Critical Path Institute: Data Drives Therapeutic Innovation in the Neurosciences

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CSO

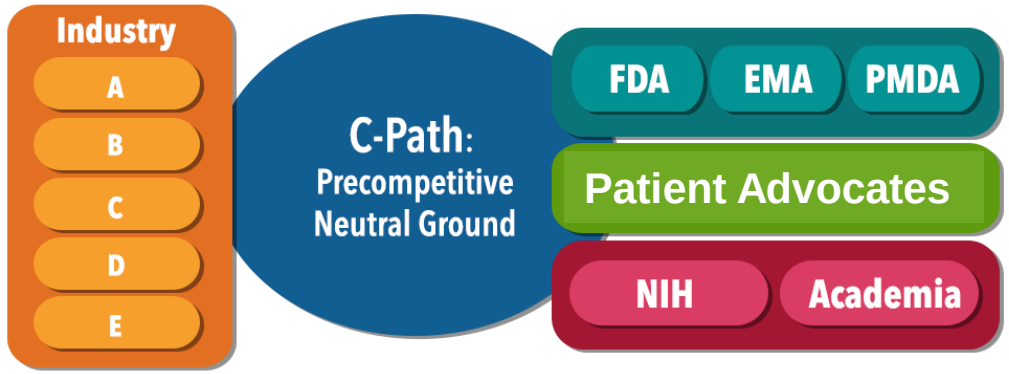
Critical Path Institute

CRITICAL PATH INSTITUTE

No conflicts of interest to disclose

C-Path: A Public Private Partnership

- Act as a trusted, neutral third party
- Convene scientific consortia of industry, academia, and government for sharing of data/expertise
  - ✓ The best science
  - ✓ The broadest experience
  - ✓ Active consensus building
  - ✓ Shared risk and costs



- Enable iterative EMA/FDA/PMDA participation in developing new methods to assess the safety and efficacy of medical products
- Official regulatory endorsement of novel methodologies and drug development tools

Clinical Data Contributed to C-Path

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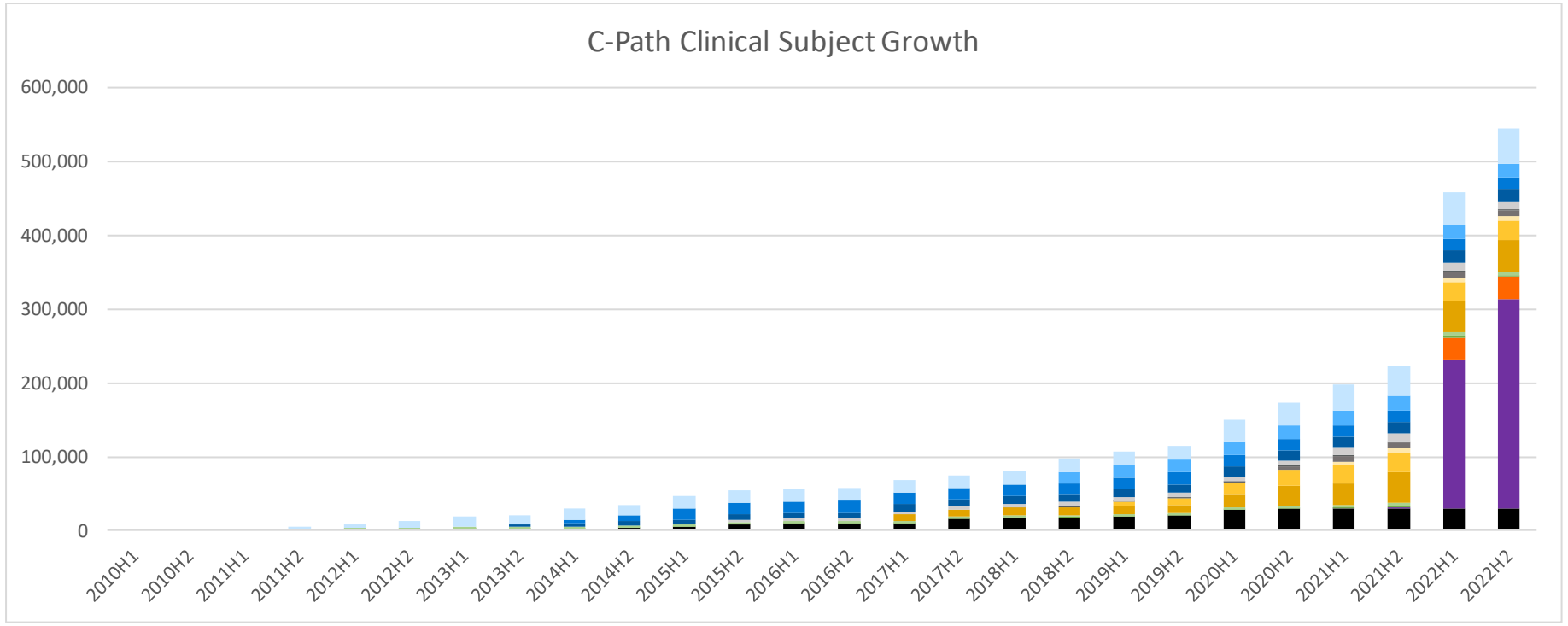


Clinical Data	
Studies	384
Subjects	**544,379**

Nonclinical Data	
Studies	148
Subjects	11,084

Neuro	
Alzheimer's Disease	46,821
Huntington's Disease	19,665
Multiple Sclerosis	15,626
Parkinson's Disease	15,702

Rare	
Duchenne's Muscular Dystrophy	11,442
Friedreich's Ataxia	1,572
Rare Diseases	8,196

IHP	
Sickle Cell Disease	6,240
Transplant Therapeutics	26,264
Type 1 Diabetes	42,581

TSSP	
Polycystic Kidney Disease	4,422
Safety Testing	2,276

CURE Drug Repurposing	29,618

Neonatal	283,565

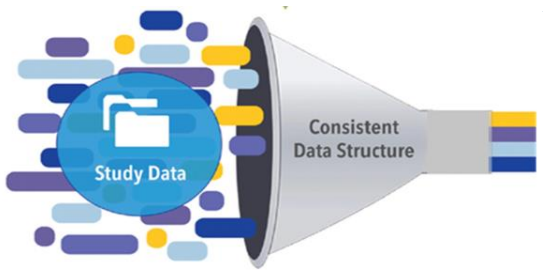
Tuberculosis	30,389

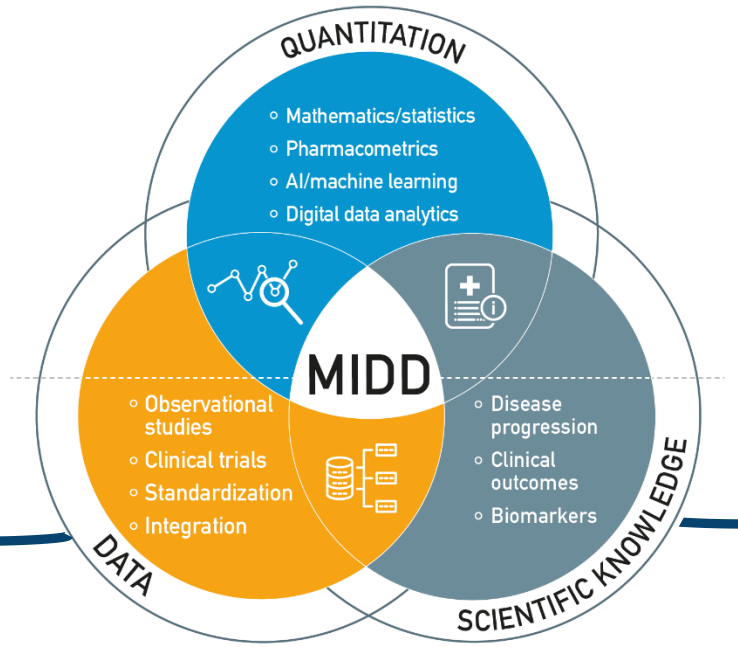
Note: Studies currently undergoing curation are only counted in Total Studies until evaluated.

C-Path Model Informed Drug Development

QUANTITATIVE MEDICINE

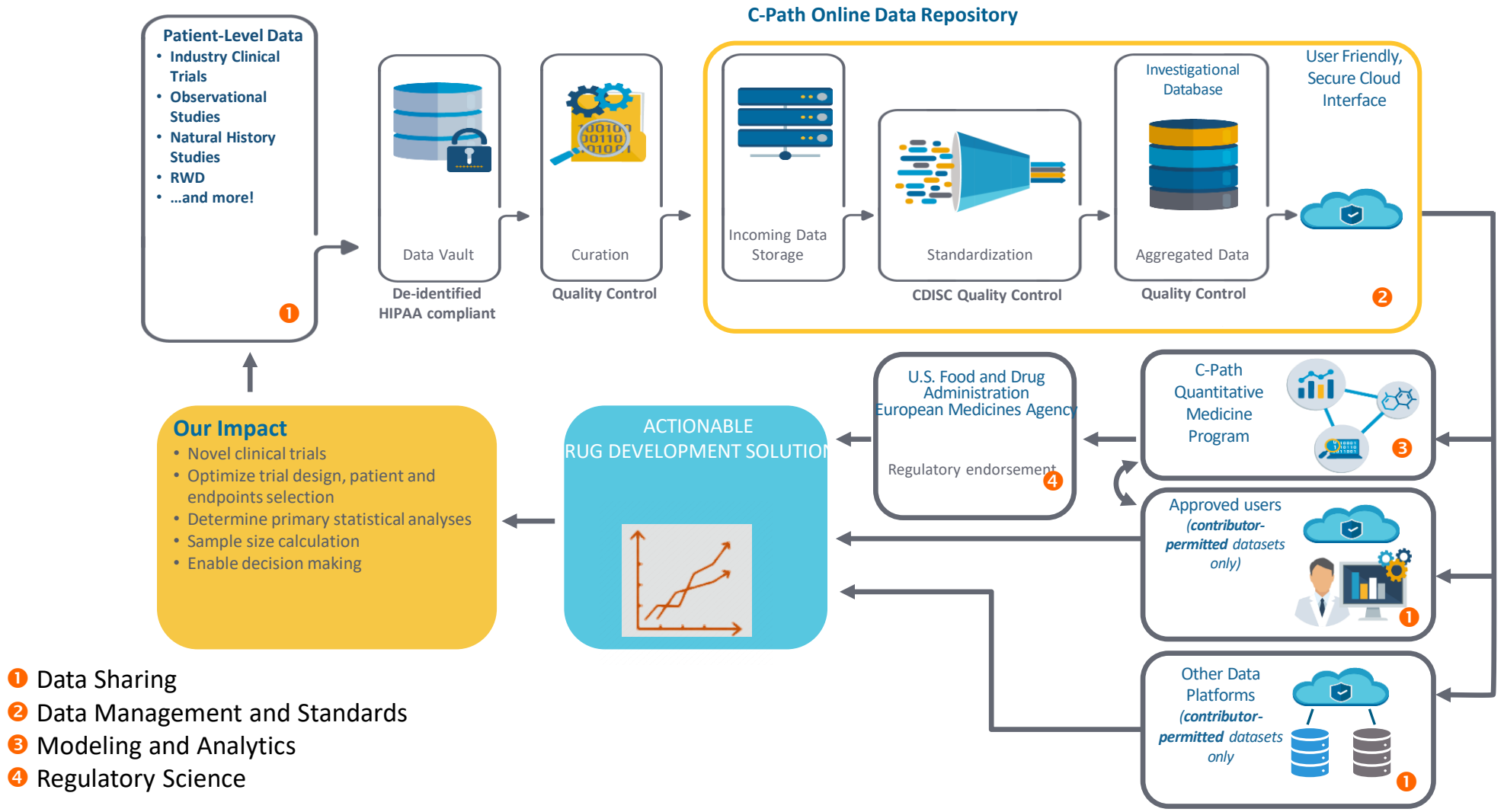
DATA COLLABORATION® CENTER





- **Alzheimer's disease**
- **Tuberculosis**
- **PKD**
- **Type 1 Diabetes**
- **Duchenne Muscular Dystrophy**
- **Kidney Transplantation**
- **Parkinson's disease**
- **Huntington's disease**

Drug Development Tools and Data Sharing



1. Data Sharing
2. Data Management and Standards
3. Modeling and Analytics
4. Regulatory Science

Definition of terms

Clarity is paramount

Data owner:

- ✓ The individual study participant is the only data owner,

Data custodian:

- ✓ The organization with which the data owner agrees to provide decision-making abilities

Data contributor:

- ✓ Typically, the data custodian, who shares patient-level data across parties

Data steward:

- ✓ The organization that receives the data contribution

Case Study #1

Barrier: Concerns about Protected Health Information and/or Sponsor Identification

How to prevent users from identifying:

- ✓ The individual's past, present, or future physical or mental health or condition,
- ✓ The provision of health care to the individual, or
- ✓ The past, present, or future provision of health care that identifies the individual or for which there is a reasonable basis to believe can be used to identify the individual.
- ✓ The study Sponsor's name, or
- ✓ The study's identifiers, or
- ✓ The active drugs evaluated in the study

Case Study #1: data anonymization

Solution: Development and application of best practices for data anonymization

Data anonymization for Protected Health Information:

- ✓ Provide the prospective data contributors with:
  - ✓ Clear description of applicable regulations (country and region-level)
  - ✓ Comprehensive guides on how to anonymize variables to reduce "distinguishability" to compliant levels with international/cross-border transfer considerations (for example, eliminate SSN and convert dates to timeframes)

Examples:

- ❑ C-Path: TB-Platform for Aggregation of Clinical Studies (TB-PACTS)
- ❑ Others: World Wide Antimalarial Resistance Network (WWARN)

Case Study #1: data anonymization

Solution: Development and application of best practices for data anonymization

For Sponsor Identification:

- ✓ Establish rules for anonymization of Sponsor's name, study's identifiers and drugs evaluated in active arms, through
- ✓ A process governed by comprehensive Data Contribution Agreements (discussed further in the next case study)

Examples:

- ❑ C-Path: Critical Path for Parkinson's Disease (CPP) Consortium Database
- ❑ Others: European Medical Information Framework (EMIF)

Case Study #2: Data Accessibility

Barrier: Concerns about accessibility, transportability and redistribution

How to ensure:

- ✓ Which parties will have access to:
  - ✓ Full data (active and control arms, extension periods, etc.)
  - ✓ Portions of the data (only control arms, only specific periods, etc.)

- ✓ Adequately answering these questions if data are to be made “publicly available”:
  - ✓ Which users can access the data?
  - ✓ Can users transport the data or only execute remote views?
  - ✓ Can the data be redistributed by “qualified researchers”?

Case Study #2: Data Accessibility

Solution (Part 1): Implementation of “Data Contribution Agreements” (DCAs) as legal documents to govern the data-sharing process

Definition of level of sharing:

- ✓ DCA provides full flexibility to contributor to define:
  - ✓ Which parties get to see which portions or the totality of data (active and control arms, versus control arms only), varying from:
    - ✓ All potential users
    - ✓ Only certain parties/organizations
    - ✓ Only single party/organization
  - ✓ Moratoria on level of sharing, varying from:
    - ✓ Only after a specific regulatory decision that is tied to the specific data is reached (drug approval, for example)
    - ✓ Only the primary analysis are concluded or published
    - ✓ Only after a fixed date

Case Study #2: Data Accessibility

Solution (Part 1): Implementation of "Data Contribution Agreements" (DCAs) as legal documents to govern the data-sharing process

Examples:

- C-Path:
  - C-Path Online Data Repository of Phase II Clinical Trials in TB
  - Duchenne Muscular Dystrophy Aggregated Clinical Trial Database
- Others:
  - European Prevention of Alzheimer's Disease Consortium
  - Biomarker Enterprise to Attack Diabetic Kidney Disease

Case Study #2: Data Accessibility

Solution (Part 2): Definition of Terms and Conditions, and Implementation of "Data Use Agreements" (DUAs)

The access request, governance and DUA execution help define:

- ✓ Which users can access the data?
  - ✓ Adequately define the criteria for determining who can be a "qualified researcher"
  - ✓ Establish and communicate a clear access request and review process
- ✓ Can users transport the data or only execute remote views?
  - ✓ Perform a comprehensive analysis of advantages of each approach, in light of objective of the data sharing effort (further research versus tangible regulatory purposes).
- ✓ Can the data be redistributed by "qualified researchers"?
  - ✓ Redistribution should generally be avoided, and provisions should be defined through specific DUA language, as well as through the acknowledgment, agreement and adherence to the terms and conditions.

Case Study #2: Data Accessibility

Solution (Part 2): Definition of Terms and Conditions, and Implementation of "Data Use Agreements" (DUAs)

Examples:

- C-Path:
  - Relational Sequencing TB Data Platform (ReSeqTB)
  - Multiple Sclerosis Outcome Assessments Consortium (MSOAC) Placebo Database

- Others:
  - The Global Alzheimer's Association Interactive Network (GAAIN)
  - Parkinson's Progression Markers Initiative (PPMI)

… To Reiterate: Key Challenges

- Proper and balanced IRB consent
- Concerns about competitive advantage
- Fear of data misuse
- Controlling scope of disclosure
- Ensuring proper level of anonymization
- Understanding privacy regulations
- Dynamic legal and regulatory requirements for different jurisdictions

Data Contribution Agreement

DATA CONTRIBUTIONS VIA FORMAL DATA CONTRIBUTION AGREEMENT

Verification that the contributor is the owner of all data and is authorized to share with C-Path

A non-confidential description of the data being contributed (meta-data)

Verification of Informed Consent review to allow sharing of data for secondary research as defined by regulations that govern in the location where the data are being held by the contributor

Confirmation that the data being contributed are anonymized to the level appropriate for the contributing entity

Defined scope of disclosure that is being permitted by the contributor

Acknowledgement and understanding that C-Path will handle data with appropriate safeguards and security

Appendices that provide registry information, detailed definitions of terms, and a full description of anonymization requirements

Terms & Conditions

DATA PROTECTION VIA USER TERMS & CONDITONS

All users must electronically review and sign the Terms and Conditions for Use before they submit an application for access to data, and again when they first log into the data platform

- Will not attempt to re-identify subjects
- Will not use or disclose data beyond purposes described in application
- Will use appropriate safeguards to protect data from misuse
- Will report breaches and other misuse of data
- Will not patent IP generated by use of data
- Will cite the data platform/project/consortia as source of data in any publications developed using data
- Will abide by terms and restrictions governing publications developed using data
- Will indemnify and hold consortium members/contributors/C-Path free of liability