Assessing the validity and reliability of MANAGE-PD tool – A clinician-reported tool to identify patients with Parkinson's disease inadequately controlled on oral medications – Results from an international survey of general neurologists

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Antonini A[1], Odin P[2], Jalundhwala YJ[3], Schmidt P[4], Skalicky AM[5], Kleinman L[5], Zamudio J[3], Onuk K[3], Kukreja P[3], Bao Y[3], Cubillos F[6], Fernandez HH[7].

[1] University of Padua, Padua, Italy; [2] Division of Neurology, Lund University, Skåne University Hospital, Lund Sweden; [3] AbbVie Inc., North Chicago, IL; [4] Brody School of Medicine, East Carolina University, Greenville, NC; [5] Evidera, Bethesda, MD; [6] Parkinson's Foundation, Miami, FL; [7] Center for Neurological Restoration, Cleveland Clinic, Cleveland, OH

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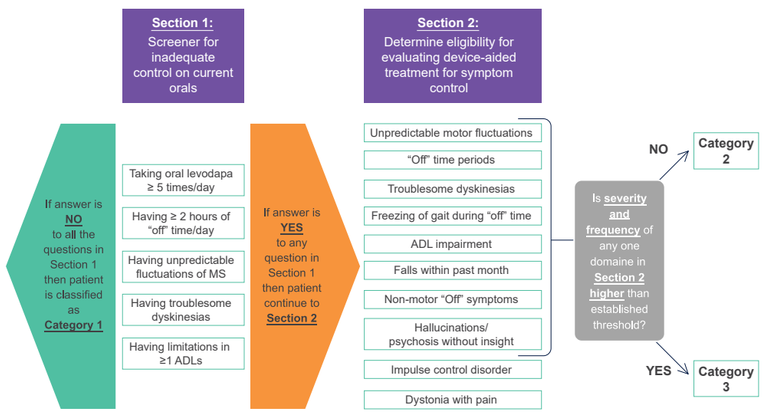
BACKGROUND

- A lack of clear definition together with the absence of gold-standard tests make diagnosis and management of symptoms challenging in patients with advanced Parkinson's disease (aPD).[1]
- Timely identification of symptoms associated with disease progression is an area for clinical practice improvement in patients with Parkinson's disease (PD). Early identification of patients uncontrolled with oral medications can lead to better decision making for proper treatment.
- Making Informed Decisions to Aid Timely Management of Parkinson's Disease (MANAGE-PD) is a simple screening tool intended to support healthcare practitioners (HCPs) make decisions making for the timely management of PD symptoms based on comprehensive evaluations of the frequency and severity of the motor, non-motor, and functional symptoms.
- The tool **(Figure 1)** was developed using a mixed-method approach[3] and building on a consensus of indicators identified by movement disorder specialists (MovDis specialists) Delphi-panel[5] and initial validity and reliability testingwith a sample of MovDis specialists[8].

Figure 1. MANAGE-PD Tool Overview[8]



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.

OBJECTIVES

- The main objective of this analysis is to assess the reliability of the MANAGE-PD tool based on an international survey of general neurologists.

METHODS

- A vignette-based validation approach was used to evaluate the inter-rater reliability and validity of the MANAGE-PD tool.

DEVELOPMENT OF CLINICAL VIGNETTES:

- A steering committee developed vignettes (n=10) representing a wide spectrum of disease severity to represent patients who are:
  - Adequately controlled on oral therapy; OR
  - Inadequately controlled on oral therapy and considering oral optimization only; OR
  - Inadequately controlled on oral therapy and considering evaluation for device-aided therapies (DAT) along with oral optimization.
- **Figure 2** presents a sample vignette of a patient who was inadequately controlled on current oral therapy and was recommended for optimization of oral therapy.[8]

Figure 2. Sample clinical vignette used for clinician validation

The patient is a 70-year-old man who was diagnosed with PD at age 64. The patient has received previous treatment with carbidopa/levodopa 25/100 three times daily and is taking carbidopa/entacapone/levodopa 37.5/200/150 mg four times daily. The patient reports two 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 VALIDITY AND RELIABILITY OF MANAGE-PD TOOL:

- Given the differences in clinical practice and level of expertise between community general neurologists(GN) and MovDis specialists, the validation and reliability was carried out in a two-step approach.
- **STEP 1:** This was conducted using a mix of open- and close-ended questions to a selected panel of leading international MovDis specialists (n=19) from 15 countries across the US and Europe to establish the gold standard. More details about the Step 1 survey have been previously presented.[8]
- **STEP 2:** This was conducted using a closed-ended survey of an internet-based panel of practicing GN from the US and UK (n=400).
- **STEP 2 WEB-SURVEY:** A panel of GN was randomly assigned to one of three blocks of vignettes. Using the MANAGE-PD tool, panelists scored one anchor vignette (used for assessing response consistency) and four randomly assigned vignettes. This approach allowed for equivalent numbers of participants to score each vignette. Based on their own clinical judgement GN also rated the treatment-management approach for each assigned vignette, and open-ended feedback was solicited on the clarity of the vignette and the tool.

STATISTICAL ANALYSIS:

- Detailed analysis approach for the validation using the MovDis specialists data has been presented before.[8]
- For the GN web-survey, an interim analysis was conducted for based on a cut-off from the ongoing survey. Descriptive analyses of scored responses were completed for each vignette.
- As a measure of reliability, weighted and unweighted kappa statistics were calculated based on the concordance of the category assigned by, GN-identified vignette category ratings (i.e., category 1, 2, 3) and MovDis specialists gold standard vignette category.
- For the sensitivity analysis, a concordance analysis was repeated with a subsample of GN with no DAT experience versus those with some DAT experience, and US versus UK GN to factors, which may influence the concordance.

RESULTS

- The survey enrollment is ongoing. In this interim analysis, 29% of the intended sample is included based on completion of the survey on or before August 25, 2019.
- Eighty-eight US (~25.2% of intended US sample) and 29 UK (~19.3% of intended UK sample) GN had completed the survey at time of the interim analysis. Responses from the interim sample (n=117) were almost equally distributed across all the three vignette blocks (i.e. Block A [n=39, 33%], Block B [n=38, 32%], and Block C [n=40, 34%]).
- The GN panelists who completed the survey had 19 ± 8 years of experience in treating PD and treated 39 ± 32 patients/per month **(Table 1)**. Compared to MovDis specialists, GN had similar years of experience in treating PD patients, but treated much fewer patients per month than MovDis specialists.

Table 1. Characteristics of the MovDis Specialists and GN

Characteristics	MovDis Specialists Sample (N=17)	GN Sample (N=117)
Gender, n (%)		
Female	12 (71%)	91 (78%)
Male	5 (29)	24 (21)
Number of years of experience in treating patients with PD		
Mean (SD)	24 (8)	19 (8)
Median [Range]	25 [10–38]	19 [4–41]
Number of PD patients treated each month		
Mean (SD)	73 (45)	39 (32)
Median [Range]	60 [10–150]	35 [0–99]
Treatment stage – PD patients seen in clinical practice (Proportion)		
PD patients optimally controlled on oral PD medication		
% Mean (SD)	39 (23)	56 (17)
% Median [Range]	40 [10–85]	60 [20–90]
PD patients not adequately controlled on oral PD medication		
% Mean (SD)	48 (29)	30 (12)
% Median [Range]	40 [0–90]	30 [20–90]
PD patients on device-aided treatment		
% Mean (SD)	18 (18)	14 (11)
% Median [Range]	12 [3–70]	10 [0–44]

Notes: *did not wish to answer (n=2, 2%).

Abbreviations: PD, Parkinson's disease; MovDis specialists, movement disorder specialists

- The highest agreement between the MANAGE-PD tool category assignment and GN clinician judgement was for the anchor vignette (vignette 1 – 98.3%) followed by vignettes in Category 3 (vignette 9 – 88.9%; vignette 7 – 84.6%; and vignette 8 – 79.5%). The agreement for the vignettes in Category 2 was relatively lower (vignette 2 – 26.3%; vignette 3 – 29.7% and vignette 4 – 35.0%) **(Table 2)**.

Table 2. Distribution of the MANAGE-PD category based on GN rating of clinical vignettes (interim data)

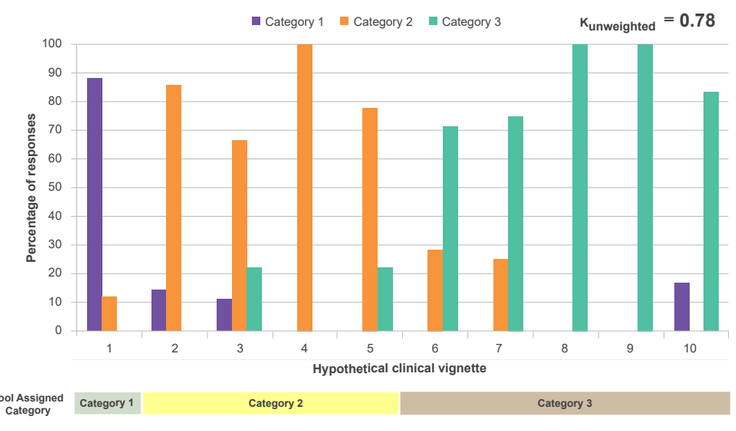
Vignette Number	Gold Standard Category*	GN Rating-based Category 1	GN Rating-based Category 2	GN Rating-based Category 3	% of Vignettes Correctly Categorized
1 (n=117)	1	115	2	0	98.3%
2 (n=38)	2	23	10	5	26.3%
3 (n=37)	2	15	11	11	29.7%
4 (n=40)	2	14	14	12	35.0%
5 (n=37)	3	9	5	23	62.2%
6 (n=38)	2	12	16	10	42.1%
7 (n=39)	3	4	2	33	84.6%
8 (n=39)	3	8	0	31	79.5%
9 (n=36)	3	3	1	32	88.9%
10 (n=39)	3	4	4	31	79.5%

Notes: *, gold standard as assigned by the MovDis Specialist and Steering Committee;
GN-rating based category reflects the category assigned based on the scoring of the MANAGE-PD tool.

Abbreviations: GN, General Neurologist

- The MANAGE-PD tool demonstrated validation based on the MovDis specialists panel survey (Intra-class co-efficient: 0.82; weighted kappa statistic: 0.71; unweighted kappa statistic: 0.78) **(Figure 3)**.[8] In contrast, the GN survey had a slightly lower concordance but moderate to substantial agreement[9] (Intra-class co-efficient: 0.32; weighted kappa statistic: 0.61; unweighted kappa statistic: 0.53).

Figure 3. Concordance between MovDis Specialist assessment and MANAGE-PD Tool scoring of the clinical vignettes[8]



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.

RESULTS (CONTINUED)

- The concordance had slight variation by geographic region: UK sample: $\kappa_{weighted} = 0.71$; compared to US sample: $\kappa_{weighted} = 0.58$. There were relatively small differences in overall agreement between GN panelists who have experience with DAT compared to those who don't.
- Amongst all the vignettes rated (n=364) by respondents classified as GN only (i.e., no movement disorders specialization), 31.5% were miscategorized (compared to MovDis specialist gold standard) by self-rating based on clinical judgement. However, based on self-rating of the vignettes using the MANAGE-PD tool, 61.7% of these vignettes could be correctly categorized.

DISCUSSIONS

STRENGTHS

- The validity and reliability of the MANAGE-PD tool is based on robust quantitative and qualitative data from both a diverse panel of leading international MovDis specialists[8] and a diverse panel of GN from the UK and US (data collection ongoing).
- The indicators in the tool are grounded in the findings of Delphi-based consensus panels including leading international MovDis specialist and have been demonstrated to have acceptable accuracy in real-world settings.[5-7]

LIMITATIONS

- Internet-based physician panel recruitment may not be generalizable to other samples of GN who may have differences in the clinical practice or specific treatment guidelines.
- The data in this poster are based on an interim analysis (~29% of intended sample).

CONCLUSIONS

- The MANAGE-PD tool validated with MovDis specialists[8] demonstrated acceptable reliability[9] with the GN (based on interim data). The variability in ratings of vignettes classified as category 2 may be due to differences in clinical practice experience and needs further Category evaluation.
- The tool demonstrated clinical utility based on the improved categorization of the vignettes via tool scoring. Real-world implementation and patient-level data are needed to further understand the clinical utility.
- Timely management of the PD patients' symptoms using a standardized and validated tool may aid in homogenizing care between MovDis specialists and GN, including the timing and need for referrals or medication change, which would reduce the time a patient remains inadequately controlled on oral medications.

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