CRITICAL PATH INSTITUTE 20 YEARS

Critical Path for Parkinson's Consortium

10-YEAR IMPACT

Diane Stephenson, PhD
Vice President, Neurology
Executive Director, CPP

Dear Friends,

When Critical Path Institute® founded a dedicated consortium focused on Parkinson's disease, our vision was clear: bring diverse stakeholders to the same table—people living with PD and their families, scientists, clinicians, and industry partners—so we could break down barriers and accelerate progress for people living with Parkinson's. As we commemorate 10 years of this extraordinary journey, I am deeply honored to reflect on what we have accomplished together. Over the past decade, that vision has come to life in ways that I only dreamed of. Our consortium has built bridges across disciplines, fostered open dialogue, and championed data sharing and collaboration as catalysts for real impact, bringing hope to people affected by Parkinson's across the world.

Our anniversary is a celebration of what the Critical Path for Parkinson's (CPP) consortium has accomplished over 10 years and a testament to the power of partnership and shared purpose. Together, we have advanced innovative research, elevated patient voices at every step of the process, and created a model for what true partnerships can look like in this field. There is still much more to do, but I am confident that with this community's unwavering dedication, we will continue to drive meaningful change for everyone impacted by Parkinson's. Thank you to every researcher, advocate, donor, regulator, industry leader and person with lived experience who has walked this journey with us—your dedication fuels our mission to create a brighter future for all those affected by Parkinson's.

Sincerely,

Diane Stephenson

David Dexter, PhD
Founder Partner,
Parkinson's UK

Marking this 10-year milestone is a testament to the power of collaboration and shared commitment to developing new therapies for Parkinson's. Through the work of the Critical Path for Parkinson's consortium, we have united researchers, clinicians, industry partners, and people affected by Parkinson's to accelerate discoveries and break down barriers that stand in the way of progress. A huge thanks to all those who have donated data to this important initiative. At Parkinson's UK, we are proud to have played a role in fostering this spirit of partnership, ensuring the research remains driven by the real needs of those living with Parkinson's. Together, we are moving closer to new treatments and, ultimately, a cure—and we remain dedicated to pushing this vital work forward.

Klaus Romero, MD, MS, FCP
CEO, Critical Path Institute

Reaching this 10-year milestone—as C-Path marks 20—we reflect on C-Path's dedication and vision to drive meaningful progress for people living with Parkinson's disease. At C-Path, we believe that advancing new tools, standards, and data-sharing approaches is only possible through true and actionable collaboration across sectors. C-Path's Critical Path for Parkinson's consortium has exemplified this spirit, uniting diverse partners to overcome challenges that no single organization can tackle alone. C-Path remains committed to building on this foundation to accelerate treatments and deliver real impact for the Parkinson's community.

Kevin Kwok, PharmD
Patient Advocate

We've moved beyond simply giving people with Parkinson's and their families a seat at the table. We're now building the table together. C-Path has shown that integrating the patient perspective early and often leads to faster and more targeted recruitment of participants, informative trials, actionable science, and optimized outcomes for those living with Parkinson's. As both an advocate and a person living with Parkinson's, I've seen the power of collaboration when industry, regulators, and patients work together with trust and purpose. For researchers, this collaboration personalizes their research efforts, and for people living with PD and their families, it provides a forum to communicate the nuanced complexities of Parkinson's and the need for urgency. This is what progress looks like, not just faster innovation, but more meaningful innovation where those affected by PD are empowered stakeholders. The next five years depend on continuing to center lived experience as a driver of change.

TABLE OF CONTENTS

WHO WE ARE

CPP is a global public-private partnership initiated in 2015 that includes industry, nonprofits, academic partners, and advisors from FDA, EMA, NIH, and people living with Parkinson's, with the goal of accelerating the path to approval of therapies that improve the lives of people with Parkinson's.

Our Mission and Approach

- The mission of C-Path's Critical Path for Parkinson's consortium is to advance the regulatory maturity of drug development tools for PD clinical trials.
- We do this by prioritizing efforts focused on broadening populations for trial recruitment; collecting, understanding and sharing patient level data; and by leveraging innovative technologies to capture what truly matters.

Key Focus Areas

- Driving innovation to accelerate drug development for Parkinson's, with powerful tools like data standards, biomarkers, and trial models.
- Advancing patient-focused drug development through modern regulatory approaches.
- Championing data sharing and early patient intervention.
- Building consensus on tools that speed Parkinson's drug development.
- Expanding global access to clinical data to unlock new disease insights.

Public-Private Partnerships and Impact

Our work is strengthened by the partnerships we've built with people living with Parkinson's and their families, nonprofit organizations, and advocacy groups. These collaborations allow us to align on shared goals, extend our reach within the community, and amplify the impact of our collective efforts. By working together, we foster trust, encourage transparency, and build momentum for change.

Industry members play a vital role in this collaborative ecosystem. Their ongoing engagement and investment make it possible to translate scientific advances into real-world solutions. Through open dialogue, shared data, and a commitment to innovation, we continue to bridge gaps across sectors—ensuring the Parkinson's community remains at the center of every conversation and every breakthrough.

C-PATH CPP BY THE NUMBERS

INNOVATION IMPACT

Regulatory-endorsed drug development solutions:

- **1st** Model-based imaging biomarker for trial enrichment
- **1st** Mechanism-based biofluid biomarker for early trials for PD and related disorders
- **6** Quantitative drug disease trial models to optimize trial design through computerized simulations

C-PATH'S CPP MEMBERS

- **3** Government Agencies
- **6** Academic Institutions
- **7** Biotechnology Companies
- **9** Nonprofits
- **9** Pharmaceutical Companies

GLOBAL DATABASE

>16,000 Individual Patient Records

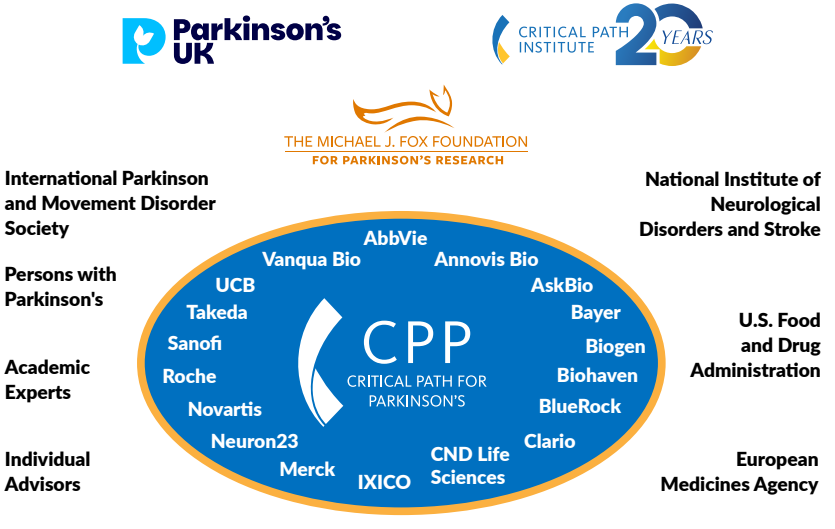
Cohorts and clinical trials from around the world aimed at maximizing learnings from ongoing and legacy data tools and models

SCIENTIFIC DISSEMINATION

- **42** Publications (Authored and co-authored by C-Path Staff)
- **6** Publications (Co-authored with people living with Parkinson's)

MEMBERS

Our work is supported by the following industry members, nonprofit and patient organizations, academic institutions, advisors and regulatory bodies. Their collaboration and investment make it possible for us to drive meaningful progress, foster innovation, and deliver real-world impact by accelerating the path to approval of therapies that improve the lives of people living with Parkinson's.



Nonprofit/Patient Organizations

- Parkinson's UK
- Parkinson Canada
- Parkinson's Europe
- Parkinson's Foundation
- The Michael J. Fox Foundation for Parkinson's Research
- Davis Phinney Foundation
- Cure Parkinson's
- PMD Alliance
- Lewy Body Dementia Association

Academic Institutions

- University of Oxford
- University of Cambridge
- Newcastle University
- University of Glasgow
- Radboud University
- University of Plymouth

ACTIONABLE REGULATORY-GRADE TOOLS

CPP Biomarkers

On behalf of its Biofluid Biomarker Work Group, the Critical Path for Parkinson's consortium successfully led the request to the FDA for the alpha-synuclein seeding amplification assay (α-syn SAA) to be used as a susceptibility/risk biomarker for enrichment of clinical trials and related neurodegenerative diseases in individuals biologically marked by misfolded α-syn pathology. The assay, developed and deployed by Amprion, uses cerebrospinal fluid (CSF) to amplify and detect α-syn seeds, positioning CSF as a critical medium for identifying disease at its earliest, pre-clinical stages.

In August 2024, the FDA's Center for Drug Evaluation and Research issued a Letter of Support (LoS) endorsing the use of α-syn SAA within a three-month record time frame. This regulatory endorsement enables more precise identification of trial participants with underlying synucleinopathy, even in the absence of clinical symptoms.

This milestone highlights CPP's leadership in advancing biomarker-driven innovation to support development of disease-modifying therapies for Parkinson's disease and related syndromes. This success also reaffirms CPP's regulatory commitment to uniting the field around shared data, laying the foundation for more efficient clinical trials.

CPP PD Patient-Centered Endpoints Team

A multistakeholder pre-competitive collaboration has been established with the sponsorship of The Michael J. Fox Foundation under the umbrella of CPP. The task force is comprised of clinical outcome assessment specialists, people with lived experience, and broader Parkinson's experts. This initiative builds on C-Path's regulatory success in advancing drug-development tools, including data sharing, regulatory alignment, and consolidated item-level evidence.

CPP Digital Health Technologies

The Digital Drug Development Tools Initiative (3DT) has advanced the regulatory maturity of DHTs in drug development by engaging with the regulators early and often. A collaborative approach with access to data from the exemplar WATCH-PD study allowed for a data-driven formulation of an intended use that formed the base for regulatory interactions. Innovative qualitative and quantitative methodologies provided the base for a rich results report to support the intended use case. A thorough review of the intended use case by the regulators, along with engaging discussions, formed the basis for rich regulatory feedback. This feedback provided the path forward for all relevant stakeholders to advance the regulatory maturity of digital health technologies.

CPP Neuroimaging

C-Path's Critical Path for Parkinson's consortium neuroimaging working group brings together neuroimaging specialists from CPP member companies and academic specialists to provide a forum to evaluate evidence for confident use of neuroimaging biomarkers in Parkinson's drug development. Presentations by key opinion leaders provide the members with new knowledge on state-of-the-art developments in neuroimaging biomarkers, while member presentations provide more insights into the practical applications of neuroimaging biomarkers in clinical trials. The working group provides a forum to develop standards for evaluation of regulatory readiness of imaging biomarkers such as dopamine transporter imaging and other modalities that are emerging.

El Tour de Tucson — riding with those living with PD


The Michael J. Fox Foundation-led Neuronal synuclein disease 2024

Cheryl Coon, Tanya Simuni, Parkinson's Study Group


Kevin Kwok, Steve Ford, Arthur Roach, Jesse Cedarbaum and Diane Stephenson at the World Parkinson's Congress


Klaus Romero, Diane Stephenson and Joseph Hedrick record C-Path's first podcast episode

A DECADE OF IMPACT - MILESTONES

Shaping the Future of Parkinson's Drug Development Through Science, Data, and Partnership

- Launched with funding from Parkinson's UK, industry, and C-Path.
- Secured FDA Letter of Support for dopamine transporter imaging in PD trials.

- Built a collaborative model to optimize early-stage PD trials.

- Earned EMA's first regulatory qualification of a PD biomarker with dopamine transporter imaging.
- Advanced personalized medicine with an endorsed progression model for LRRK2 carriers and early-intervention trials.

- Launched 3DT initiative to advance digital tools in PD trials.
- Partnered with FDA to align validation of DHT studies.
- Engaged EMA on digital tools for early PD trials.

› 2022

- Gained EMA support for a trial simulation platform to optimize PD efficacy studies.

› 2023

- Earned FDA positive review for a model-based PD trial simulation tool.
- Formed a patient-focused Advisory Council to guide trial endpoints.

› 2024

- Developed a biological staging framework for PD, culminating in a Lancet Neurology publication.
- Secured FDA support for α-syn SAA as an enrichment biomarker in early PD trials.
- Hosted a full-day FDA meeting to align strategies for the 3DT initiative.

› 2025

- Received EMA qualification advice on digital health tools for early PD trials.
- Launched GEM-PD to advance treatment for women through data-driven insights.
- Featured on C-Path's podcast linking regulatory strategies in PD and type 1 diabetes.

COLLABORATIVE DATA SHARING TO ACCELERATE THERAPEUTIC INNOVATION

Data Background

C-Path has developed infrastructure and data expertise in standards development, patient-level data privacy, security, and controlled access methods. Its ability to curate, standardize, aggregate, and securely receive large volumes of data has enabled CPP to build a rich repository for generating new discoveries and expanding its impact.

To date, CPP has acquired nearly 16,000 patient-level records across 26 observational studies and clinical trials conducted over the past 30 years. These datasets are housed in the CPP Integrated Parkinson's Database, a comprehensive resource with access available to academic, industry, and global researchers. CPP has provided access to more than 100 users at over 40 organizations in 13+ countries. This database enables researchers to extract subsets of patient-level data to develop disease progression models, simulate clinical trials, with future applications centered around artificial intelligence and machine learning algorithms.

Impact

CPP's Integrated Parkinson's Database promotes the sharing of key insights from clinical trials and observational studies, accelerating the development of innovative tools, improving clinical trial design, and enhancing the efficacy of candidate drug development pipelines. In addition to supporting research, the repository's impact is reflected in its growing number of publications (Table 1).

Looking to the Future

Leveraging the database, CPP is developing a data analytics platform and a clinical trial simulation tool to promote data sharing across organizations and accelerate the development of new treatments for Parkinson's disease.

Learn more about CPP's Integrated Parkinson's Database:

Table 1

Title	Research Topic	Reference
Validating new symptom emergence as a patient-centric outcome measure for PD clinical trials	MDS-UPDRS, emergent symptoms	Zou et al., Parkinsonism Relat Disord. 2024 Nov;128:107118. doi: 10.1016/j.parkreldis.2024.107118.
The effect of cardiovascular risk on disease progression in *de novo* Parkinson's disease patients: An observational analysis	Cardiovascular risk in PD, disease modification, longitudinal modeling, hypertension, causal inference	Oosterwegel et al., Front Neurol. 2023 Apr 12;14:1138546. doi: 10.3389/fneur.2023.1138546.
Using Movement Disorder Society Unified Parkinson's Disease Rating Scale Parts 2 and 3 Simultaneously: Combining the Patient Voice with Clinician Rating	MDS-UPDRS, exploratory factor analysis, patient voice	Guo et al., Mov Disord. 2023 Mar;38(3):453-463. doi: 10.1002/mds.29308.
Application of longitudinal item response theory models to modeling Parkinson's disease progression	Multidimensional longitudinal IRT modeling, item response theory, MDS-UPDRS	Zou et al., CPT Pharmacometrics Syst Pharmacol. 2022 Oct;11(10):1382-1392. doi: 10.1002/psp4.12853.
A disease progression model to quantify the non-motor symptoms of Parkinson's disease in participants with leucine-rich repeat kinase 2 mutation	LRRK2, idiopathic PD, MDS-UPDRS, PPMI, beta regression, non-linear mixed-effects modeling, non-motor symptoms	Ahamadi et al., Clin Pharmacol Ther. 2021 Aug;110(2):508-518. doi: 10.1002/cpt.2277
Development of a disease progression model for leucine-rich repeat kinase 2 in Parkinson's disease to inform clinical trial designs	PPMI, ICICLE, LRRK2, clinical trial design, disease progression	Ahamadi et al., Clin Pharmacol Ther. 2020 Mar;107(3):553-562. doi: 10.1002/cpt.1634.
The Qualification of an Enrichment Biomarker for Clinical Trials Targeting Early Stages of Parkinson's Disease	Enrichment biomarkers, biomarker reproducibility and reliability, DAT, regulatory engagement	Stephenson et al., J Parkinsons Dis. 2019;9(3):553-563. doi: 10.3233/JPD-191648.
Dopamine Transporter Neuroimaging as an Enrichment Biomarker in Early Parkinson's Disease Clinical Trials: A Disease Progression Modeling Analysis	Enrichment biomarker in early PD, DAT, SWEDD	Critical Path for Parkinson's (CPP) Parkinson's Disease Modeling and Simulation Working Group, Clin Transl Sci. 2018 Jan;11(1):63-70. doi: 10.1111/cts.12492.

Note: This is a summary of known publications citing CPP's Integrated Parkinson's Database.

REGULATORY SUCCESSES

2015: FDA Letter of Support

Exploratory prognostic biomarkers for enrichment in early-stage Parkinson's disease clinical trials; molecular neuroimaging biomarker: dopamine transporter

2016: EMA Letter of Support

Molecular imaging of the dopamine transporter biomarker as an enrichment biomarker for clinical trials for early Parkinson's disease

2018: EMA Qualification Opinion

Molecular neuroimaging of the dopamine transporter as biomarker to identify patients with early manifest Parkinsonism in Parkinson's disease

2019: FDA Critical Path Innovation Meeting

Digital drug development tools for early Parkinson's disease clinical trials

2019: EMA Innovative Task Force

Digital drug development tools for early Parkinson's disease clinical trials

2022: EMA Letter of Support

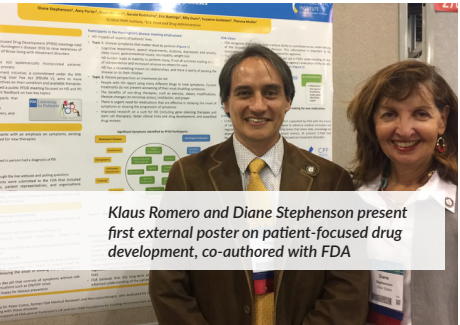
Model-based clinical trial simulation platform to optimize design of efficacy evaluation studies in Parkinson's disease

2024: FDA Letter of Support

Application of binary assessment of α-synuclein seeding amplification assay as an enrichment biomarker for patient selection in clinical trials of neurodegenerative disorders characterized by a common synuclein biology

CPP 3DT team attends the FDA Critical Path Innovation meeting

CPP Executive Director Dr. Diane Stephenson's first visit to Parkinson's UK in London



Klaus Romero and Diane Stephenson present first external poster on patient-focused drug development, co-authored with FDA

David Dexter, Caroline Williams Gray, Diane Stephenson and Klaus Romero present first Data Sharing Pioneer Award

PATIENT ADVISORY COUNCIL

Overview

People with lived experience in Parkinson's disease are key stakeholders of the Critcal Path for Parkinson's consortium and contribute the consortium's goals. Formed in October 2023 under the auspices of CPP's PD Endpoints Working Group, the Advisory Council is a partnership between people with lived experience and eight nonprofit organizations. The council includes 11 members with lived experience in Parkinson's, including at-risk individuals, those with early- and late-stage Parkinson's, and core partners. Representation is diverse, with its members spanning the U.S., Canada, Europe, and the United Kingdom.

Purpose

Leverage the lived experience voice to gather feedback on candidate clinical endpoints aligned with FDA's Patient-Focused Drug Development Guidance and with an emphasis on what is meaningful to people affected by Parkinson's disease.

Why

People with lived experience are eager to share how Parkinson's affects their day-to-day lives. CPP has partnered with other nonprofit organizations to leverage their expertise in advocating for people living with Parkinson's.

Nonprofit Partners

Parkinson's UK

The Michael J. Fox Foundation

Parkinson's Europe

Parkinson Canada

Cure Parkinson's

Parkinson's Foundation

Parkinson's Foundation, LBDA

PMD Alliance

Davis Phinney Foundation

TOPICS

COGNITION

NEUROIMAGING

CLINICAL TRIALS

ENDPOINTS

FUTURE FOCUS

Our vision for the next three to five years is to accelerate progress by accelerating drug development tools that improve the efficiency of clinical trials for Parkinson's and related disorders. A broader scope that includes other neurodegenerative diseases will be key to enhancing global recognition of copathologies and sharing learnings across the global ecosystem.

Central to this vision is our commitment to elevating the patient voice, ensuring that the lived experiences of people with Parkinson's guide our priorities, shape meaningful endpoints, and inspire solutions that matter. By strengthening our partnerships with patient advocacy groups, nonprofit organizations, and our industry and academic collaborators, we will continue to foster a vibrant public-private partnership that breaks down silos and drives progress with a sense of urgency.

Together, we aim to build a future where our collaborative impact goes beyond any single disease, empowering those affected, accelerating science, and delivering new hope for people and families affected by Parkinson's and other neurodegenerative conditions worldwide.

"It's powerful to see how lived experiences, combined with scientific expertise, can drive progress so people with Parkinson's benefit sooner. On the CPP Patient Advisory Council, I've valued meaningful discussions on biological staging, prevention, and the ethical challenges of research. What stands out most is the collaborative spirit—people worldwide sharing diverse experiences and symptoms. As a caregiver, I bring a different perspective, noticing daily struggles that might go unspoken. These insights ensure research, treatment, and policy stay centered on people and relationships at the heart of Parkinson's."

-Claire Boles, CPP Advisory Council Member and PD Caretaker

Bending the Curve: Sarah Zenner-Dolan's Advocacy Journey with Parkinson's Disease

Podcast: Connecting the Dots Between T1D and Parkinson's

GLOBAL REPRESENTATION

United States

Canada

United Kingdom

EU

26
Datasets

110+
Researchers

15k
Participants

40+
Organizations

MEET THE CPP TEAM

Laura Carrillo, MPH - Senior Project Manager

Laura supports CPP's Parkinson's Disease Endpoints Working Group and Patient Advisory Council and manages the Integrated Parkinson's Database. She also contributes to C-Path's GEM-PD initiative.

Originally from Alaska, Laura earned her MPH from George Washington University. Prior to joining C-Path, she served as the principal executive officer of the Alaska Board of Pharmacy and continues to consult on national pharmacy regulation. As a parent of a child with rare neurodevelopmental conditions, Laura is deeply committed to advancing patient-driven innovation in drug development.

Shasta Jorgensen, MPH - Senior Project Manager

Shasta supports CPP's efforts to accelerate PD therapeutic development. She brings 20+ years of experience in public health and healthcare, with expertise in systems change, health education, and quality improvement.

She earned her BA in International Relations from the University of Redlands and her MPH from Boston University, with a concentration in Social and Behavioral Science.

Erin Lowry, PACE - Senior Project Coordinator

Erin has dedicated over four years to supporting collaborative and regulatory science at C-Path. A PACE-certified coordinator, she brings more than 20 years of experience in operations and stakeholder engagement from the travel industry, ensuring seamless project execution across multi-partner initiatives.

Martijn Müller, PhD - Senior Scientific Director

Dr. Müller is a psychologist with two decades of experience in PD research and a focus on developing patient-relevant treatments.

He brings multidisciplinary expertise in neuropsychology, mobility, neurodegeneration, and neuroimaging. Previously a research associate professor at the University of Michigan, Martijn now leads CPP scientific efforts to advance regulatory tools that improve clinical trial outcomes.

Anne Pedata - Scientific Director

Anne supports CPP with over 20 years of experience in neuroscience, cancer biology, and clinical diagnostics across academia and industry.

She holds degrees in psychology and chemistry from Northern Arizona University and in pharmacology and neuroscience from Wake Forest University. Her work focuses on biomarker applications for brain disorders.

Diane Stephenson, PhD - Vice President, Neurology and Executive Director

Dr. Stephenson is a neuroscientist with 30 years of experience in academic research and drug discovery. She has led work in ALS, Alzheimer's, Parkinson's disease and stroke, and has authored 125 publications and six patents.

Diane is a recognized leader in public-private partnerships, with expertise in neuroimaging and translational neuroscience. She earned her biochemistry degree from UC Santa Barbara and her PhD in medical neurobiology from Indiana University. At C-Path, she leads cross-sector teams working to accelerate therapies for neurodegenerative diseases.

CRITICAL PATH INSTITUTE 20 YEARS

c-path.org

c-path.org/cpp

LET'S WORK TOGETHER

cppadmin@c-path.org

c-path.org/fda-acknowledgement