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Leveraging PROMIS and HealthMeasures to Develop Non-Motor Patient-Reported Outcome Measures for Early Parkinson's Disease Trials

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Background

- Parkinson's disease (PD) involves motor and non-motor symptoms (cognitive impairment, sleep disturbances, fatigue, autonomic dysfunction) that emerge early and significantly impact quality of life[1,2]
- No fit-for-purpose clinical outcome assessments (COAs) exist for early PD that meet FDA guidance to support clinical trial endpoints
- PROMIS® and HealthMeasures provide item banks for efficient, precise assessment of symptoms and function across populations

Objective

- To develop fit-for-purpose PRO measures for early PD that assess non-motor symptoms using HealthMeasures item banks (primarily PROMIS), aligned with FDA guidance to support clinical trial endpoints.

Methods

Phase 1: Development

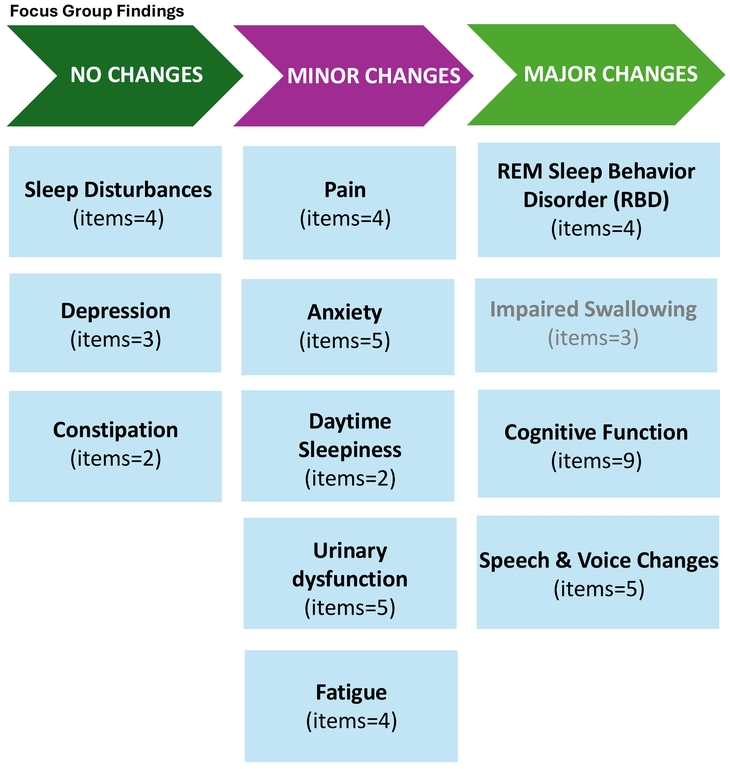
1. **Concept Identification:** Identified **c**andidate concepts of interest (e.g., symptom domain) through literature reviews and stakeholder feedback
2. **Concept Refinement:** Refined concepts through secondary analysis of symptom maps from the Wearable Assessments in The Clinic and at Home in PD (WATCH-PD) qualitative sub-study (N=40)
3. **Item Mapping:** Mapped priority symptoms to existing HealthMeasures items (PROMIS, Neuro-QoL™, NIH Toolbox®, FACIT, ASCQ-Me®, LURN SI-29)
4. **New Item Development:** Drafted new items to address gaps in early PD non-motor symptom assessment
5. **Item Reduction:** PRO experts and stakeholders reviewed and removed items, finalizing 12 Draft Early PD PRO Measures (v1.1)

Phase 2: Focus Groups

1. NU Team collaborated on WATCH-PD Qualitative Study Extension (MJFF-022743) to conduct focus groups with a subset of WATCH-PD participants (N=12) in two independent groups (5-6 per group)
2. Each group completed four consecutive weekly sessions (8 total sessions, February-March 2025)
3. Evaluated item clarity, relevance, response options, and missing content

Stakeholders (individuals with PD, clinicians, PRO measurement experts, FDA representative) provided input throughout both phases

Figure 1. Draft PRO Measures (v1.1) Organized by Degree of Modification Based on Focus Group Findings



Results

Phase 1: Development

- Developed 12 draft early PD PRO measures (v1.1) with 51 total items assessing the most relevant early PD non-motor symptoms to support clinical trial endpoints (Figure 1)
- WATCH-PD symptom map analysis (N=40) enabled identification of key terms and phrases to refine candidate concepts and guide item mapping
- Mapped content from HealthMeasures item banks (primarily PROMIS, supplemented by Neuro-QoL, NIH Toolbox, ASCQ-Me) and other systems/measures (FACIT, LURN SI-29), and drafted new items where gaps were identified
- 8 of 12 measures assess potential pre-motor symptoms (daytime sleepiness, REM sleep behavior disorder (RBD), pain, anxiety, depression, urinary dysfunction, constipation, cognitive function)

Results (cont.)

Phase 2: Focus Groups

- Focus group data analyzed to inform measure refinements organized by degree of modification needed: no changes, minor changes, or major changes (Figure 1)
  - **Impaired swallowing** measure dropped (low prevalence in early PD); **RBD** reduced to 1-item screener
  - **Items added, removed, and modified** across measures based on participant feedback; no changes to sleep disturbances, depression, or constipation
- Preliminary revisions reviewed with stakeholders and validated with patient advisors (N=4), finalizing 10 Draft Early PD Non-motor PRO measures (v1.2): 48 items plus 1 RBD screening item (49 total)

Conclusion

- Developed and refined 10 draft early PD non-motor PRO measures (v1.2) and 1 RBD screening item through rigorous, multi-phase iterative process involving stakeholder and patient advisor input
- 7 of 10 measures and the RBD screening item assess potential pre-motor symptoms (daytime sleepiness, pain, anxiety, depression, urinary dysfunction, constipation, cognitive function, RBD),[3,4] aligning with current research on disease modification and early intervention strategies
- Cognitive interview testing planned with individuals with early PD (all measures) and care partners (RBD, cognitive function)
- This collaborative, multi-phase process supports creation of fit-for-purpose clinical trial endpoints sensitive to early disease changes and suitable for evaluating disease-modifying treatments in future registration trials
- Leveraging existing HealthMeasures content can accelerate PRO development while maintaining psychometric rigor and regulatory compliance

References

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