Optimizing scoring algorithms of the MDS-UPDRS Part 3 for clinical trials in early-stage Parkinson's disease

Submitter Nicolai D. Ayasse

Affiliation Critical Path Institute

SUBMISSION DETAILS

I agree to provide poster pdf for attendee download. Yes

What is the Methodological Issue Being Addressed? As the focus of interventional trials in Parkinson's disease (PD) shifts from symptomatic treatment to disease-modifying therapies, the population of interest is moving earlier in the disease course. Existing measures, including the MDS-UPDRS, and common clinical trial endpoints were developed with the full spectrum of PD severity in mind and are not optimized for early-stage PD (Hoehn & Yahr ≤2).

Introduction As one component of a multi-stakeholder collaboration to optimize endpoints for early intervention that are clinically meaningful and sensitive to change in early PD,[1] quantitative methods were employed to investigate subsets of items and alternative scoring strategies that might improve MDS-UPDRS Part 3 measurement properties and responsiveness (sensitivity to change) in early PD.

Methods Based on input from PD experts and existing patient-focused qualitative and quantitative data,[1] multi-dimensional measurement models were hypothesized that, importantly, correspond to interpretable alternative scoring algorithms, and items were identified that are less relevant for early-stage PD. Potential measurement models and their corresponding scoring algorithms were tested using a series of confirmatory factor analysis (CFA) models. Change (3- or 5-points) on the patient-reported Part 2 score was used as an anchor for examining the responsiveness of these potential scores, specifically looking at the effect size, standardized response mean, and Guyatt's responsiveness statistic for groups who reported improvement or worsening. These potential scores were further investigated using bootstrap-based power analyses.

All analyses were conducted in a sample of people with early PD (Hoehn & Yahr ≤2) across 1 observational (PPMI; baseline N=983) and 7 interventional (baseline N=1159) trials available in the Critical Path for Parkinson's database. Included participants had the MDS-UPDRS collected in the absence of effects from symptomatic treatment (either treatment naïve or in the "off" medication state) and no missing item-level data.

Results When total scores were computed using scoring algorithms corresponding to the best-fitting CFA models, both responsiveness and power increased for this early PD sample compared to the traditional scoring algorithm. Specifically, alternative scoring algorithms decreased the required sample size to achieve power=0.80 at 6 months by, for example, up to 50 (e.g., from 225 to 175), and increased responsiveness by up to 0.12 (on an effect size scale), for this early PD sample. CFA models achieved acceptable model fit when they included 4-5 dimensions based on

symptom clusters, re-framed right and left sides into most- and least-affected sides, and accounted for inter-item relationships stemming from repeated tasks (e.g., rigidity assessed separately for each limb); fit further improved when either 3 or 5 items identified as less relevant in early PD were removed.

Conclusion These results highlight the importance of tailoring chosen clinical outcome assessment-based endpoints to the population of interest, and that suitable endpoints for earlier stages of a condition are likely not the same as those developed to assess meaningful benefit of novel treatments in later stages of the same condition. They also demonstrate the effectiveness of using patient-focused qualitative and quantitative data to guide decisions.

Co-Authors

Nicolai D. Ayasse[1], Fraser D. Bocell[1], Yuge Xiao[2], Catherine M. Kopil[2], Diane Stephenson[1]

[1] Critical Path Institute

[2] The Michael J. Fox Foundation for Parkinson’s Research

Keywords

Keywords
Parkinson's disease
Clinical Outcome Assessments
Endpoint optimization

Guidelines I have read and understand the Poster Guidelines

Disclosures The authors report no conflicts of interest for this work.
Critical Path Institute is supported by the Food and Drug Administration (FDA) of the Department of Health and Human Services (HHS) and is 43% funded by the FDA/HHS, totaling $20,724,703, and 57% funded by non-government source(s), totaling $27,346,613. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement by, FDA/HHS or the U.S. Government.

Related Tables and Supporting Materials References Doc_ISCTM Fall 2026 Poster Abstract.docx