Data Reuse: Navigating the Regulatory Environment

Klaus Romero
Chief Executive Officer, Chief Science Officer,
Critical Path Institute

Virginia Nido
Global Head, Product Development Industry Collaborations,
Roche, Co-Founder, **CRDSA**

Welcome

Keynote

The Intersection of Data Sharing and Equitable Healthcare: Challenges and Opportunities

Innovative Trial Design: Data Reuse Opportunities and Regulatory Considerations

CRDSA
Clinical Research Data Sharing Alliance









Advancing Drug Development.

Improving Lives.

Together.

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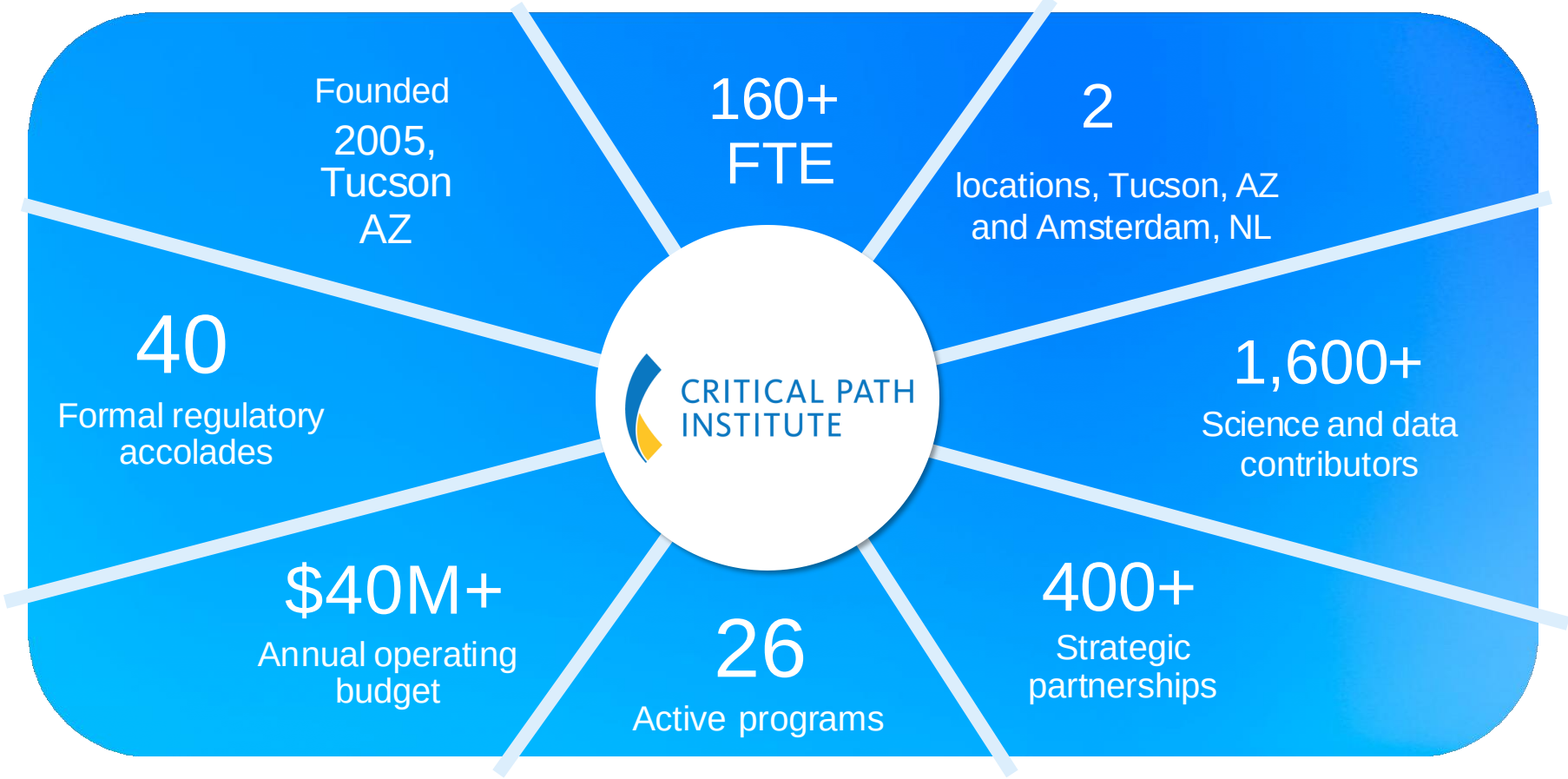
C-Path's Mission:

C-Path leads collaborations that accelerate drug development, advancing better treatments for people worldwide.


Founded
2005,
Tucson
AZ
160+
FTE
2
locations, Tucson, AZ
and Amsterdam, NL
40
Formal regulatory
accolades
CRITICAL PATH
INSTITUTE
1,600+
Science and data
contributors
$40M+
Annual operating
budget
26
Active programs
400+
Strategic
partnerships

Driven, Resilient Leadership with Deep Expertise

Klaus Romero, MD, MS
Chief Executive Officer

Kristen Swingle, MS
President, Chief Operating Officer

Rick Liwski
Chief Technology Officer,
Director, Data Collaboration Center

Cheryl D. Coon, PhD
Vice President, Clinical Outcome Assessment Program

Collin Hovinga, PharmD, MS, FCCP
Vice President, Rare and Orphan Disease Programs

Shu Chin Ma, MSc, M.Phil, PhD, EMBA
Vice President, Model-Informed Drug Development, Quantitative Medicine

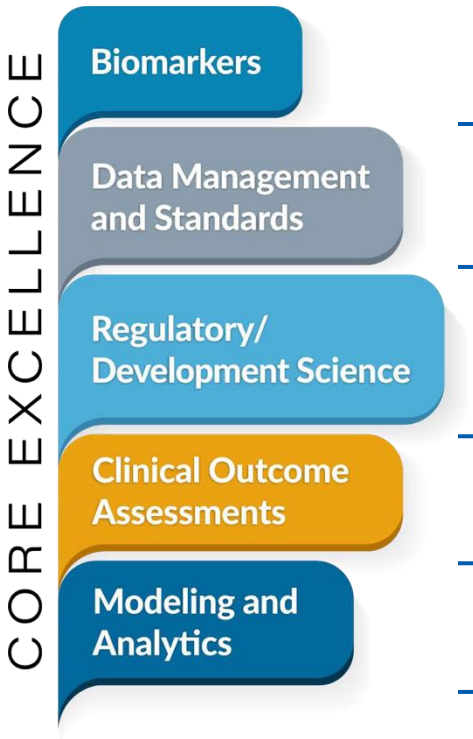
Cécile Ollivier, MS
Vice President,
Global Affairs

Diane Stephenson, PhD
Vice President,
Neurology

Jennifer Kendra
Vice President,
Strategic Relationships

C-Path's Core Excellence

CRITICAL PATH INSTITUTE 20 YEARS



Biomarkers	Identifying and validating biomarkers to enhance drug development efficiency.
Data Management and Standards	Developing and implementing cutting-edge data management practices and universal standards.
Regulatory/ Development Science	Advancing the field of regulatory science to streamline the review and approval processes.
Clinical Outcome Assessments	Crafting and refining tools for accurate and meaningful measurement of clinical benefit.
Modeling and Analytics	Generating state-of-the-art quantitative solutions for optimized predictions and evaluations.

C-Path's Public-Private Partnership Model

- Patient Groups
- Regulators
- Academia
- WHO
- NIH
- ICH
- Industry Partners

Active consensus building

Shared risk and costs

Collaborative expertise for the best science

1. **Develop of New Evaluation Tools**
   Inform drug development and regulatory decision-making
2. **Scientific Consortia**
   Convene industry, academia, and government for sharing of data, networks, and expertise
3. **Regulatory Participation**
   Enable iterative EMA/FDA/PMDA participation in developing new methods
4. **Regulatory Endorsement**
   Obtain official regulatory endorsement of novel drug development methodologies and research tools

Decreasing the Burden of Disease

CRITICAL PATH INSTITUTE 20 YEARS

UNMET MEDICAL NEED

DDTs and Other Solutions

C-Path expedites treatment in people of all ages, including both rare and non-rare conditions.

- Alpha-1 Antitrypsin Deficiency
- Alzheimer's Disease
- Amyotrophic Lateral Sclerosis
- Asthma
- Crohn's Disease
- Chronic Heart Failure
- Depression
- Duchenne Muscular Dystrophy
- Friedreich's Ataxia
- Functional Dyspepsia
- Huntington's Disease
- Irritable Bowel Syndrome
- Kidney Transplant
- Lysosomal Diseases
- Multiple Sclerosis
- Myelofibrosis
- Neonatal Conditions of Prematurity
- Non-small Cell Lung Cancer
- Parkinson's Disease
- Polycystic Kidney Disease
- Progressive Supranuclear Palsy
- Rheumatoid Arthritis
- Sickle Cell Disease
- Small Cell Lung Cancer
- Spinocerebellar Ataxia
- Tuberculosis and other infectious diseases
- Type 1 Diabetes

The Solution: C-Path Removes the Bottlenecks

Forge diverse collaborations to identify hurdles

- Industry & research scientists
- Regulatory agencies
- Patient and patient advocacy groups
- Industry leaders
- Donors and philanthropic community

Craft tools and solutions

Achieve regulatory success

FDA

- 8 Qualifications Decisions
- 11 Letters of Support
- 1 Fit for Purpose endorsement

EMA

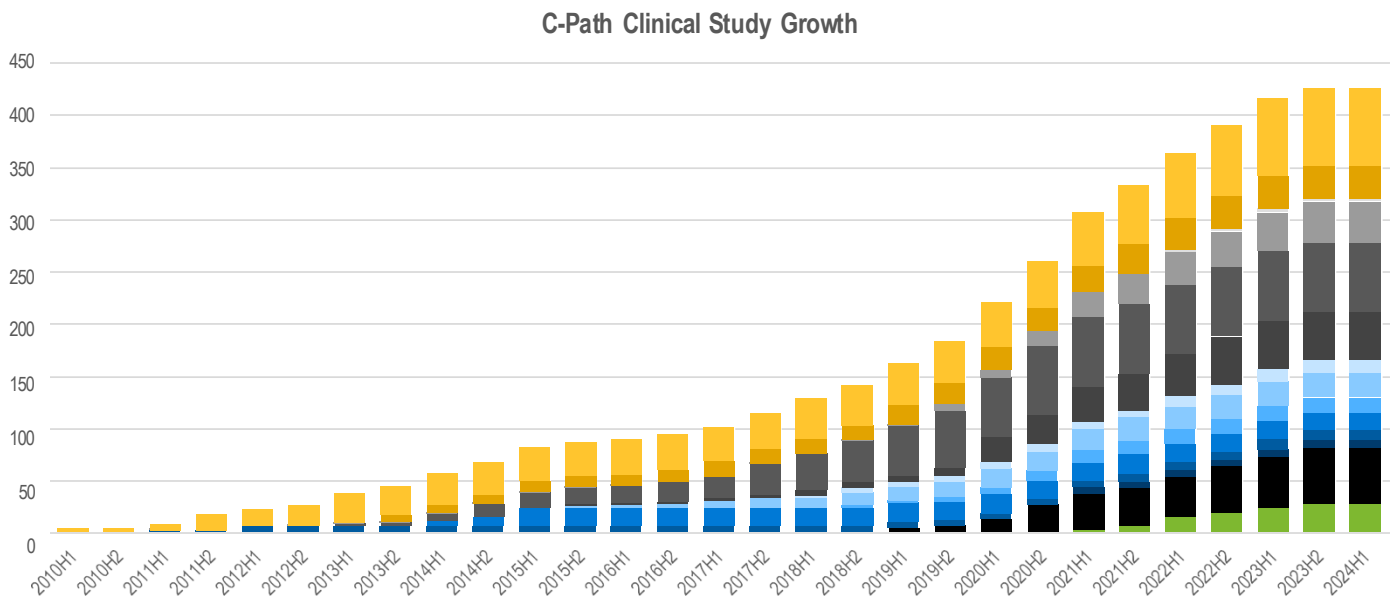
- 9 Qualification Opinions
- 10 Letters of Support

PMDA

- 1 Qualification Decision

Clinical Impact

Data Contributors Trust C-Path



Clinical Data	
Studies	**425**
Individuals	694,401

Non-clinical Data	
Studies	153
Subjects	13,190

Neurology	
Alzheimer's Disease	75
Parkinson's Disease	31

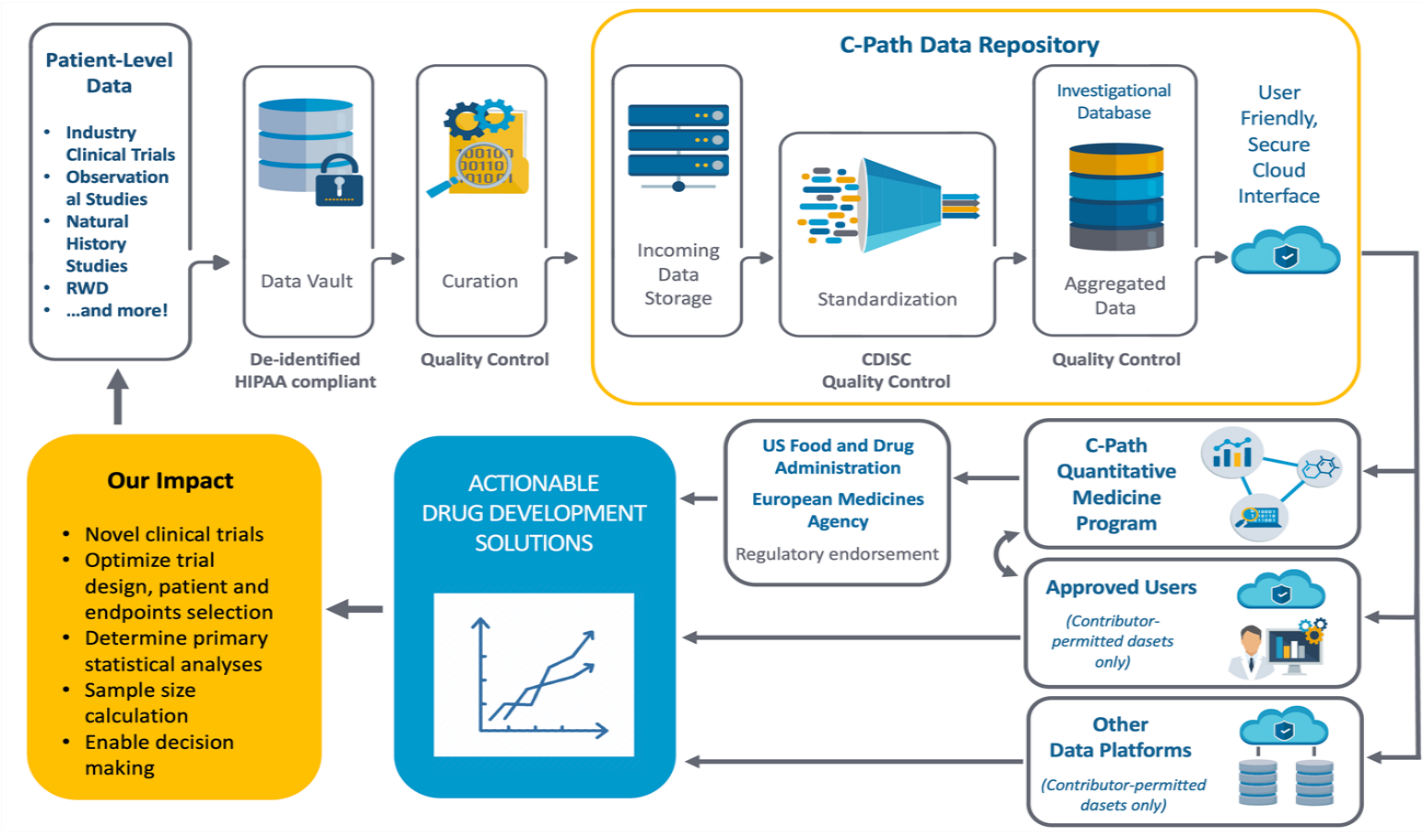
Public Health	
COVID-19	3
Safety	38
Tuberculosis	67
Type 1 Diabetes	46

Rare/Orphan			
Ataxias	12	Multiple Sclerosis	18
Duchenne's Muscular Dystrophy	24	Polycystic Kidney Disease	9
Huntington's Disease	13	Sickle Cell Disease	8
		Other Rare Diseases	53

Neonatal	28

*as of Jan 22, 2025
"Subjects" represents a combination of human, animal, device, and cell line data

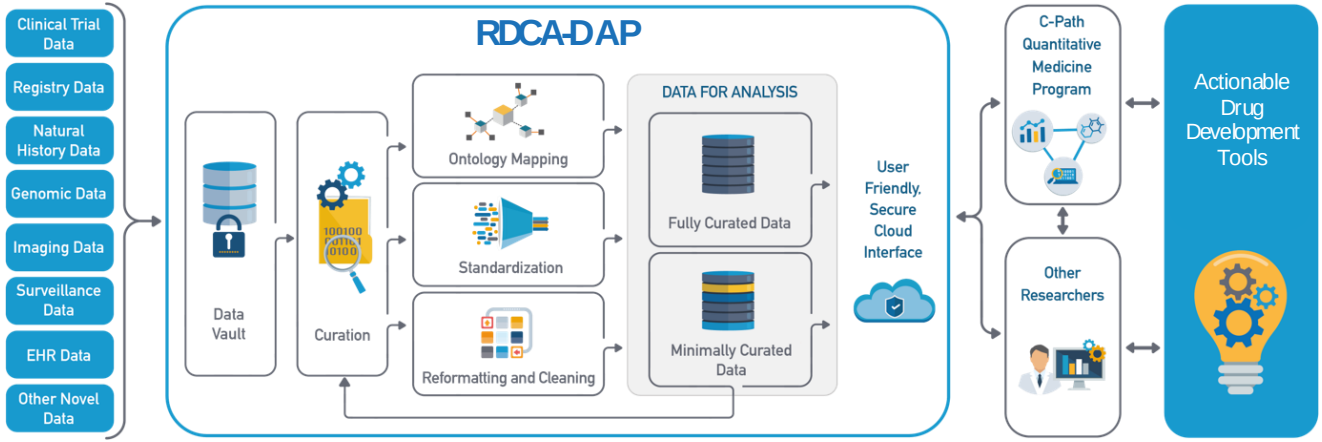
From Data to Actionable Knowledge



Clinical Impact

Indication	C-Path's Solution	Clinical Impact
Alzheimer's disease	2 Clinical Trial Simulation (CTS) Tools, 2 biomarkers	First disease-modifying drugs
Tuberculosis	Multiple quantitative tools	First new drug and drug regimen
Polycystic Kidney Disease	CTS Tool and model-based imaging biomarker	First disease-modifying drug
Type 1 Diabetes	Model-based biomarkers	First prevention drug
Irritable Bowel Syndrome with constipation	PRO measure of symptom severity	Label expansion for symptomatic drug
Friedrich's ataxia	Data & Analytics Platform to support generation of external controls	First disease-modifying drug
Duchenne Muscular Dystrophy	5 disease progression models, 3 CTS tools, 1 biomarker	First non-steroidal treatment for all variants
Kidney Transplantation	Composite biomarker endpoint	Accelerated treatment options with improved drug tools and trial strategies for faster clinical development
Parkinson's disease	3 CTS tools, 1 biomarker, multiple DHT solutions	
Huntington's disease	Staging system, 3 disease progression models	

Totality of Evidence: Impacting FA Patients



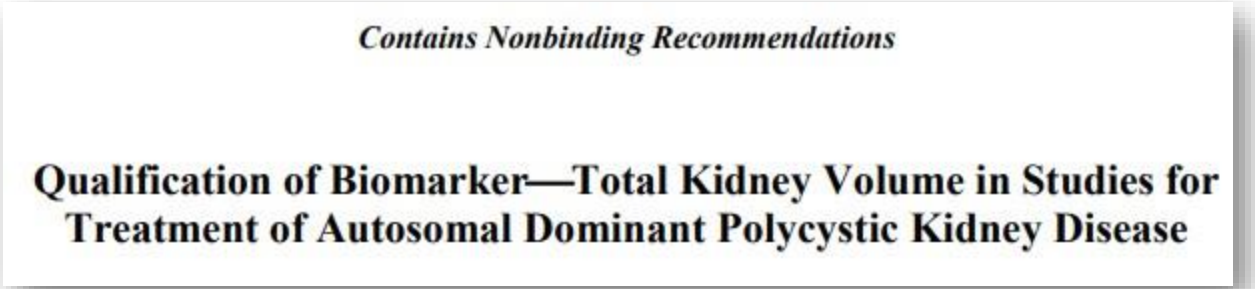
Friedreich's Ataxia aggregated database
Standardized & Accessible to Industry

Database exploration, FA-COMS study selection:
Propensity match analysis to support MOXIe open-label extension trial

First drug approved for FA

"The data collected in the natural history study were critical to showing the drug's benefit"
(Reata CEO J. Warren Huff in "FDA Widens Path for Rare-Disease Treatments With New Approval," WSJ, March 1st 2023)

First Regulatory Qualification of an Orphan Disease Biomarker

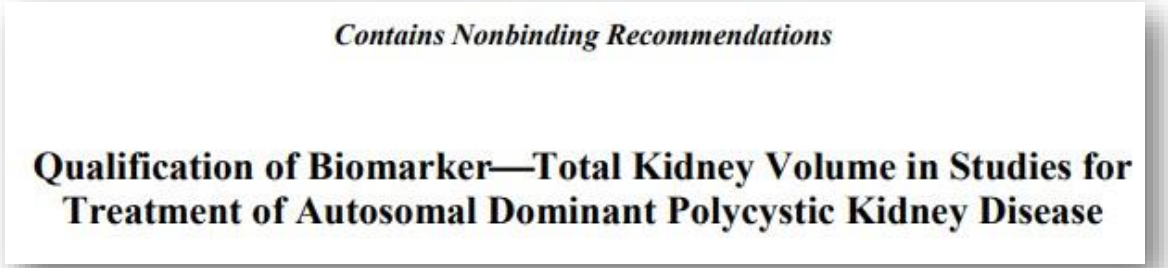


Contains Nonbinding Recommendations

Qualification of Biomarker—Total Kidney Volume in Studies for Treatment of Autosomal Dominant Polycystic Kidney Disease

- FDA qualification decision:
- Baseline TKV is a prognostic enrichment biomarker to select patients with ADPKD at high risk for a progressive decline in renal function (defined as a confirmed 30% decline in the patient's eGFR), for inclusion in interventional clinical trials.

This Was a **Model-Based** Qualification



Contains Nonbinding Recommendations

Qualification of Biomarker—Total Kidney Volume in Studies for Treatment of Autosomal Dominant Polycystic Kidney Disease

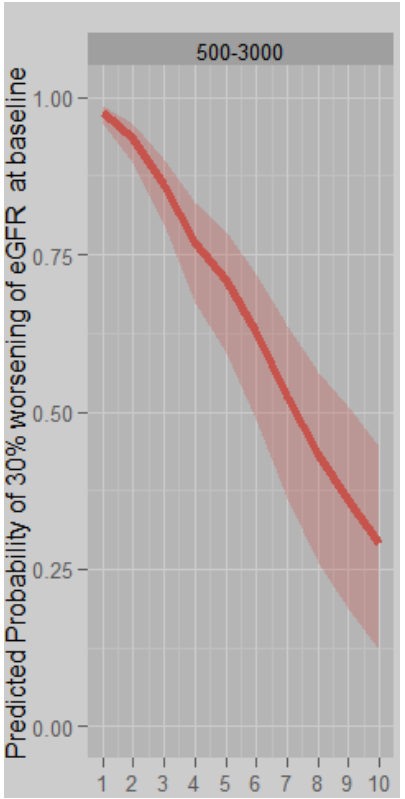
Underlying evidence for the regulatory qualification of TKV as a prognostic biomarker:

- Joint model:
  - TKV progression model (continuous model endpoint over time)
  - Survival model (time-varying probability of reaching a 30% decline in eGFR)
  - Including covariates such as baseline eGFR and age

Actionable application

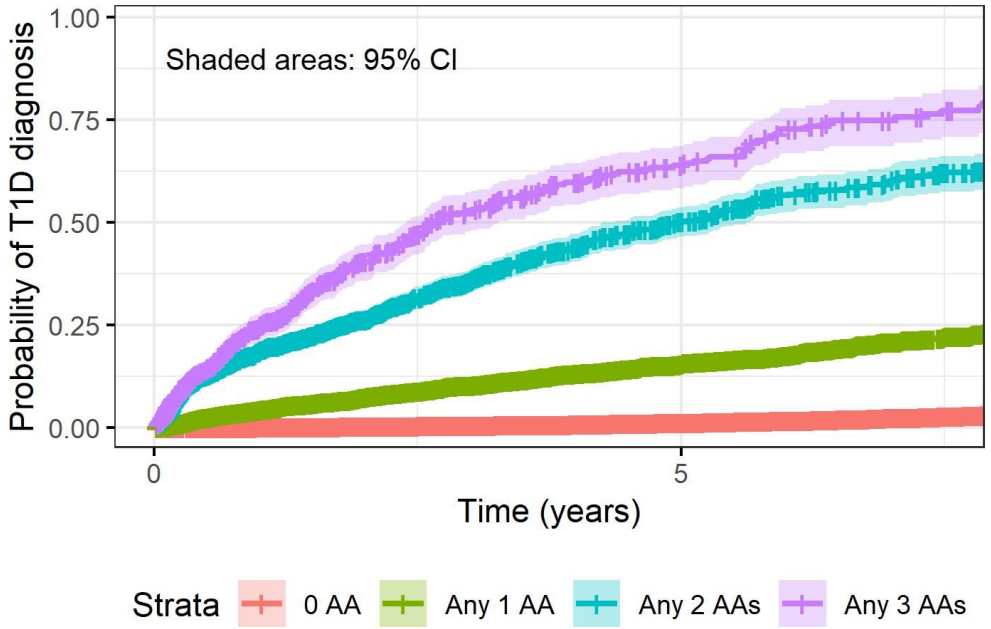
- Joint model:
  - TKV progression model (continuous model endpoint over time)
  - Survival model (time-varying probability of reaching a 30% decline in eGFR)
  - Including covariates such as baseline eGFR and age

Age	TKV	Follow-Up Period	1-Probability of 30% Worsening of eGFR		
			Median	Lower	Upper
Baseline age=30yrs	Baseline TKV 1.7L	1	0.98	0.96	0.99
		2	0.93	0.90	0.96
		3	**0.86**	0.80	0.90
		4	0.77	0.67	0.83
		5	0.71	0.59	0.79
		6	0.63	0.49	0.72
		7	0.52	0.36	0.64
		8	0.43	0.26	0.56
		9	0.36	0.19	0.51
		10	0.29	0.12	0.45

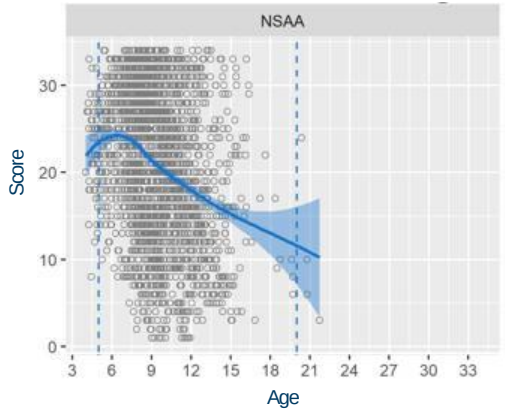


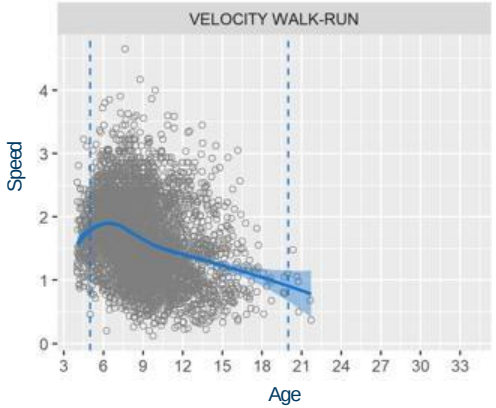
Application in T1D prevention

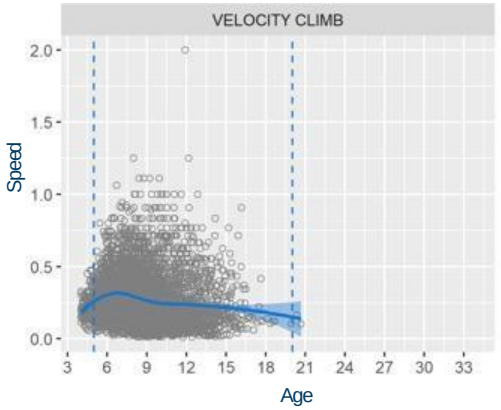
- Survival model to predict T1D diagnosis, based on islet AA positivity.
- The model will change the landscape for RCTs for T1D prevention.

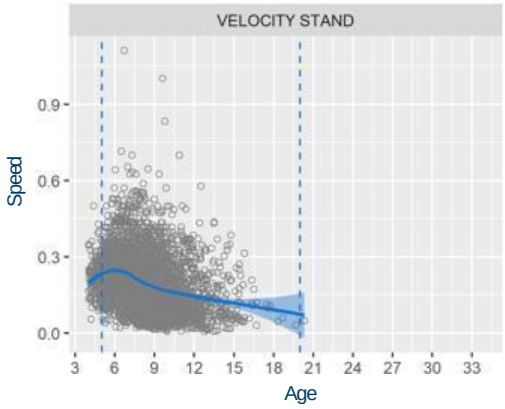


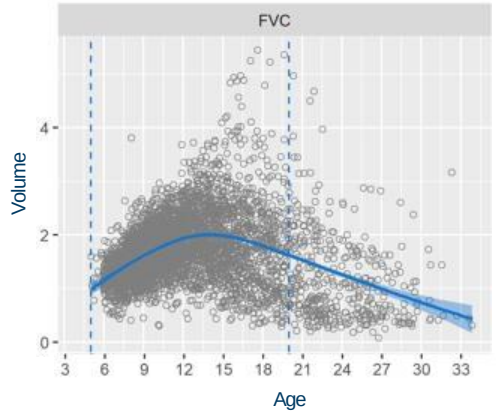
Application in Duchenne muscular dystrophy











Multiple endpoints over time in Duchenne Muscular Dystrophy (DMD).

CRITICAL PATH INSTITUTE 20 YEARS OF IMPACT

Help us advance better treatments for people worldwide.

C-Path is ready to explore meaningful partnerships that can benefit your area of focus in drug development.

Together, we can collaborate to drive innovation and shape the future of healthcare.

c-path.org

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Advancing Drug Development.
Improving Lives. Together.

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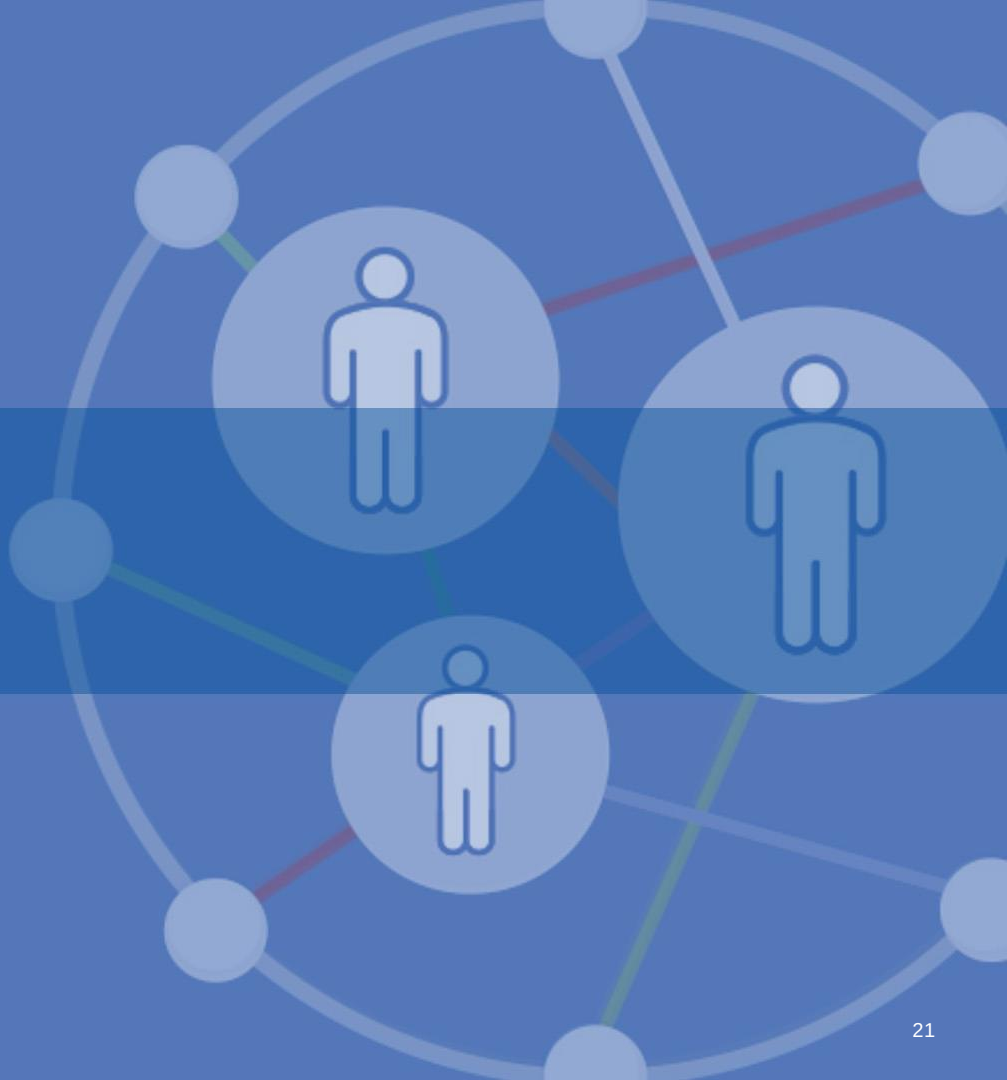
Q&A



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The Intersection of Data Sharing and Equitable Healthcare: Challenges and Opportunities

Pierre Theodore
Head Patient Inclusion and Health Equity, **Genentech**

D&I Diversity & Inclusion

THE INTERSECTION OF DATA SHARING AND EQUITABLE HEALTHCARE: CHALLENGES AND OPPORTUNITIES

Exploring the challenges and opportunities in leveraging data sharing in healthcare

危机

January 28, 2025

Pierre R. Theodore, MD, MPH
Head Patient Inclusion and Health Equity
Genentech – Roche Pharmaceuticals

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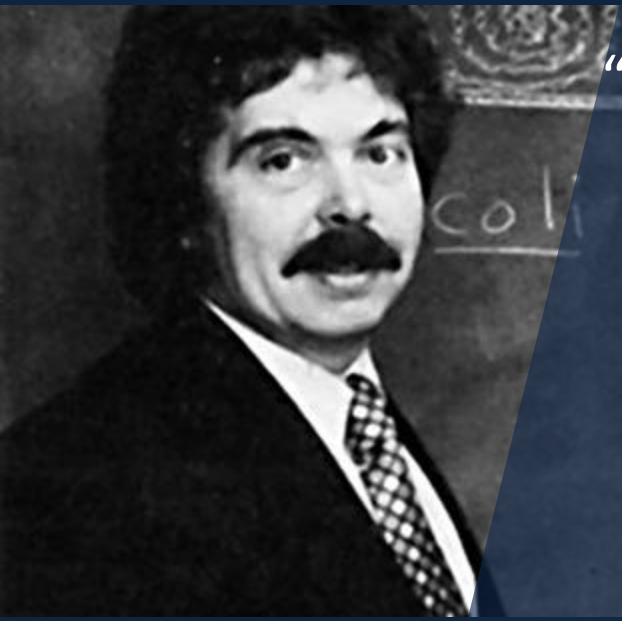

“We didn’t set out to invent genetic engineering, but to understand basic biological phenomena had important practical applications.”

THE PROMISE OF DATA SHARING

Accelerates Innovation

Enables Population Health Insights

Supports Precision Medicine

Equity Challenges
Perpetuating biases

Equity - built in from the inception of data sharing initiatives - is crucial to realize its full potential

KEY CHALLENGES OF DATA SHARING IN EQUITABLE HEALTHCARE

- **Representation Gaps in Shared Data**
- **Privacy Concerns Disproportionately Impact Vulnerable Populations**
- **Geographic and Socioeconomic Barriers**
- **Algorithmic Bias in Data-Driven Tools**

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Representation Gaps in Shared Data

Underrepresentation of ethnic minorities

Clinical datasets often lack sufficient samples from racial and ethnic minority populations,

Lack of rural community data

Rural and remote areas are frequently underrepresented in healthcare data,

Insufficient data on low-income individuals

underrepresented in medical research and data, contributing to disparities

Addressing the underrepresentation of marginalized groups in healthcare datasets is crucial to ensuring equitable and effective clinical decisions, research outcomes, and resource allocation.

Privacy Concerns and Vulnerable Populations

Historical Abuses

exploitation and unethical data use practices in the past, leading to distrust of data-sharing

Stigma and Discrimination Fears

data could be used to **stigmatize or discriminate** against them, discouraging participation.

Deportation Concerns

Immigrant communities may avoid data-sharing out of fear that their information could be used for deportation or other legal action.

Addressing the deep-rooted privacy concerns of marginalized groups is crucial for building trust and ensuring equitable participation in data-sharing initiatives.

Geographic and Socioeconomic Barriers

Limited EHR Interoperability

Lack of integration between electronic health record (EHR) systems in low-income and rural areas

Insufficient Broadband Infrastructure

Unreliable or unavailable high-speed internet access in underserved communities

Inadequate Digital Literacy

Impeding the adoption and effective use of data-sharing platforms.

The disparities in access to advanced data-sharing technologies in low-income and rural areas lead to incomplete health data, which in turn reinforces inequities in resource allocation and healthcare outcomes.

Algorithmic Bias in Data-Driven Tools

Biased Datasets

Datasets used to train AI models may contain **systemic biases** reflecting historical inequities and discrimination, leading to flawed algorithmic decisions.

Lack of Diversity

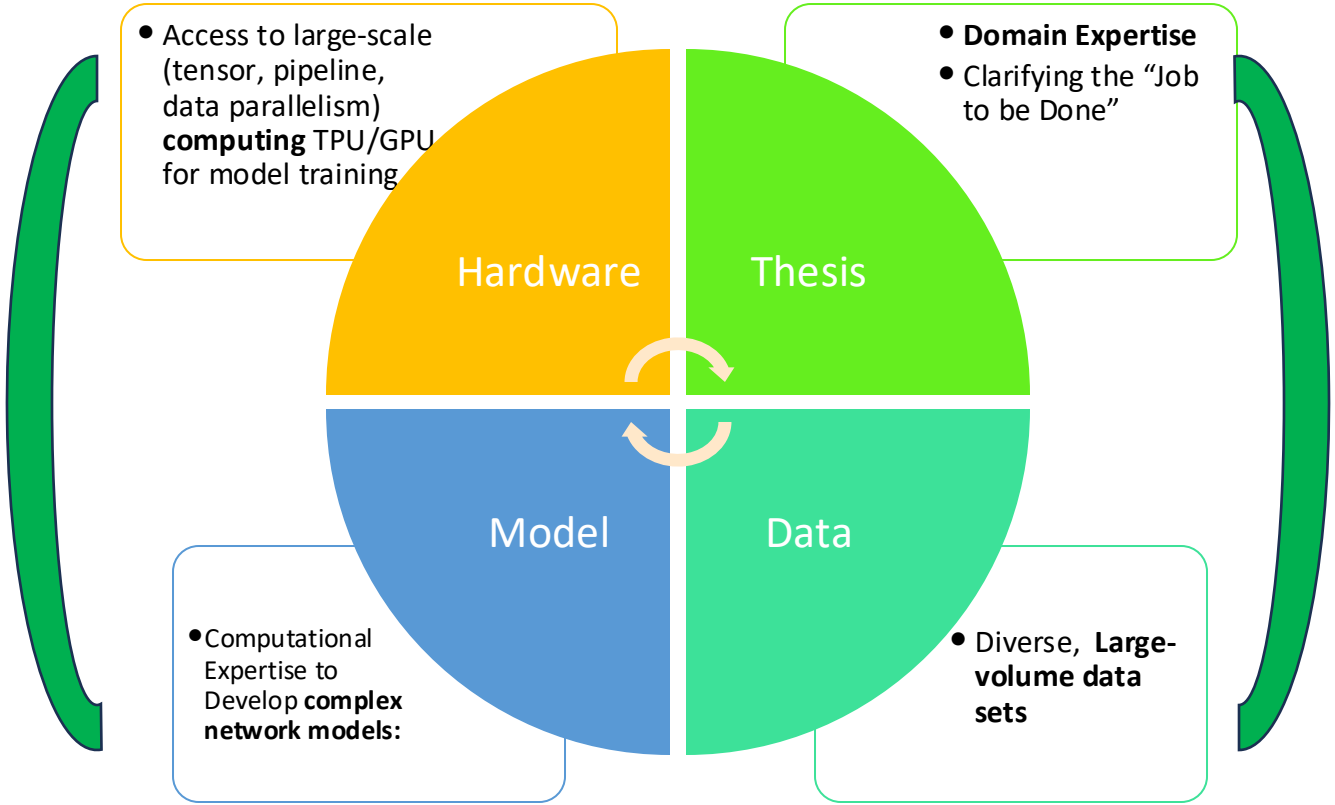
Underrepresentation of marginalized groups in shared datasets results in AI models that fail to generalize well and make unfair predictions for those populations.

Amplification of Bias

AI-powered tools that rely on biased data can **perpetuate and amplify unfair outcomes,** further entrenching existing disparities in healthcare access and treatment.

Addressing algorithmic bias in data-driven tools is crucial to ensure equitable healthcare outcomes for all, particularly for vulnerable and marginalized populations.

Core Components:Intersection of Health Equity and Bioinformatics



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INCLUSIVE RESEARCH EFFORTS ACROSS THE DRUG DEVELOPMENT PROCESS

END-TO-END OPPORTUNITIES FOR DATA SHARING AND HEALTH EQUITY

PRE-CLINICAL | PHASE I FIRST IN HUMAN | PHASE II PROOF OF CONCEPT | PHASE IIB | PHASE III | FILE FOR APPROVAL | LAUNCH

Phase 1 and First in Human Trials

Access to Diverse Data Sets

IDENTIFYING PHASE II SITES ACROSS MULTIPLE THERAPEUTIC AREAS

(CVRM - Neuro - Ophthalmology)

Industry- leading Sub-population and Investigator Initiated Studies

EARLIER STAGE CLINICAL DEVELOPMENT | LATER STAGE CLINICAL DEVELOPMENT | POST-APPROVAL

Genentech Research and Early Development (gRED) & **Pharma Research and Early Development** (pRED) included in Site Alliance Scope

Product Development

(PD SSF)

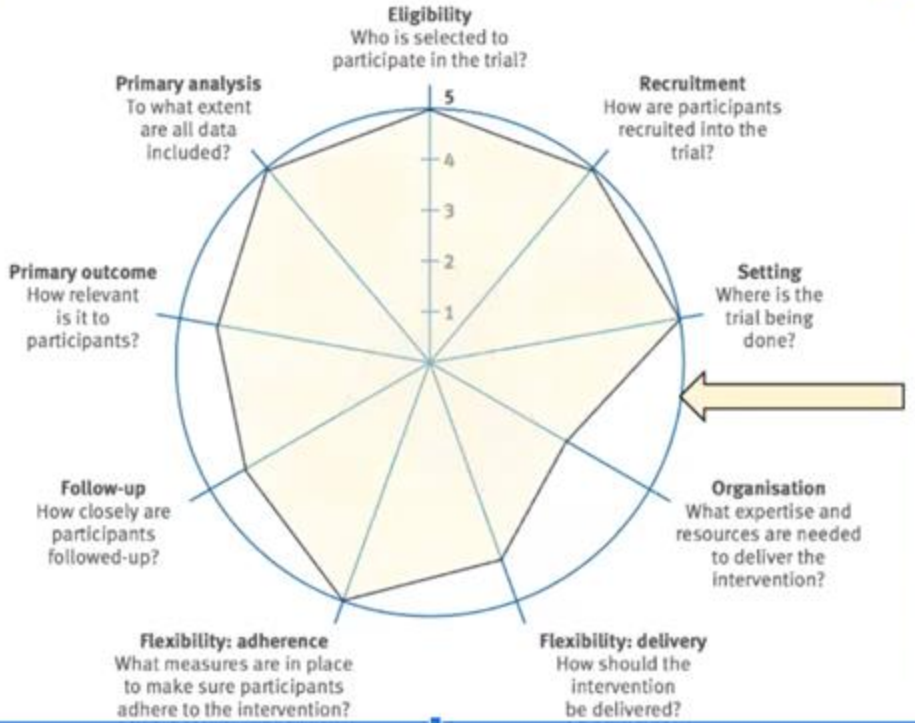
Commercial, Medical, and Government Affairs

EVOLVING CONTROLLED TRIALS WITH DATASETS TO PERMIT GREATER INCLUSION:

Explanatory

Can an intervention work under optimal conditions?

- Strict eligibility criteria
- Recruit with targeted effort
- Academic/specialized settings
- Increased staff and training
- Strict protocol and monitoring
- Seek to improve adherence
- More frequent, longer visits
- Surrogate outcomes
- Includes only completers



Pragmatic

Does an intervention work under usual conditions?

- Broad eligibility criteria
- Recruit at usual appointments
- Mirror routine settings
- Usual experience and resources
- Identical flexibility to usual care
- Usual encouragement
- Usual follow up
- Participant-focused outcomes
- Intent-to-treat analysis

BALANCING PRIVACY AND EQUITY

FDA NEWS RELEASE

FDA Issues Comprehensive Draft Guidance for Developers of Artificial Intelligence-Enabled Medical Devices

Guidance Shares Strategies to Address Transparency and Bias, while Providing Key Considerations and Recommendations on Product Design, Development and Documentation

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Reference: https://www.fda.gov/news-events/press-announcements/fda-issues-comprehensive-draft-guidance-developers-artificial-intelligence-enabled-medical-devices

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ALIGNING WITH FDA GUIDANCE

Defining the Question of Interest

Clearly articulate the **specific problem** the AI model aims to address in the context of data sharing and health equity.

Assessing the Context of Use

Specify how and **under what conditions the AI model will be employed** to inform data sharing practices and their impact on different patient populations.

Evaluating AI Model Risk

Assess potential risks associated with the model's use, particularly concerning patient safety, privacy, and the potential to exacerbate health disparities.

Establishing AI Model Credibility

Develop a comprehensive plan to **validate the model's reliability,** effectiveness, and fairness within its intended context of use for equitable healthcare delivery.

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A CALL TO ACTION: *Cultivate a Culture of Equity*

Cross-Sector Collaboration

align data-sharing practices with equity goals among a diverse array of stakeholders and communities

Prioritize Ethical Innovation

Tools and services that address needs of marginalized populations
Allocate Resources to improve data- sharing capabilities for geographic and socio-economically marginalized

Establish Equity Metrics

Define and track key performance indicators to measure the impact of data-sharing initiatives on health equity, ensuring accountability.

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Q&A

Innovative Trial Design: Data Reuse Opportunities and Regulatory Considerations

Moderator: Aaron Mann
Chief Executive Officer, **CRSDA**

Mwango Kashoki
SVP, Global Head of Regulatory Strategy, **Parexel**

Pierre Theodore
Head Patient Inclusion and Health Equity, **Genentech**

Veronica Miller
Director, **Forum for Collaborative Research,** Adjunct Professor, **Berkeley Public Health**

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Thank you!

Please join us tomorrow for "Demystifying the EU Data Sharing Space"

For additional resources and information, please visit:

https://crdsalliance.org/resources