

# HEALTH STATUS COMPARISON BETWEEN STABLE PARKINSON'S DISEASE PATIENTS AND THOSE EXPERIENCING "OFF-TIME"

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## BACKGROUND

- End-of-dose "wearing-off" is commonly experienced by Parkinson's disease (PD) patients who have used dopaminergic therapy for several years.
- Although investigations of "wearing-off" have traditionally focused on motor fluctuations, it is increasingly recognized that non-motor symptoms also vary between periods of "on-time" (when PD symptoms are minimized due to medication) and "off-time" (when PD symptoms return).
- The impact of symptom fluctuations on health-related quality of life (HRQL) remains poorly understood.

## OBJECTIVES

This study characterizes the self-reported health status of PD patients who experienced "off-time" fluctuations as compared to those who were stable.

## METHODS

### Study Design

• A sample of adults from the U.S. age  $\geq 30$  with self-reported doctor-confirmed PD were recruited, screened, and consented online from a Knowledge Networks panel [1].

• **Inclusion criteria:** ever experienced resting tremors and at least one of the following symptoms due to their Parkinson's disease: slowed ability to start and continue movements; rigidity or the inability to complete a movement, stiffness; difficulty with balance, instability; stooped, forward-leaning posture; freezing or sudden, brief inability to move the feet. **Exclusion criteria:** self reported history of brain surgery to treat PD symptoms; declined consent.

• Frequency of "off-time" was measured using the Unified Parkinson's Disease Rating Scale Part IV.

### Measures

• **12-item Short-Form Health Survey version 2 (SF-12v2)** [2]: generic 12-item instrument assessing HRQL in eight health domains and two summary measures (Physical Component Summary [PCS] and the Mental Health Component Summary [MCS]). Higher scores represent greater health.

• **Parkinson's Disease Questionnaire-8 (PDQ-8)** [3]: 8-item questionnaire measuring the physical and psychosocial impact of PD. Although each item represents one domain, a summary score based on all 8 items - the PDQ-8 Summary Index (PDQ-8 SI) - can be derived. The PDQ-8 SI was evaluated as the sum of the 8 items divided by the maximum possible score (32), expressed as a percentage.

• **Wearing off Questionnaire-9 (WOQ-9)** [4]: The "wearing-off" Questionnaire -9 [4] is a 9-item survey that asks about the reduction of or improvement of PD symptoms in relation to the timing of medication. For each symptom, the respondent is first asked whether they experience the symptom (Yes/No). Respondents who answer "Yes", are then asked whether the symptom is reduced or disappears after taking the next dose of PD medication (Yes/No). WOQ-9 scores were derived using the following calculations:

- the number of symptoms that are present on a normal day, evaluated as the sum of affirmative answers to question 1;
- the total number of fluctuating symptoms, evaluated as the number of affirmative answers to question 2, provided the respondent also answered Yes to question 1 for the same item;

## RESULTS

### Sample Characteristics

Key demographic and clinical characteristics are presented in Table 1.

Table 1. Demographic and Clinical Characteristics, by Fluctuator/Stable Status

	Entire Sample (n=165)	Stable (n=25)	Fluctuators (n=140)	p-value
Age				
Mean (SD)	66.6 (11.9)	68.9 (11.6)	66.3 (11.9)	0.4015
Gender				
Male	87 (52.7)	13 (52.0)	74 (52.9)	0.9370
Race				
White, Non-Hispanic	81 (82.7)	13 (92.9)	68 (81.0)	0.7592
Black, Non-Hispanic	7 (7.1)	1 (7.1)	6 (7.1)	
Other, Non-Hispanic	4 (4.0)	0 (0.0)	4 (4.8)	
Hispanic	6 (6.1)	0 (0.0)	6 (7.1)	
Employment				
Working	39 (23.6)	7 (28.0)	32 (22.9)	0.2163
Not working	31 (18.8)	1 (4.0)	30 (21.4)	
Retired	95 (57.6)	17 (68.0)	78 (55.7)	
Years since PD diagnosis				
Mean (SD)	7.1 (5.24)	6.1 (6.1)	7.3 (5.1)	0.4177
Currently taking Levodopa	104 (63.0)	13 (52.0)	91 (65.0)	0.3430
How long have you been taking Levodopa?				
< 1 year	20 (19.2)	3 (23.1)	17 (18.7)	0.7068
$\geq 1$ year	84 (80.8)	10 (76.9)	74 (81.3)	

± statistical significance of differences between stable and fluctuators assessed with the t-test for mean differences in age and years since PD diagnosis; significance testing for all other variables conducted with the Chi-Square test.

### Differences in Health Status Between Stable PD patients and Fluctuators

• SF12v2 summary scores showed significantly greater impairment in physical health ( $p < 0.01$ ) and mental health ( $p = 0.02$ ) for *fluctuators* when compared to *stable* patients (Table 2). The scores of *fluctuators* were 0.5 standard deviations below average SF12v2 scores for individuals aged 65-74 years, in the general US population [2].

• The mean PDQ-8 SI of stable subjects was nearly 5 points lower than the mean of PD patients with fluctuations ( $p < 0.01$ ; Table 2).

• The mean number of self-reported symptoms in the WOQ-9 was significantly higher (+1) among *fluctuators*, as was the mean number of symptoms improving after medication (+1.6).

• Differences in specific PD symptoms (Figure 1), as captured by the WOQ-9, didn't reach statistical significance, with the exception of stiffness (*stable*: 46%; *fluctuator*: 70%;  $p = 0.019$ ). Statistically significant differences were observed in symptoms which improve after taking the medication: tremor (*stable*: 43%; *fluctuators*: 85%;  $p < 0.001$ ), reduced dexterity (*stable*: 31%; *fluctuators*: 64%;  $p = 0.012$ ) and cloudy mind (*stable*: 39%; *fluctuators*: 63%;  $p = 0.036$ ).

Table 2. Health Status by Fluctuator/Stable Status

	Entire Sample			Stable			Fluctuator			p-value
	Mean	SD	N	Mean	SD	N	Mean	SD	N	
PCS	38.1	(10.7)	165	42.1	(7.5)	25	37.4	(11.1)	140	0.0102
MCS	44.8	(11.0)	165	49.6	(10.8)	25	44.0	(10.8)	140	0.0220
PDQ-8 SI	19.4	(7.0)	164	15.3	(6.2)	24	20.2	(6.9)	140	0.0015
WOQ-9 Symptoms	5.7	(2.1)	154	4.9	(2.0)	24	5.9	(2.0)	130	0.0503
WOQ-9 Fluctuating Symptoms	3.6	(2.2)	143	2.2	(2.0)	20	3.8	(2.2)	123	0.0026

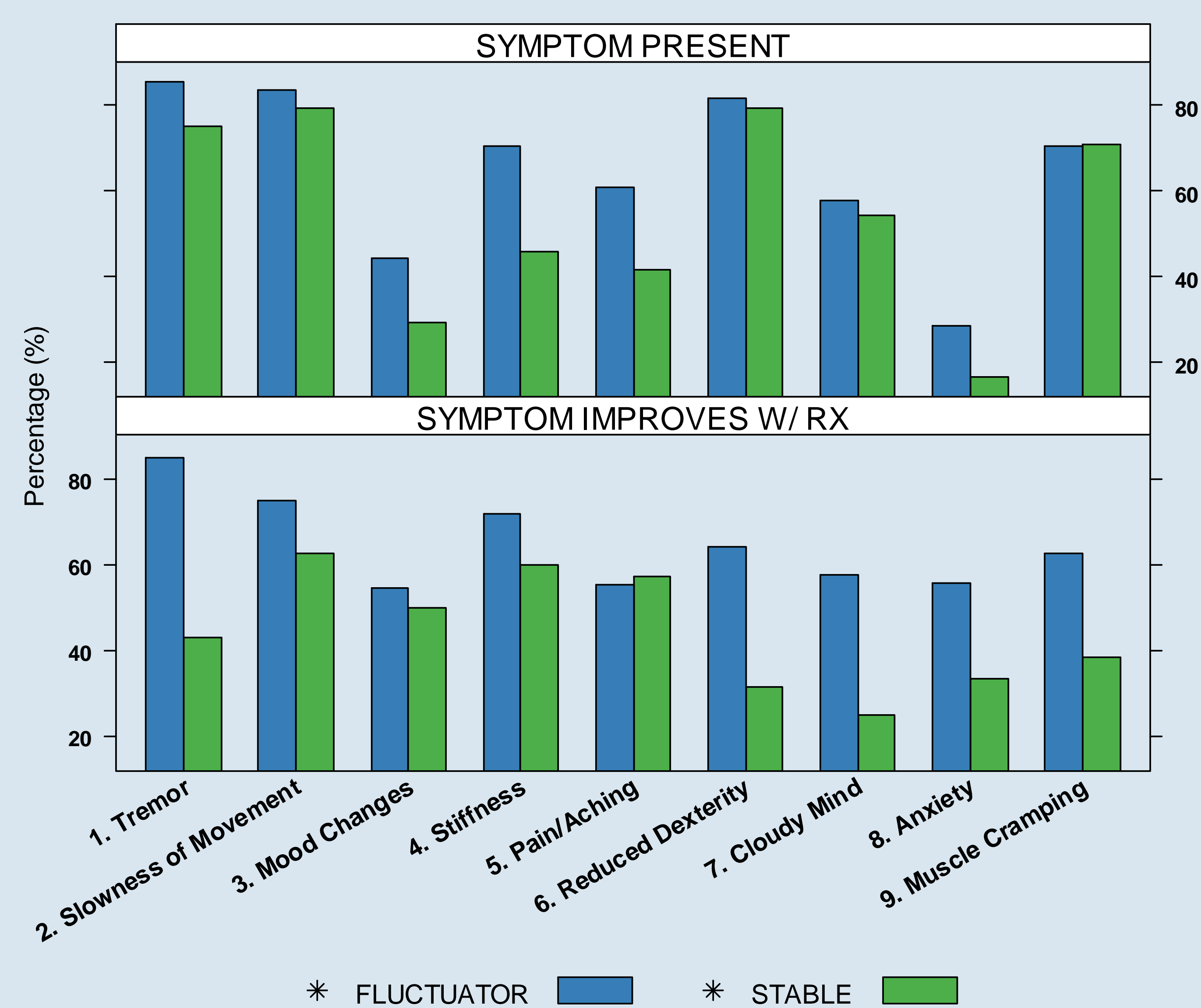


Figure 1. Frequency and "wearing-off" of PD symptoms

Note: statistically significant ( $p < 0.05$ ) differences between stable and fluctuators were found for stiffness (symptom present) and for tremor, reduced dexterity and cloudy mind (symptom improves after medication).

## LIMITATIONS

- Online recruitment of participants could have introduced bias by excluding individuals lacking appropriate skills and/or resources.
- The presence of "off-time"-time was self-reported which could have caused misclassification and/or differed from clinician assessed presence of "off-time"-time.
- Cross-sectional study design.

## CONCLUSIONS

- PD patients who experienced at least some "off-time" on a typical day (*fluctuators*) reported worse overall physical and mental well-being than *stable* patients.
- Both motor and non-motor "wearing-off" symptoms differed between the two patient groups.
- Additional research to understand the consequences of "off-time" would be useful, especially as it pertains to non-motor symptoms.

## REFERENCES

- [1] <http://www.knowledgenetworks.com/knpanel/KNPanel-Design-Summary.html>. 2010
- [2] Ware JE, Jr., Kosinski M, Turner-Bowker DM, Gandek B. How to Score Version 2 of the SF-12® Health Survey (With a Supplement Documenting Version 1). Lincoln, RI: QualityMetric Incorporated, 2002.
- [3] Jenkinson C, Fitzpatrick R, Peto V, Greenhall R, Hyman N. The PDQ-8: development and validation of a short-form Parkinson's disease questionnaire. *Psycho Health* 1997; 12:805-814.
- [4] Stacy MA, Murphy JM, Greeley DR, Stewart RM, Murck H, Meng X. The sensitivity and specificity of the 9-item "wearing-off" Questionnaire. *Parkinsonism Relat Disord* 2008; 14(3):205-212.