Clinical Data Neutrality: its Role in Transforming Data into Solutions

Transforming data into actionable knowledge for drug development

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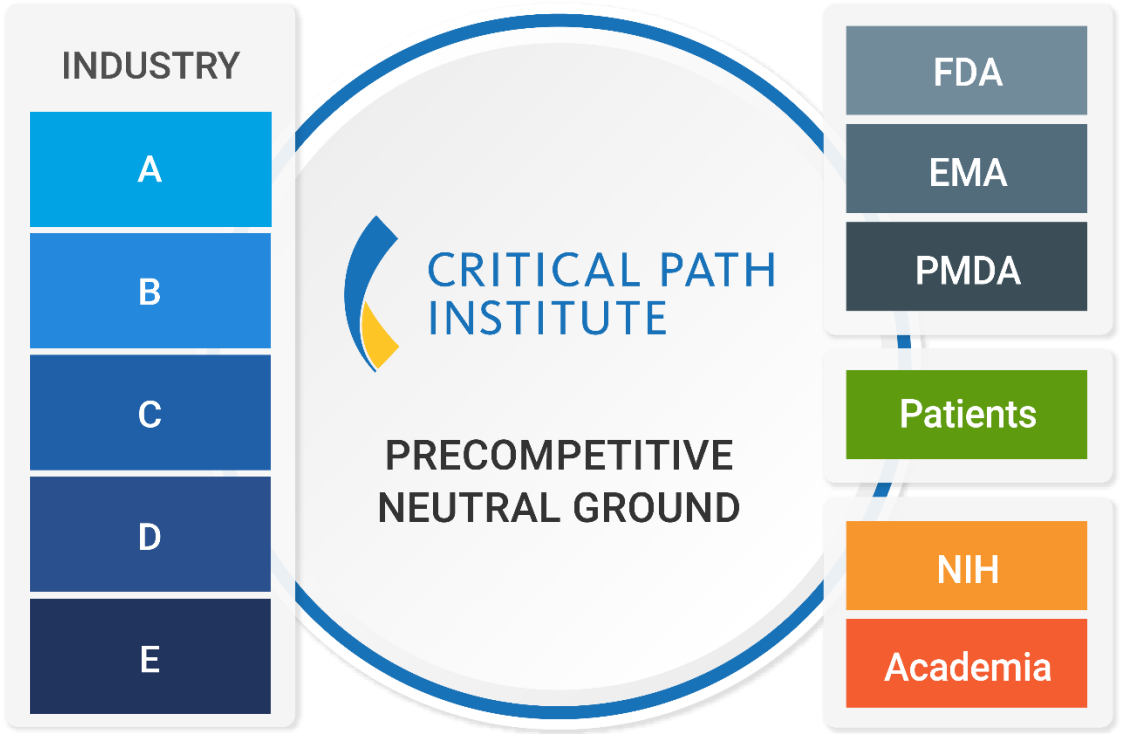
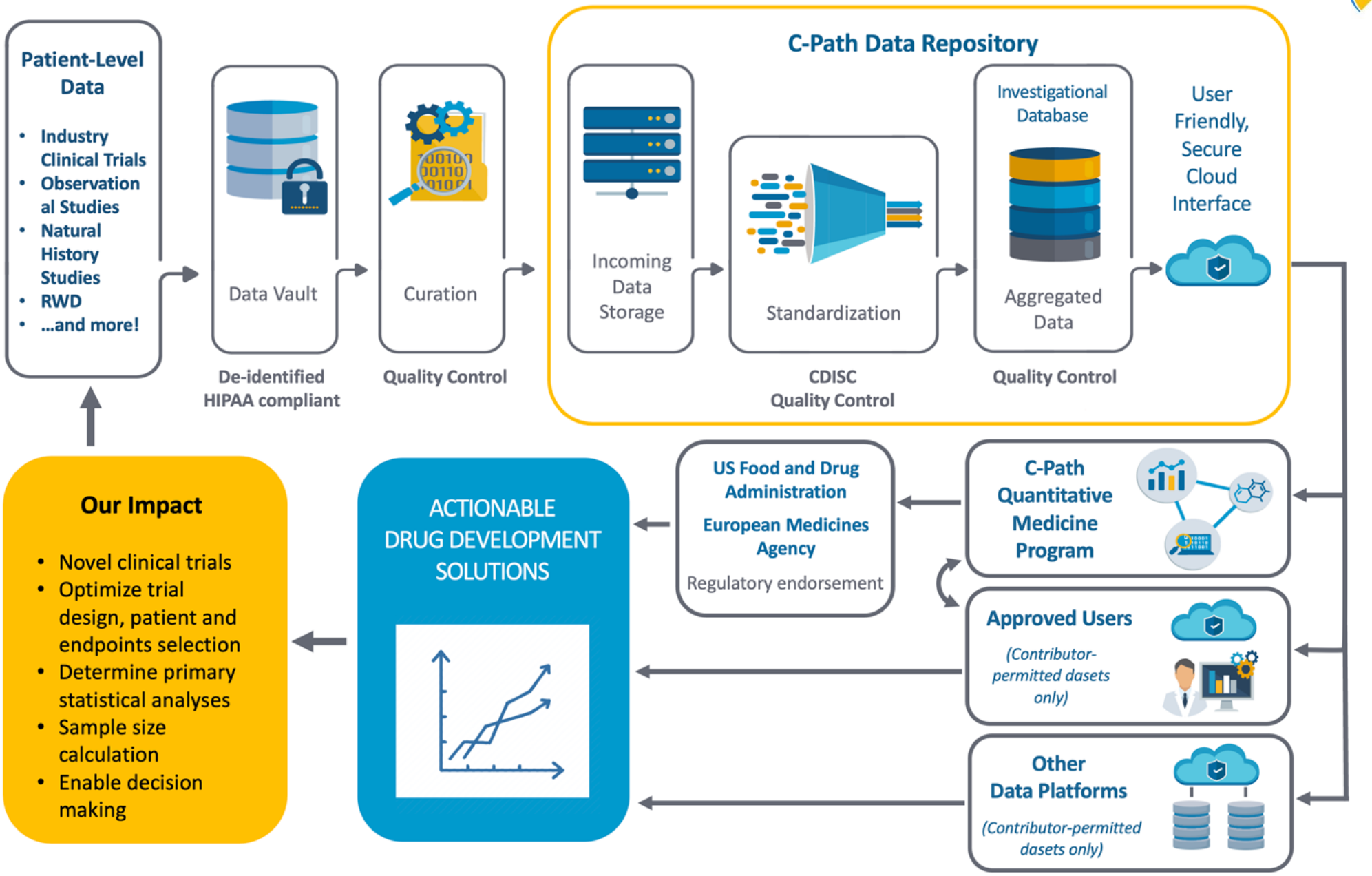
The Critical Path Institute: A Neutral Party

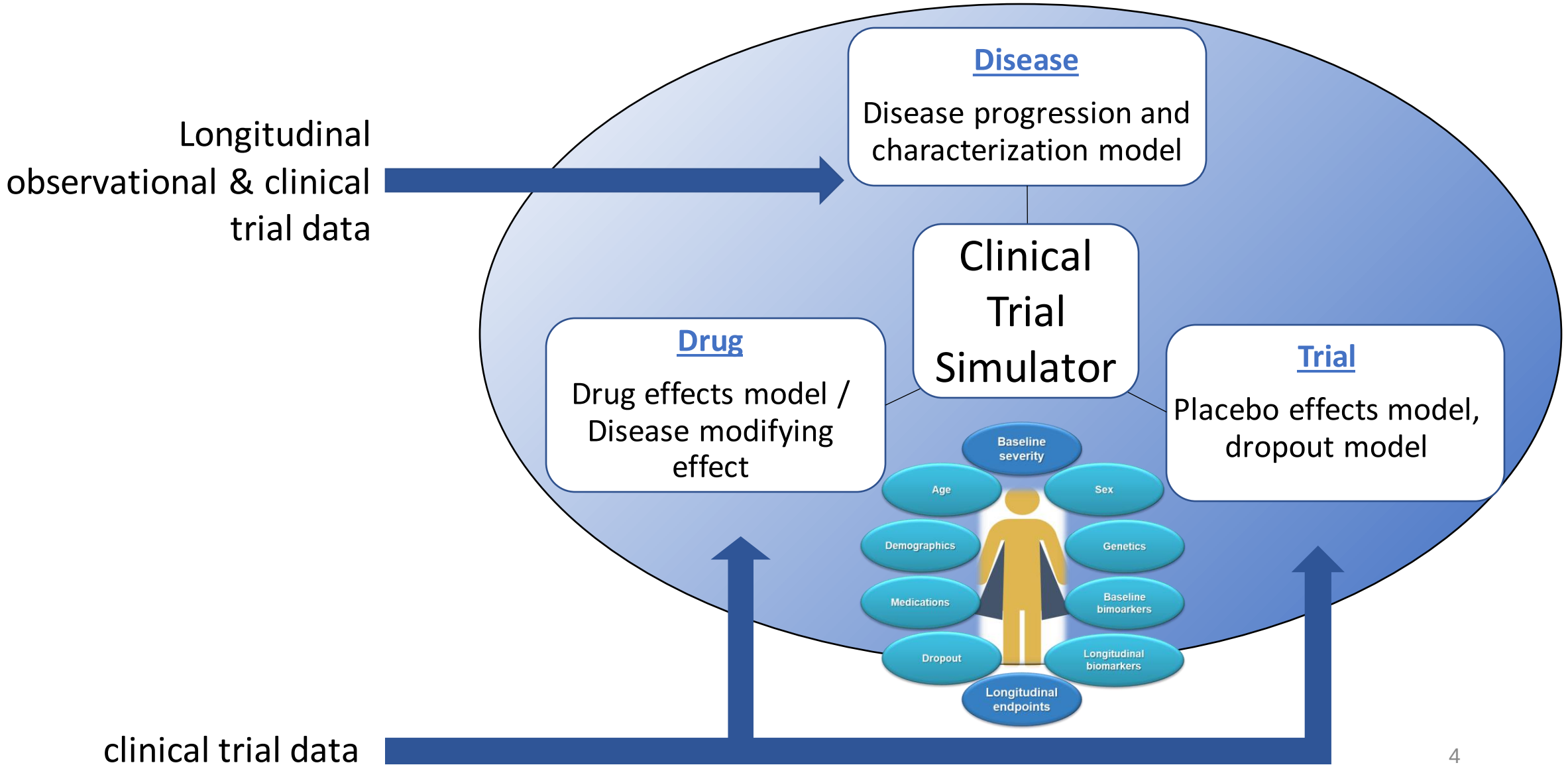
- Public-Private Partnerships (PPP)
- Convene scientific consortia of industry, academia, and government for sharing of data/expertise
  - ✓ The best science
  - ✓ The broadest experience
  - ✓ Active consensus building
- Enable iterative EMA/FDA/PMDA participation in developing new methods to assess the safety and efficacy of medical products
- Official regulatory endorsement of novel methodologies and drug development tools



Collaboration Contributed to a Transformation



Example: drug-disease-trial modeling



Alzheimer's Disease

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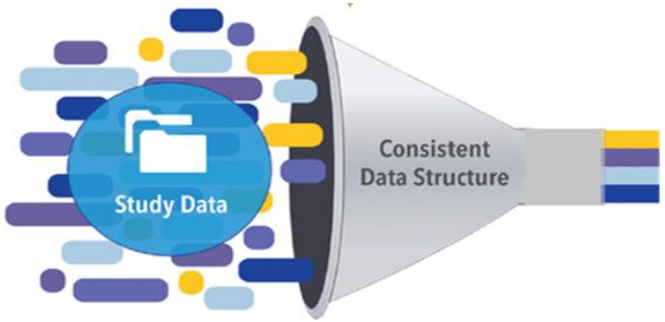

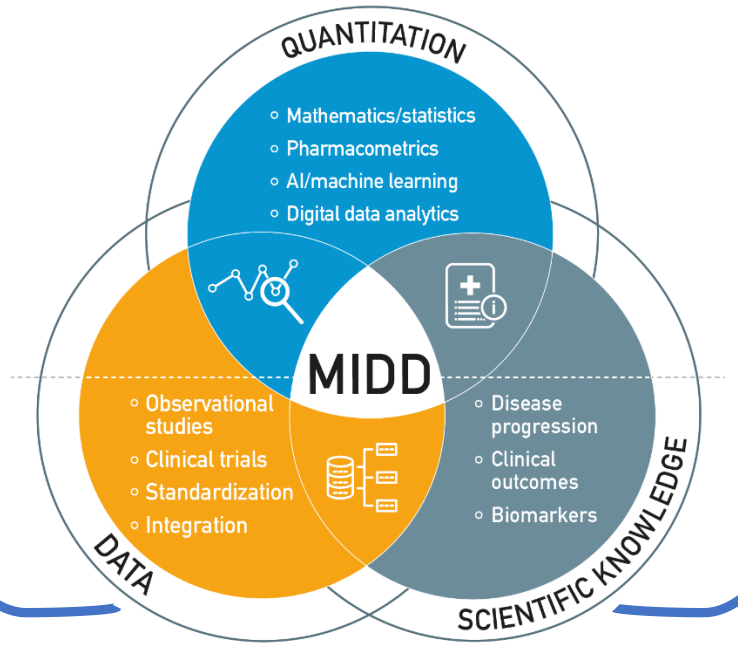

CPAD
CRITICAL PATH FOR ALZHEIMER'S DISEASE

First Regulatory Endorsement of a Quantitative Drug Development tool

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Drug Development Tools: Fit-for-Purpose Initiative

2013 FDA endorsement decision:

- Clinical trial simulations relying on this model can provide support for the choice of trial design features and can facilitate protocol review by Center for Drug Evaluation and Research (CDER) staff. End-of-Phase 2A meeting requests can be supported through the use of trial simulations based on this model or a modified version when clearly described.

There was a need to go earlier into the disease continuum

Letter of support for Model-based CT enrichment tool for CTs in aMCI

2018 EMA Letter of Support decision:

- The EMA supports the primary objectives of the applicant and has decided to issue a Letter of Support to the CPAD Consortium, while also encouraging the CPAD team to disseminate and provide access to the current version of the model for implementation by sponsors actively designing clinical trials in amnesic mild cognitive impairment (aMCI).

Incorporating Lessons From the Pandemic

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CPAD
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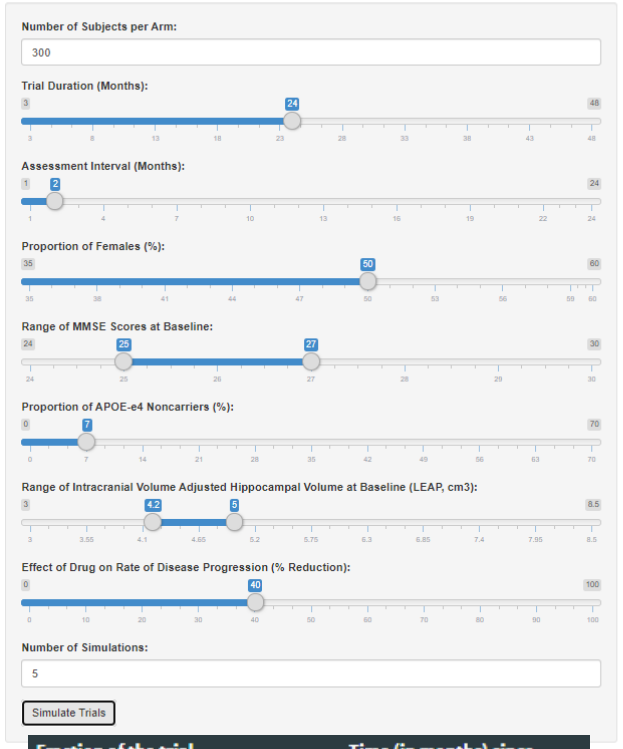
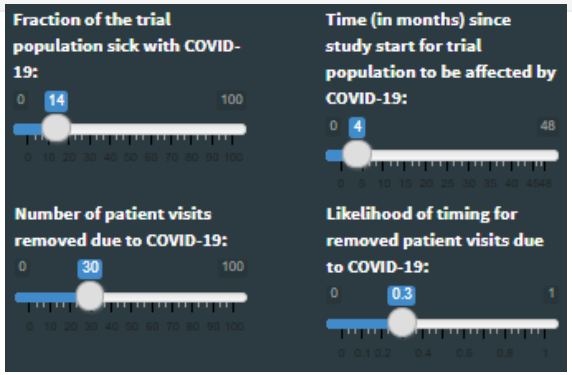
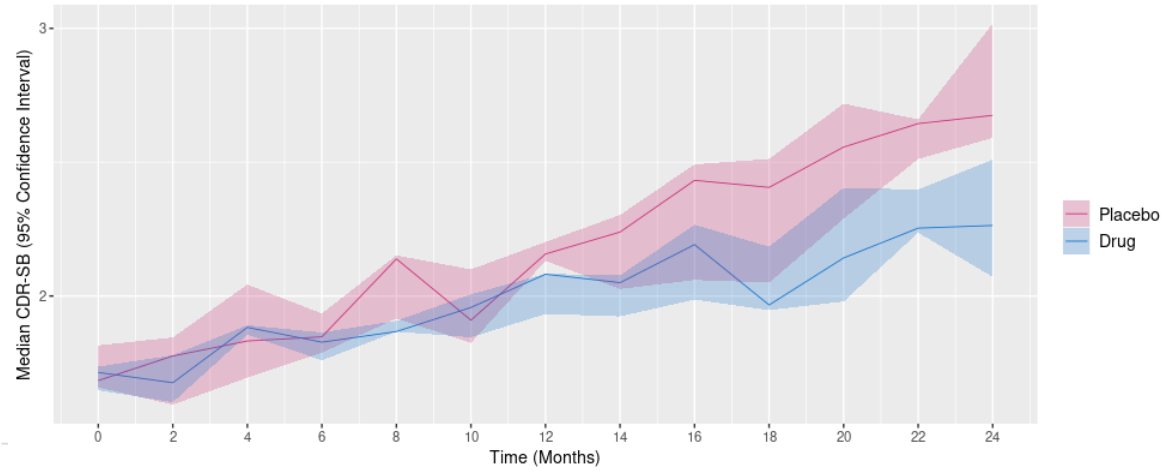
Hippocampal Neuroimaging-Informed Amnestic MCI Clinical Trial Simulator

Simulate clinical trials on patients with amnestic mild cognitive impairment







Total Number of Subjects	600
Study Duration (Months)	24
Assessment Interval (Months)	2
Effect of Drug on Rate of Disease Progression (% Reduction)	40
Proportion of Female (%)	50
Range of MMSE Scores at Baseline	[25, 27]
Proportion of APOE-e4 Noncarrier (%)	7
Range of Intracranial Volume Adjusted Hippocampal Volume at Baseline (cm3)	[4.2, 5]
Median Age at Baseline (95% Confidence Interval) (Years)	74 (74, 74)
Median MMSE Score at Baseline (95% Confidence Interval) (Points)	26 (26, 26)
Median Intracranial Volume Adjusted Hippocampal Volume at Baseline (95% Confidence Interval) (cm3)	4.7 (4.7, 4.7)
Number of Simulations	5
Monte-Carlo Standard Error for Calculation of Confidence Interval for Statistical Power (%)	0
Statistical Power (%, 95% Confidence Interval)	100 (47.8, 100)

From data, to solutions, to impact

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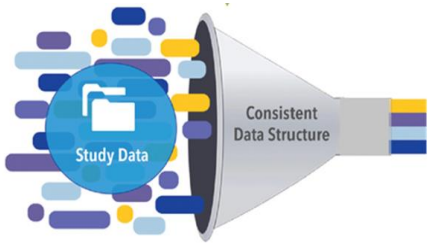

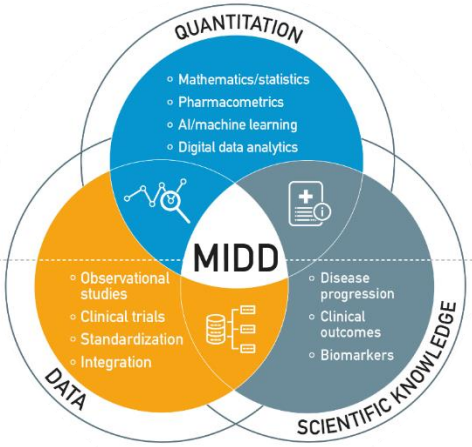

Indication	Solutions	Impact
Alzheimer's disease	2CTS tools, 2 biomarkers	First 2 disease-modifying drugs
Tuberculosis	Multiple quantitative tools	First new drug and drug regimen
PKD	PKD	First disease-modifying drug
Type 1 Diabetes	Model-based biomarkers	First prevention drug
Duchenne Muscular Dystrophy	5 disease progression models	Transformed trial design paradigm
Kidney Transplantation	Composite biomarker endpoint	Transformed trial design paradigm
Parkinson's disease	3 CTS tools, 1 biomarker, multiple DHT solutions	Transformed trial design paradigm
Huntington's disease	Staging system, 3 disease progression models	Transformed trial design paradigm

Thank you!

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Improving Lives.

Together.

Back up slides

C-Path's Active Programs

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Active Consortia/Programs

BmDR	Biomarker Data Repository	**DCC**	Data Collaboration Center	**PSTC**	Predictive Safety Testing Consortium
CDRC	Cure Drug Repurposing Collaboratory	**D-RSC**	Duchenne Regulatory Science Consortium	**QuantMed**	Quantitative Medicine
CPA-1	Critical Path for Alpha-1 antitrypsin deficiency (pre-consortium)**	**eCOA Consortium**	Electronic Clinical Outcome Assessment Consortium	**RDCA-DAP**	Rare Disease Cures Accelerator- Data and Analytics Platform
CPAD	Critical Path for Alzheimer's Disease	**ERA4TB**	European Regimen Accelerator for Tuberculosis*	**RD-COAC**	Rare Disease Clinical Outcome Assessment Consortium
CPLD	Critical Path for Lysosomal Disorders (pre-consortium)**	**HD-RSC**	Huntington's Disease Regulatory Science Consortium	**T1D**	Type 1 Diabetes Consortium
CPP	Critical Path for Parkinson's Disease	**INC**	International Neonatal Consortium	**TOMI-T1D**	Trial Outcome Markers Initiative in T1D Consortium
CPTA	Critical Path to Therapeutics for the Ataxias	**MSOAC**	Multiple Sclerosis Outcome Assessment Consortium	**TRxA**	Translational Therapeutics Accelerator
CP-SCD	Critical Path for Sickle Cell Disease	**PKDOC**	Polycystic Kidney Disease Outcomes Consortium	**TTC**	Transplant Therapeutics Consortium
CPTR	Critical Path to TB Drug Regimens	**PredicTox KE**	PredicTox Knowledge Environment	**UNITE4TB**	Worldwide Accelerator for Tuberculosis*
CP-RND	Critical Path for Rare Neurodegenerative Diseases	**PRO Consortium**	Patient-Reported Outcome Consortium		

****Pre-Consortia** *** C-Path Europe**