

Worldwide collaborative framework for optimizing new Parkinson's treatment trials with patient centric outcome measures

Diane Stephenson¹, Yuge Xiao², Catherine Kopil², Karen Lee³, David T. Dexter⁴, Martijn Müller¹, Klaus Romero¹, Helen Matthews⁵, Gary Rafaloff⁶, Jodie Forbes⁶, Sarah Zenner Dolen⁶, Carroll Siu⁶, Johan Hellsten⁶, John Crawford⁶, Mark Maybank⁶, Tanya Simuni⁷

¹Critical Path Institute, Tucson, AZ, ²The Michael J. Fox Foundation, New York, NY, ³Parkinson's Canada, Ontario, Canada ⁴Parkinson's UK, London, England, ⁵Cure Parkinson's, London, England, ⁶Parkinson's Patient/Researchers/Advocates, ⁷Northwestern University, Chicago, IL.

Background

- A rich pipeline of promising therapies is in development for Parkinson's with a growing number targeting early intervention. (McFarthing et al., 2021)
- Historically, endpoints used in Parkinson's trials have relied on clinician-based outcome assessments and/or in-clinic performance outcome (PerfO) assessments for example, UPDRS.
- The FDA is driving a new era of Patient-Focused Drug Development, requiring trials to use patient-centered endpoints.
- Multi-stakeholder collaborations are needed to develop new patient reported outcome measures for Parkinson's.
- A consensus roundtable focused on endpoints was held in Washington DC, November 2-3, 2022.

Objectives

To build precompetitive alignment on methodologies and regulatory insights for:

- 1 Development of patient-centric clinical outcome assessments (COAs) for early Parkinson's measurement.
- 2 Integration of the patient's perspective through linking the voice of the patient to digital health technologies (DHTs) to facilitate faster and cohesive advancement in developing improved tools for measuring changes in early Parkinson's.



Parkinson Canada



PARKINSON'S
CHANGE ATTITUDES.
FIND A CURE.
JOIN US.



Appendix B. Endpoints Roundtable Participants

An asterisk indicates a member of The Michael J. Fox PD Endpoints Advisory Group.

Meeting Chair

*Tanya Simuni, MD, Northwestern University

Hosts

Angelica Ais, MSc, Parkinson Canada
Zachary Chaney, The Michael J. Fox Foundation
Shona Clegg, Parkinson's UK
Sohini Chowdhury, MA, The Michael J. Fox Foundation
David Dexter, PhD, Parkinson's UK
Mark Fraser, PhD, The Michael J. Fox Foundation
*Catherine Kopil, PhD, The Michael J. Fox Foundation
Karen Lee, PhD, Parkinson Canada
*Yuge Xiao, The Michael J. Fox Foundation

Funders, Conveners, and Community Partners

Francisco Cardoso, MD, PhD, FAAN, International Parkinson and Movement Disorder Society
Hyun Joo (Sophie) Cho, MD, National Institute of Neurological Disorders and Stroke
*Rebecca Fuller, PhD, Cure Huntington's Disease Initiative
Jennifer Goldsack, MBA, Digital Medicine Society
Helen Matthews, Care Parkinson's
Martijn Müller, PhD, Critical Path Institute
Karlin Schroeder, MA, Parkinson's Foundation
Rebecca Speck, PhD, MPH, Critical Path Institute
*Diane Stephenson, PhD, Critical Path Institute

Patient Advocates

Johan Hellsten, PhD
Mark Maybank
*Gary Rafaloff
Carroll Siu

Regulatory Agencies

Michelle Campbell, PhD, U.S. Food and Drug Administration
Billy Dunn, MD, U.S. Food and Drug Administration

Academia

David Cella, PhD, Northwestern University
Walter Mastaler, MD, Kiel University
Jennifer Mammen, PhD, APRN-CNP, University of Rhode Island
*Ken Marek, MD, Institute of Neurodegenerative Disorders
Connie Marras, MD, PhD, University of Toronto
*Anat Mirelman, PhD, Tel Aviv Medical Center
Togo Mestre, MD, PhD, Ottawa Hospital Research Institute, University of Ottawa
*Lynn Rochester, PhD, Newcastle University
*Glenn Stebbins, PhD, Rush University
Daniel Weintraub, MD, University of Pennsylvania

Industry

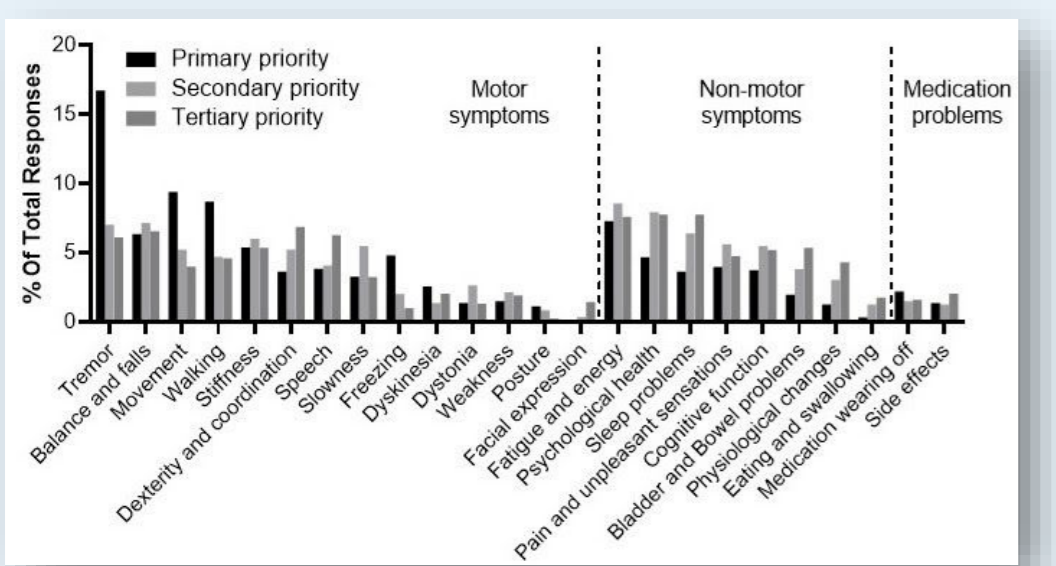
Milton Biagioni, MD, CMD, UCB
*Peter Chin, MD, MSHS, Denali Therapeutics
Tem Dam, MD, Biogen
Evan Davies, MSc, Hoffman-La Roche
Rita Kapur, PhD, Verily Life Sciences
Michael Lindemann, PhD, MBA, Hoffman-La Roche

RAND Team

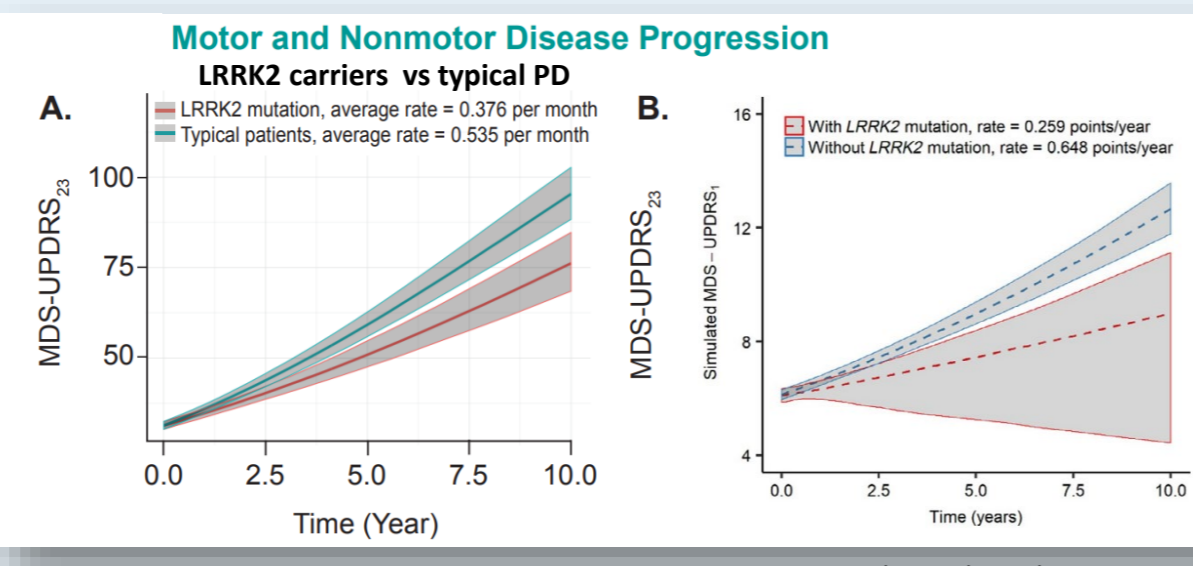
Claire E. O'Hanlon, PhD, MPP, RAND Corporation
Carrie M. Farmer, PhD, RAND Corporation
Jamie Ryan, MPH, MPH, RAND Corporation

Problem People with early Parkinson's report many motor and nonmotor symptoms, often present prior to diagnosis

Port et al., 2021



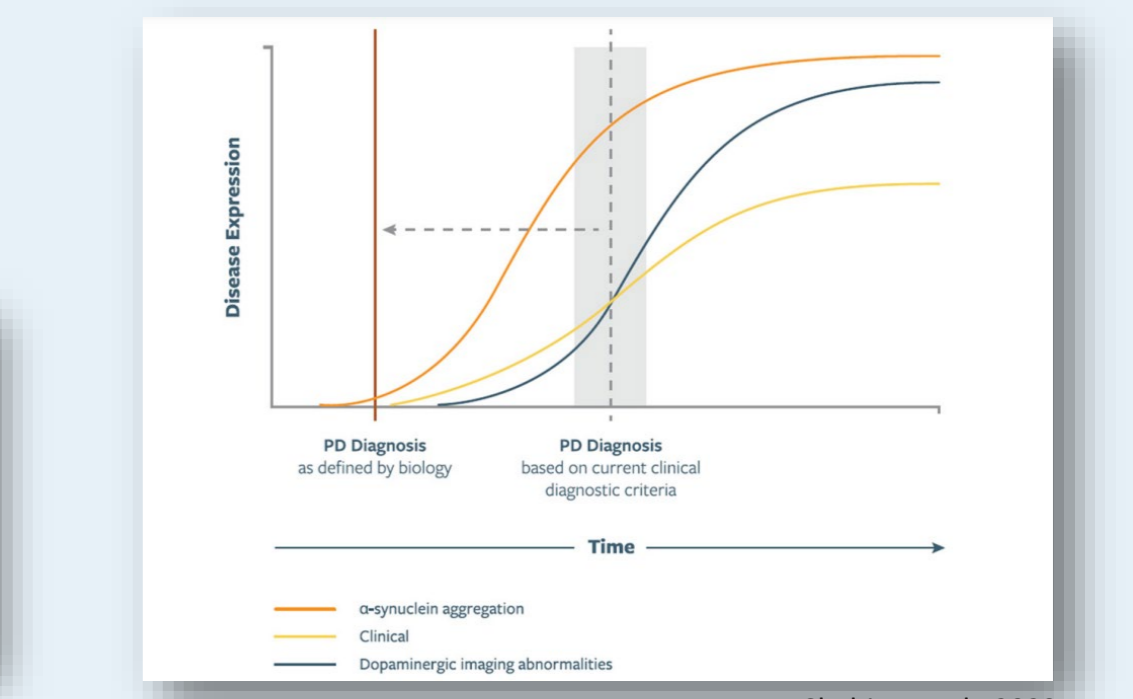
Current State Endpoints used in trials today are not ideal, especially at early stages



Efforts Underway An array of different approaches for better endpoints are being advanced by experts across the globe

- Industry led efforts tied to drug trials
- Academic led research initiatives
- Nonprofit driven initiatives and research
- Movement Disorder Society outcomes expert led program
- Global strategies via Public Private Partnerships in the area of digital health technologies

Implementing a biological staging system accelerates progress, regardless of the approach taken.



What are the possible approaches to development of patient-centric endpoints recommended by FDA?

Patient-Focused Drug Development: Incorporating Clinical Outcome Assessments Into Endpoints For Regulatory Decision-Making
Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders
DRAFT GUIDANCE

Draft - Guidance 4: Patient-Focused Drug Development: Incorporating Clinical Outcome Assessments Into Endpoints for Regulatory Decision-Making

Final - Guidance 1: Patient-Focused Drug Development: Collecting Comprehensive and Representative Input, Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

Heterogeneity In Diseases
Multiple outcome variables associated with a disease

Construct a multi-component endpoint
At within-subject combination of two or more components

Final - Guidance 2: Patient-Focused Drug Development: Methods to Identify What Is Important to Patients

Heterogeneity In Diseases
Multiple outcome variables associated with a disease

Construct a personalized endpoint

Draft - Guidance 3: Patient-Focused Drug Development: Selecting, Developing or Modifying Fit-for-Purpose Clinical Outcomes Assessments

Heterogeneity In Diseases
Multiple outcome variables associated with a disease

Construct separate endpoints for each aspect of health

- Methods**
- A diverse array of stakeholders from around the world were engaged as active participants in the workshop.
 - Precompetitive collaboration and willingness to share regulatory insights are key requirements for all roundtable participants, including contributing organizations.
 - A panel of people with lived experience with Parkinson's led a dynamic panel discussion.
 - Complementary to ongoing initiatives: CPP endpoints, MJFF advisory council, DHT efforts.

Results

- Reviewed a total of 8 case studies at Nov. 2-3 meeting and within the C-Path CPP's Patient-Centric Outcomes Team
- FDA issues call to action for new biological staging framework.
- Published November workshop proceedings report (open access):

Clinical Outcome Assessments and Digital Health Technologies Supporting Clinical Trial Endpoints in Early Parkinson's Disease
Roundtable Proceedings and Roadmap for Research
O'Hanlon et al. 2023

- Actions and next steps**
- Develop a consensus conceptual model for [early] Parkinson's from qualitative data
 - Expand CPP's 3DT effort to centralize intelligence on digital clinical measures in development for Parkinson's and expand the list of publicly available information.
 - Develop Parkinson's Concepts of Interest (COI) item bank.
 - Maintain ongoing forums: CPP's Patient-Centric Outcomes Team & MJFF's Endpoints Advisory Council

You can help by participating in research

- Fox Trial Finder <https://www.michaeljfox.org/trial-finder>
- Fox Insight Online Study <https://foxinsight.michaeljfox.org/>
- Buddy Network: study postings in the "Research" group board <https://parkinsonsbuddynetwork.michaeljfox.org/v2/>

For more information about CPP please contact Executive Director Dr. Diane Stephenson (dstephenson@c-path.org). View the poster video here >

References:
Ahamadi M., et al. (2019) *Clinical Pharmacology & Therapeutics*. 107(3), 553–562. <https://doi.org/10.1002/cpt.1634>
Ahamadi M., et al. (2021) *Clinical Pharmacology & Therapeutics*. 110(2), 508–518. <https://doi.org/10.1002/cpt.2277>
Chahine L., et al. (2023) *Journal of Parkinson's disease*, 13(3), 297–309. <https://doi.org/10.3233/JPD-225111>
McFarthing K, et al., (2023) *J Parkinsons Dis.* ;13(4):427-439. <https://pubmed.ncbi.nlm.nih.gov/37302040/>
O'Hanlon C., et al. (2023). https://www.rand.org/pubs/conf_proceedings/CF2550-1.html.
Port R.J., et al. (2021) *Journal of Parkinson's disease*, 11(2), 715–724. <https://doi.org/10.3233/JPD-202346>