MANAGE-PD: A Clinician-Reported Tool to Identify Patients with Parkinson's Disease Inadequately Controlled on Oral Medications—Results from Vignette-Based Validation

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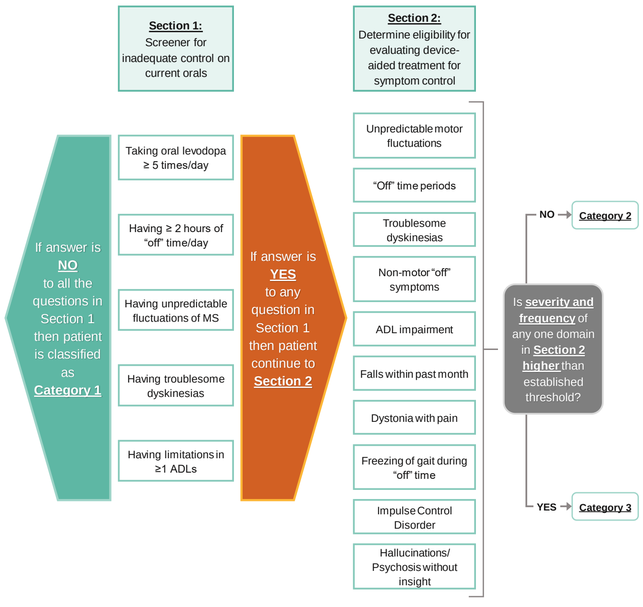
BACKGROUND

- A lack of clear definition of advanced Parkinson's Disease (aPD) together with absence of gold standard tests make diagnosis and management of symptoms challenging.[1]
- In patients whose symptoms are not adequately controlled on oral medications, the likely challenges with gastric emptying may require appropriate utilization of device-aided therapies (e.g. deep brain stimulation, sub-cutaneous apomorphine infusion and levodopa-carbidopa intestinal gel).[2]
- Making Informed Decisions to Aid Timely Management of Parkinson's Disease (MANAGE-PD) is a simple screening tool intended to be used by health care providers. The tool is aimed to support HCP's decision making for the timely management of PD symptoms based on comprehensive evaluation of frequency and severity of the motor, non-motor and functional symptoms.
- The tool **(Figure 1)** was developed based on feedback from a global panel of leading movement disorder specialists using a mixed-method approach.[3]

OBJECTIVE

- The main objective of this study was to evaluate the validity and reliability of the MANAGE-PD tool.

Figure 1. MANAGE-PD Tool Overview



Notes: Frequency of domains measured as: (i) none of the time/ never, (ii) rarely, (iii) frequent/some of the time, and (iv) most/all of the time (daily); Severity of domains measured as: (i) mild i.e. detectable to clinician but not interfering with daily life (not or minimally troublesome to the patient), (ii) moderate i.e. detectable to clinician and influences daily life (troublesome to the patient), and (iii) severe i.e. detectable to clinician and significantly influences daily life (very troublesome to the patient).
Category 1: Patient is adequately controlled on current oral therapy; **Category 2:** Patient is inadequately controlled on current oral therapy and optimization of oral therapy is recommended; **Category 3:** Patient is inadequately controlled on current oral therapy and along with optimization of oral therapy, evaluation for device-aided therapies is recommended. **Abbreviations:** MS, Motor symptoms; ADLs, Activities of Daily Living.

METHODS

- For this study, a vignette-based validation approach was used; a multi-step mixed-methods approach which included two major components:
  1. Develop clinical patient vignettes representing real-world PD patients
  2. Evaluate the inter-rater reliability and validity of the MANAGE-PD tool

DEVELOPMENT OF CLINICAL PATIENT VIGNETTES

- A Steering Committee (SC) developed ten hypothetical patient vignettes to represent a wide spectrum of frequency and severity of motor symptoms, non-motor symptoms and functional limitations of PD. Vignettes included the current management approach for the patient.
- A vignette of a patient inadequately controlled on current oral therapy and recommended optimization of oral therapy is described in **Figure 2**.
- The SC classified vignettes into one of three categories:
  - **Category 1:** adequately controlled on current oral therapy (n=1 vignette);
  - **Category 2:** inadequately controlled on current oral therapy and recommend optimization of oral therapy (n=4 vignettes);
  - **Category 3:** inadequately controlled on current oral therapy and recommend along with optimization of oral therapy, need for evaluation for device-aided therapies (n=5 vignettes).

Figure 2. Sample Clinical Vignette Used for Clinician Validation

> The patient is a 70-year-old man diagnosed with PD at age 64. The patient has received previous treatment with carbidopa/levodopa 25/100 three times daily and presently is taking carbidopa/entacapone/levodopa 37.5/200/150 mg, four times daily. The patient reports 2 hours of the day with "off" time with stiffness, slowness of movement and moderate walking difficulties at the end of effect of levodopa. He also experienced mild dyskinesias in the afternoon or late in the evening. These dyskinesias were noticed by his spouse more than the patient. His spouse also reports slight mood changes and slowness in thinking, although rarely. The patient has no limitations in his daily activities and continues with his daily walks each morning.

EVALUATING THE RELIABILITY AND VALIDITY OF MANAGE-PD TOOL

Web-based Survey

- Approximately 20 Parkinson's disease specialists (PD-specialists) from 15 countries (US and Europe) were identified based on their expertise in comprehensively treating aPD patients, experience in development of regional/national clinical guidelines and conduct of clinical trials and real-world studies including two or more device-aided therapies and invited to participate.
- A web survey was completed by each panelist. Using the MANAGE-PD tool, panelists scored one anchor vignette (used for assessing response consistency) and four randomly assigned vignettes.
- PD-specialists scored each vignette evaluating the frequency and severity of motor symptoms, non-motor symptoms, and functional impacts along with the current medication (including frequency of oral levodopa doses taken per day).
- Based on their own clinical judgement PD-specialists also rated the treatment management approach for each assigned vignette and open-ended feedback was solicited on the clarity of the vignettes and the tool.

Analysis

- Descriptive and scoring analyses of responses were completed for each vignette.
- The degree of agreement among PD-specialist raters on the severity of each vignette was evaluated.
- Intra-class co-efficient weighted kappa statistics were calculated for concordance for the categories[4] between clinical judgement for management of patient versus MANAGE-PD SC classification.
- Cognitive interview feedback (from five of the panelists) was evaluated for common themes or identified issues.

RESULTS

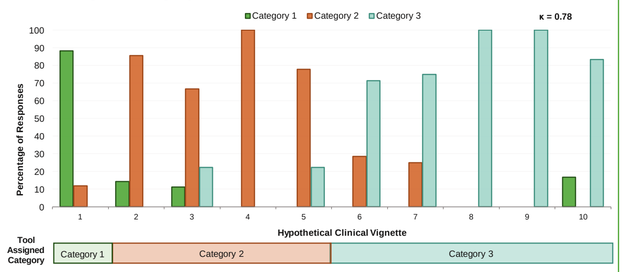
- The response rate for the panelist survey was 89% (n=17/19).
- The panelists who completed the survey had extensive experience in treating PD (mean years of treating PD patients: 24.4 ± 7.6 years (**Table 1**); mean number of patients treated/month: 73.2 ± 45.4 patients).
- The agreement between the MANAGE-PD tool and clinician rating was 88.23%, 82.35% and 88.23% for the three categories respectively.
- A high concordance between clinical judgement of the PD-specialists and MANAGE-PD tool rating for the vignette was observed (Intra-class co-efficient: 0.82; weighted kappa statistic: 0.71; unweighted kappa statistic: 0.78) (**Figure 3**).
- In open-ended survey feedback, panelists reported no issues with usage of the tool.
- In-depth interviews from five panelists provided recommendations for enhancing the item wording, response options, and vignette wording.

Table 1. Characteristics of the PD-Specialist Panel

Characteristics	Total Sample (N=17)
Gender, n (%)	
Female	12 (70.6%)
Male	5 (29.4%)
Number of years of experience in treating patients with PD	
Mean (SD)	24.4 (7.6)
Median [Range]	25 [10.0–38.0]
Number of PD patients treated each monthly	
Mean (SD)	73.2 (45.4)
Median [Range]	60 [10.0–150.0]
Treatment stage-PD patients seen in clinical practice (Proportion)	
PD patients optimally controlled on oral PD medication	
% Mean (SD)	38.8% (23.2)
% Median [Range]	40% [10.0–85.0]
PD patients not adequately controlled on oral PD medication	
% Mean (SD)	47.6% (29.4)
% Median [Range]	40% [0.0–90.0]
PD patients on device-aided treatment	
% Mean (SD)	18.1% (17.8)
% Median [Range]	12% [3.0–70.0]

Notes: Characteristics of only the PD-specialists who completed the entire validation exercise are shown. The response rate for the survey was 89.47% (i.e. 2 PD-specialists did not complete the entire validation exercise).
Abbreviations: PD, Parkinson's Disease

Figure 3. Concordance of PD-specialist Assigned Category and MANAGE-PD Tool Assigned Category



Notes: Category 1: Patient is adequately controlled on current oral therapy; **Category 2:** Patient is inadequately controlled on current oral therapy and optimization of oral therapy is recommended; **Category 3:** Patient is inadequately controlled on current oral therapy and along with optimization of oral therapy, evaluation for device-aided therapies is recommended. **Abbreviations:** κ, unweighted Kappa statistic; PD-specialists, Parkinson's Disease Specialists

DISCUSSION

STRENGTHS

- The MANAGE-PD tool is based on robust quantitative and qualitative data from a panel of leading PD-specialists from multiple countries.
- The indicators in the tool are grounded in the findings of Delphi-based consensus panels including leading international PD-specialists and have demonstrated acceptable accuracy in real-world settings.[5-7]
- The high experience and homogeneity of the panel add to the robustness of the findings.

LIMITATIONS

- The results of the survey may not be generalizable to other samples of PD-specialists who may have differences in the clinical practice or specific treatment guidelines.

CONCLUSION

- The MANAGE-PD tool demonstrated high reliability and validity within a sample of internationally renowned PD-specialists.
- Timely management of the PD patient symptoms using a standardized and validated tool may aid in homogenizing care for patients between PD-specialists and general neurologists (GNs) including the timing and need for referrals or medication change, and reducing the time a patient remains inadequately controlled on oral medications.
- A planned large global survey of GNs will further fine-tune the item wording and response options and provide opportunities to optimize the scoring algorithm and evaluate the psychometric properties.
- Future studies should evaluate the clinical utility of the tool for increasing care quality and efficiencies in real-world clinical practice.

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DISCLOSURES

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