Vivli

CENTER FOR GLOBAL CLINICAL RESEARCH DATA

Vivli – Global Clinical Trials Data Sharing Platform

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Vivli Co-Founder
Professor of Medicine, UCSF
December 11, 2020

COVID-19 Vaccine Clinical Trials

Vivli: The Difference Data Re-Use Can Make

Agenda

- Overview of clinical trial data sharing
- How can Vivli help me share my clinical study data?
- How can I request data from other completed studies?

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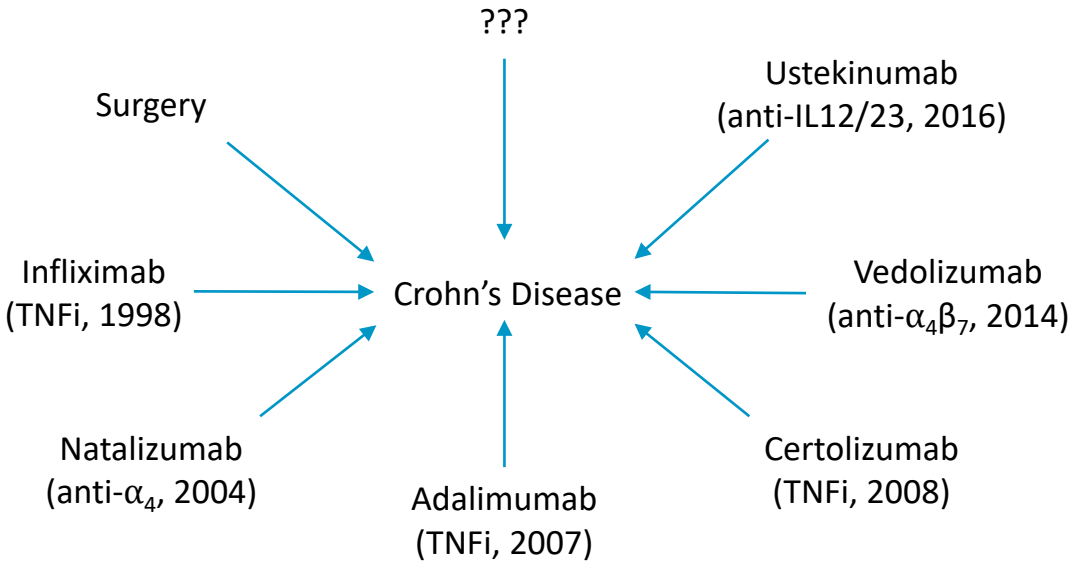
Today's Menu of Crohn's Treatments



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Questions, questions…

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?

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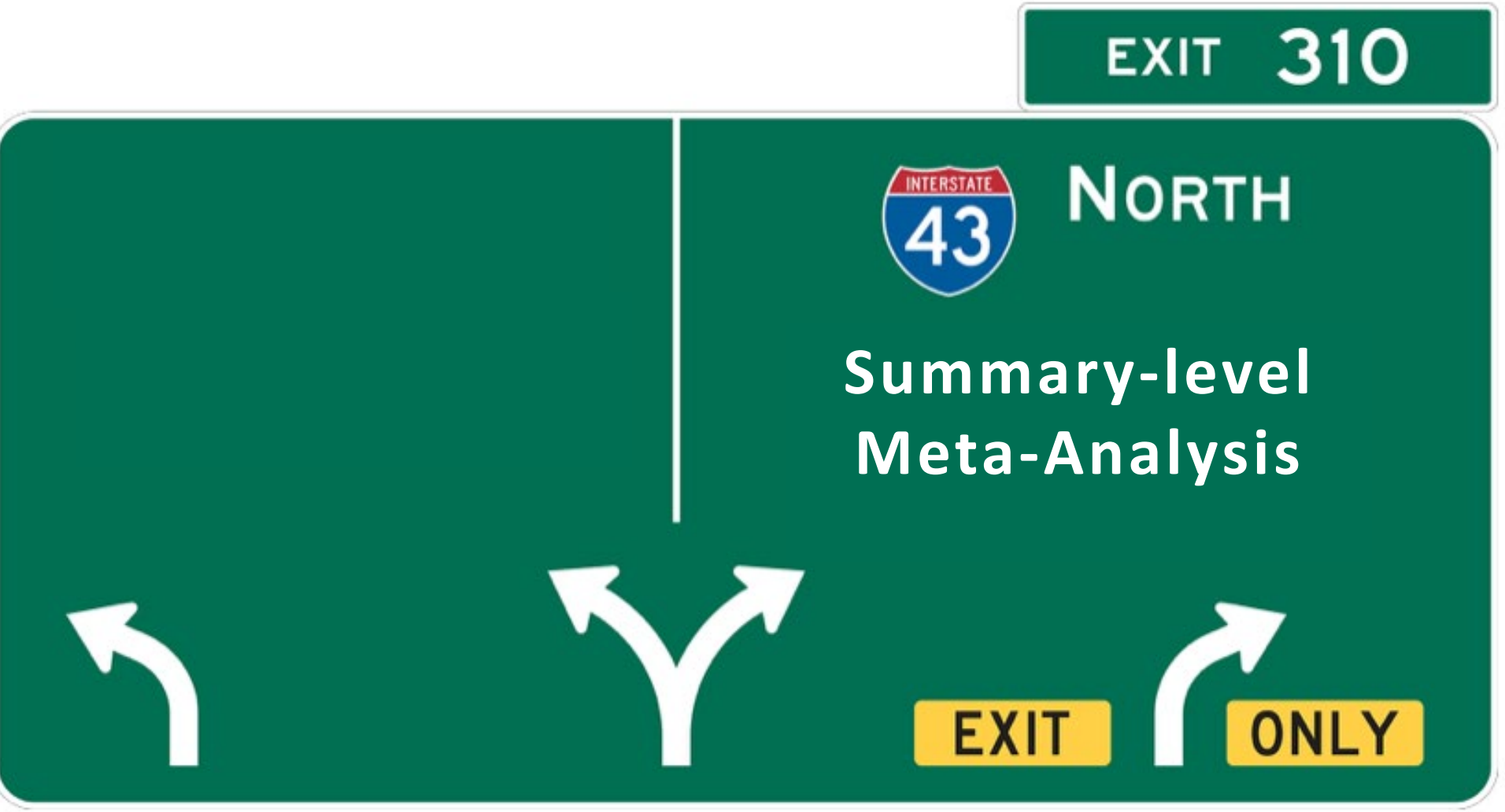
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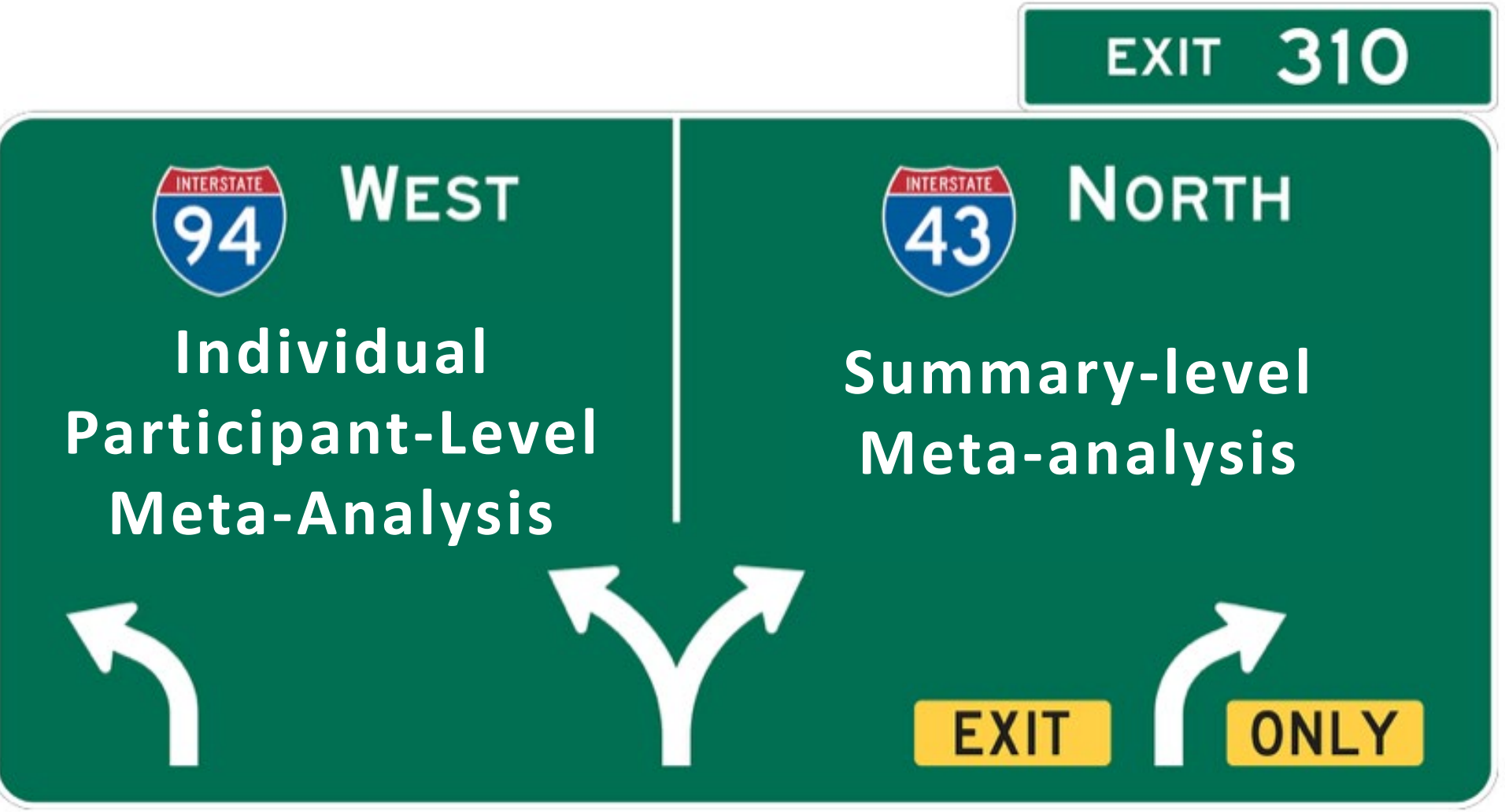
INTERSTATE
43
NORTH
Summary-level
Meta-Analysis
EXIT
ONLY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Individual Participant-Level Meta-Analysis
Summary-level Meta-analysis
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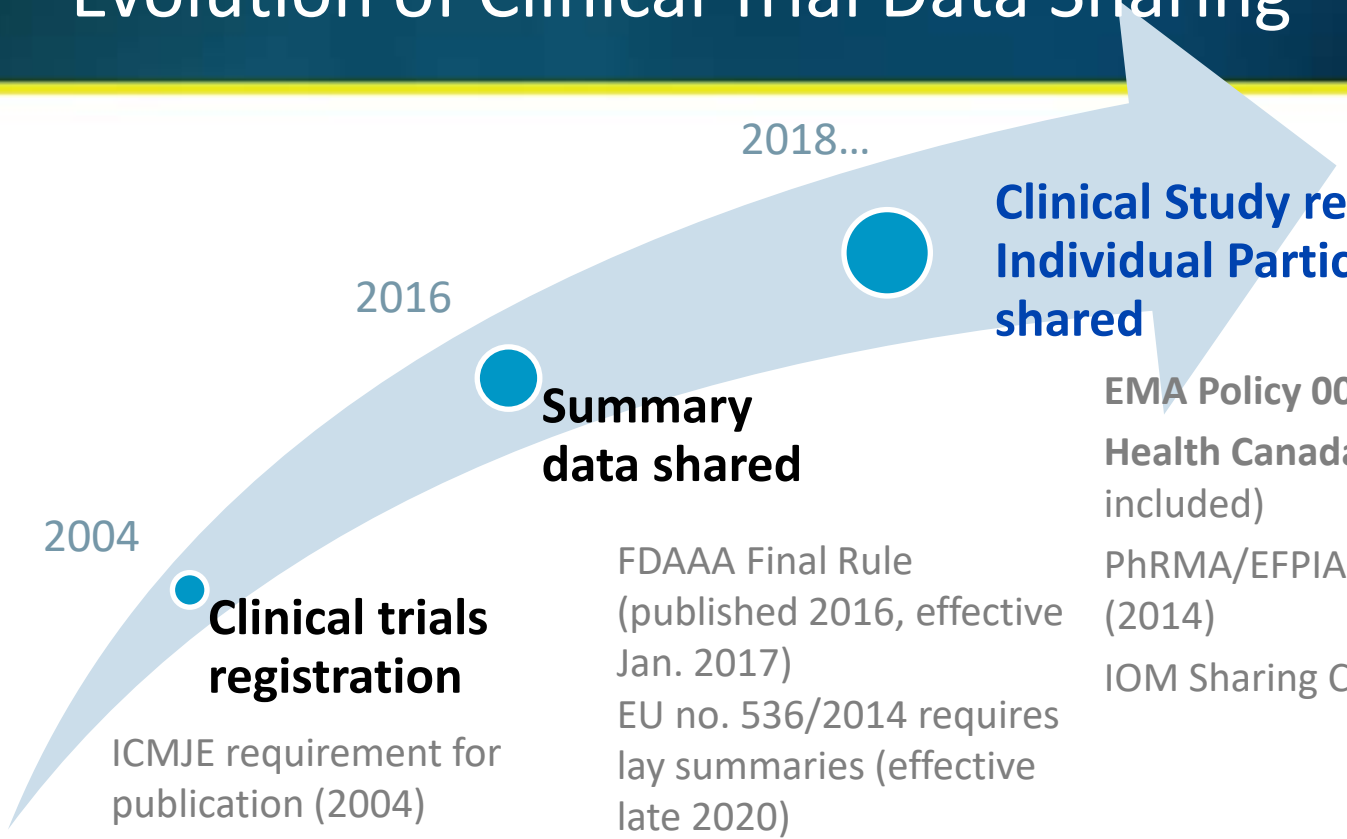
ONLY

Evolution of Clinical Trial Data Sharing



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2018: Major Journals Require IPD Sharing Statement

- Trial manuscript submissions must include a data sharing statement
  - who, what, when, where, and why and how IPD will be shared
- Some journals routinely request IPD be shared
  - e.g., BMJ, PLoS Medicine, Lancet

ICMJE: International Committee of Medical Journal Editors

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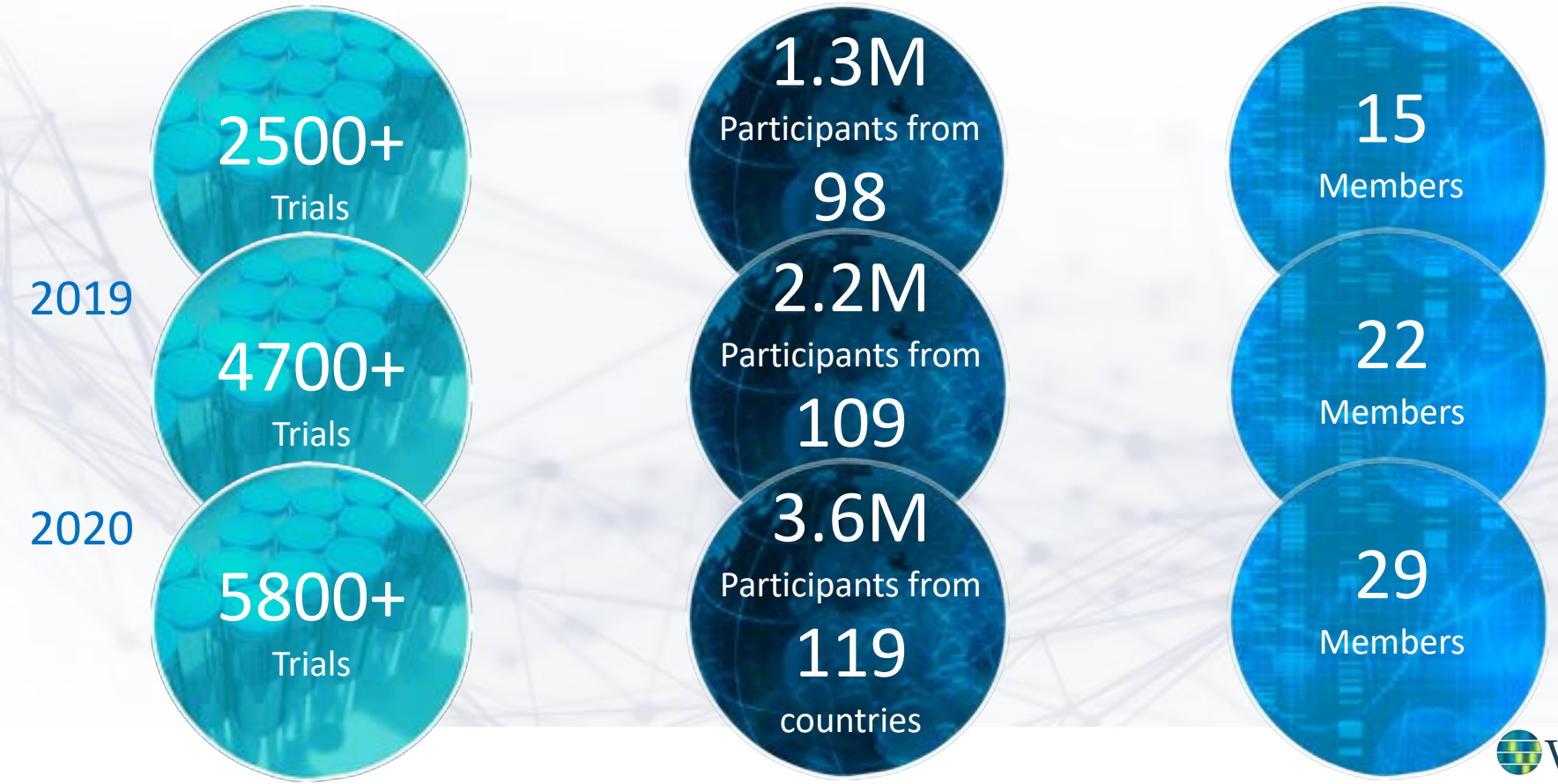
Mid-2018: Vivli Launches



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2019: Data Sharing Plans at Trial Registration

- Data sharing plans added to ClinicalTrials.gov registration
- ICMJE requires that you included a 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.

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

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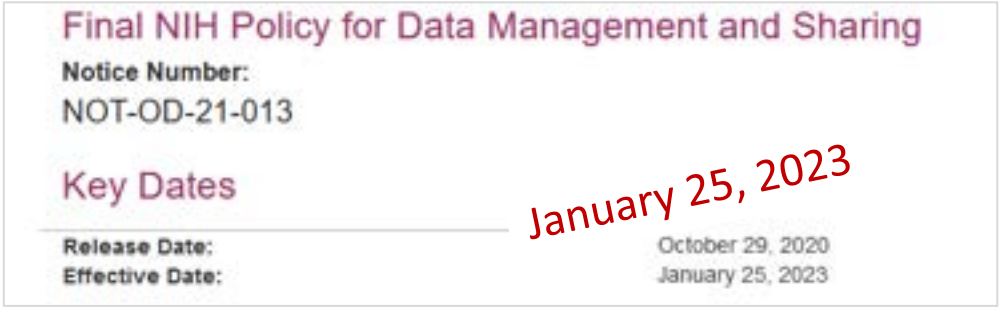
2023: NIH Requiring Data Sharing Plans

- Data sharing plan must be included in NIH grant proposals
  - but will not be scored as part of peer review
- Allowed to budget for data sharing costs
- Encourages use of established repositories (including Vivli)



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Benefits of IPD Sharing

- **Honors** the commitments of participants
- **Strengthens trust** in the clinical research enterprise
- **Prevents repetitive trials** and putting additional patients at risk
- **Enables new discovery** and scientific insights through combining data from disparate sources

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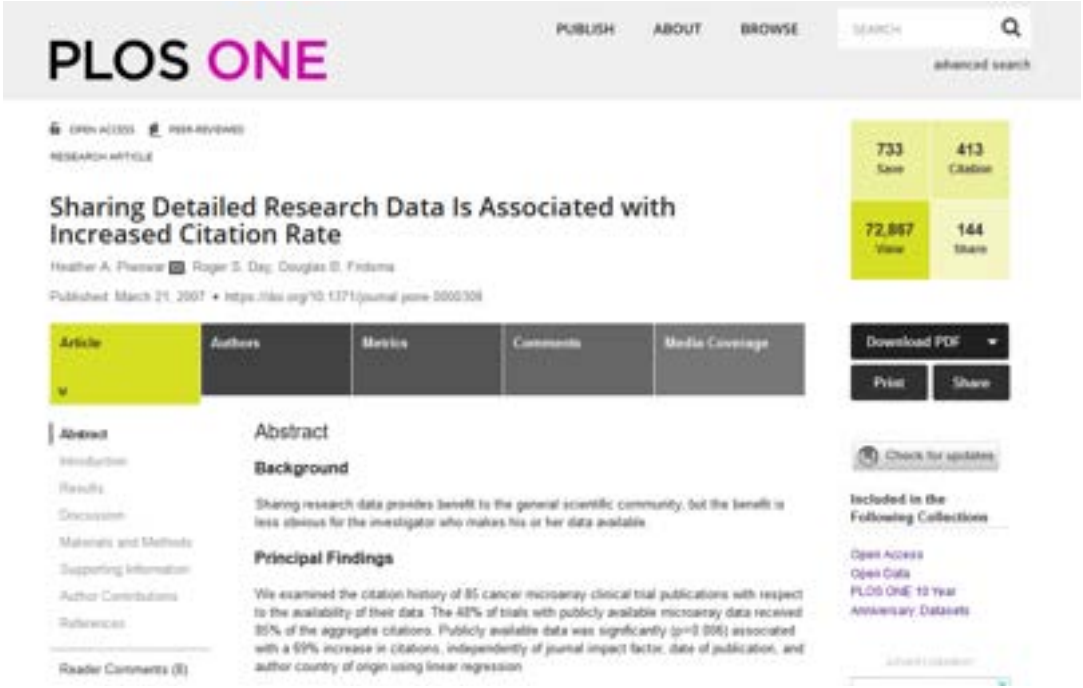
Increases Citations Too!



"The 48% of trials with publicly available microarray data received 85% of the aggregate citations. Publicly available data was significantly ($p = 0.006$) associated with a 69% increase in citations"

https://doi.org/10.1371/journal.pne.0000308

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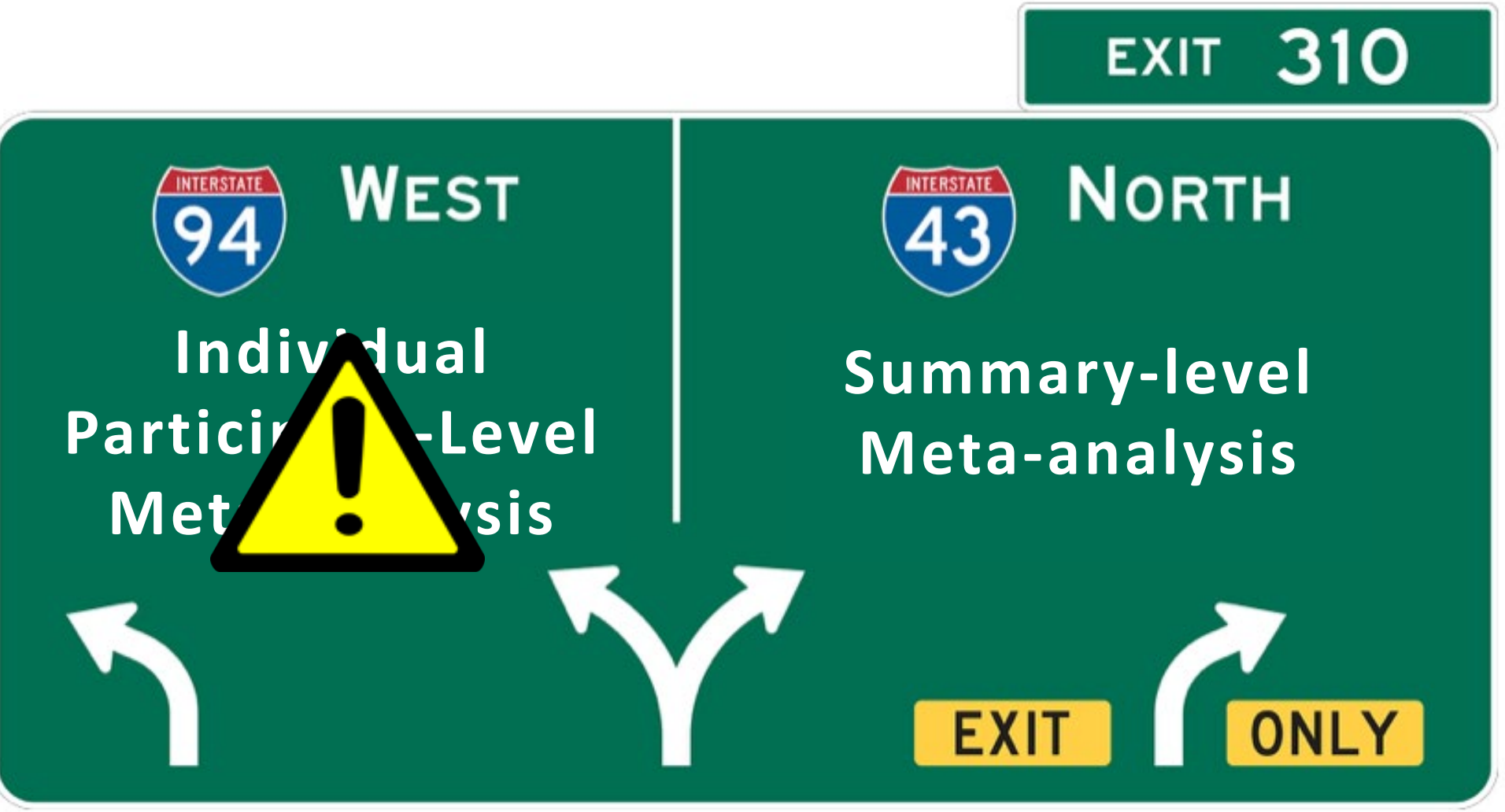
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INTERSTATE 94
WEST
INTERSTATE 43
NORTH
Individual Participant-Level Meta-analysis
Summary-level Meta-analysis
EXIT ONLY

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

HOW TO SHARE DATA VIA VIVLI

Balancing Risks and Benefits

Openness

Maximizing the value of the data collected respects participants' contributions

Privacy

Protecting participant privacy

Approaches to Sharing Human Data

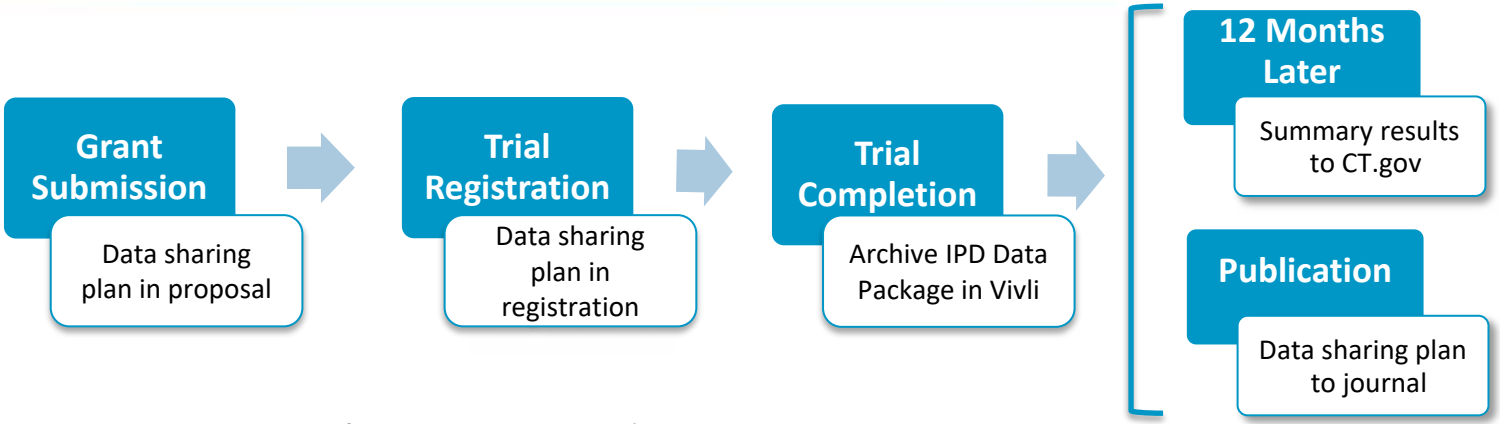
Type	Key Features	Examples
Open access	Anyone can access, simple account creation, simple on-line data use agreement (DUA)	Health CAN, EMA, Project Datasphere
Managed access	• for scientific purposes only (standard request form) • (independent) review process • secure environment for data access • clear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

Vivli Members

When to Use Vivli

		Unrestricted access ok	Sharing only within team	Sharing only within consortium	**Wide but managed access**
	IPD Sharing Requirements	**Figshare & Dryad**	**Internal University Repositories**	**"Walled Gardens"**	**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			X	✓
	Independent request review available				✓
Data Users	One-stop shop for finding IPD on any therapeutic area from any contributor worldwide			X	✓
	Harmonized data request form				✓
	Additional data and software can be brought into the research environment				✓
	Uniform security standards and policies				✓

IPD Sharing over Study Lifecycle



IPD Data Package required contents

- IPD
- Protocol
- Data Dictionary
- Statistical Analysis Plan

Optional: Informed consent, case report form, analytic code…

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IPD Must be Anonymized

Protecting private or sensitive information by perturbing data

- De-identification: identifiers are removed to reduce the risk that a person can be re-identified from the data
- Anonymization: erasing or encrypting all identifiers that connect an individual to stored data

Privacy Analytics partnership

- Special discounted pricing and turn around time for Vivli members (industry sponsors and academics)
- Secure and audited environment for performing the anonymization
- Risk-based quantitative anonymization approach: consistent with current best practices as recommended by EMA and Health Canada

PRIVACY ANALYTICS
an IQVIA company

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Data Contributor Agreement – Key provisions

Key Vivli DCA provisions.

Researcher agrees

- The data are provided in an anonymized form (meaning that measures have been taken to reduce the risk of re-identification of individual participants)
- Researcher has the rights to share the data and continues to maintain pre-existing ownership rights

Vivli agrees – That Recipients must sign the DUA for access

Data Use Agreement – Key provisions

- Vivli manages DUA process for members who use the Vivli harmonized DUA
- Vivli members who are partner platforms may use their own DUA as long as it does not conflict with the Vivli DUA (cross-platform sharing)

Key Vivli DUA provisions. Researcher agrees:

- To adhere to a research plan
- To make reasonable efforts to publish
- Not to re-identify participants

Costs Per Study

	Study Curated and Listed on Vivli	Anonymized IPD Storage	Independent Review Panel	One-off Cost
Study ready for sharing and needs storage	✓	✓		$4,000
Study ready for sharing and needs Storage and Independent Review Panel	✓	✓	✓	$9,500
Anonymization	✓	✓	✓	Provided by Privacy Analytics (additional $2,000-$5000 / dataset)

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Institutional Membership

- Institutions can join Vivli as a member
  - covers data depositions from that institution
- Steps
  1. Sign membership agreement
  2. Agree to harmonized Data Contributor Agreement / Data Use Agreement (DCA/DUA)
  3. Post membership page on Vivli website explaining how requests will be reviewed, etc.
- Contact jwood@vivli.org

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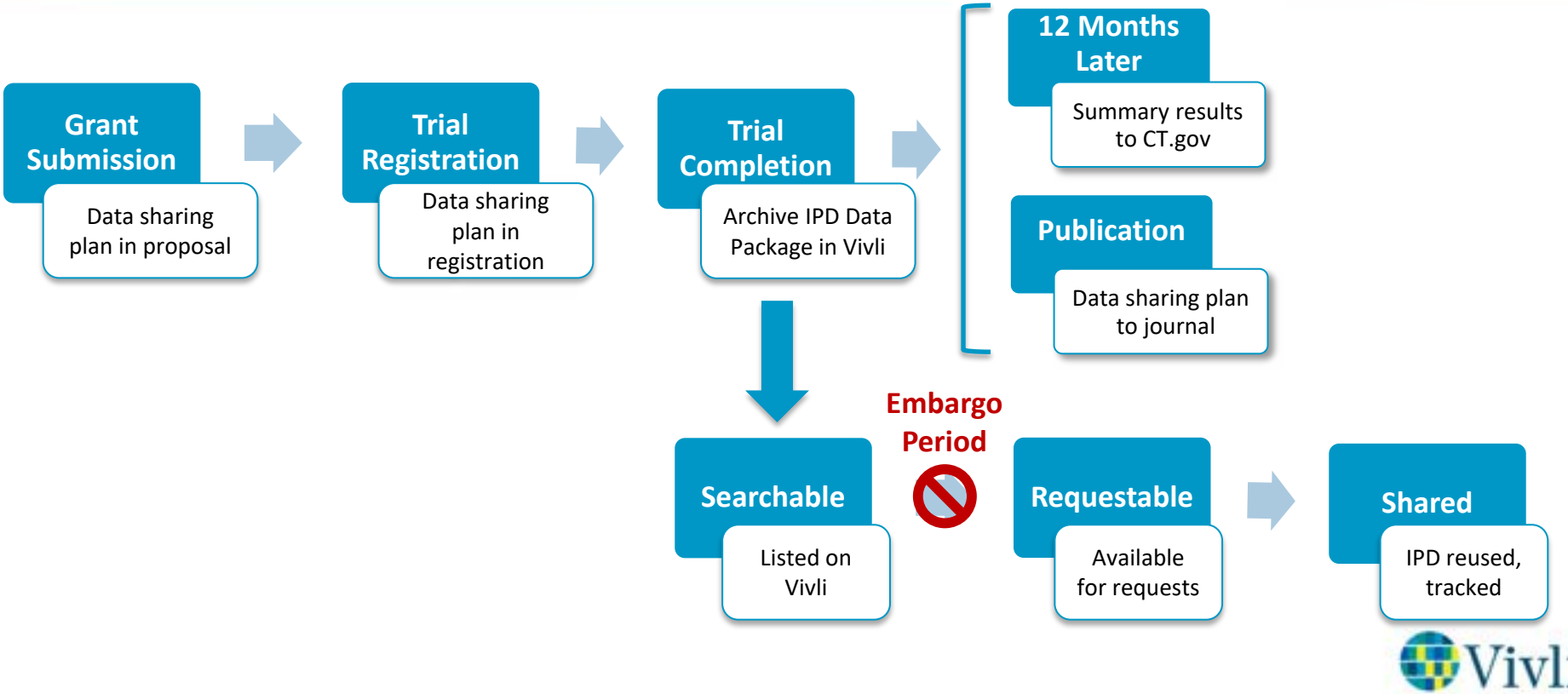
IPD Package is Listed and Requestable



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Informed Consent and IPD Sharing

- Typically, data are shared in “de-identified” or “anonymized” form
- Vivli accepts only anonymized data
- The extent to which consent remains relevant following de-identification or anonymization is a debated issue
- Common view is that promises made to research subjects at the time of consent must be respected, regardless of whether data have been de-identified or anonymized

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Informed Consent: Example 1

Informed Consent explicitly prohibits secondary uses of data

> "your trial data from the XYZ breast cancer study will be made available to XYZ investigators at UCSF and regulators who may need to review your data for regulatory purposes."

- Implies that data would not be shared beyond original trial purpose (even if anonymized)
- Best practice would recommend not using this data for secondary research purposes
- Participants may be re-consented for secondary uses of their data

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Informed Consent: Example 2

ICF is silent regarding secondary uses of data **(most common)**

- No explicit promises were made to the contrary, secondary uses of data are thought permissible if the data are "anonymized" or "de-identified"
  - Consider additional consent / notice requirements of particular regulatory regime

- Increasing trend to require notice of and/or consent to future uses of de-identified or anonymized data **(Revised Common Rule)**

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HOW TO REQUEST DATA VIA VIVLI

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Agnostic to Disease, Funder or Data Contributor

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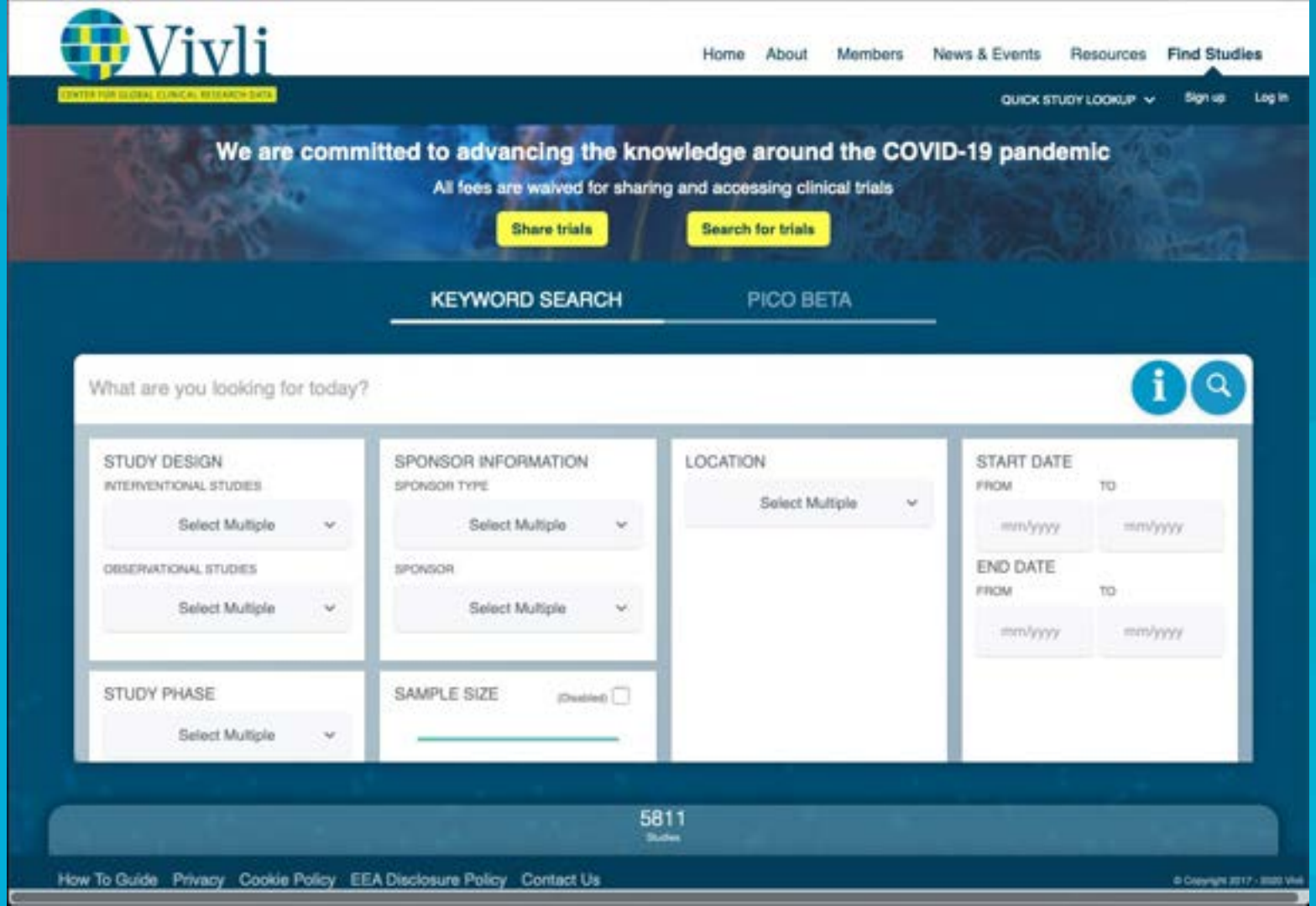
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Search for trials
KEYWORD SEARCH
PICO BETA
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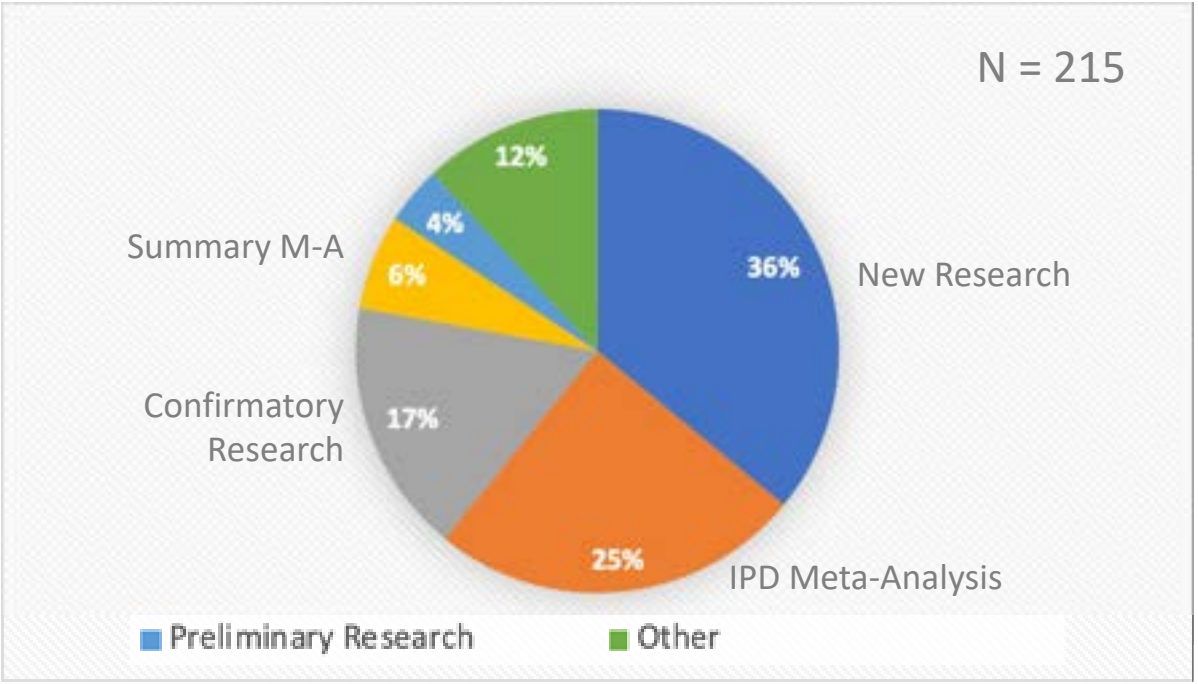
STUDY DESIGN
INTERVENTIONAL STUDIES
Select Multiple
OBSERVATIONAL STUDIES
Select Multiple
SPONSOR INFORMATION
SPONSOR TYPE
Select Multiple
SPONSOR
Select Multiple
LOCATION
Select Multiple
START DATE
FROM
TO
mm/yyyy
mm/yyyy
END DATE
FROM
TO
mm/yyyy
mm/yyyy
STUDY PHASE
Select Multiple
SAMPLE SIZE
(Disabled)
5811
Studies
How To Guide
Privacy
Cookie Policy
EEA Disclosure Policy
Contact Us

18 Therapeutic Areas Covered by Vivli Requests

TYPE	Number of Requests
Cardiovascular	25
Dermatology	7
Endocrinology	6
Gastroenterology	9
Hematology	3
Infectious Disease	5
Methods	12
Neurology	25
Oncology	52
Orthopedics	5
Psychiatry	13
Pulmonary	18
Rheumatology	30
Other	7
Total	217

215 Requests as of November 2020

Types of Planned Secondary Research



NIDDK-related studies on Vivli

- 400+ studies available in NIDDK-related fields

- Sample of requests already approved related to NIDDK
  1. **Chronic Kidney Disease** Epidemiology – Clinical Trials Consortium (CKD-EPI CT)
  2. TRIAL-INFORMED **DKA** MITIGATION EDUCATIONAL TOOL
  3. Stratification of SGLT2 inhibitor glucose lowering therapy in **Type 2 diabetes**
  4. The impact of biological interventions on health-related quality of life in adults with **Crohn's disease**
  5. Predictors of Mucosal Healing in **Ulcerative Colitis**: A Post-hoc Analysis of VARSITY

7 of the most requested studies on Vivli are in IBD

Gastroenterology	**Crohn's Disease**	**5**
	UC	**2**
Rheumatology	RA	14
Cardiology	AFIB	1
	Stroke	1
	Bladder	3
Oncology	Breast	1
	NSCLC	4
	RCC	1
	Covid 19	1
Other	Depression	1
	Duchenne	1
	Hidradinitis	2

400+ NIDDK topic studies available for request

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Getting to Answers…

Dr. Vivek Rudrapatna
Assistant Professor, UCSF

Vivli Pioneer Award Winner

All phase 2/3, completed, randomized, double-blinded, placebo-controlled, trials of FDA-approved drugs for moderate-to-severe Crohn's Disease (at the FDA-approved dose) in adults, extending to at least 24 weeks in duration

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REQUEST

Request IPD Data sets.

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

REVIEW

Reviewed by sponsor or independent review panel.

Sponsor provides **IPD, data dictionary, protocol, statistical analysis plan.**

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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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

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Vivli Secure Environment Bridges Multiple Platforms

abbvie

Biogen

Johnson & Johnson
FAMILY OF COMPANIES

Takeda

ucb Inspired by patients. Driven by science.

Vivli Secure Environment

30+ tools
- SAS
- STATA
- MS Office
- R, + over 300 pkgs
- Jupyter Notebook
- Python, + over 250 pkgs
- Spark
- Anaconda

BYO data, scripts, software on request

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Vivli FAIR Data Sharing

- Findable
  - metadata model, annotated using Cochrane vocabulary (SNOMED, WHO ATC, MedDRA)
  - Dataset DOIs minted by DataCite
- Accessible
  - from fully downloadable to available only in secure MS Azure environment
- Interoperable, Reusable
  - SDTM format recommended but not required
  - No requirement for common variables

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Outcomes of Vivli Data Sharing

- 10 publications so far (1st data requests submitted July 2018)
  - e.g., JNCI, Annals of Oncology, Clin Exp Dermatol, J Am Acad Derm, Ann of Rheum Dis, BMC Medicine
- Scientific value: case example of hidradenitis suppurativa

Dr. John Frew
Rockefeller University

"I was at a conference in Europe last month and a half a dozen speakers were citing my research as the basis for re-thinking trial designs and the outcome measures used and whether multiple measures need to used or a new one developed to take these findings into account."

"Having all this data available via the Vivli platform is a key tenet to evaluating the epidemiological aspects of this condition. This is beyond valuable."

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CHALLENGES/FUTURE

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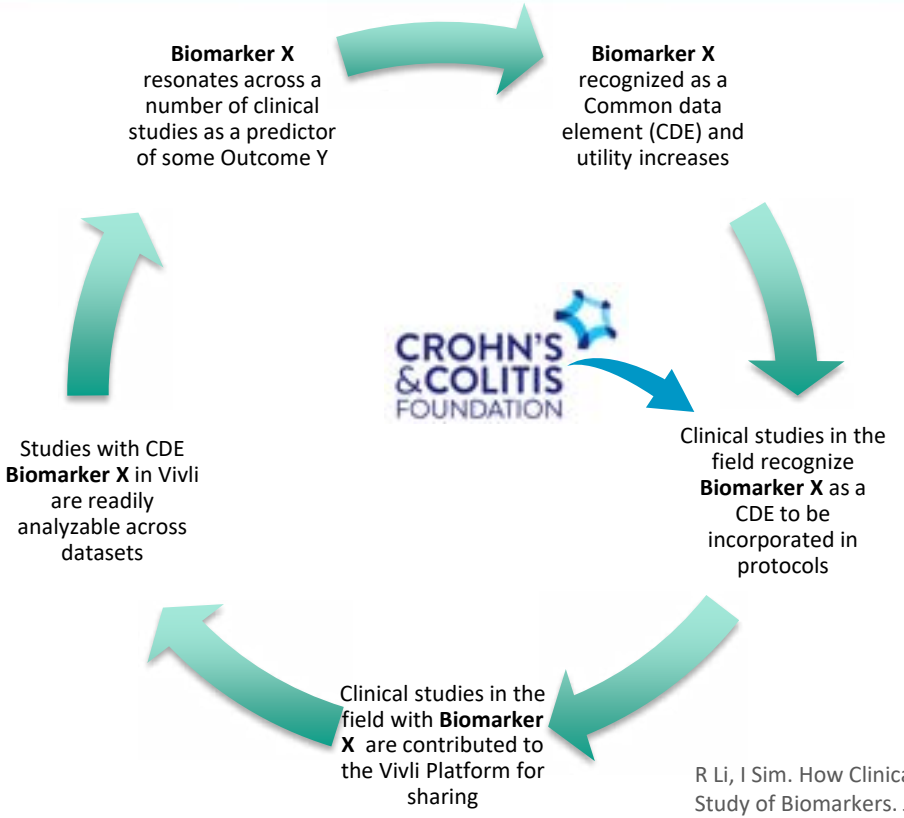
Can Data Sharing Drive Common Biomarker Development and Adoption?



- PhenX, ICHOM, …NIH CDE Repository contains over 27,000 CDEs
  - limited adoption overall
- Data sharing and re-use makes effort of Common Biomarkers directly visible and scientifically valuable
- Most successful when led by disease-specific investigator communities e.g.,
  - Traumatic Brain Injury
  - pediatric obesity

R Li, I Sim. How Clinical Trial Data Sharing Platforms Can Advance the Study of Biomarkers. J Law Med Ethics, 2019. 47(3):369-373.

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Challenges in Sharing of Clinical Trial Data

- Utilization lags behind data contribution
- Academic participation
- Data harmonization
- Awareness of data sharing initiatives

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Summary

Vivli distinguishing features

- Trusted venue for sharing with the entire scientific community (not a “walled garden”)
- Established working relationships across industry, academia, and non-profit and government funders
- Enables data from multiple sources to be combined securely
- Given the urgency, we will support sharing of some interim participant-level data followed by the final dataset

Contact support@vivli.org

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Explore Vivli

Log on to

Vivli.org

To explore the ~5,800 trials and begin the search

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