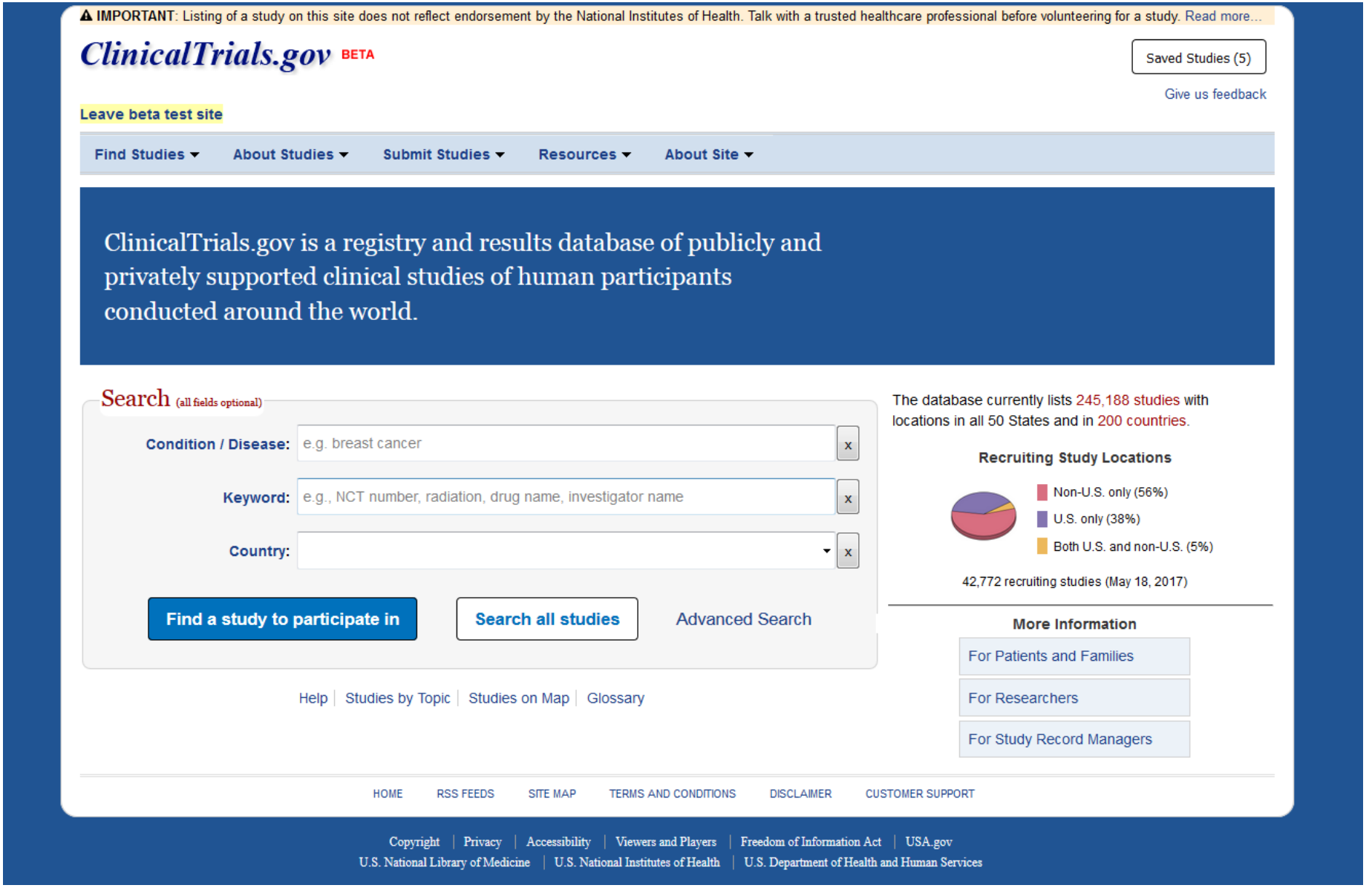
NIH and other ClinicalTrials.gov Reporting Requirements

Deborah A. Zarin, M.D.
Director, ClinicalTrials.gov
Senior Scientist, NIH
May 2017

DISCLAIMER

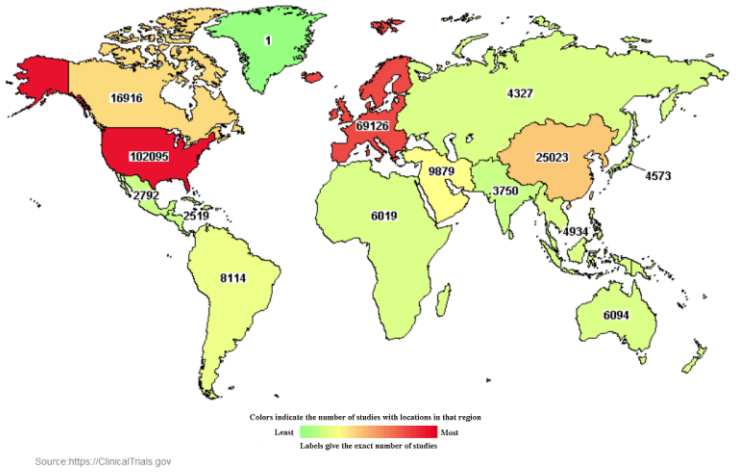
Views are mine and do not necessarily represent views of NIH or HHS

ClinicalTrials.gov Background


IMPORTANT: Listing of a study on this site does not reflect endorsement by the National Institutes of Health. Talk with a trusted healthcare professional before volunteering for a study. Read more...
ClinicalTrials.gov BETA
Saved Studies (5)
Give us feedback
Leave beta test site
Find Studies
About Studies
Submit Studies
Resources
About Site
ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world.
Search (all fields optional)
Condition / Disease:
e.g. breast cancer
Keyword:
e.g., NCT number, radiation, drug name, investigator name
Country:
Find a study to participate in
Search all studies
Advanced Search
Help | Studies by Topic | Studies on Map | Glossary
The database currently lists 245,188 studies with locations in all 50 States and in 200 countries.
Recruiting Study Locations
Non-U.S. only (56%)
U.S. only (38%)
Both U.S. and non-U.S. (5%)
42,772 recruiting studies (May 18, 2017)
More Information
For Patients and Families
For Researchers
For Study Record Managers
HOME
RSS FEEDS
SITE MAP
TERMS AND CONDITIONS
DISCLAIMER
CUSTOMER SUPPORT
Copyright | Privacy | Accessibility | Viewers and Players | Freedom of Information Act | USA.gov
U.S. National Library of Medicine | U.S. National Institutes of Health | U.S. Department of Health and Human Services

About ClinicalTrials.gov

- Clinical studies registry and results database
  - >245,000 studies (trials, observational studies, & expanded access)
  - Studies with locations in all 50 states and 200 countries
  - Privately and publicly funded studies involving humans
  - Study information submitted by study sponsors or investigators
- Website & registry launched in February 2000
  - Results database, in September 2008
  - >26,000 studies with posted results
- Intended Audience
  - Registry: Public
  - Results Database: Readers of the medical literature
  - Both: Downloaders for other content analysis
- Usage
  - 76,000 unique visitors per day



ClinicalTrials.gov

Content of a Study Record
(Minimum Information Requirements)

- **Registration section**
  - Submitted **at** trial initiation
  - Summarizes information from trial protocol: e.g.,
    - Condition
    - Interventions
    - Study Design
  - Includes recruitment information (e.g., eligibility, locations)

- **Results section**
  - Submitted **after** trial completion
  - Summarizes trial results
    - Participant flow
    - Baseline characteristics
    - Outcome measures (including statistical analyses)
    - Adverse events
  - Full Protocols & SAPs

ClinicalTrials.gov

ClinicalTrials.gov Reporting Volume
(as of 22 May 2017)

- Registration
  - 245,000 study records
  - 600 submissions/week
  - 16,500 data providers (sponsors and investigators)
- Summary Results Reporting
  - 26,000 records with results posted
  - 140 submissions/week
  - 2,800 data providers
- Usage Stats
  - 199+ million page views/month
  - 1.1M+ unique visitors/month

ClinicalTrials.gov Statistics

(as of May 22, 2017)

	Registration	Results
Total*	245,188	26,354
Type of Trial		
Observational	47,815 (20%)	1,695 (6%)
Interventional**	196,214 (80%)	24,659 (93%)
– Drug & Biologic	118,353	19,811
– Behavioral, Other	58,401	4,192
– Surgical Procedure	21,132	1,312
– Device***	23,273	2,886
Study Sites (200 countries)		
US only	88,536 (36%)	13,464 (51%)
Non-US only	114,559 (47%)	6,632 (25%)
US & Non-US mixed	13,559 (6%)	3,621 (14%)
Not Specified	28,534 (12%)	2,637 (10%)

*Includes 433 expanded access programs

**A study record may include more than one type of intervention

***Does not include 726 applicable device clinical trials submitted, but qualify for "delayed posting" under FDAAA

Source: https://clinicaltrials.gov/ct2/resources/trends

ClinicalTrials.gov

ClinicalTrials.gov Reporting Requirements

ClinicalTrials.gov – Milestones

- 1997 – FDA Modernization Act (FDAMA)
- 2000 - ClinicalTrials.gov launched
- 2005 - International Committee of Medical Journal Editors (ICMJE) trial registration policy
- 2007 - FDAAA 801* (Title VIII of Public Law 110-85)
  - Expanded clinical trial registration requirement and imposed new results submission requirements
  - Added enforcement provisions including up to $10,000/day in civil monetary penalties and withholding remaining or future grant funds
- 2016 – FDAAA 801 Final Rule (42 CFR Part 11) & NIH Clinical Trials Disclosure Policy

*FDAAA 801 = Section 801 of the Food and Drug Administration Amendments Act of 2007

Enhancing Clinical Trial Transparency
ClinicalTrials.gov

Under the law, it says you must report. If you don't report, the law says you shouldn't get funding. I'm going to find out if it's true [that the research centers aren't reporting the results] and if it's true, I'm going to cut funding. That's a promise.

Vice President Joe Biden
June 29, 2016

ClinicalTrials.gov

Key Clinical Trial Reporting Requirements

Reporting Requirement	ICMJE Policy (Effective in 2005)	FDAAA Final Rule (Issued in 2016)	Final NIH Policy (Issued in 2016)
Scope	Registration	Registration & Results Reporting	Registration & Results Reporting
Funding Source	Any	Any	NIH
Intervention Type	All	Drugs, Biologics, & Devices regulated by the FDA (Except Phase 1)	All (e.g., including Phase 1, behavioral interventions)
Submission Timing	Before enrollment of first participant	Registration: Within 21 days after first participant Results: Not later than 1 year after Primary Completion Date (some Delays permitted)	Registration: Within 21 days after first participant Results: Not later than 1 year after Primary Completion Date (some Delays permitted)
Enforcement	Refusal to publish	Criminal proceedings and civil penalties (up to $10,000/day); Loss of HHS funding to grantee institution	Loss of NIH funding (term and condition of award)

ICMJE Trial Registration Policy

- **Scope** – All clinical trials, regardless of intervention type, phase, or sponsor
- **Reporting Due Date** – Registration before enrollment of the first participant
- **Potential Consequences of Non-Compliance** – Editor's refusal to publish trial results

ClinicalTrials.gov

FDAAA/Final Rule Overview

- **Scope** –
  - **Applicable Clinical Trials**: Include non-phase 1 trials of drugs, devices, and biologicals (including IND/IDE exempt trials)
  - **Responsible Party**: Study sponsor or designated PI
- **Reporting Due Dates** –
  - **Registration**: No later than 21 days after enrollment of the first participant
  - **Results Reporting**: No later than 1 year after the "primary completion date,"* with delayed submission for limited circumstances
- **Potential Consequences of Non-Compliance** –
  - **FDA**: Criminal proceedings and civil penalties (up to $10,000/day)
  - **HHS**: Loss of HHS funding to grantee institution

*Date final participant was examined or received intervention for the primary outcome as specified in the protocol

NIH Policy

- **Scope** –
  - **NIH-funded Trials**: Funded in whole or in part, including phase 1 trials and non-drug/device trials (e.g., behavioral, dietary supplements)
  - **Responsible Party**: NIH-funded awardees and investigators, as part of terms and conditions
- **Reporting Due Dates** –
  - **Registration**: No later than 21 days after enrollment of the first participant
  - **Results Reporting**: No later than 1 year after the "primary completion date"*
- **Potential Consequences of Non-Compliance** –
  - Loss of NIH funding to grantee institution

*Date final participant was examined or received intervention for the primary outcome as specified in the protocol

ClinicalTrials.gov

Outcome Measure Reporting – Required

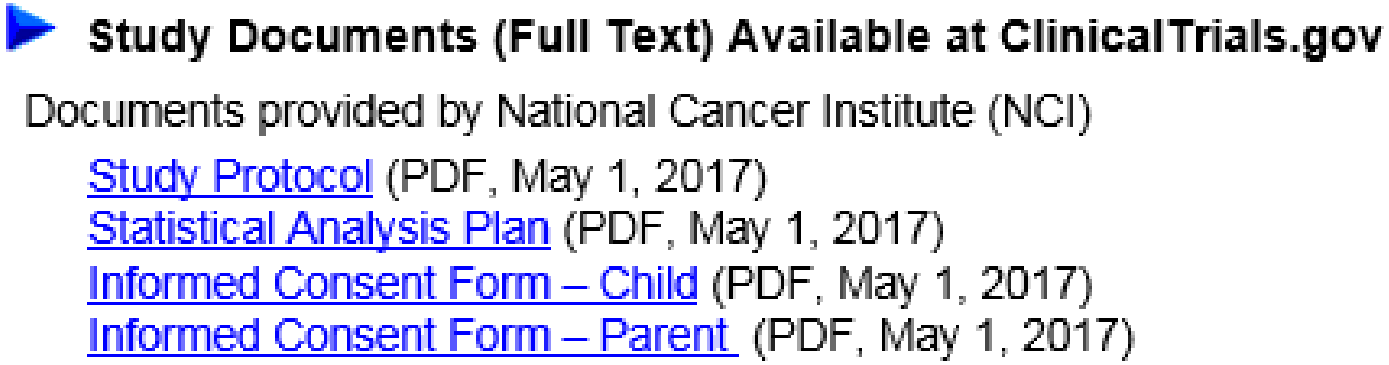
- **Primary outcome measure*** - Outcome measure(s) of greatest importance specified in the protocol, usually the one(s) used in the power calculation. Most clinical studies have one primary outcome measure, but a clinical study may have more than one.
- **Secondary outcome measure*** - Outcome measure that is of lesser importance than a primary outcome measure, but is part of a pre-specified analysis plan for evaluating the effects of the intervention or interventions under investigation in a clinical study and is not specified as an exploratory or other measure. A clinical study may have more than one secondary outcome measure.

Outcome Measure Reporting - Optional

- **Other pre-specified outcome measure** - Any other measurements, excluding post-hoc measures, that will be used to evaluate the intervention(s) or, for observational studies, that are a focus of the study.

Submission of Protocols and SAPs

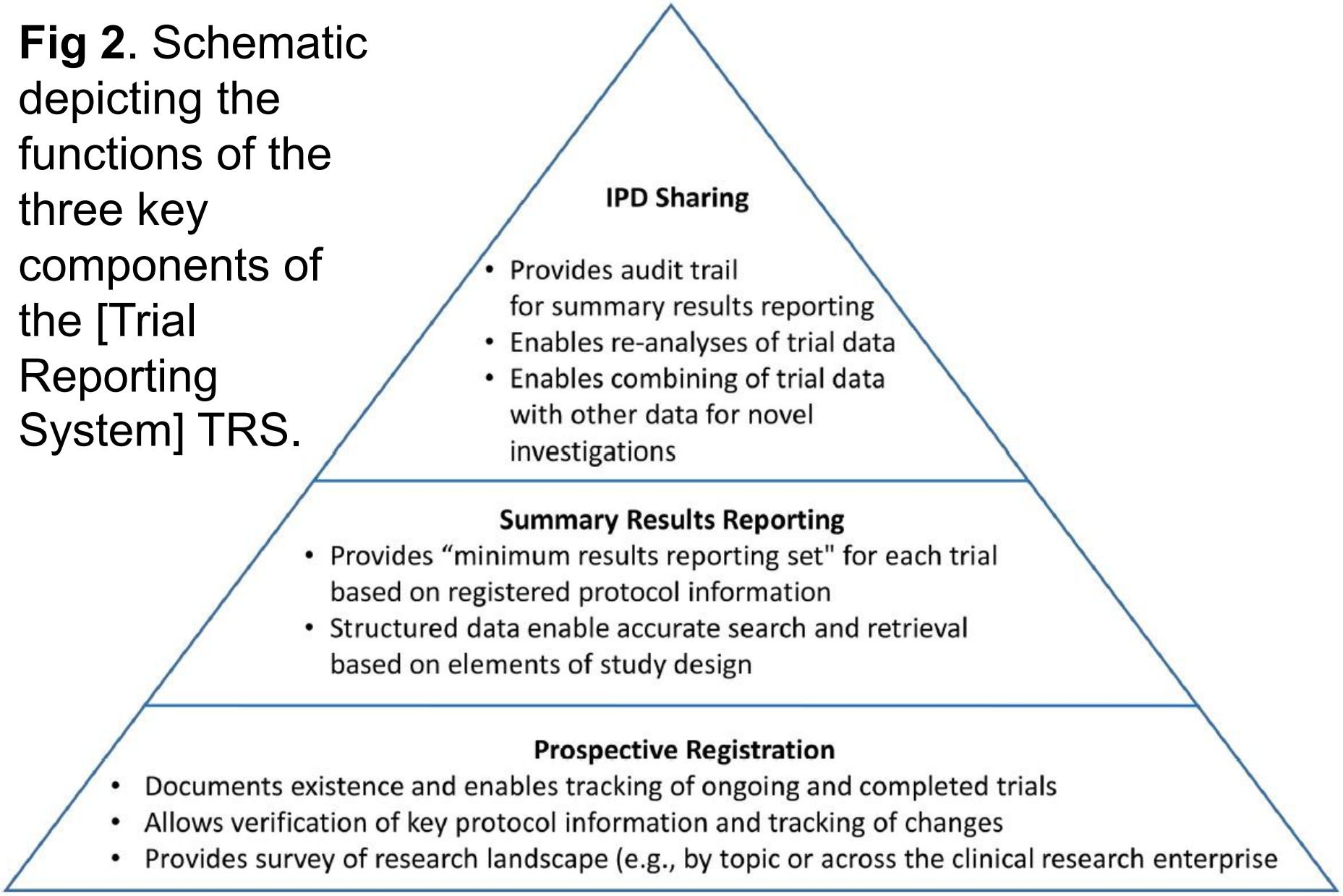
- Full protocol documents (and statistical analysis plans) required as Final Rule results submission
- Document upload feature to be available in June
  - Format: Portable Document Format Archival (PDF/A)
  - Mockup of study record display



ClinicalTrials.gov

IPD Data Sharing Information

Fig 2. Schematic depicting the functions of the three key components of the [Trial Reporting System] TRS.



Source: Zarin DA, Tse T. *PLoS Med*. 2016.

Plan to Share Individual Participant Data (IPD) Data Element - Current

- **At Time of Registration** (Oversight module)
  - **Plan to Share IPD**
    - Definition: Indicate whether there is a plan to make individual participant data (IPD) collected in this study available to other researchers (typically after the end of the study). Select Yes/No/Undecided.
  - **Plan Description**
    - Definition: If IPD collected in this study are to be made available to other researchers (typically after the end of the study), briefly describe what participant data sets and/or documents are to be shared, when data will be available, and how the data may be obtained. An explanation may be provided for why IPD will not be shared.

Individual Participant Data (IPD) Sharing Statement - Planned

- Plan to Share IPD (Yes/No/Undecided)
  - **IPD-Sharing Description**: specific participant data sets to be shared
  - **IPD-Sharing Additional Information Type**
    - Study Protocol
    - Statistical Analysis Plan
    - Informed Consent Form
    - Clinical Study Report
    - Analytic Code
  - **IPD-Sharing Time Frame**: when IPD and supporting information will become available and for how long
  - **IPD-Sharing Access Criteria**: with whom, for what types of analyses, and by what mechanism IPD will be shared
  - **URL**: web address used to find additional plan information

MOCKUP of IPD Sharing Statement DE

Plan to Share IPD?
(including data dictionaries)

Yes ▽

Yes
No
Undecided

IPD Description:

Additional Document Types
(Select all that apply)

- ☐ Study Protocol
- ☐ Statistical Analysis Plan
- ☐ Informed Consent Form
- ☐ Clinical Study Report
- ☐ Analytic Code

IPD-Sharing Time Frame

Describe when IPD/additional documents will be available for sharing including start and end dates or period of availability (e.g., 2 years).

Key Access Criteria

Describe access criteria including who may request access (e.g., “open” or “controlled”), types of data analyses permitted, process for requesting data/documents, who will decide (e.g., third party), and criteria for reviewing requests (e.g. “qualifications,” “quality of request”).

Website providing more information

URL:

Plan to Share Individual Participant Data (IPD) Data Element - Current

- **At Time of Registration** (Oversight module)
  - **Plan to Share IPD**
    - Definition: Indicate whether there is a plan to make individual participant data (IPD) collected in this study available to other researchers (typically after the end of the study). Select Yes/No/Undecided.
  - **Plan Description**
    - Definition: If IPD collected in this study are to be made available to other researchers (typically after the end of the study), briefly describe what participant data sets and/or documents are to be shared, when data will be available, and how the data may be obtained. An explanation may be provided for why IPD will not be shared.

Available Study Data/Documents Data Element -- Current

- **Available Study Data/Documents**

  Definition: Study data sets and documents that are being shared. Provide the following information for each:

  - **Type**

    Definition: The type of data set or document being shared.

    - Individual Participant Data Set
    - Study Protocol
    - Statistical Analysis Plan
    - Informed Consent Form
    - Clinical Study Report
    - Analytic Code
    - Other (specify)

  - **URL**

    Definition: The Web address used to request or access the data set or document.

References Module: Available Study Data/Documents Data Element

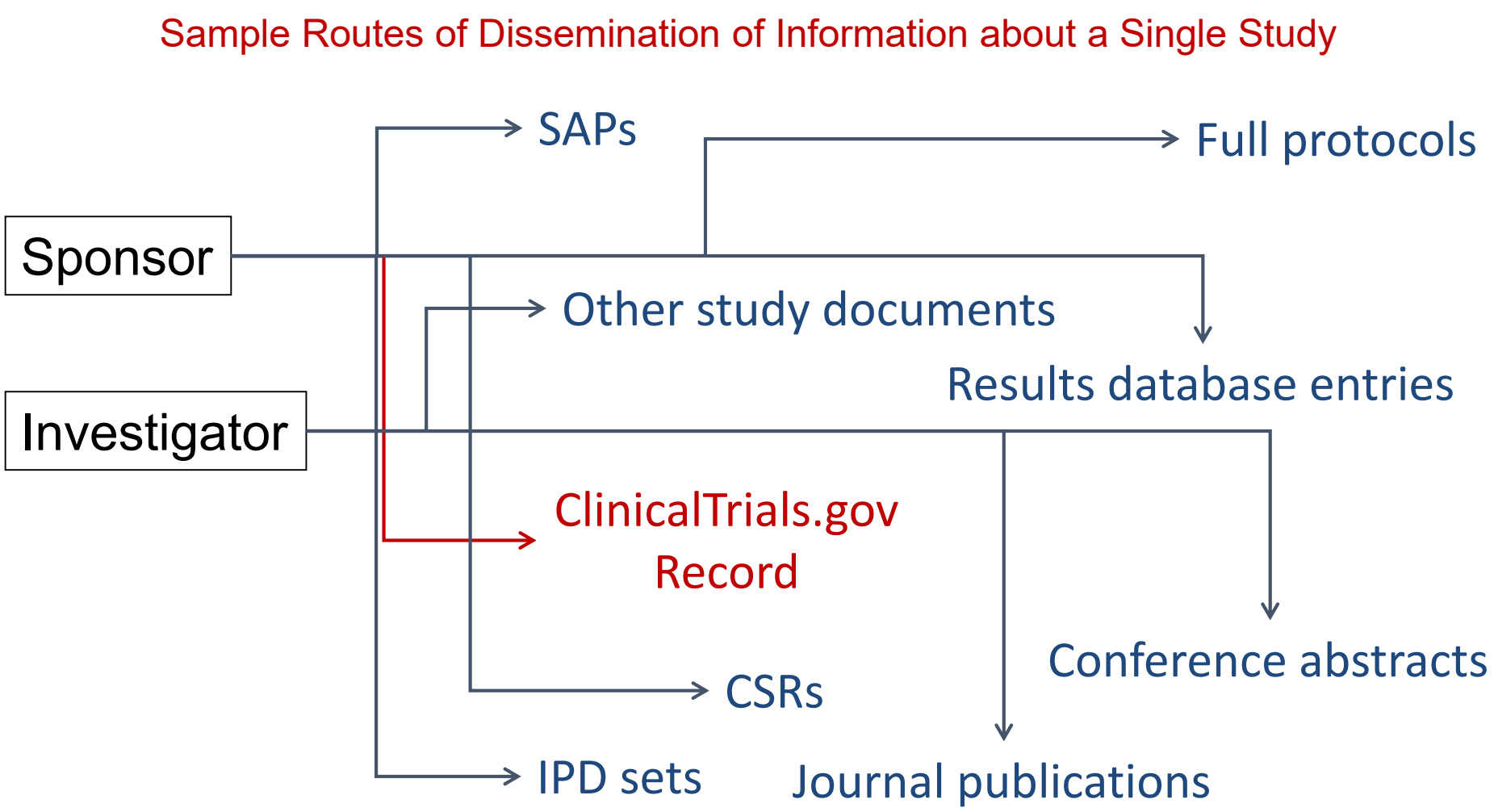
- **Available Study Data/Documents (cont.)**
  - **Identifier**

    Definition: The unique identifier used by a data repository for the data set or document.
  - **Comments**

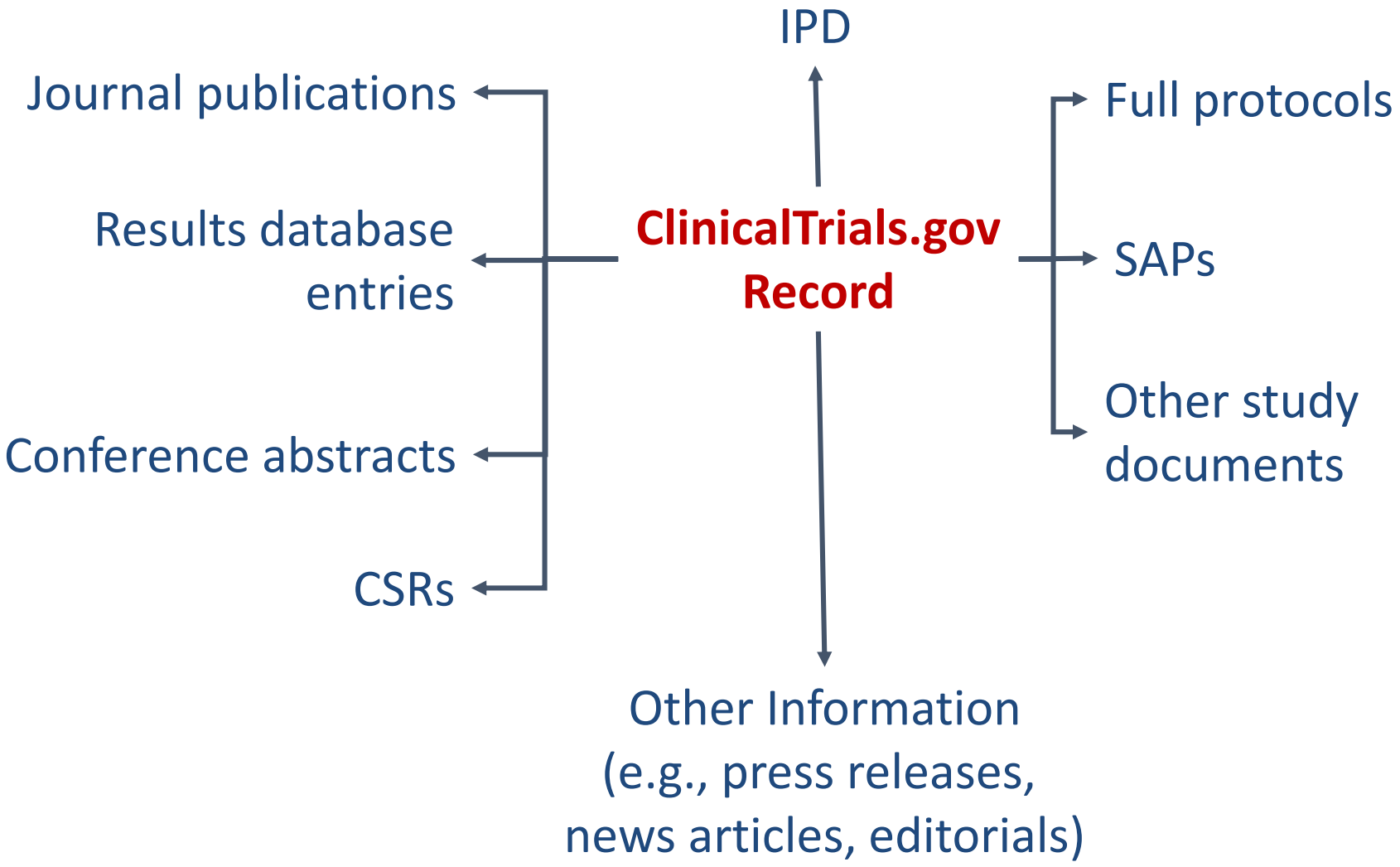
    Definition: Additional information including the name of the data repository or other location where the data set or document is available. Provide any additional explanations about the data set or document and instructions for obtaining access, particularly if a URL is not provided.

“Informational Chaos”

Diffuse, hard-to-access information about a single study



ClinicalTrials.gov: Informational Scaffold



Q&A