate, IBD Plexus

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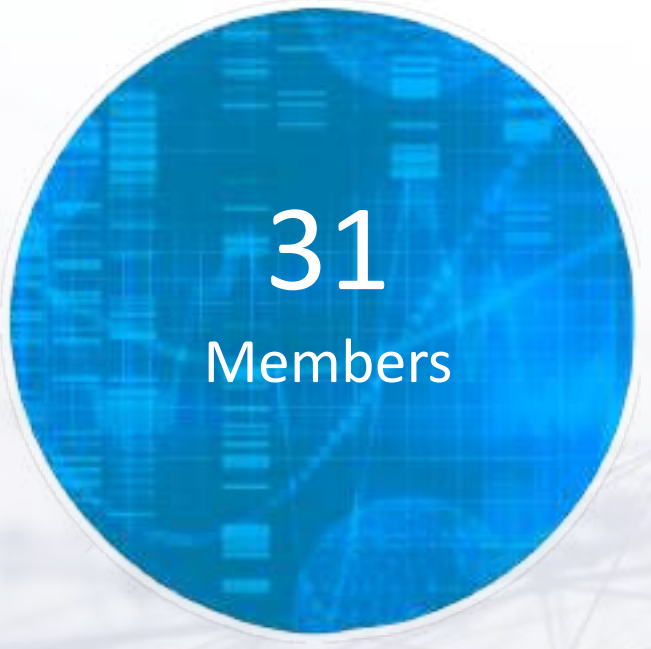
Vivli – A Case Study

the largest global IPD data sharing platform

Vivli by the numbers …today



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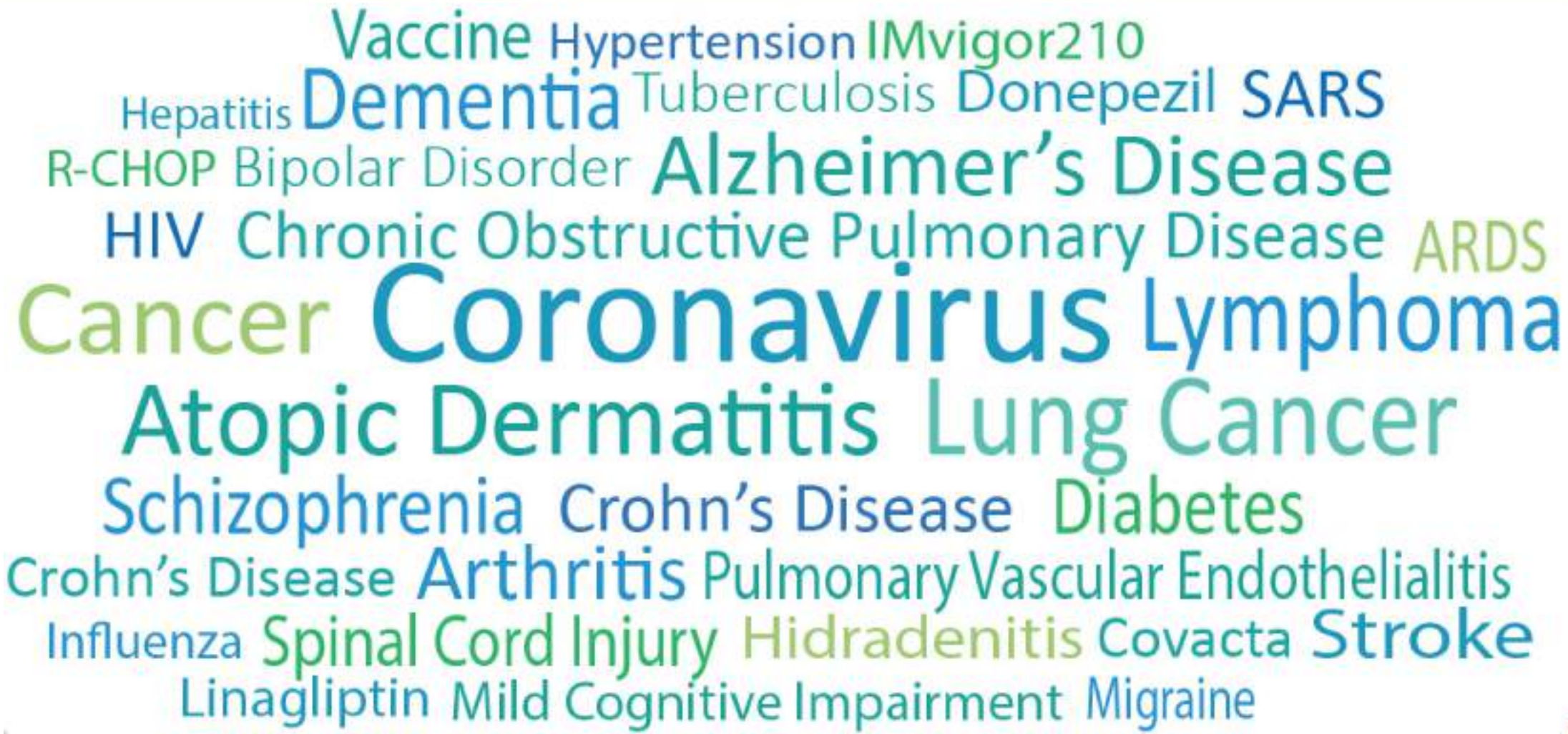
Vivli Members

Example of Research groups recently sharing on Vivli

Study	Organization	Study
NCT03085329 (Seattle-Pap 002)	Abigail Wexner Research Institute	Neonatal CPAP randomized study (Gates funded)
DUKE CATH	Duke University	ACATHD dataset (also known as DukeCath) contains records on cardiac catheterization procedures performed on adult patients at Duke University Medical Center.
PACE trial	UK Medical Research Council	RCT Chronic Fatigue Syndrome /myalgic encephalomyelitis or encephalopathy
COVID-19 study	Hannover Medical School, Germany	Respiratory failure due to ARDS caused by SARS – Cov2 or influenza

Vivli is a Global Data Platform
Snapshot of Frequently Searched Terms



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More than 100 data requests approved from researchers based in 25+ countries

Australia
Austria
Belgium
Canada
China
Croatia
Denmark
France
Germany
Ireland
Israel
Italy
Japan
Lebanon
Netherlands
New Zealand
Portugal
South Korea
Spain
Sweden
Switzerland
Thailand
United Kingdom
United States

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Data Contributors Provide Individual Participant-Level Data (IPD) to Vivli for Re-use

Item	Description
Recommended Data Package Set	
Study Protocol	**Final protocol with all amendments**
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 analysis described in the protocol**
IPD dataset	**Final cleaned individual participant-level data, de-identified/anonymized**
Optional	
Analytic code	Software code used to carry out prespecified and additional analyses
Analysis ready IPD data set	Dataset in a format used to carry out a sponsor's 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 form the study (after regulatory decision)

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

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How Vivli works

SEARCH

Search Vivli platform for information about available studies.

REQUEST

Request IPD Data sets.

Each Data Request will be **reviewed** according to contributors' publicly stated requirements.

ACCESS

Data from approved requests can be **accessed** 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** will be assigned a DOI.

Researchers may use the Vivli platform to meet their **publication** requirements.

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Vivli's Secure Environment Bridges Multiple Platforms

BioLINCC
Biologic Specimen and Data Repository Information Coordinating Center

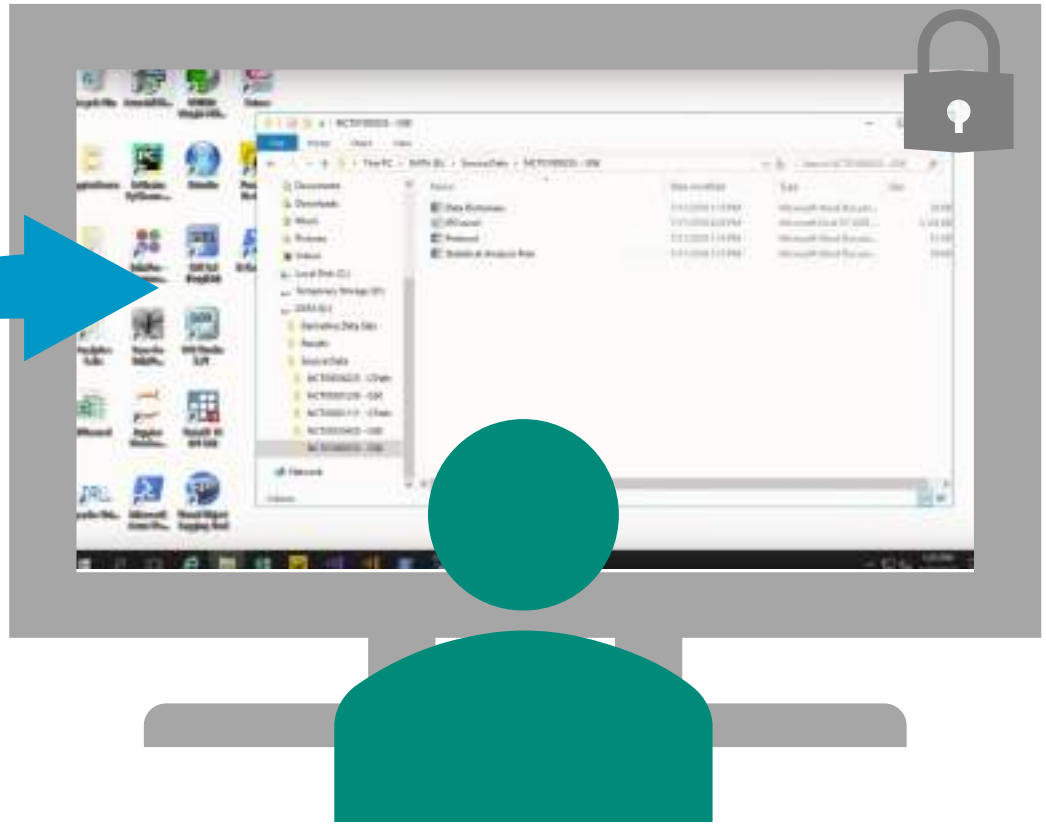
Johnson & Johnson

IMMPORT
BIOINFORMATICS FOR THE FUTURE OF IMMUNOLOGY

Project Data Sphere

gsk
do more
feel better
live longer

Vivli Secure Environment



- STATA
- MS Office
- R
- Jupyter Notebook
- Python
- SAS

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Vivli enables a secure yet flexible research environment

Software available in the research environment:

- R (Version 3.4.1) and Rstudio Desktop
- Python, 3.5
- Jupyter Notebook 4.3.0
- Microsoft Office 2016 Standard edition, including Word, Excel and PowerPoint
- Anaconda
- JuliaPro 0.5.1.1 and the Juno IDE for Julia
- PyCharm Community Edition - 2017.2.3
- Apache Spark 2.2.0
- SparkML and pySpark
- Apache Drill 1.11.0
- MAPR Drill driver
- VIM 8.0.606
- TensorFlow
- MXNet, MXNet Model Server
- Microsoft Cognitive Toolkit (CNTK)
- Weka
- Vowpal Wabbit
- xgboost
- Team Data Science Process (TDSP) Utilities
- VOTT (Visual Object Tagging Tool) 1.6.11
- Microsoft Machine Learning Server
- PowerBI
- Docker version 17.06.1-ee-2
- SQL Server Developer Edition (2017), including Management Studio and SQL Server Integration Services (SSIS)
- Visual Studio Community Edition (2017)
- Nodejs
- 7-zip
- STATA 15.1
- SAS 9.4 (academic license)

Flexibility: Researchers can bring in their own data sets, statistical software and scripts to their secure research environment

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19 Therapeutic Areas Covered by Vivli Proposals through 2021

Therapeutic Areas
Cardiovascular
Dermatology
Endocrinology
Gastroenterology
Gynecology
Hematology
Infectious Disease
Methods /Training
Neurology
Oncology
Ophthalmology
Orthopedics
Psychiatry
Pulmonary
Rheumatology
Urology
Vaccines

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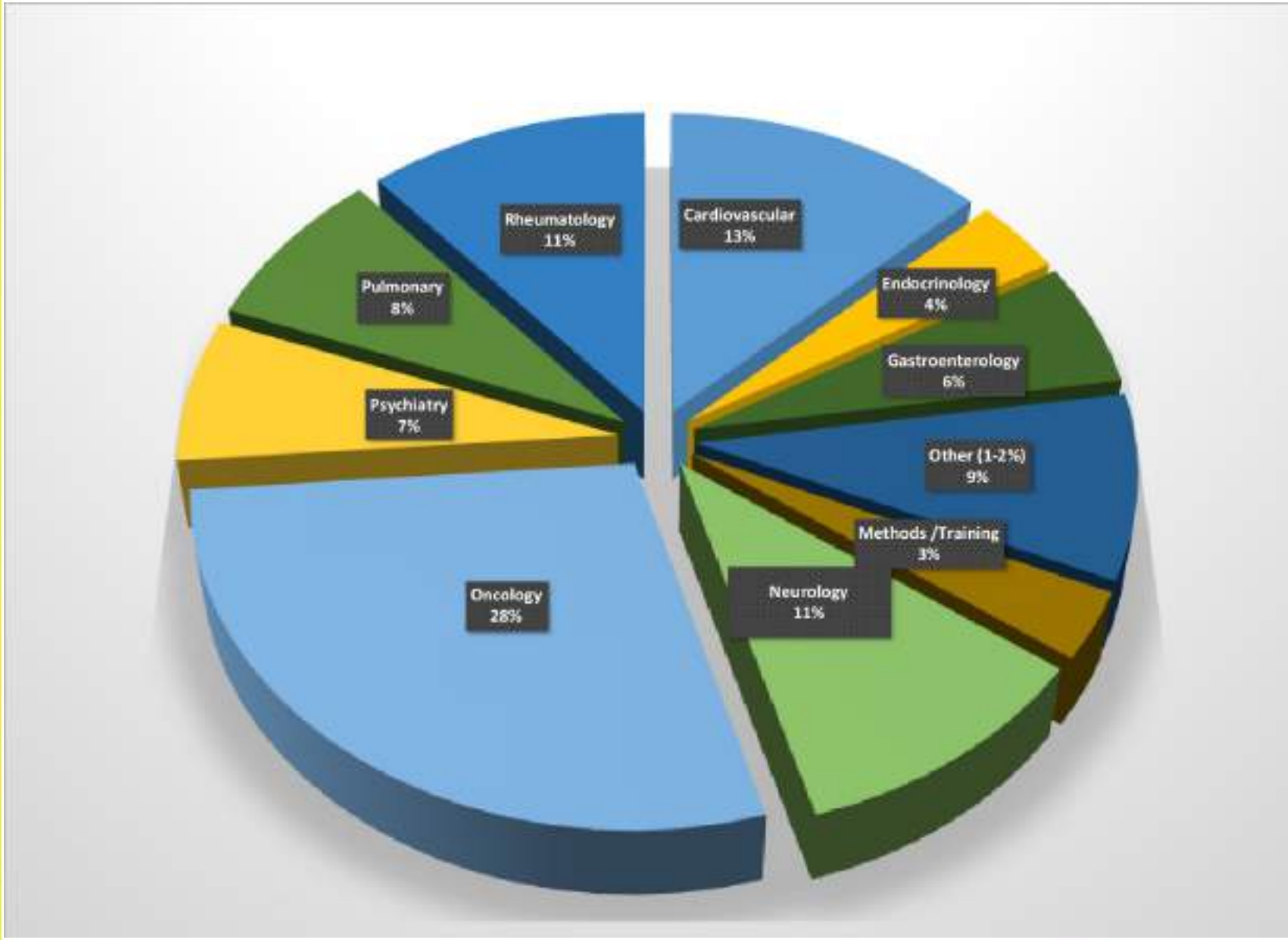
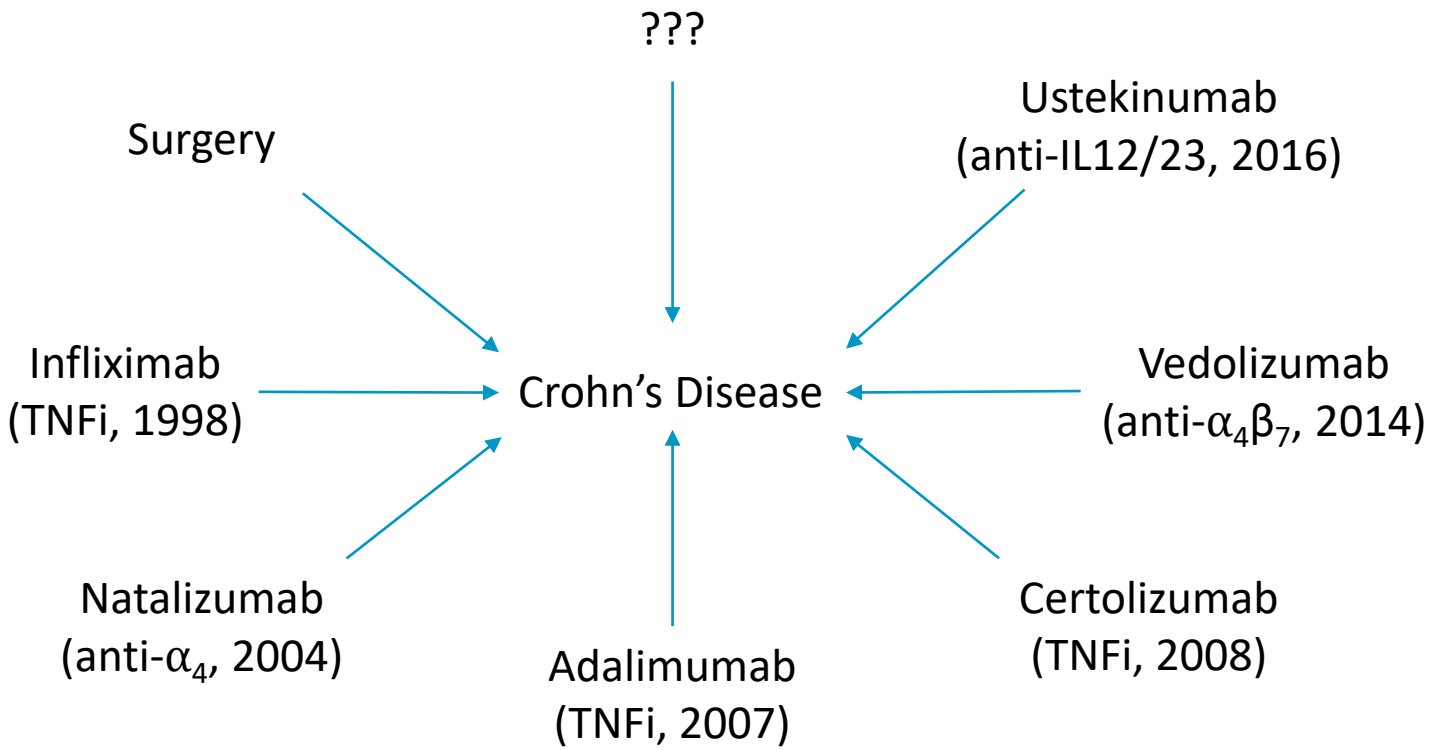
Top 40 Requested Studies 2021

Oncology	Bladder	3
	Breast	6
	NSCLC	4
	RCC	1
Gastroenterology	Crohn's Disease	4
Rheumatology	RA	14
	UC	2
Cardiology	AFIB	1
Other	Covid 19	1
	Duchenne	1
	Hidradinitis	1
	T2 Diabetes	1

Therapeutic Areas represented by Submitted Proposals as of 2021 (Requests)



EXAMPLE: Today's Menu of Crohn's Disease Treatments



Vivek Rudrapatna, UCSF

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We can ask Efficacy and Safety questions of the data

Trials	Drug
PRECISE 1/2	Certolizumab
CLASSIC 1/2	Adalimumab
GEMINI 2	Vedolizumab
ENACT	Natalizumab
ACCENT 1/2	Infliximab
UNITI	Ustekinumab
CERTIFI	Ustekinumab

Efficacy questions

- Are there subgroups that preferentially respond to some drugs over others?
- How much time do we need to confidently determine if a patient will favorably respond? What data do we need to make this determination?

Safety

- Are there certain subgroups more susceptible to certain severe adverse effects (SAEs) than others?
- What does this tell us about the biology of SAEs as they relate to drug mechanism of action?

Vivek Rudrapatna, UCSF

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Studies Requested; IPD Obtained

Trials	Drug	Sponsor	Original Data Sharing Platform
PRECISE 1/2	Certolizumab	UCB	CSDR
CLASSIC 1/2	Adalimumab	AbbVie	Vivli
GEMINI 2	Vedolizumab	Takeda	Vivli
ENACT	Natalizumab	Biogen	Vivli
ACCENT 1/2	Infliximab	Janssen	YODA
UNITI	Ustekinumab	Janssen	YODA
CERTIFI	Ustekinumab	Janssen	YODA

Individual participant-level data (IPD) from **5011** patients in **10** trials

Vivek Rudrapatna, UCSF

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Recent Publications from the Vivli Platform

PI and Institution	Data Request	Journal	Data Contributors
Chris Gale, University of Leeds	Efficacy and safety of edoxaban versus warfarin in patients with atrial fibrillation and frailty insights from the ENGAGE AF-TIMI 48 trial	BMC Med	Daiichi Sankyo
Thomas Metkus, Johns Hopkins University School of Medicine	Severe sepsis in the cardiac intensive care unit: management strategies and outcomes	Critical Care Medicine	Lilly
Jose da Silva, Universidade de Coimbra, Portugal	Long-term predictive value of patient global assessment regarding radiographic damage and physical function in patients with Rheumatoid Arthritis individual patient data meta-analysis	Annals of the Rheumatic Diseases	AbbVie, Pfizer Inc., Roche, UCB
Ahmad Abuhelwa, University of South Australia	Predictors of exposure, therapeutic and adverse effects of certolizumab pegol, baricitinib and tocilizumab used in the treatment of rheumatoid arthritis	Scientific Reports	Lilly, Roche, UCB
Michael Ward, National Institutes of Health (NIH)	Predicting Treatment Response to Tumor Necrosis Factor Inhibitors in Patients with Ankylosing Spondylitis	Arthritis Rheumatol.	Abbott, Pfizer

Explore Vivli

Log on to

Vivli.org

To explore the ~6,000 trials and begin the search

Questions: Contact me at RLI@VIVLI.ORG

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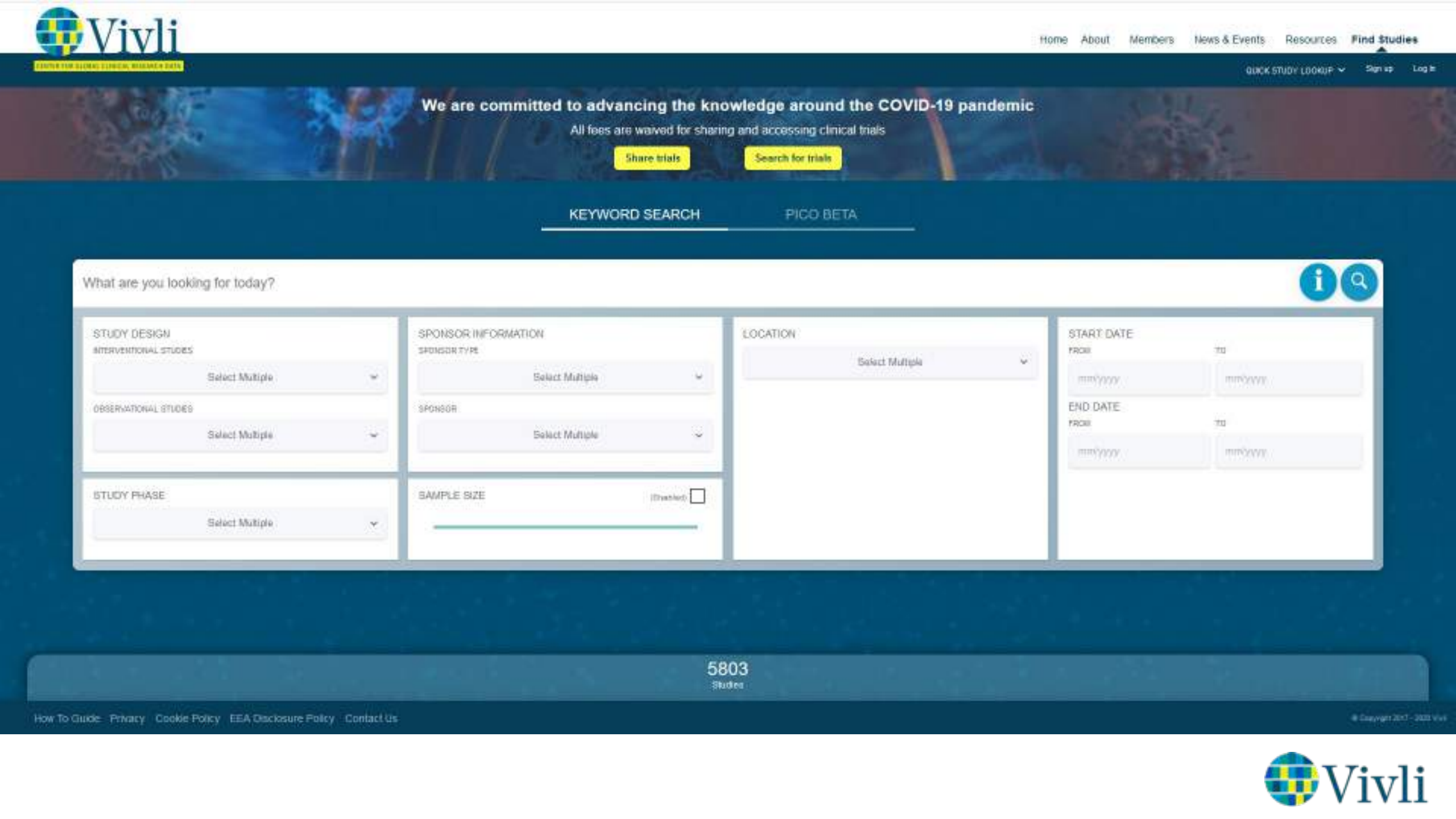
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We are committed to advancing the knowledge around the COVID-19 pandemic
All fees are waived for sharing and accessing clinical trials
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PICO BETA
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STUDY DESIGN
INTERVENTIONAL STUDIES
Select Multiple
OBSERVATIONAL STUDIES
Select Multiple
SPONSOR INFORMATION
SPONSOR TYPE
Select Multiple
SPONSOR
Select Multiple
LOCATION
Select Multiple
START DATE
FROM
TO
mm/yyyy
mm/yyyy
END DATE
FROM
TO
mm/yyyy
mm/yyyy
STUDY PHASE
Select Multiple
SAMPLE SIZE
(Disabled)
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