

# COMPENDIUM OF BASIC AND CLINICAL RESEARCH IN PARKINSON'S DISEASE

*Highlights from the*

## 2018 INTERNATIONAL CONGRESS OF PARKINSON'S DISEASE AND MOVEMENT DISORDERS

### A CANADIAN PERSPECTIVE

OCTOBER 5-9 | WAN CHAI, HONG KONG

Were you unable to attend the International Congress this year? Or do you feel you missed key abstract presentations and poster sessions? This *Compendium* offers expert reviews of the latest research on Parkinson's disease. Five Canadian neurologists who attended the Congress collaborated to present you with meeting highlights as well as their thoughts on how advances in the field and the latest technological tools will impact the future management of Parkinson's disease in Canada.



# 2018

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## EDITOR'S NOTE

This year's Congress focused the spotlight on technological advances in movement disorders; it was a fitting topic given the myriad of novel technologies featured in this year's presentations. In keeping with this theme, we have reviewed a few of the most promising candidates in this year's *Compendium*. There were also several studies that stood out as they informed on best practices in the management and assessment of Parkinson's disease (PD). In addition to the abstracts reviewed within the *Compendium*, there were many insightful studies worth mentioning that advanced our knowledge and will impact the field in the future.

### INNOVATIVE CELL THERAPY

Cell therapy is a strategy that employs stem cells to replace dopaminergic neurons and reverse disease progression in PD. There are, however, many roadblocks with this approach, including the poor survival of neuronal transplants, lack of in situ control of neuronal identity, and ensuing tumour risk. Researchers from France have developed controlled neural organoids (CNOs) to overcome these limitations as they allow for more control over cell size and content. When tested in hemiparkinsonian rats, CNO transplants appear to promote functional recovery. Following future validation in human subjects, this promising strategy could present an alternative to drug-based treatment in PD.

### NOVEL TREATMENT TARGET

A team in Spain found evidence of an overlapping mechanism in the pathogenesis of diabetes and PD. Past studies have alluded to a form of peripheral insulin resistance in the brains of PD patients without diabetes.<sup>1</sup> In the same vein, a clinical trial found glucagon-like peptide-1 (GLP-1) agonist exenatide improved off-medication scores in PD patients without diabetes.<sup>2</sup> This latest study found alpha-synuclein deposits in the pancreatic beta cells of patients with PD, as well as in neurologically asymptomatic patients with diabetes. The researchers also found that alpha-synuclein interacted with the islet amyloid polypeptide precursor (IAPP) in the pancreas of these patients. IAPP has been shown to promote alpha-synuclein oligomer formation. In light of these findings, the researchers propose that this interaction could pose a novel treatment target in PD and that exenatide is a pharmacological candidate with potential neuroprotective effects.



## PREDICTING DEMENTIA RISK IN PD

Researchers from the UK evaluated the potential of visual testing to identify PD patients at risk of dementia. The same group had previously found a link between visuo-perceptual deficits and cognitive decline in PD.<sup>3</sup> Retinal thinning was shown to correlate to dopamine active transporter (DaT) scan and positron emission tomography (PET) findings indicative of neuronal degeneration. In their study, retinal optical coherence tomography (ROCT) was used to assess retinal thickness. PD patients at risk for dementia<sup>4</sup> exhibited more retinal thinning compared to those at low risk for dementia. Pending further validation, retinal thinning assessed using ROCT may serve as a viable biomarker for the presence of dementia in PD.

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## CONGRESS SUMMARY



The annual International Congress of Parkinson's Disease and Movement Disorders took place in Wan Chai, Hong Kong from October 5–9. Hailing from 86 countries across the globe, more than 4,000 participants attended this year and over 1,800 abstracts were presented.

The theme of this year's Congress was *Technology in the diagnosis, monitoring, and management of movement disorders*. True to form, there were many emerging technologies presented that are likely to transform the field of movement disorders. These included a nanotechnological stimulation device to improve gait (Peppe et al.), wearable sensors to monitor Parkinson's disease symptoms (Daneault et al.), and novel imaging techniques, such as neuromelanin magnetic resonance imaging (MRI).

As in previous meetings, the poster and plenary sessions were dominated by presentations on potential disease biomarkers – particularly for Parkinson's disease (PD). Of note, regression analysis of prospective data on a large cohort of patients has enabled the identification of certain biomarkers years prior to onset of motor symptoms. In gene therapy news, the preliminary data from the first antisense oligonucleotide (ASO) trial in Huntington's disease showed a reduction in huntington (HTT) levels in a dose-dependent fashion.

While there was no major therapeutic breakthrough announced in PD, a mass of evidence was presented on the safety, feasibility, and functional benefits of various alternative and exercise modalities (cycling, dance, boxing, tai chi). In the quest to diagnose advanced PD earlier, a study by Odin et al. identified and evaluated certain clinical indicators that could be used in practice. In a large Hong Kong study by Chan et al., low body weight—a common characteristic in PD—was found to relate to poorer functional status in PD. Weight loss was also seen in a small study by Fernández-Rodríguez et al. of patients on levodopa-carbidopa intestinal gel (LCIG) therapy when compared to those undergoing deep brain stimulation (DBS). While LCIG treatment was shown to improve motor symptoms and quality of life (QOL) in a study by Chorbazdzheva, an associated vitamin deficiency was also found.

Our Canadian experts attending the Congress this year also reported there were many exciting developments revealed in both the basic science and clinical realms. In an overview of the latest findings in PD pathology, new information revealed that alpha-synuclein and tau—both proteins implicated in neurodegeneration—can cross-talk through cellular proteostasis. In neurosurgical research, gamma knife radiosurgery appears to provide a safe and effective option for the management of refractory tremor, according to a study by Perez-Sanchez et al. Finally, a study by Seier et al. found that alternating DBS programming weekly may help prolong tremor control compared to the standard DBS approach.

# PHARMACOLOGICAL MANAGEMENT

## Rationale and Design of an Open-Label, Randomized, 26-Week Study Comparing Levodopa-Carbidopa Intestinal Gel to Optimized Medical Treatment on Non-Motor Symptoms in Patients with Advanced Parkinson's Disease – INSIGHTS Study

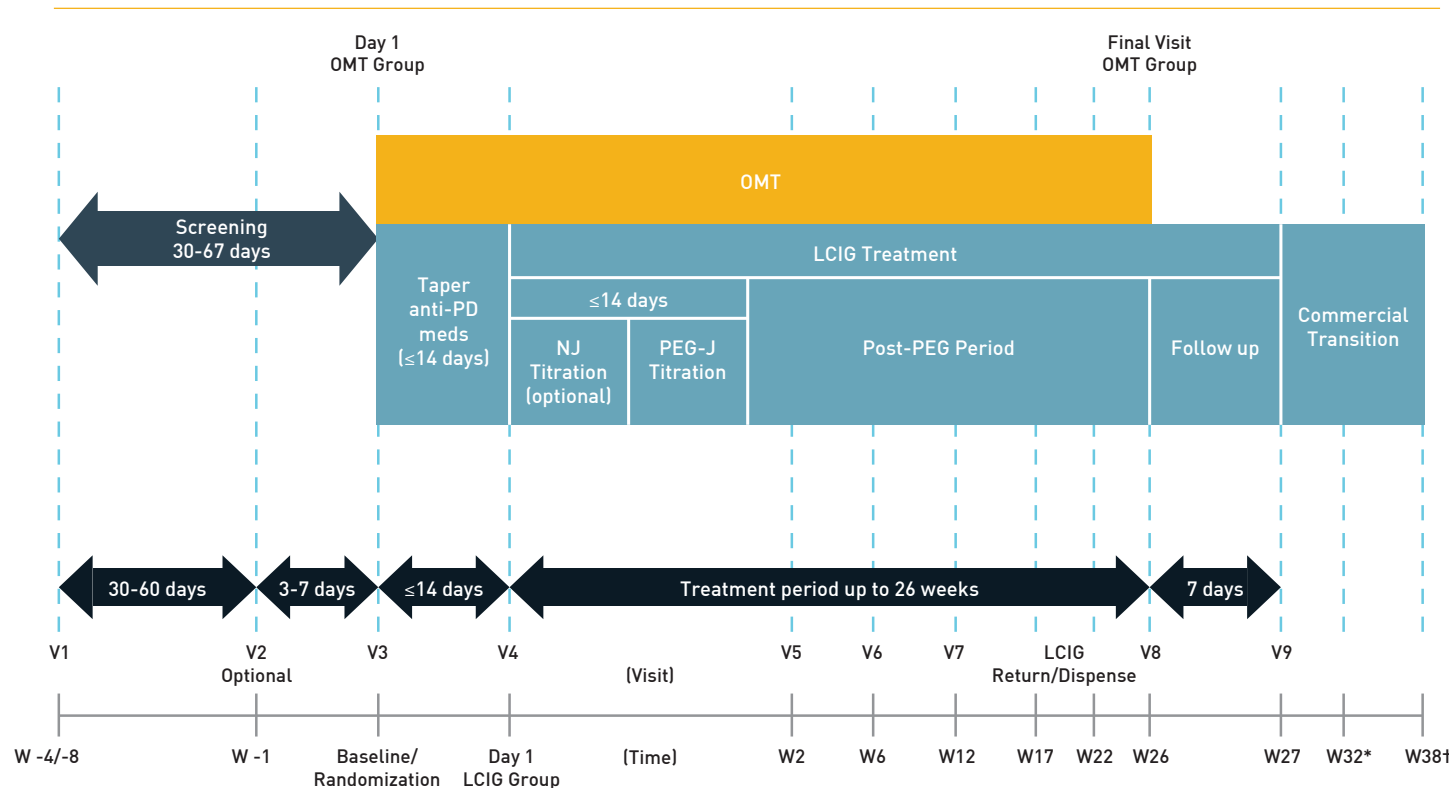
K. Ray Chaudhuri, D. Weintraub, A. Antonini, W. Robieson, M. Li, K. Chatamra, J. Benesh, M. Facheris (London, United Kingdom)

SUMMARY BY DR. JULIUS ANANG

Many patients with advanced Parkinson's disease (PD) have nonmotor symptoms (NMS) that remain inadequately controlled despite reduced "off" time and increased "on" time with conventional therapies. This study compares the effects of levodopa-carbidopa intestinal gel (LCIG) to those of optimized medical treatment (OMT) on NMS in advanced PD.

INSIGHTS is a Phase IIIb, randomized, open-label, multicentre study that is looking to compare the effects on NMS of LCIG or OMT in a 1:1 ratio over 26 weeks in 88 patients (Figure 1). Patients who were levodopa-responsive with motor fluctuations (no longer controlled with oral PD medications) and who experienced sleep disturbances were included in the study. Sleep disturbances were confirmed using the modified PD Sleep Scale (PDSS-2) and was defined as a score of >18. Excluded from the study were patients with prior PD related to neurosurgery, prior treatment with LCIG (or contraindication for its use), and clinically significant sleep attacks or impulse control behaviour (within 3 months of screening).

FIGURE 1: INSIGHTS study design



\*During the commercial transition, patients will return used LCIG cassettes and have LCIG dispensed every 6 weeks. †Safety Assessments will be performed every 12 weeks. LCIG = levodopa-carbidopa intestinal gel; Meds = medications; NJ = nasojejunal; OMT = optimized medical treatment; PD = Parkinson's disease; PEG-J = percutaneous endoscopic gastrojejunostomy with J tube extension; W = week; V = visit.

Adapted with permission from Ray Chaudhuri et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 424.





The primary endpoints of the study include capturing changes from baseline to the 26-week mark in the NMS Scale (NMSS) and PDSS-2 total scores. Secondary endpoints include measuring activities of daily living (ADL), quality of life (QOL), and safety assessments. When this study was presented at the Congress, 42 patients had been enrolled – nearly all are white (2 nonwhite) with a mean age of 69.1 years (Table 1).

**TABLE 1: Baseline characteristics of patients enrolled in INSIGHTS study**

Baseline Characteristic	Mean (standard deviation) Range
<b>PD disease duration (since diagnosis, years)</b>	14.3 (5.56) 4.9 - 29.9
<b>NMSS total score</b>	108.1 (48.5) 23.0 - 208.0
<b>PDSS-2 total score</b>	31.2 (8.2) 16.0 - 50.0
<b>PDQ-8 summary index</b>	41.8 (16.05) 9.4 - 81.3

Adapted with permission from Ray Chaudhuri et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 424.

At this preliminary stage, all patients' PDSS-2 scores confirm they are poor sleepers and their short-form 8-item Parkinson's Disease Questionnaire (PDQ-8) total scores—which are a reflection of the presence of NMS—indicate reduced QOL at baseline. The authors note the data from this study will help provide important guidance to physicians, patients, and caregivers when assessing treatment options and weighing the benefits of different PD treatments.

## EXPERT TAKEAWAY

This study would be the first prospective randomized study to compare the effects of LCIG and OMT on NMS and sleep. It's an important endeavor, as NMS contributes considerably to QOL and represents a significant amount of disease burden on PD patients. The study size of 88 patients might pose a limitation. A larger size study would provide more robust and reliable data.



## POTENTIAL FUTURE IMPACT

The outcomes from this study would provide comprehensive data on the benefits (other than motor benefits) of advanced treatments that will be valuable to physicians, patients, and caregivers. The data could help treatment teams further optimize therapies in patients with advanced disease. In future, a similar randomized study comparing the effects on NMS of OMT and other available advanced therapies, such as deep brain stimulation (DBS) and apomorphine infusion therapy would be useful. This data would help further facilitate decision making in the selection of specific device-aided therapies for patients.

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## PHARMACOLOGICAL MANAGEMENT

### Weight variation in Parkinson's disease patients treated with levodopa-carbidopa intestinal gel infusion

B. Fernández-Rodríguez, J. Dupouy, E. Harroch, MH. Fabre-Delcros, C. Barthélémy, P. Loubière, K. Barange, C. Brefel-Courbon, O. Rascol, F. Ory-Magne (Toulouse, France)

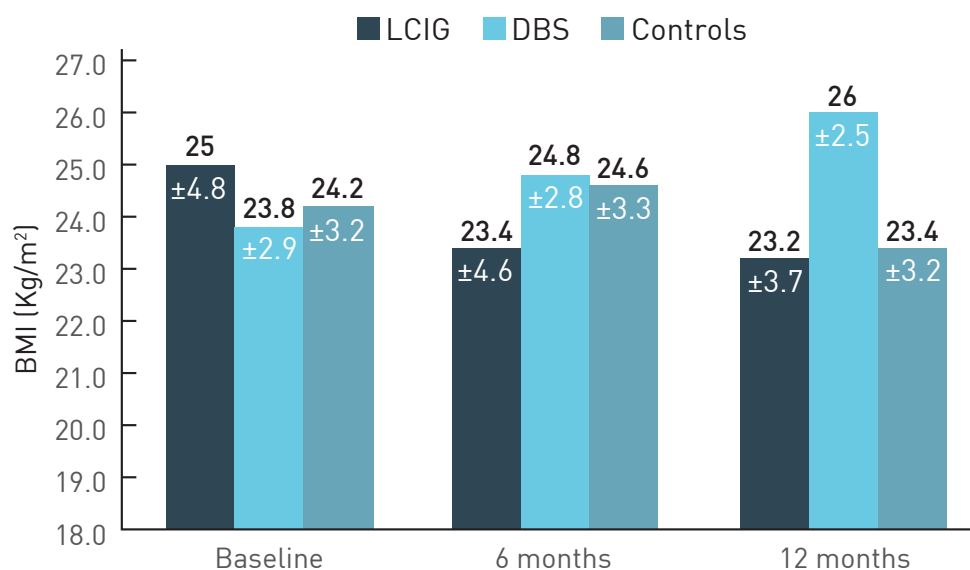
SUMMARY BY DR. ALFONSO FASANO

An increase in weight is a well-known complication associated with subthalamic nucleus deep brain stimulation (STN-DBS). Currently, weight loss has been reported only in some studies in patients on continuous levodopa-carbidopa intestinal gel (LCIG). The purpose of this study was to determine if treatment with LCIG infusion has an impact on a patient's weight and also to establish the timeline of weight changes. To achieve this objective, weight variations were compared across three cohorts of patients with advanced Parkinson's disease (PD). The three cohorts consisted of 19 patients in their first year of treatment with LCIG, 18 patients in their first year of treatment with STN-DBS, and 18 patients on conventional oral therapy.

Weight variations and body mass index (BMI) were studied retrospectively in the three cohorts. Patients with systemic disorders (e.g. diabetes, cancer, etc.) within 5 years before baseline were excluded from the study. The patients on LCIG therapy who were included were matched to the STN-DBS patients and oral therapy patients by gender, age ( $\pm 4$  years), disease duration ( $\pm 3$  years), and the Hoehn and Yahr (H&Y) scale on levodopa (L-dopa). Weight, height, treatment, cognitive impairment, medical history, and blood tests were assessed at baseline, 6 months, and 12 months.

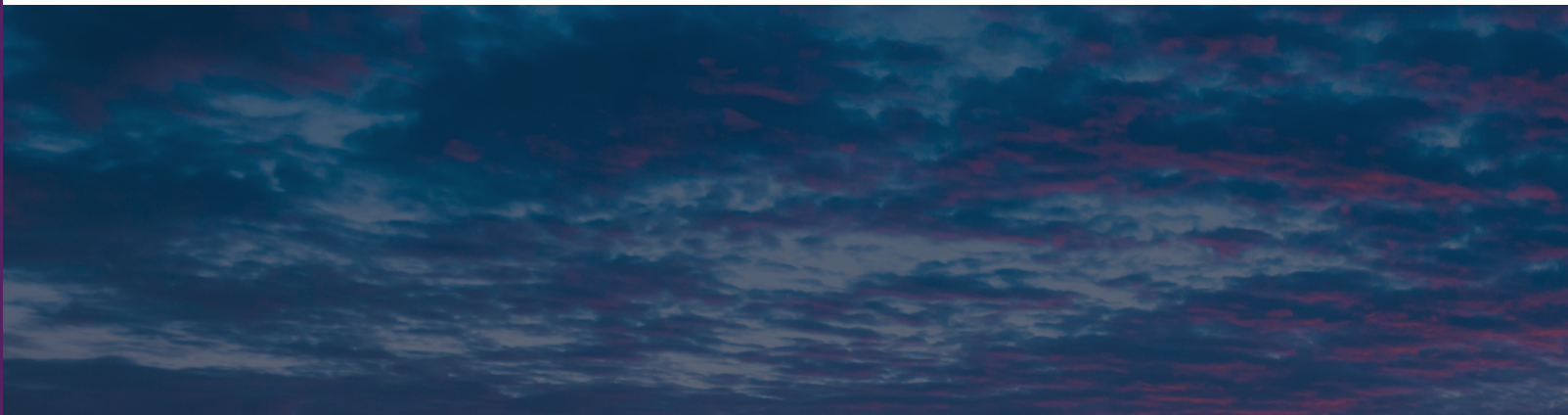
At 12 months, a mean weight reduction of  $5.78 \pm 6.8$  Kg was found in the LCIG group. Of the 19 patients in this group, 15 lost weight, and 2 gained weight, while 1 patient remained stable and another stopped treatment at 4 months. At the end of the year, the mean BMI decrease was  $2.1 \pm 2.6$  Kg/m<sup>2</sup> in the LCIG group (Figure 1). The group on oral therapy showed a mild decrease in BMI of  $0.55 \pm 1.1$  Kg/m<sup>2</sup> while the group that underwent STN-DBS showed an increase in BMI of  $1.97 \pm 1.7$  Kg/m<sup>2</sup>.

**FIGURE 1: BMI variation from baseline to 12 months (Kg/m<sup>2</sup>)**



Adapted with permission from Fernández-Rodríguez et al. *Mov Disord.* 2018; 33 [suppl 2], abstract 314.





The study found that LCIG treatment was associated with a risk of weight reduction that is higher than the loss typically observed with the disease alone. The authors stress that understanding the mechanism driving this weight loss is imperative to prevent malnutrition or vitamin deficiency in patient with advanced PD.

## EXPERT TAKEAWAY

This study shows there is weight loss with LCIG and that this happens largely in the first 6 months of therapy. Notably, there was no difference in weight loss seen between the LCIG and the oral therapy group at 12 months (Figure 1). The sample size for the study is small and not pure as seven patients in the LCIG therapy group had undergone STN-DBS therapy previously. It would also be useful to have data on the cognition measures, other drugs used by patients in the cohort studies, the levodopa equivalent daily dose (LEDD) reduction, vitamin levels, and occurrence of neuropathy.

## POTENTIAL FUTURE IMPACT

The link between weight loss and LCIG treatment remains unclear. Prospective studies with larger samples of patients with PD would help provide more information on the extent of the weight loss and shed more light on the potential factors at play.

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## PHARMACOLOGICAL MANAGEMENT

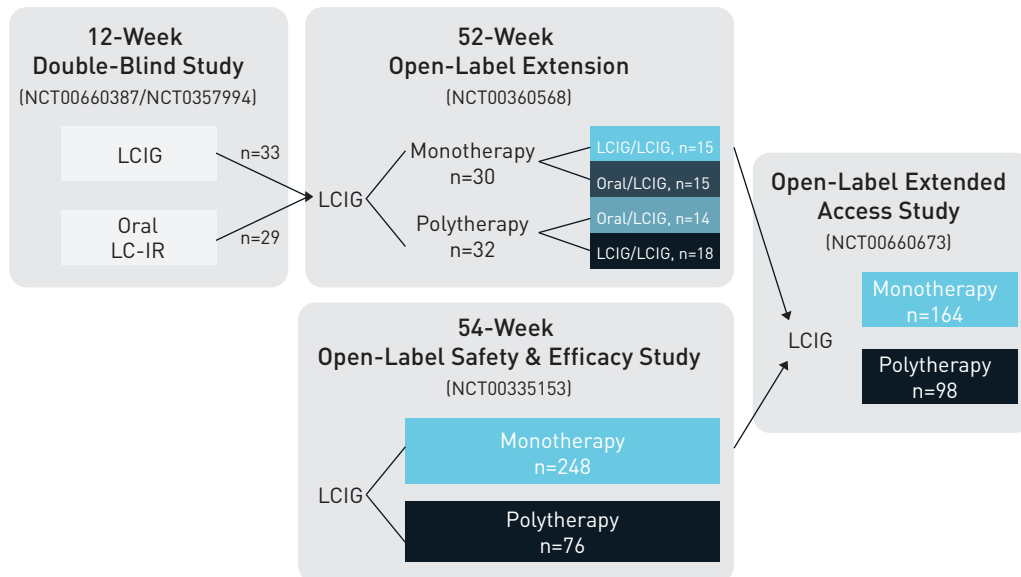
### Safety and Efficacy of Levodopa-Carbidopa Monotherapy in Patients with Advanced Parkinson's Disease

J. Boyd, C. Zadikoff, M. Siddiqui, J. Benesh, J. Zamudio, W. Robieson, P. Kukreja (Burlington, VT, USA)

SUMMARY BY DR. ALFONSO FASANO

Adjunctive therapies are often needed when treating motor complications in Parkinson's disease (PD). Continuous levodopa-carbidopa intestinal gel (LCIG) administration is an option that could help reduce pill burden. The purpose of this study was to evaluate the safety and efficacy of continuous LCIG daytime monotherapy for advanced PD compared to polytherapy (LCIG with more than one adjunctive therapy). Note: LCIG monotherapy was administered with or without night-time oral carbidopa-levodopa. The data used in the study were derived from the extension of three Phase III studies. The first study was a 52-week open-label extension, the second was a 54-week open-label study, and the third was an extended-access study (Figure 1). In all, 386 patients with a mean LCIG duration of 3 years were included in the study. LCIG monotherapy was administered continuously for 16 hours per day using percutaneous endoscopic gastrojejunostomy (PEG-J).

**FIGURE 1: Patient groups included from three Phase III trials**



LCIG = levodopa-carbidopa intestinal gel; LC-IR = immediate-release levodopa-carbidopa.

Adapted with permission from Boyd et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 374.

Across all three studies, patients on daytime LCIG monotherapy reported similar reductions in “off” time and improvement in “on” time as those on polytherapy in their PD diary. Likewise, adverse events were comparable between the daytime LCIG monotherapy group and the polytherapy group. Interestingly, in the first study (52-week open-label extension study), freezing was more common in the LCIG monotherapy group (Table 1) whereas constipation was reported more often in the polytherapy group (Table 2) in the second study (54-week open-label extension study).

**TABLE 1: Adverse events reported in the 52-week open-label extension study (study 1)**

Preferred Term <sup>a</sup>	Patients, n (%)	
	LCIG/LCIG or Oral/LCIG Monotherapy n=30	LCIG/LCIG or Oral/LCIG Polytherapy n=32
Any adverse event	27 (90.0)	32 (100)
Non-procedure/device-related adverse events (>15% of patients in any group)		
Fall	7 (23.3)	6 (18.8)
Vitamin B6 decreased	6 (20.0)	7 (21.9)
Nausea	5 (16.7)	4 (12.5)
Freezing phenomenon	5 (16.7)	2 (6.3)
Constipation	3 (10.0)	6 (18.8)
Urinary tract infection	3 (10.0)	6 (18.8)
Blood homocysteine increased	2 (6.7)	5 (15.6)
Parkinson's Disease <sup>b</sup>	2 (6.7)	6 (18.8)
Insomnia	1 (3.3)	8 (25.0)
Orthostatic hypotension	1 (3.3)	5 (15.6)
Seborrheic keratosis	1 (3.3)	7 (21.9)
Depression	0	5 (15.6)

<sup>a</sup> A single event could be coded to >1 preferred term.

<sup>b</sup> Refers to a reemergence of Parkinson's disease symptoms.

Adapted with permission from Boyd et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 374.




**TABLE 2: Adverse events reported in the 54-week open-label extension study (study 2)**

Preferred Term <sup>a</sup>	Patients, n (%)	
	Daytime Monotherapy n=248	Polytherapy n=76
Any adverse event	225 (90.7)	73 (96.1)
Non-procedure/device-related adverse events (>10% of patients in any group)		
Nausea	39 (15.7)	15 (19.7)
Fall	39 (15.7)	10 (13.2)
Insomnia	34 (13.7)	10 (13.2)
Constipation	32 (12.9)	15 (19.7)
Urinary tract infection	27 (10.9)	10 (13.2)
Weight decreased	22 (8.9)	9 (11.8)
Vomiting	19 (7.7)	9 (11.8)
Parkinson's Disease <sup>b</sup>	19 (7.7)	10 (13.2)
Depression	18 (7.3)	8 (10.5)
Back pain	17 (6.9)	8 (10.5)
Dyskinesia	16 (6.5)	15 (19.7)

<sup>a</sup> A single event could be coded to >1 preferred term.

<sup>b</sup> Refers to a reemergence of Parkinson's disease symptoms.

Adapted with permission from Boyd et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 374.

The study concluded that daytime LCIG monotherapy had a similar efficacy and safety profile as polytherapy in advanced PD across the three Phase III extension studies examined.



## EXPERT TAKEAWAY

There are some concerns to address with this comparison study that may have affected the outcome. Firstly, the study was open-label and flexible. Secondly, typically, patients who require polypharmacy have more advanced PD. Although the side effect profiles were found to be similar between the groups, there were some differences noted when the studies were looked at separately. This discrepancy may indeed be indicative of more severe disease in the polytherapy group.

## POTENTIAL FUTURE IMPACT

As PD progresses, the number of medications and frequency of dosing tends to increase, which correlates with reduced patient compliance and subsequently, suboptimal control of symptoms. Although the comparison of the two groups (monotherapy vs. polytherapy) may have been somewhat problematic, this study proposes another potential option for the treatment of PD patients that would help simplify therapy.

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## PHARMACOLOGICAL MANAGEMENT

### Treatment with levodopa/carbidopa intestinal gel of advanced Parkinson's disease patients: Bulgarian experience

E. Chorbazhieva (Sofia, Bulgaria)

SUMMARY BY DR. JUSTYNA SARNA

Typically, levodopa-carbidopa intestinal gel (LCIG) is used to ensure stable plasma infusion in Parkinson's disease (PD) patients to help reduce motor fluctuations. This study was done to assess the efficacy of LCIG on motor symptoms and quality of life (QOL), and to determine the association between LCIG, polyneuropathy, and vitamin B levels.

The retrospective analysis was conducted on 61 patients with advanced PD. In all, 50 men and 11 women aged  $61.84 \pm 7.38$  years who were treated from 2009 to 2016 at the St. Naum movement disorder department in Bulgaria were included in the study. Patients were evaluated at Day 1 and at 12 months using the Unified Parkinson's Disease Rating Scale (UPDRS) III and IV, the 39-item Parkinson's Disease Questionnaire (PDQ-39 [QOL]), levodopa equivalent dose (LED), and electrophysiology measures (Table 1).

**TABLE 1: Patient characteristics and evaluations at Day 1 and at 12 months**

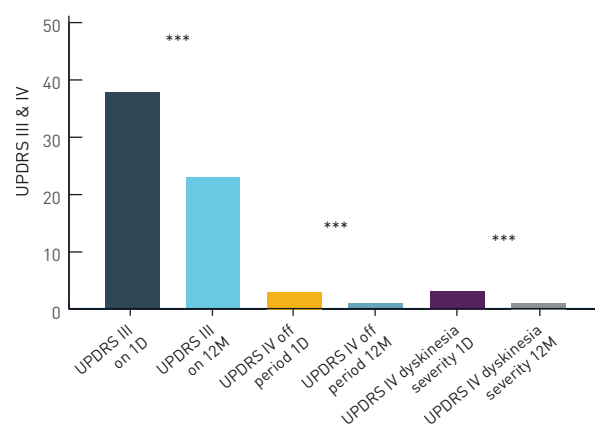
Characteristics	LCIG 1D	LCIG follow-up 12M	P value
Gender (m/f)	50/11	-	-
Age (years)	$61.84 \pm 7.38$	-	-
PD duration (years)	$15.13 \pm 4.90$	-	-
LCIG duration (months)	$29.28 \pm 21.29$	-	-
H&Y	$3.98 \pm 0.23$	-	-
UPDRS III on	$38.14 \pm 10.07$	$21.97 \pm 6.23$	<0.001
UPDRS IV off duration	$2.30 \pm 0.53$	$1.03 \pm 0.18$	<0.001
UPDRS IV dyskinesia severity	$2.10 \pm 0.68$	$1.03 \pm 0.49$	<0.001
LED (mg)	$1361.07 \pm 508.73$	$1419.90 \pm 318.29$	0.014
PDQ-39SI	$67.51 \pm 11.84$	$40.81 \pm 10.22$	<0.001
Cobalamin (246-911 pg/ml)	$306.7 \pm 27.8$	$233.3 \pm 25.78$	0.063
Folic acid (>5 ng/ml)	$8.40 \pm 0.84$	$6.26 \pm 0.80$	0.077
Homocysteine (<15 umol/l)	-	$32.08 \pm 12.77$	-

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When patients were evaluated on the first day of LCIG treatment compared to 12 months later, significant improvements were seen in motor fluctuations and PD-related symptoms, specifically in UPDRS III “on” duration, UPDRS IV “off” duration and UPDRS IV dyskinesia severity (Figure 1). Similarly, a significant improvement in QOL measures was seen at 12 months.

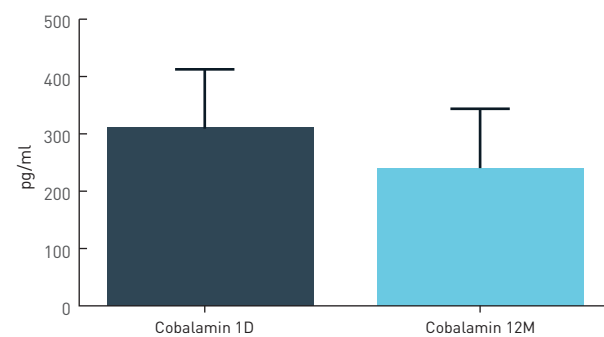
**FIGURE 1: Changes in motor fluctuations and PD-related symptoms at 12 months**



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When vitamin levels were evaluated, cobalamin levels (vitamin B12) were low at Day 1 and at 12 months (Figure 2) as were folate levels, while homocysteine levels were twice as elevated. The fluctuation in homocysteine elevation was significantly correlated to the drop in vitamin levels.

**FIGURE 2: Cobalamin levels at Day 1 and at 12 months**

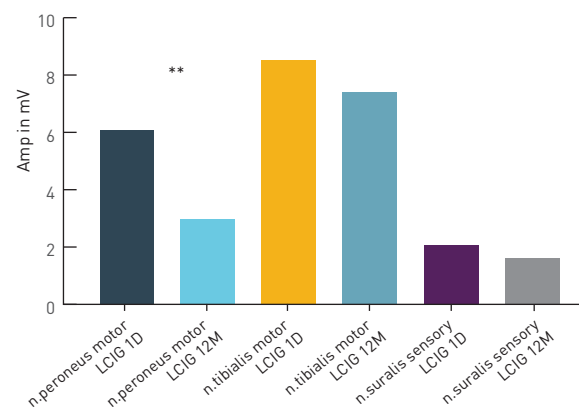


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A quarter (25%) of the group evaluated experienced motor axonal neuropathy and 16.7% had demyelinating polyneuropathy that was more pronounced at 12 months. It would appear that polyneuropathy corresponded to low vitamin levels and elevated homocysteine levels. (Figure 3).

**FIGURE 3: Incidence of neuropathies at Day 1 and at 12 months**



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The author concludes there was a marked improvement in motor symptoms for patients on LCIG therapy as reflected by UPDRS III and IV results after 12 months of treatment. There was also a marked improvement in QOL as assessed by PDQ-39 at 12 months. However, a reduction in cobalamin (vitamin B12) and folate, as well as an elevation of homocysteine levels were noted after 12 months of LCIG treatment, and these findings correlated with the incidence of polyneuropathies.

## EXPERT TAKEAWAY

The findings from this study supported those from previous studies that examined the link between LCIG and vitamin deficiency as well as the incidence of polyneuropathy. The results from this study contribute to the growing body of literature on this link.



## POTENTIAL FUTURE IMPACT

In light of the results of this study and past literature, it would be useful to have clinical practice guidelines for screening for vitamin deficiencies in PD as well as the provision of vitamin supplementation in these patients.

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## PHARMACOLOGICAL MANAGEMENT

### Study on Patient- and Caregiver-Reported Symptoms and Outcomes With Levodopa-Carbidopa Intestinal Gel for the Treatment Of Advanced Parkinson's Disease. ADEQUA Study

F. Valldeoriola, M.J. Catalán, F. Escamilla-Sevilla, E. Freire, J. Olivares, E. Cubo, D. Santos, J.C. Parra, G. Arroyo, J.M. Arbelo (Barcelona, Spain)

#### SUMMARY BY DR. JUSTYNA SARNA

One of the main goals driving treatment in Parkinson's disease (PD) is to improve a patient's quality of life (QOL). The primary objective of this study was to assess the impact of levodopa-carbidopa intestinal gel (LCIG) therapy on the QOL in patients with advanced PD. The secondary objective was to assess the constellation of other PD symptoms in patients on LCIG therapy as well as the impact on their caregivers' QOL. Symptoms evaluated for patients included motor and nonmotor symptoms, mood, fatigue, apathy, depression, anxiety, and treatment satisfaction. For caregivers, their QOL, anxiety, depression, burden of the disease, work productivity, and activity impairment were assessed.

This prospective, observational, multicentre study was conducted in 20 centres across Spain. Patients with advanced PD who were levodopa-responsive (at least 2 hours "off" time or 2 hours of dyskinesia) and who scored  $\geq 26$  on the Mini-Mental State Examination (MMSE) were included in the study. In addition, the decision to treat these patients with LCIG must have been made by the physician prior to any decision to approach the patient to enrol in the study. Patients were assessed using the 39-item Parkinson's Disease Questionnaire (PDQ-39 [QOL]), Unified Parkinson's Disease Rating Scale (UPDRS) III, Non-Motor Symptoms Scale (NMSS) SATMED-Q (Treatment Satisfaction with Medicines Questionnaire), Norris/Bond & Lader VAS (Visual Analogue Scale [mood]), PFS (Parkinson's Disease Fatigue Scale), AS (the Starkstein Apathy Scale), BDI-II (the Beck Depression Inventory second edition [depression and anxiety]). Caregivers were assessed using SQCL (Scale of Quality of Life of Care-Givers), Zarit Burden Interview (ZBI [burden of disease]), GADS (the Goldberg Anxiety and Depression Scale) and WPAI (Work Productivity and Activity Impairment questionnaire).

In the final analysis, 62 patients were enrolled in the study, of which 52 completed follow-up to the six-month mark (Table 1).

**TABLE 1: Baseline characteristics of patients**

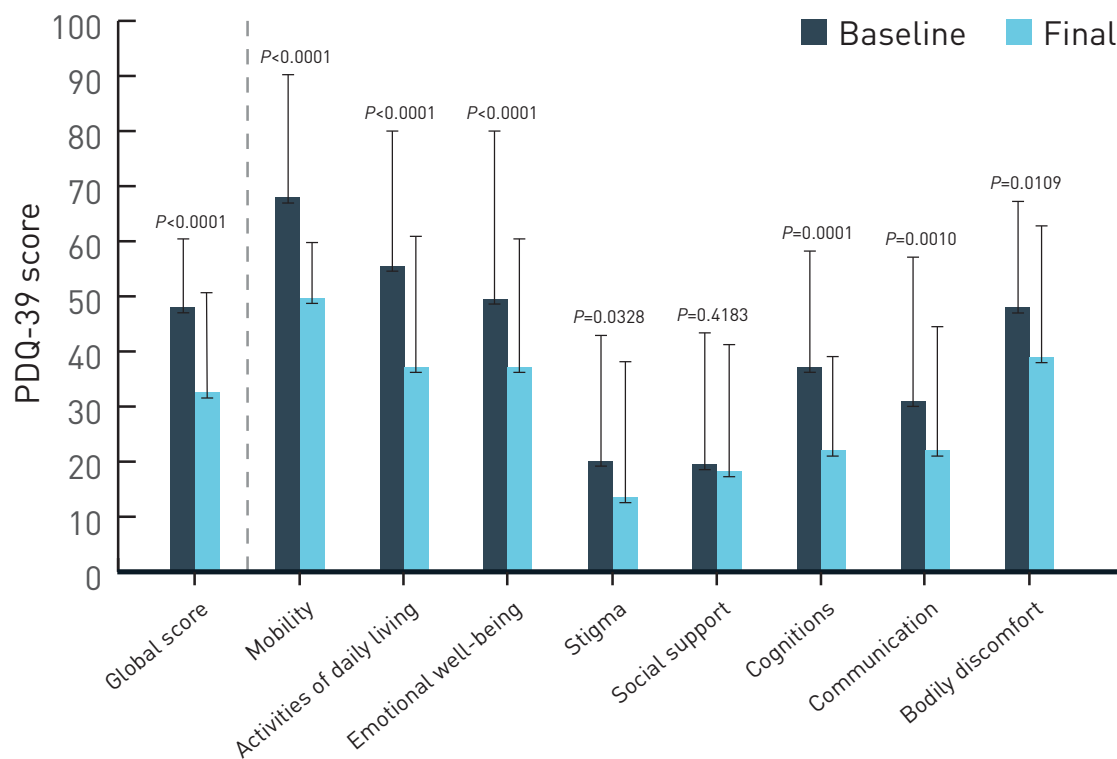
Baseline Characteristics	
Age, years (mean $\pm$ DE)	67.9 $\pm$ 7.5
Sex, male (%)	61.0
Race, Caucasian (%)	100
Marital status (%)	
Single	3.4
Married/Couple's relationship	76.3
Separated/Divorced	8.5
Widower/Widow	11.9
Highest level of education (%)	
None	22
Primary school	57.6
Secondary school	5.1
Vocational education	5.1
University	10.2
Duration of the disease, years (mean $\pm$ DE)	12.7 $\pm$ 6.0
UPDRS-IV (mean $\pm$ DE)	3.5 $\pm$ 2.0
Schawb&England ADL (ON) (mean $\pm$ DE)	70.3 $\pm$ 23.1
Schawb&England ADL (OFF) (mean $\pm$ DE)	31.0 $\pm$ 18.6
PDQ-39 (mean $\pm$ DE)	46.7 $\pm$ 13.6
UPDRS-III (ON) (mean $\pm$ DE)	30.1 $\pm$ 14.2
NMSS (mean $\pm$ DE)	83.2 $\pm$ 32.6
Norris/Bond-Lader VAS (mean $\pm$ DE)	42.6 $\pm$ 17.6
PFS-16 (mean $\pm$ DE)	3.7 $\pm$ 0.8
AS (mean $\pm$ DE)	11.4 $\pm$ 6.4
BDI-II (mean $\pm$ DE)	18.1 $\pm$ 9.7
BAI (mean $\pm$ DE)	19.8 $\pm$ 9.4
SATMED-Q (mean $\pm$ DE)	52.8 $\pm$ 15.7

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After 6 months of LCIG therapy, patients showed significant improvement in QOL measures. The baseline PDQ-39 score of  $46.7 \pm 13.59$  dropped to  $33.94 \pm 16.91$  at 6 months (Figure 2). The improvements across all PDQ-39 domains were statistically significant – except for “social support.”

**FIGURE 2: Patient PDQ-39 scores (global and per domain) at baseline and at 6 months**



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In caregivers, there was a trend toward a correlation between their QOL and that of the patients (Table 2).

**TABLE 2: Correlation between change in patient and caregiver QOL and change in study variables**

Variable	with Variable	n	Correlation	Fisher's z	P-value
PDQ-39	UPDRS-IV	52	0.36489	0.38251	0.0074
PDQ-39	NMSS	52	0.42533	0.45419	0.0015
PDQ-39	BAI	52	0.29707	0.30631	0.0320
PDQ-39	BDI-II	52	0.44258	0.47544	0.0009
PDQ-39	AS	51	0.33330	0.34654	0.0164
PDQ-39	PFS	51	0.55515	0.62579	<0.0001
PDQ-39	Norris Bond-Lader (Vigilant/Sedated)	52	0.34554	0.36037	0.0116

Adapted with permission from Valldeoriola et al. *Mov Disord.* 2018; 33 [suppl 2], abstract 271.

The authors concluded that LCIG therapy improves the QOL of patients and caregivers as well as motor and nonmotor symptoms of patients with advanced PD after 6 months of therapy.

## EXPERT TAKEAWAY

This study contributes to the growing body of literature that shows QOL and motor, as well as nonmotor symptoms, improve for patients in the initial 6 months of LCIG therapy. However, there is an issue with this type of study design as no goal attainment scale was set or recorded from the outset.



## POTENTIAL FUTURE IMPACT

While this study did look at caregiver QOL, the impact on caregivers should be more extensively studied in future. Caregivers often fear the burden of using LCIG when patients switch from oral medications to the percutaneous endoscopic gastrostomy jejunostomy (PEG-J) tube pump delivery system. As such, it would be useful to confirm how this therapeutic switch actually affects their QOL in the long term.

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# NEUROSURGICAL THERAPY

## Gamma knife radiosurgery for essential and parkinsonian tremor: Long-term experience in a Spanish centre

JR Perez-Sanchez, R Martinez-Alvarez, NE Martinez Moreno, I Cuervo-Arango, G Rey Portoles, I Parees, A Del Barrio, J Linera and MM Kurtis (Madrid, Spain)

SUMMARY BY DR. JULIUS ANANG

Gamma knife thalamotomy (GKT) presents a minimally invasive surgical option, particularly for fragile and elderly patients with medically refractory tremor. Recent studies have produced positive results in GKT safety and efficacy but long-term evidence is lacking. This single centre study describes the long-term outcomes of GKT for medically refractory essential tremor (ET) and parkinsonian tremor.

Over the span of 5 years (2013–2017), 12 patients were followed for at least 12 months in this prospective, observational study. At baseline and yearly follow up, motor and neuropsychiatric evaluations were done, which comprised the Fahn-Tolosa-Marin (FTM) tremor rating scale; tremor items of the motor Unified Parkinson's Disease Rating Scale (UPDRS) and Clinical Global Impressions Scale (CGI); EuroQoL-5D (QoL); and neuropsychological assessment (Montreal Cognitive Assessment (MoCA), Hamilton Depression Scale). Of the 12 patients enrolled, 5 had asymmetric tremor predominant Parkinson's disease (PD), 4 had intractable ET, while 3 had ET-PD (Table 1). The mean age of participants was 78.8 years with 6 patients older than age 75 years. For the intervention, the Leksell Gamma Knife was used to target the ventral intermediate nucleus (VIN) using a radiation dose of 130 Gy.

**TABLE 1: Baseline characteristics of study participants**

	Age (y)	Diagnosis	Disease Duration (y)	Follow-up (months)	Anticoagulant
Patient 1	69	PD	10	54	-
Patient 2	71	PD	5	24	-
Patient 3	79	PD	9	24	-
Patient 4	70	PD	3	14	Yes
Patient 5	78	PD	11	12	-
Patient 6	62	ET	47	36	-
Patient 7	81	ET	20	22	Yes
Patient 8	83	ET	68	13	Yes
Patient 9	82	ET	15	12	-
Patient 10	67	ET+PD	14+11	47	-
Patient 11	75	ET+PD	55+4	22	-
Patient 12	80	ET+PD	74+6	12	Yes

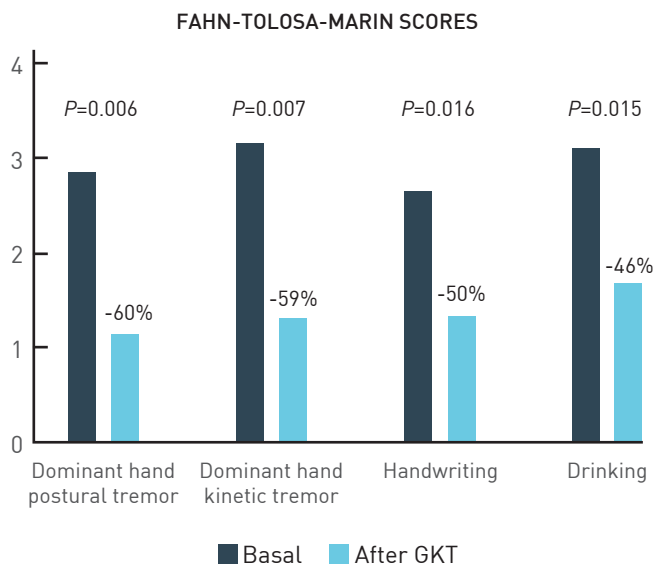
Adapted with permission from Perez-Sanchez et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 1174.



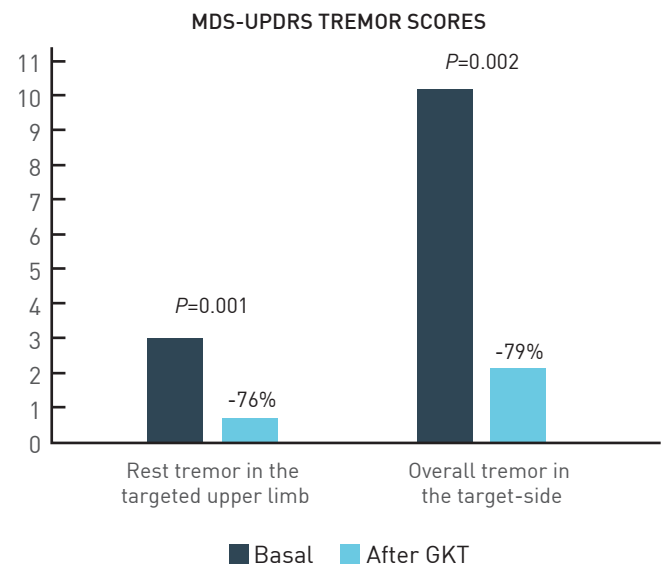


After a median follow up of 22 months (12–54 months), 11 patients showed improvement on their tremor scores, with significant decreases in FTM scores (n=6) as well as UPDRS tremor scores (n=7) (Figure 1 and 2). Similarly, EuroQoL-5D improved significantly and no severe adverse events were found. One patient reported transient hand paresthesia, another experienced cognitive disturbance without changes in neuropsychological tests (MoCA) while a third patient had depression.

**FIGURE 1 AND 2: Mean scores on FTM rating scale and tremor items of UPDRS**



Adapted with permission from Perez-Sanchez et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 1174.



Adapted with permission from Perez-Sanchez et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 1174.

The authors concluded that this study suggests GKT is a safe and efficacious option for medically refractory ET and asymmetric tremor predominant PD, and that it may present a good alternative in cases where deep brain stimulation (DBS) is contraindicated. This long-term follow-up study showed sustained clinical benefit and a good safety profile.

## EXPERT TAKEAWAY

Although small, this study demonstrates sustained and robust long-term benefits from GKT without any significant adverse events or complications. This is in contrast to what is at times seen with magnetic resonance-guided focused ultrasound (MRgFUS) where there is a decay in tremor benefit. Typically, postradiation necrosis or extension of the lesion is a concern with radiation, yet this was not seen in this study.



## POTENTIAL FUTURE IMPACT

Given that MRgFUS is not available at most centres—especially nontertiary centres—GKT with the right protocol and operator could present a cheaper and more available alternative for the management of refractory tremor. The debate on lesioning vs. DBS at the 2018 Congress underscores the fact that there is no universally better option for all patients. It is best to begin implementing personalized or individualized care in PD and GKT presents a promising option for refractory tremor in PD.

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## NEUROSURGICAL THERAPY

### Alternating thalamic deep brain stimulation for Essential Tremor: A trial to reduce habituation

M. Seier, A. Hiller, J. Quinn, C. Murchison, M. Brodsky, S. Anderson (Omaha, NE, USA)

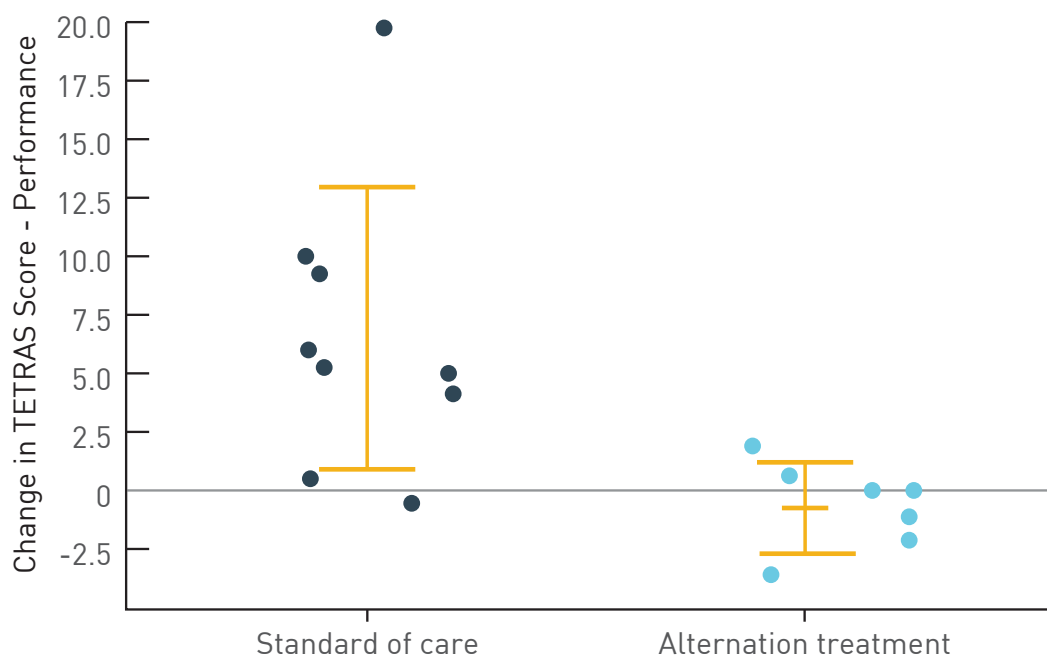
SUMMARY BY DR. JULIUS ANANG

Ventral intermediate nucleus (VIN) deep brain stimulation (DBS) is a promising treatment for essential tremor (ET), which is debilitating yet common in Parkinson's disease (PD). The gradual loss of tremor control can occur over time due in part to habituation to chronic DBS. Currently, DBS entails constant parameter settings. This study investigates the treatment potential of regularly alternating DBS programming in the VIN to reduce habituation and sustain tremor control.

In this placebo-controlled trial, 16 patients were randomized to either the experimental treatment arm to receive alternating stimulation patterns weekly (n=7) or only standard DBS care with fixed stimulation settings (n=9) for the 12 weeks. The alternating stimulation program exposed patients to a minimum of two changing variables each week – either electrode configuration, voltage, milliamps, frequency or pulse width. The essential tremor rating assessment scale (TETRAS) was used to register any change in performance from baseline and at 12 weeks.

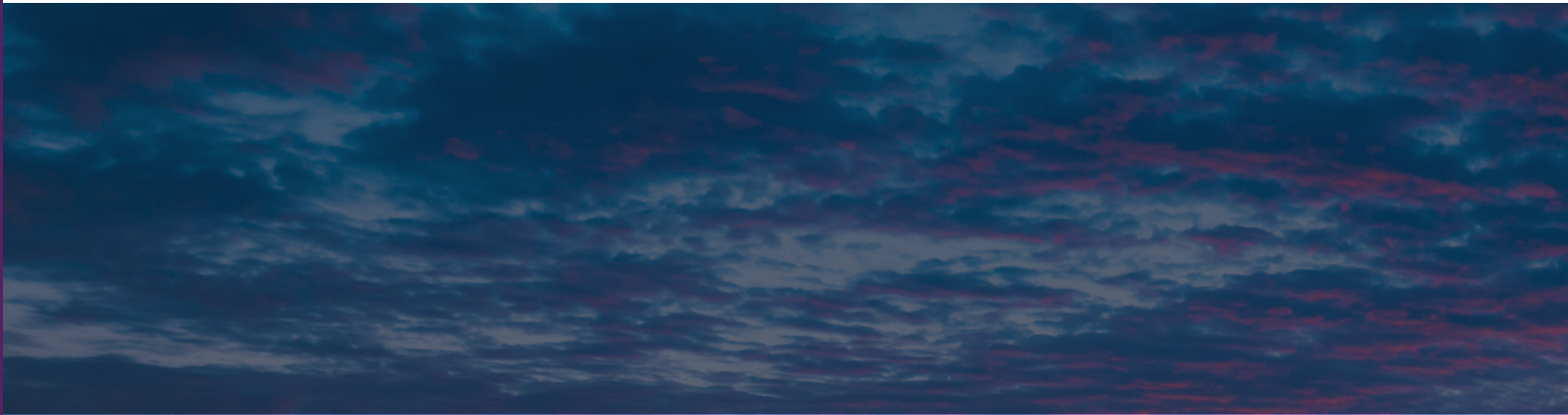
More sustained tremor control was found in the experimental arm (-0.6 point change) when compared to the standard therapy arm (6.7 point change) (Figure 1). Overall there was a 7.3 point change on the TETRAS score between the two groups ( $p=0.006$ ). Side effects reported were minimal and comparable between the two groups.

**FIGURE 1: Change in TETRAS score performance**



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The authors concluded that alternating thalamic DBS may be a good way to delay habituation to stimulation and prolong tremor control in ET patients who require VIN DBS.

## EXPERT TAKEAWAY

Using TETRAS, this novel approach shows more sustained tremor control when patients with tremor undergo alternating DBS programming as opposed to standard DBS programming where the programming is fixed. This study would have to be replicated on a larger scale to confirm these results, but the initial outcome is promising.

## POTENTIAL FUTURE IMPACT

Alternating VIN DBS stimulation on a weekly basis in ET may be an approach to mitigate the effects of habituation and provide better and sustained tremor control compared to the current approach. This programming strategy could be easily reproduced with current technology. However, further studies are needed that investigate if this outcome is sustained in the long-term before this treatment can be widely recommended.

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## NEUROSURGICAL THERAPY

### Poor responders to STN-DBS in Parkinson's disease: One-year follow-up study

M. Zibetti, L. Ricciardi, E. Montanaro, M. Sarchioto, M. Edwards, L. Lopiano, F. Morgante (Turin, Italy)

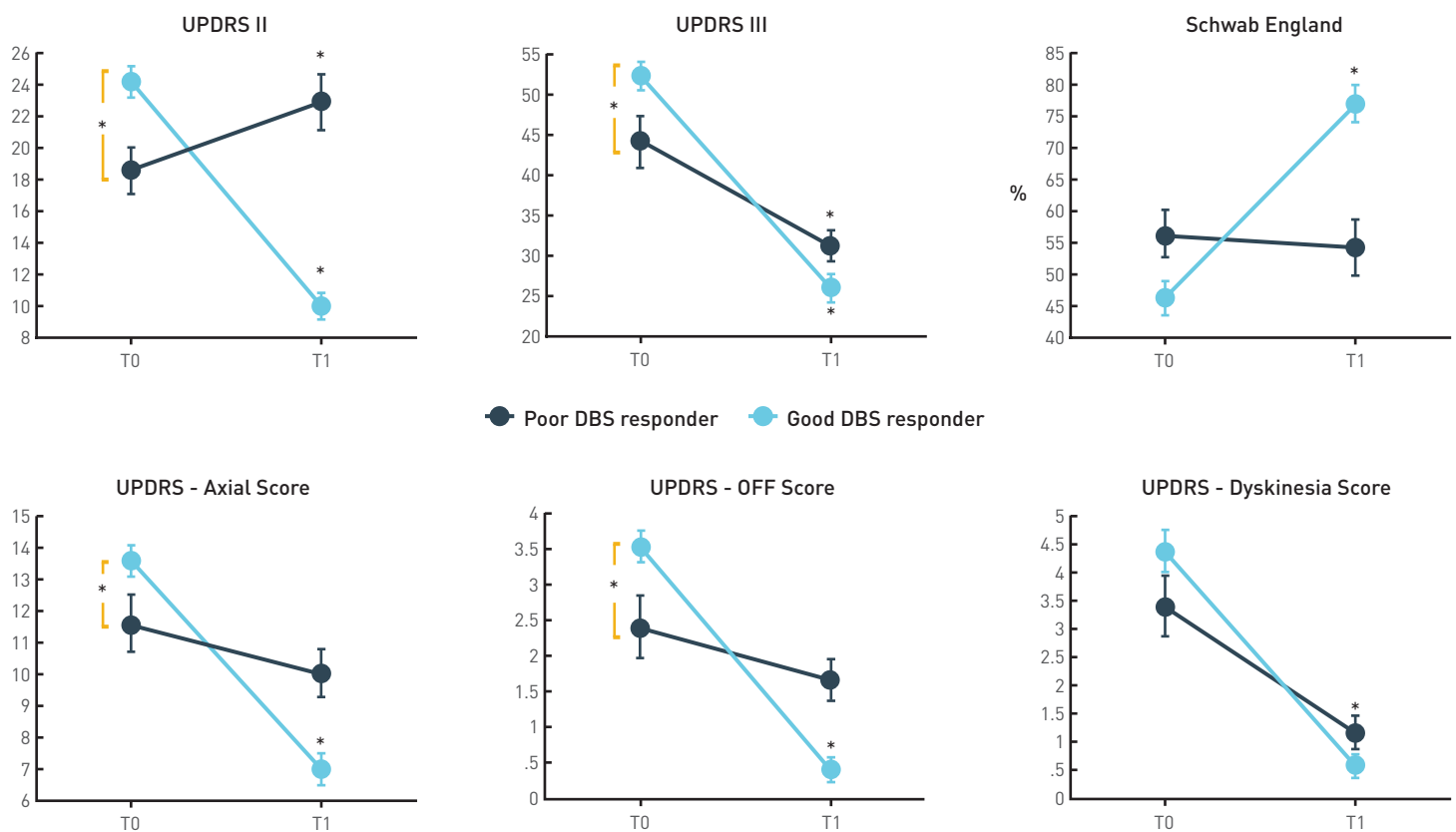
SUMMARY BY DR. ALFONSO FASANO

Despite the demonstrated efficacy of subthalamic nucleus deep brain stimulation (STN-DBS), there are patients who report unsatisfactory outcomes. This study set out to determine what parameters might contribute to a poor outcome after 1 year of STN-DBS treatment. To this end, a retrospective analysis was done of prospectively acquired data from the University of Turin's DBS Centre.

Of 203 patients with Parkinson's disease (PD) who were treated consecutively at the Centre, 126 had complete data and were included in the study (i.e. available Unified Parkinson's Disease Rating Scale [UPDRS] II scores before surgery and at one-year follow-up). Poor DBS responders were defined as those who showed <20% improvement on UPDRS II at the practically defined "off" state (off medication) after 1 year of STN-DBS (on stimulation). Using this criteria, 35 poor responders and 91 good responders were identified. These groups were compared at baseline and at 1 year post-DBS. Specifically, the final analysis included demographic and clinical variables, Schwab-England Scale (SE), UPDRS III (off med) at baseline and in off med/on stim at one year. Psychiatric assessments included the Beck Depression Inventory (BDI), and State-Trait Anxiety Inventory (STAI-X1 and X2).

At baseline, UPDRS II, UPDRS III, and axial UPDRS III were significantly less impaired and motor fluctuations were less severe in the poor DBS responder group (Figure 1). At one year, UPDRS III improved in both poor DBS and good DBS responder groups ( $p < 0.0001$ ). In good DBS responders, UPDRS II, SE, UPDRS axial scores, dyskinesia scores, and "off" time scores showed significant improvement after 1 year. In poor DBS responders, the study found that UPDRS II significantly worsened ( $p = 0.0001$ ), SE remained unchanged ( $p = 0.7$ ), UPDRS axial scores decreased but not significantly ( $p = 0.06$ ) and "off" time scores were unchanged ( $p = 0.17$ ) at the one-year mark. In the poor DBS responder group, only dyskinesia scores ( $p = 0.0025$ ) and total UPDRS IV showed improvement ( $p = 0.0055$ ). BDI decreased only in good responders ( $p < 0.01$ ) while STAI-X1 and X2 did not differ between groups.

**FIGURE 1: Comparison of results at baseline and outcomes at 1 year for good vs. poor DBS responders**



Adapted with permission from Zibetti et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 544.

Despite improvements seen in UPDRS III in off med/on stim in poor responders after STN-DBS, the authors concluded that a poor outcome on activities of daily living might be caused by an improvement of axial symptoms that is only deemed “mild” and of “off” time scores in this group (Figure 1).



## EXPERT TAKEAWAY

This study shows axial symptoms play a major role in quality of life (QOL) and in some patients, this variable is worsened with STN-DBS therapy. In future, it would be of interest to find out how outcomes for axial symptoms in STN-DBS patients compare with patient groups who undergo globus pallidus interna (GPi) DBS or levodopa-carbidopa intestinal gel (LCIG) infusion.

## POTENTIAL FUTURE IMPACT

Despite accurate patient selection and electrode positioning, there can be poor responders to STN-DBS therapy. It would be useful to determine if poor DBS responders are more common in patients with limited axial impairment at baseline.

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# NEUROSURGICAL THERAPY

## Simple Programming Method in STN-DBS using directional lead

K. Kimura, H. Kishida, T. Kawasaki, K. Hamada, N. Ueda, F. Tanaka (Yokohama, Japan)

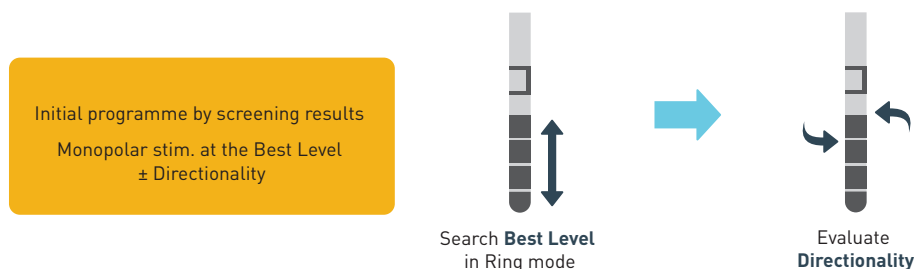
SUMMARY BY DR. ALFONSO FASANO

This study sought to identify a stimulation programming method that could be performed easily and quickly for patients who require deep brain stimulation with directional leads (dDBS). The study enrolled 12 patients with Parkinson's disease (PD) who were receiving subthalamic nucleus deep brain stimulation (STN-DBS) with the Boston Scientific Vercise PC implantable pulse generator (IPG) and Cartesia Directional Lead. On average, patients in the study were aged  $62.1 \pm 5.7$  years with a disease duration of  $8.0 \pm 4.3$  years. The average Unified Parkinson's Disease Rating Scale (UPDRS) III score when patients were off medications was  $41.0 \pm 23.6$ .

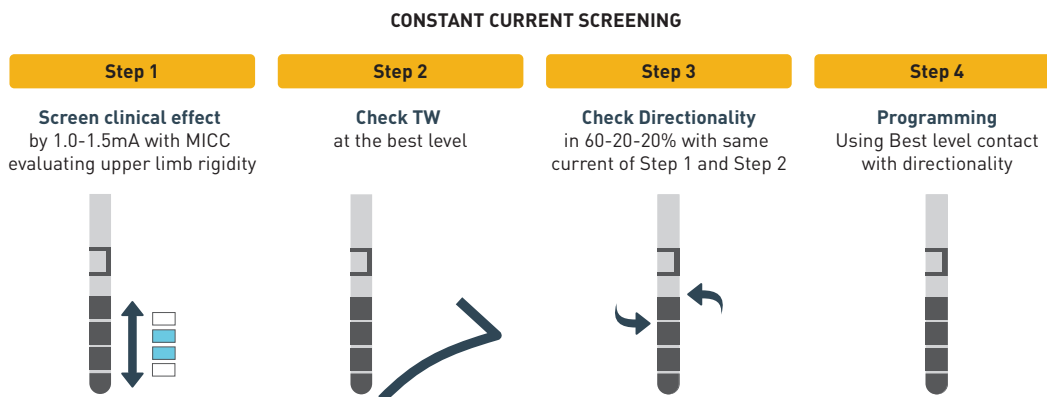
Patients were divided into two groups. In one group (Group A), each contact was screened in Ring (R) mode (Figure 1). The current value sufficient for motor symptom improvement and at which capsular side effects were apparent was determined for this group. The second group (Group B) was screened at a constant current setting of 1.5 mA. The researchers determined what the optimal stimulation level was while continuously stimulating each contact from the bottom to the top (Figure 1). For both groups, optimal contact was determined and then R vs. directional (D) mode was compared. The study assessed screening time, motor control after 12 weeks, and the number of setting changes needed for both groups.

FIGURE 1: Clinical outcomes based work flow

### GROUP A



### GROUP B

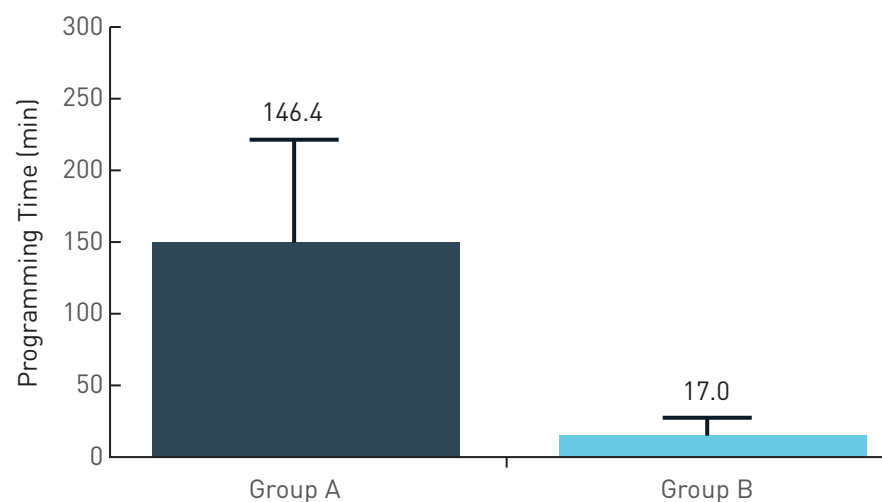


Adapted with permission from Kimura et al. *Mov Disord.* 2018; 33 [suppl 2], abstract 559.



Among the 12 cases (6 per group), 75% of electrodes were set in D mode stimulation. The stimulation effect for motor control as determined using UPDRS III was almost equal for both groups at  $-66.7 \pm 20.6\%$  for Group A and  $-64.6 \pm 19.5\%$  for Group B. The screening time was longer for Group A at  $2.44 \pm 1.22$  hours compared to  $17.0 \pm 8.4$  minutes for Group B (Figure 2). In Group B, the screening time was shorter as was the burden on the patient. The authors concluded the Group B setting method was a more efficient method for stimulation programming in PD patients who require dDBS.

**FIGURE 2: Screening time required for Group A vs. Group B**



Adapted with permission from Kimura et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 559.

## EXPERT TAKEAWAY

The STN is a small structure and DBS currents may easily stray from the target, causing stimulation evoked adverse events. The use of directional leads can help adjust the spread of currents in the horizontal direction, which will likely improve the effects of STN-DBS. This study examined simple programming methods and found one possible way to reduce screening time and the burden on patients requiring dDBS. However, this study is limited by its open-label nature, the unclear randomization schedule, and a small sample size.



## POTENTIAL FUTURE IMPACT

It is expected that the stimulus setting range for dDBS will be expanded, which will enhance the effect of STN-DBS therapy. However, programming is becoming more complicated and there are currently no guidelines. The method proposed by the study (Group B setting) is mainly saving screening time along the vertical axis which is useful for all types of electrodes and not specific to just directional leads. A larger, randomized study of this programming method may prove useful.

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## ASSESSING DISEASE SEVERITY

### Activities of Daily Living and Quality of Life in Patients with Advanced Parkinson's Disease who are Treated with or Planning to use Device-Aided Treatments

A. Fasano, K. Seppi, V. Fung, Z. Pirtosek, J.C. Parra, L. Bergmann, O. Sanchez-Solís, B. Elibol, K. Onuk (Toronto, ON, Canada)

SUMMARY BY DR. JULIUS ANANG

The impact of specific disease characteristics on activities of daily living (ADL) and the link to quality of life (QOL) is not well understood in patients with advanced Parkinson's disease (PD). Often as the disease progresses, motor fluctuations become increasingly difficult to control with oral medications alone, requiring the use of device-aided treatments (DATs). This study sought to identify characteristics in patients with advanced PD that may be predictive of QOL and ADL responses in those who require DATs. The study consisted of a post hoc analysis of the OBSERVE-PD study – a cross-sectional, observational study conducted at 128 centres in 18 countries. ADL were assessed using the Unified Parkinson's Disease Rating Scale (UPDRS) II while QOL was assessed using the short-form 8-item Parkinson's Disease Questionnaire (PDQ-8). For this study, DATs comprised deep brain stimulation (DBS), levodopa-carbidopa intestinal gel (LCIG) infusion, and continuous apomorphine subcutaneous infusion. The correlation between ADL and QOL was assessed in patients using Pearson correlation coefficients.

The study included 384 patients (mean age 65.1 years, mean disease duration 14.2 years, mean duration of motor fluctuations 7.1 years) on ongoing DAT and 164 patients (mean age 64.3 years, mean disease duration 10.1 years, mean duration of motor fluctuation 4.2 years) who planned to initiate DAT. Compared to patients waiting to initiate DAT, better ADL and QOL scores were found in patients already on DAT despite longer disease duration and higher age (Table 1). The researchers also found the group of patients on DAT who had endured more than 4 years of motor fluctuation and more than 10 years of PD also had slightly better scores for ADL and QOL compared with patients who were DAT-naïve.



**TABLE 1: UPDRS II and PDQ-8 scores in patients with advanced PD**

	N [%] <sup>a</sup>	UPDRS Part II	PDQ-8
		Mean (SD)	Mean (SD)
<b>Ongoing DAT</b>	<b>384</b>	<b>15.8 (8.7)</b>	<b>36.6 (19.3)<sup>b</sup></b>
Duration of motor fluctuations			
< 2 years	10 (3)	14.6 (7.7)	39.7 (19.6)
2 - 4 years	96 (25)	14.8 (8.9)	36.2 (19.6)
> 4 years	245 (64)	16.4 (8.6)	36.9 (19.6) <sup>c</sup>
Time since PD diagnosis			
< 5 years	6 (2)	18.8 (11.4)	51.6 (17.4)
5 - 10 years	80 (21)	14.6 (8.6)	35.8 (18.0)
> 10 years	286 (74)	16.2 (8.7)	36.7 (19.5) <sup>d</sup>
<b>Planned DAT</b>	<b>164</b>	<b>17.5 (7.8)</b>	<b>39.1 (18.4)</b>
Duration of motor fluctuations			
< 2 years	20 (12)	15.3 (8.2)	33.8 (18.3)
2 - 4 years	69 (42)	17.6 (8.0)	39.0 (18.8)
> 4 years	63 (38)	18.4 (7.5)	41.9 (17.9)
Time since PD diagnosis			
< 5 years	18 (11)	15.4 (7.0)	39.1 (18.8)
5 - 10 years	74 (45)	16.9 (7.4)	37.6 (16.2)
> 10 years	68 (41)	18.5 (8.3)	39.6 (18.8)

<sup>a</sup>Subgroupings do not total 100% because of missing data; <sup>b</sup>n = 381; <sup>c</sup>n = 242; <sup>d</sup>n = 283.

DAT = device-aided treatment; PD = Parkinson's disease; PDQ-8 = Parkinson's disease 8-item questionnaire; SD = standard deviation; UPDRS = Unified Parkinson's Disease Rating Scale

Adapted with permission from Fasano et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 385.

The data suggest that DAT improves patient-reported outcomes in the long-term. Overall, ADL and QOL were strongly correlated for patients in both groups ( $p < 0.0001$ ). Together these data show the importance of assessing ADL and QOL in patients with advanced PD.



## EXPERT TAKEAWAY

We know that ADL influences QOL for patients with advanced PD. However, it is unknown how disease characteristics, such as motor fluctuation and PD duration, affect ADL and QOL for patients. In routine care, a lot of emphasis is often placed on motor fluctuations in assessing benefits from advanced treatment or DAT. This study underscores the fact that patients most appreciate benefits from interventions based on their functional performance and QOL and not simply in terms of UPDRS units gained.

## POTENTIAL FUTURE IMPACT

More studies are revealing the benefits of DATs in improving nonmotor symptoms and QOL in PD. This study provides mounting evidence for the need to incorporate QOL measures in the decision making and assessment processes as well.

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# ASSESSING DISEASE SEVERITY

## Advanced Parkinson's disease Diagnosis and Treatment Trends in Israel – Sub-Analysis of the OBSERVE-PD Multi-Country, Cross-Sectional Study

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SUMMARY BY DR. MANDAR JOG

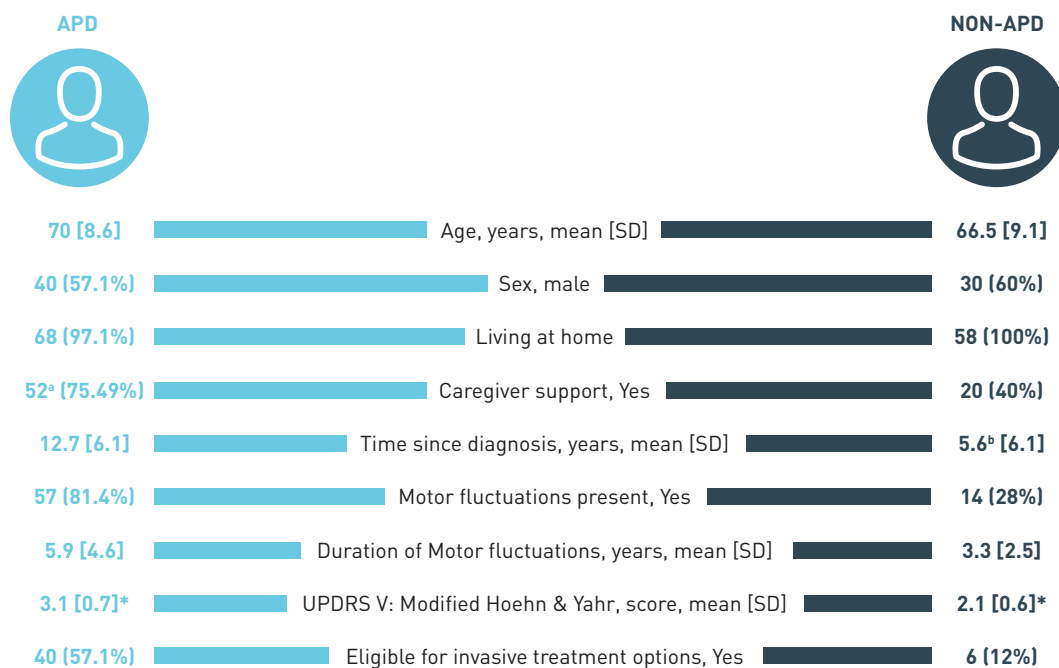
A definitive consensus is currently lacking on the diagnosis and treatment of advanced Parkinson's disease (APD), making it difficult to provide this patient population with adequate and timely care and resources, such as device-aided treatment (DAT). This observational, cross-sectional study investigated the correlation between Delphi consensus criteria and physician judgment when classifying patients as APD (Table 1).

**TABLE 1: Delphi method criteria for APD**

Delphi Criteria Question	Patient has
Troublesome motor fluctuations, severity level	Moderate or severe
"Off" time, hours/waking day	2-4 or > 4
Night time sleep disturbances, severity level	Moderate or severe
Troublesome dyskinesia, hours/waking day	2-3 > 3
Non-motor fluctuations present	Yes
"Off" time at least every 3 hours	Yes
≥ 5 times daily oral levodopa dosing	Yes
Activities of daily living limitation, severity level	Moderate or severe
Falling, frequency	Most of the time or all of the time
Dementia, severity level	Moderate or severe
Psychosis, severity level	Moderate or severe

Adapted with permission from Djaldetti et al. *Mov Disord.* 2018; 33 [suppl 2], abstract 31.

Overall, 120 patients who frequented four movement disorder centres (MDCs) for a mean of 5.4 years were evaluated. Physician assessment classified 58.3% of patients as APD compared to 78% of APD determined using the Delphi criteria. Of the 58.3% patients identified as APD, 81.4% experienced motor fluctuations for a mean of 12.7 years while 28% of non-APD patients experienced motor fluctuations for a mean of 5.6 years (Figure 1).


**FIGURE 1: Characteristics of APD vs. non-APD patients**


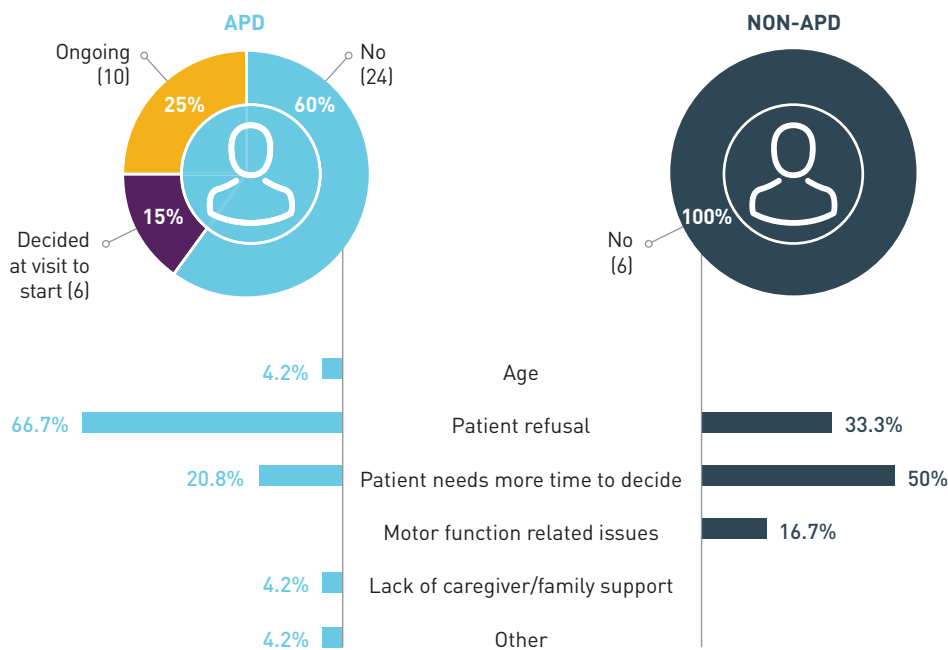
N for 'Advanced' PD, 'Non Advanced' PD: a. 69 b. 49 c. 52.14  $P < 0.0001$  (\*); UPDRS=Unified Parkinson's Disease Rating Scale  
 NMSS=NonMotor Symptom Scale; PDQ 8=8 item Parkinson's Disease Questionnaire

Adapted with permission from Djaldetti et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 31.



Even though DAT was recommended for 57.1% of APD patients and 12% of non-APD patients, only 40% of eligible patients were given or scheduled to receive DAT. On further investigation, the main reason that eligible patients were not on DAT was “patient refusal” (Figure 2).

**FIGURE 2: Reasons captured for why eligible patients were not receiving DAT**



Adapted with permission from Djaldetti et al. *Mov Disord.* 2018; 33 [suppl 2], abstract 31.

A moderate correlation was found between physician classification and Delphi consensus-based criteria for APD ( $K=0.384$ , 95% CI [0.226, 0.543]). The criteria with the highest agreement between physician judgment and Delphi consensus were activities of daily living (ADL), daily “off” hours and motor fluctuations. The authors concluded that there was agreement between physician assessment of APD and Delphi consensus criteria. Despite this, many eligible patients were not receiving DAT – with the main barrier to advanced therapies being patient refusal.



## EXPERT TAKEAWAY

This study found the main obstacle to DAT therapy for eligible APD patients was patients refusing advanced therapy. It would be valuable to follow up with these patients to understand why they were reticent to receive this advanced therapy.

## POTENTIAL FUTURE IMPACT

Future studies are warranted to understand more fully what barriers exist to DAT and why patients would refuse advanced therapies despite problematic PD symptoms.

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## ASSESSING DISEASE SEVERITY

### Low body weight is associated with poor functional status in Parkinson's disease (PD)

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SUMMARY BY DR. MANDAR JOG

Low body weight is common in Parkinson's disease (PD). Loss of appetite, gastric emptying delay, and loss of smell may be potential causes of weight loss in this patient population. At the same time, poor nutrition may be linked to dysphagia, depression, and dementia in PD. Currently, there is a dearth of data on the association between low body weight, malnutrition, and poorer function in PD. This study sought to investigate if low body weight and poor nutrition is associated with poor function in PD.

This retrospective chart review was conducted at the Queen Elizabeth Hospital in Hong Kong from October 2014 to January 2018. All patients enrolled in the study had a clinical confirmed diagnosis of PD. A BMI  $<20 \text{ kg/m}^2$  was used to indicate an increased risk of malnutrition. Average height for patients was 1.65 m. Thus, the cut-off value to indicate low body weight was set at 54.5 kg. Patients were divided into two groups: those weighing  $\geq 54.5 \text{ kg}$  and those weighing  $<54.5 \text{ kg}$ . Motor and nonmotor function, quality of life (QOL), and drug dosage were assessed and compared between both weight groups.

The results showed that patients with lower body weight had poorer motor function as well as functional status (Schwab and England Activities of Daily Living [S&E ADL] Scale) (Table 1). This group had a higher Hoehn and Yahr (H&Y) score and was more likely to have higher Unified Parkinson's Disease Rating Scale (UPDRS) scores. There was no significant difference in nonmotor function, QOL, and drug dosage between both patient groups.


**TABLE 1: Clinical measures for patients by body weight groups**

	Body weight (kg)	N	Mean ± Std Deviation	P value
Motor function				
UPDRS III	≥ 54.5	379	22.33 ± 11.88	P = 0.028
	< 54.5	206	24.71 ± 13.62	
Modified H&Y stage	≥ 54.5	379	2.47 ± 0.89	P = 0.034
	< 54.5	206	2.64 ± 1.02	
TUG test	≥ 54.5	310	14.93 ± 11.64	P = 0.058
	< 54.5	165	17.19 ± 13.62	
Non-motor function				
NMSS total score	≥ 54.5	378	51.87 ± 33.48	P = 0.478
	< 54.5	205	49.79 ± 34.33	
Functional status				
UPDRS II	≥ 54.5	379	11.47 ± 6.44	P = 0.113
	< 54.5	206	12.40 ± 7.20	
S&E ADL score	≥ 54.5	377	81.26 ± 15.63	P = 0.005
	< 54.5	205	77.24 ± 17.87	
Quality of life				
PDQ39 summary index	≥ 54.5	377	23.80 ± 15.13	P = 0.282
	< 54.5	206	22.44 ± 13.43	
Daily medication consumption				
LEDD	≥ 54.5	378	641.00 ± 501.17	P = 0.355
	< 54.5	206	684.06 ± 598.29	

Adapted with permission from Chan et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 1661.

The authors concluded that low body weight and poor nutrition appear to be associated with poorer motor function and functional status.





## EXPERT TAKEAWAY

The results of this study are important and can inform clinical practice today. More studies on the link between BMI and functional status in PD may help us better understand the interplay between nutritional status, body weight, and disease severity in PD.

## POTENTIAL FUTURE IMPACT

In light of this study, monitoring body weight should be done routinely in PD patients – especially in those who are losing weight. In these cases, referral to a nutritionist/dietician could prove valuable.

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## ASSESSING DISEASE SEVERITY

### Clinical indicators of advanced Parkinson's disease: Evaluating diagnostic properties from retrospective analysis of multi-country, cross-sectional observational study

P. Odin, Z. Pirtosek, R. Rodriguez, P. Martinez-Martin, D. Shah, P. Kandukuri, O. Koray, J. Zamudio, Y. Bao, Y. Jalundhwala, A. Antonini (Lund, Sweden)

SUMMARY BY DR. TIAGO A. MESTRE

Early recognition of advanced Parkinson's disease (APD) can help drive timely and effective interventions and optimize management. There is currently no global consensus for a clinical definition of APD, making it difficult to identify those who require advanced therapies to control symptoms. The availability of clinical indicators of APD can promote the screening of these patients in regular practice. The current retrospective study set out to assess the diagnostic value of clinical markers of APD that were previously identified in a cross-sectional, multi-country, observational study (OBSERVE-PD).

A total of 2,595 PD patients from 128 movement disorder centres in 18 countries were included in the study (Fasano 2017). Of these, approximately half were considered to have APD (51.56%). Symptoms of patients were evaluated using clinician assessment as well as patient self-reports. The final diagnosis of APD was confirmed based on the gold standard of physician assessment. Patients were also assessed for clinical characteristics of APD using a previous global Delphi-based consensus study (Antonini 2018). Different diagnostic features were assessed as "diagnostic" markers for APD based on sensitivity, specificity, and area under the curve (AUC). Discriminant validity was assessed by comparing mean scores on quality of life (QOL), activities of daily living (ADL) and nonmotor symptoms (Unified Parkinson's Disease Rating Scale II [UPDRS II]), the short-form 8-item Parkinson's Disease Questionnaire (PDQ-8), and Non-Motor Symptoms Scale [NMSS]).

Among individual APD indicators, the ones that performed the best were i) having moderate/severe limitations with ADL, ii) having moderate/severe troublesome motor fluctuations, iii) taking oral levodopa  $\geq 5$  times/day, iv) having "off" symptoms for  $\geq 2$  hours of the waking day, v) having NMS fluctuations, vi) having "off" time at least every 3 hours and vii) having  $\geq 2$  hours of troublesome dyskinesias/day (Table 1). All individual indicators of APD were also shown to possess discriminant validity since patients identified as having APD based on these markers also had worse QOL (Figure 1) as well as higher impairment of ADL (UPDRS-II) and higher NMS burden (NMSS).

**TABLE 1: Performance of individual APD diagnostic indicators**

	Clinical indicators	APD indicators	N	AUC
1	What level of troublesome motor fluctuations does your patient have?	Moderate/severe troublesome motor fluctuations	759	0.70
2	How many hours of the waking day does your patient have "OFF" symptoms?	≥ 2hrs off-time/day	814	0.6
3	What level of night time sleep disturbances does your patient have?	Moderate/severe sleep disturbances	784	0.60
4	How many hours of the day with troublesome dyskinesia does your patient have?	≥ 2hrs troublesome dyskinesia/day	431	0.65
5	Does your patient have NMS (non-motor symptoms) fluctuations?	Has NMS motor fluctuations	1012	0.67
6	Does your patient have "OFF" time at least every 3 hours?	Has off-time at least every 3 hours	585	0.64
7	Does your patient have at least 5 times daily oral levodopa dosing?	Has at least 5 times oral levodopa/day	814	0.6
8	What level of limitation of ADL (activities of daily living) capacity does your patient have?	Moderate/severe limitations with ADLS	921	0.67
9	What frequency of falls does your patient have?	Falls most/all of the time	138	0.53
10	What degree of dementia (cognitive impairment) does your patient have?	Has at least mild dementia	1163	0.57
11	What degree of psychosis does your patient have?	Moderate/severe psychosis	105	0.51

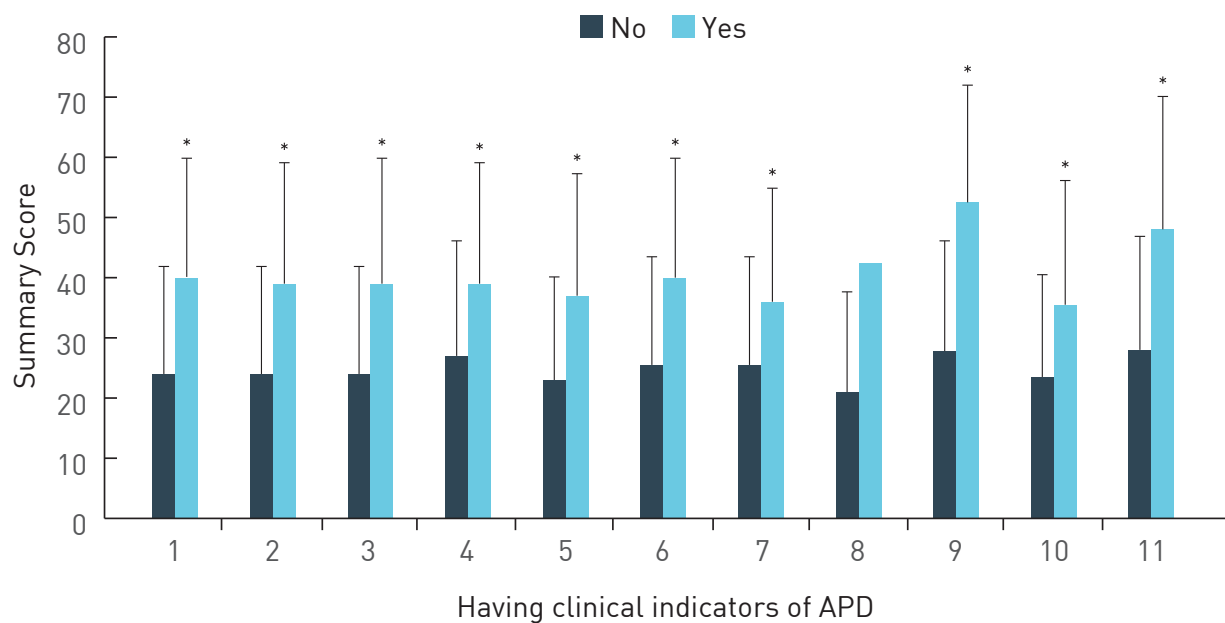
Notes: Global assessment of APD was used as a gold standard for all comparisons. N, the number of PD patients in the study who have the clinical indicators of PD.

Abbreviations: AUC, area under the curve

Adapted with permission from Odin et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 1031.



**FIGURE 1: Discriminant validity of individual APD diagnostic indicators based on QOL (PDQ-8) scores**



Notes: 1, Having moderate/severe troublesome motor fluctuations; 2, Having  $\geq 2$  hrs "off"-time/day; 3, Having moderate/severe sleep disturbances; 4, Having  $\geq 2$  hours of troublesome dyskinesias/day; 5, Having non-motor symptoms fluctuation; 6, Having "off"-time at least every 3 hours; 7, Taking  $\geq 5$  times oral levodopa/day; 8, Having moderate/severe limitations with ADLs; 9, Experiencing falls most/all of the time; 10, Having cognitive impairment (mild dementia or more severe); 11, Having moderate/severe psychosis; \*,  $p < 0.001$  for t-test comparing mean scores of patients classified as being in advanced stage of Parkinson's Disease (based on individual clinical indicator) and not having advanced Parkinson's Disease.

Adapted with permission from Odin et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 1031.



When assessed, different combinations of objective indicators of APD further improved on diagnostic performance compared to individual indicators (Table 2).

**TABLE 2: Performance of combinations of diagnostic indicators of APD**

	Combinations of clinical indicators	Sensitivity	Specificity	AUC
1	Taking oral levodopa ≥ 5 times /day	53.14	82.22	0.68
2	Taking oral levodopa ≥ 5 times/day OR having off symptoms for ≥ 2 hours of waking day	68.31	81.94	0.75
3	Taking oral levodopa ≥ 5 times/day OR having off symptoms for ≥ 2 hours of waking day OR having ≥ 2 hours of troublesome dyskinesia/day	72.87	80.83	0.77
4	Taking oral levodopa ≥ 5 times/day OR having off symptoms for ≥ 2 hours of waking day OR having moderate/severe limitations with activities of daily living	80.64	75.10	0.78
5	Taking oral levodopa ≥ 5 times/day OR having off symptoms for ≥ 2 hours of waking day OR having ≥ 2 hours of troublesome dyskinesia/day OR having moderate/severe limitations with activities of daily living	82.14	74.07	0.78

Notes: Sensitivity and specificity were calculated against physician clinical judgement of a patient currently being in an advanced stage of Parkinson’s disease. Abbreviations: AUC, Area under the curve based on ROC analyses.  
Adapted with permission from Odin et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 1031.

The authors concluded that these simple, objective indicators may aid in streamlining screening for APD in clinical practice. Further, validated clinical indicators may help to simplify the identification of patients with APD who are suboptimally controlled on oral medications.



## EXPERT TAKEAWAY

This study shows that 1–3 clinical features could be used to successfully identify APD patients with fairly good accuracy. Interestingly, the frequency of falls and the presence of dementia had a lower specificity and consequently smaller AUCs, suggesting that the definition of APD in this study leans toward the presence of motor complications. As for grouping indicators, some combinations functioned better than others. That said, the use of combined indicators may affect specificity and sensitivity, and the best combination of indicators needs to be tailored to the ultimate purpose of use.

## POTENTIAL FUTURE IMPACT

There is much clinical value for clear diagnostic indicators to help identify APD in practice as there is currently a lot of heterogeneity in how this diagnosis is achieved. However, further validation of these clinical indicators would be needed before a robust diagnostic tool is finalized for use in practice.

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## NOVEL TECHNOLOGIES

### The Levodopa Response Trial and the Parkinson Disease Digital Biomarker Challenge: Monitoring symptoms of Parkinson's disease in the lab and home using wearable sensors

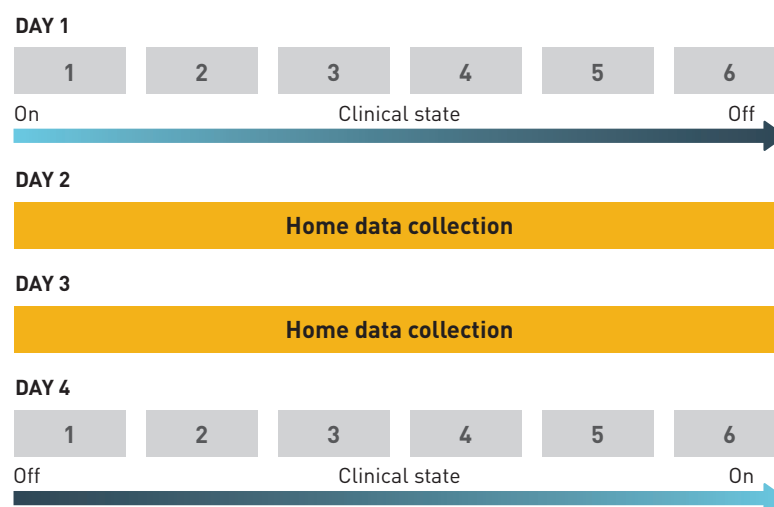
J. Daneault, G. Vergara-Diaz, G. Costante, E. Fabara, G. Ferreira-Carvalho, F. Golabchi, F. Parisi, S. Sapienza, Y. Chae, P. Snyder, P. Aubin, P. Banda, D. Brunner, R. Dorsey, L. Mangravite, W. Marks, E. Neto, U. Rubin, E. Soderberg, D. Daeschler, S. Moore, S. Sieberts, L. Omberg, P. Bonato, The Parkinson's Disease Digital Biomarker DREAM Challenge Consortium (Newark, NJ, USA)

#### SUMMARY BY DR. MANDAR JOG

Wearable sensors have been gaining in popularity as they enable clinicians to monitor symptoms. This type of tool is especially relevant as motor fluctuations increase as Parkinson's disease (PD) progresses. This study aimed to record continuous data for a group of PD patients in the clinic and at home. The data was then uploaded and shared with a community of researchers who collectively helped determine the best algorithm to estimate PD symptom severity.

Over the span of 4 days, patients with PD (n=29) wore two watches on their wrists that recorded tremor as well as a smartphone on their waist. Data were recorded for two sessions in-clinic and two sessions at home. Day 1 entailed a visit to the clinic where participants performed 20 scripted tasks while on their regular medication regimen (tasks were done 6 times to coincide with medication dosage) (Figure 1). At this visit, symptom severity scores for tremor, bradykinesia, and dyskinesia were assessed by a clinician. Days 2 and 3 were spent at home while sensor data were collected by the devices. Patients returned to the clinic on Day 4 to perform the same tasks as Day 1 except they were off their medications at the start (for at least 10 hours prior). Data recordings were taken before and after medication consumption. Clinician assessments were used as the gold standard to evaluate the sensor data captured.

**FIGURE 1: Data collection protocol**



Adapted with permission from Daneault et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 1138.

A subset of the data was then shared with a community of researchers who used different approaches (signal processing, machine learning, etc.) to develop algorithms to accurately assess symptom severity for tremor, bradykinesia, and dyskinesia. The teams who participated achieved an area under the precision-recall curve (AUPR) of 0.444–0.75 for tremor, 0.413–0.95 for bradykinesia,



and 0.175–0.477 for dyskinesia. Overall, the data demonstrated much variability in both symptom severity and response to medication. This exercise shows that harnessing the ingenuity of a community can help create robust algorithms that could help accurately estimate PD symptom severity. The authors conclude that more exercises such as this will aid in the collection of a higher calibre of data that can then be more accurately interpreted.

## EXPERT TAKEAWAY

The exercise in this study focused on feature extraction instead of predictive modelling. As such, algorithm submissions were evaluated only on the ability to estimate symptom severity. Significant variability was found in the data recordings. Overall, clinically supervised recordings were better. In the final analysis, data on tremor was easier to extract compared to bradykinesia and dyskinesia.

## POTENTIAL FUTURE IMPACT

Currently, feature extraction accuracy remains inadequate for unsupervised data collection at home. More sensors may be needed to provide detailed recordings, particularly when capturing data on balance and gait. Further fine-tuning and studies are needed before wearable sensors can be used in practice or in clinical trials to capture data on symptom severity.

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## NOVEL TECHNOLOGIES

### Smartphone App-Based Assessment of Gait in patients with Parkinson's disease

D. Su, Z. Liu, W. Yu, H. Zhu, O. Lo, B. Manor, T. Feng, J. Zhou (Beijing, China)

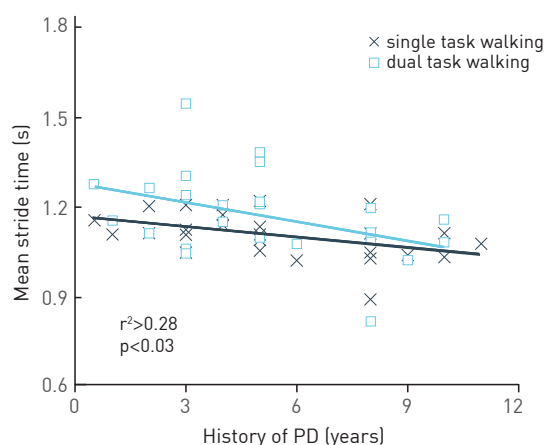
SUMMARY BY DR. MANDAR JOG

As the disease progresses, a lack of gait control leads to more falls in patients with Parkinson's disease (PD). As loss of control can vary widely throughout the day and with medication use, it would be helpful to have tools to assess gait in PD patients, especially in an unsupervised setting. This study evaluates the use of a smartphone app to evaluate gait at home. More specifically, the study investigates if the metrics captured by the app correlated with clinical symptoms and functional performance in PD patients.

In the final analysis, 28 patients aged  $61 \pm 14$  years used the app to capture gait metrics while they performed a 45-second walking trial with single and dual tasks (e.g. walking while performing serial subtractions). The app would instruct patients on its use and the phone was placed in a pant pocket to collect data on gait (acceleration, angular velocity, and magnetometer data). The mean stride time (ST) was calculated for the walking trial as well as the ST variability (STV). All participants were also evaluated using the Unified Parkinson's Disease Rating Scale (UPDRS) III and Montreal Cognitive Assessment (MoCA) measures.

The authors found that ST and STV were not correlated across participants. Patients with more severe disease had shorter ST (Figure 1).

**FIGURE 1: Linear regression model (age adjusted) for ST and duration of disease**

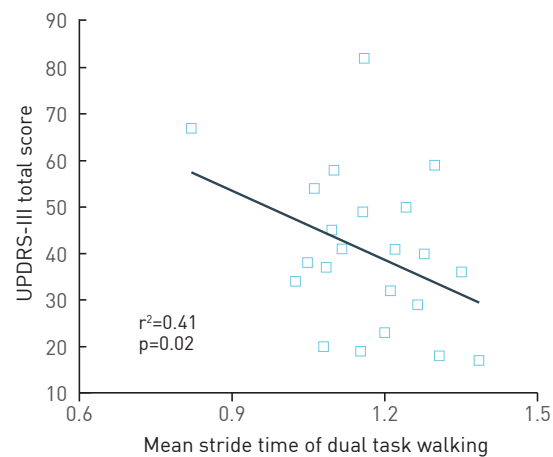


Adapted with permission from Su et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 1100.



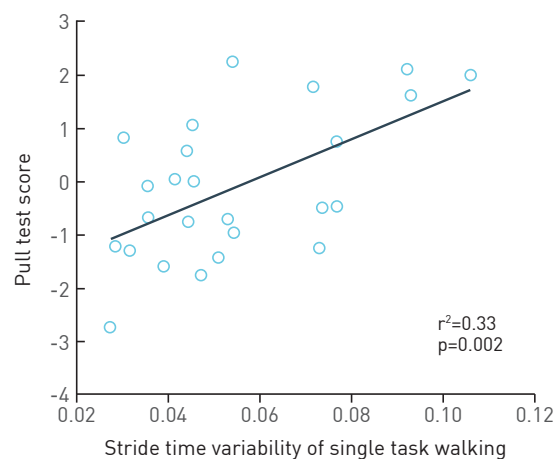
Patients with shorter ST in dual tasking had worse UPDRS III scores (Figure 2) while those with greater STV in single task walking exhibited higher pull test scores (Figure 3).

**FIGURE 2: Age-adjusted mean ST for dual task walking and UPDRS III total scores**



Adapted with permission from Su et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 1100.

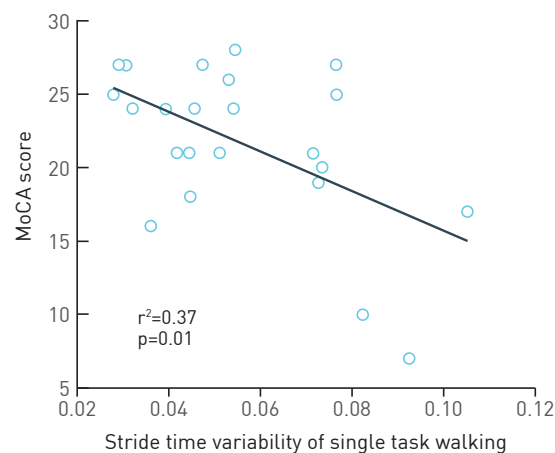
**Figure 3: Age-adjusted STV for single task walking and pull test scores**



Adapted with permission from Su et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 1100.

The study found that higher STV was also correlated with poorer cognitive function (worse MoCA scores) (Figure 4).

**FIGURE 4: Age-adjusted STV for single task walking and MoCA scores**



Adapted with permission from Su et al. *Mov Disord*. 2018; 33 (suppl 2), abstract 1100.

The authors concluded that this novel smartphone app is a useful tool to capture clinically-meaningful gait metrics in PD patients outside of a clinical setting. They note that more studies are needed to confirm the validity and reliability of the tool.

## EXPERT TAKEAWAY

Currently, this digital tool is not robust enough to capture metrics on stride length, which would be helpful. Further studies are needed before this app can be recommended for use in an unsupervised setting as well as in a clinical one.

## POTENTIAL FUTURE IMPACT

This novel approach to monitoring gait at home could prove useful and provide important data to clinicians on their PD patients.

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## NOVEL TECHNOLOGIES

Proprioceptive Focal Stimulation (Equistasi®) may improve quality of gait in moderate-advanced Parkinson's disease patients. Double-blind, double-dummy, randomized, crossover, Italian Multicentric study.

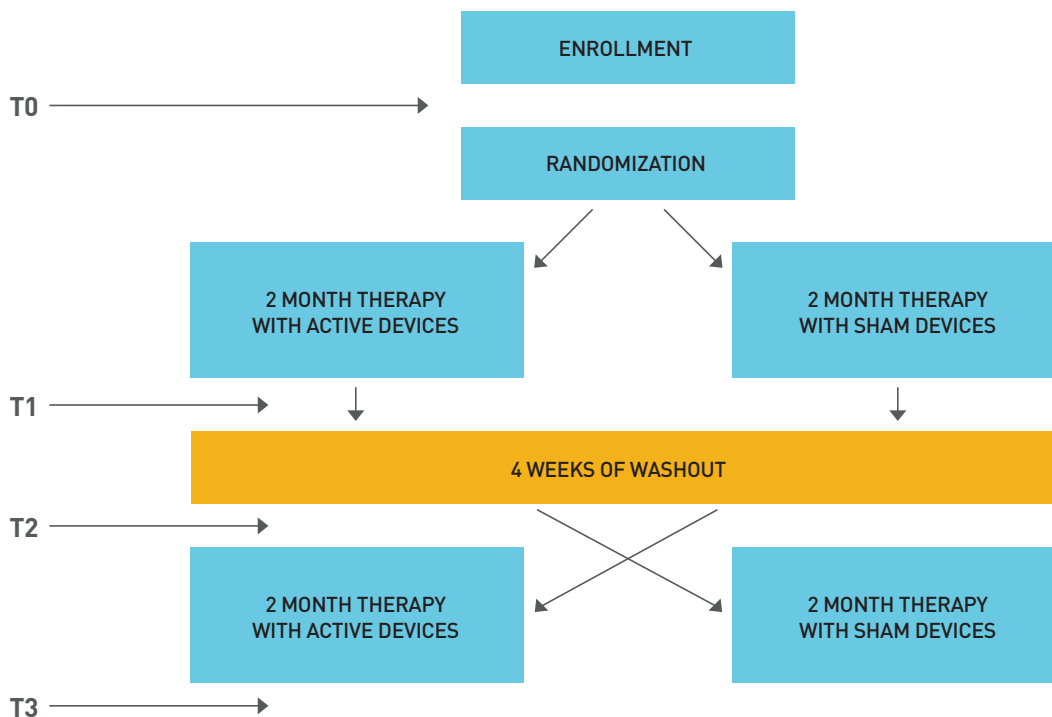
A. Peppe, P. Paone, S. Paravati, M. G. Baldassarre, L. Bakdounes, F. Spolaor, A. Guiotto, D. Pavan, Z. Sawacha, D. Clerici, N. Cau, A. Mauro, G. Albani, M. Avenali, G. Sandrini, C. Tassorelli, D. Volpe (Roma, Italy)

### SUMMARY BY DR. MANDAR JOG

This crossover, randomized, double-blind study evaluated the efficacy of the vibrotactile device Equistasi, that provides proprioceptive focal stimulation to improve gait in patients with moderate to advanced Parkinson's disease (PD). Enrolled in this study were 40 PD patients with a mean age of 68.7 years (disease duration 8.34 years; therapy duration 7.3 years, Hoehn and Yahr [H&Y] score 2.52).

Stimulation (vibration) was applied externally to the soleus muscles of both legs and at C7 using the Equistasi device. All patients were randomized to receive stimulation on the "on" or "off" state (Figure 1). All gait analysis was done in the "on" state and in the morning. Four recordings of gait were taken with the stimulation and without.

**FIGURE 1: Study protocol**

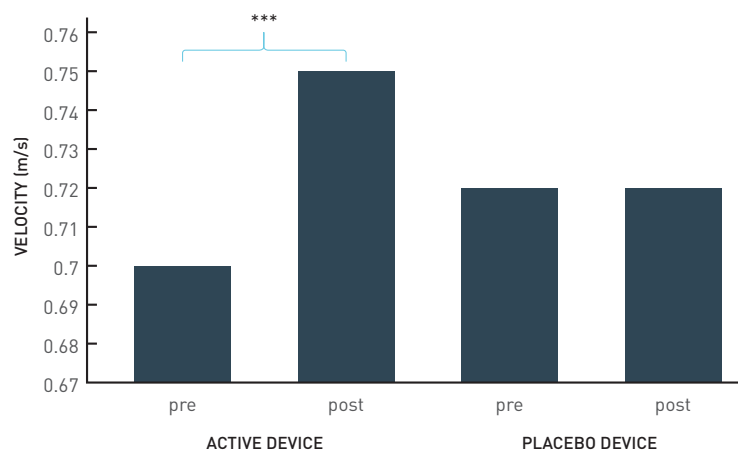


Adapted with permission from Peppe et al. *International Congress of Parkinson's Disease and Movement Disorders*, 2018; LBA 8.



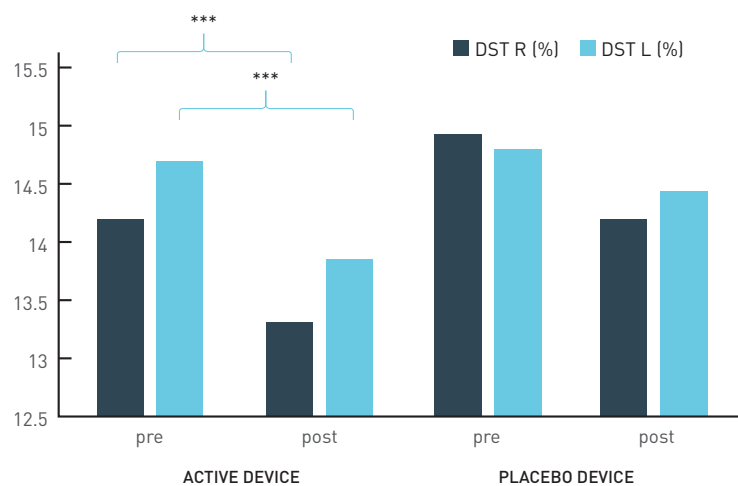
The results showed significant improvement in patients using the device in stride velocity (Figure 1), stride length (right and left) as well as double support stance (DST) (right and left) (Figure 2).

**FIGURE 2: Stride velocity in patients on active and placebo devices**



Adapted with permission from Peppe et al. *International Congress of Parkinson's Disease and Movement Disorders*, 2018; LBA 8.

**FIGURE 3: DST in patients on active and placebo devices**



DST: Double Support Stance in Left (L) + Right (R) stride

Adapted with permission from Peppe et al. *International Congress of Parkinson's Disease and Movement Disorders*, 2018; LBA 8.



The authors conclude that the results of this study confirm the potential of the Equistasi nanotechnological device to provide focal vibration in patients with PD to improve gait.

## EXPERT TAKEAWAY

Interestingly, there was an improvement seen in Unified Parkinson's Disease Rating Scale (UPDRS) III scores when the device was in both the active and inactive mode. This study sample was small, but the results do warrant further investigation into the use of this vibrotactile device in gait improvement for PD patients.

## POTENTIAL FUTURE IMPACT

The efficacy of this device—especially in more severe PD patients—is promising and opens up novel possibilities in the management of gait in patients.

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## ALTERNATIVE MEDICINE

### Artisanal formulations of Cannabis in Movement Disorders. The real-life perspective in a population from Buenos Aires, Argentina. Preliminary report

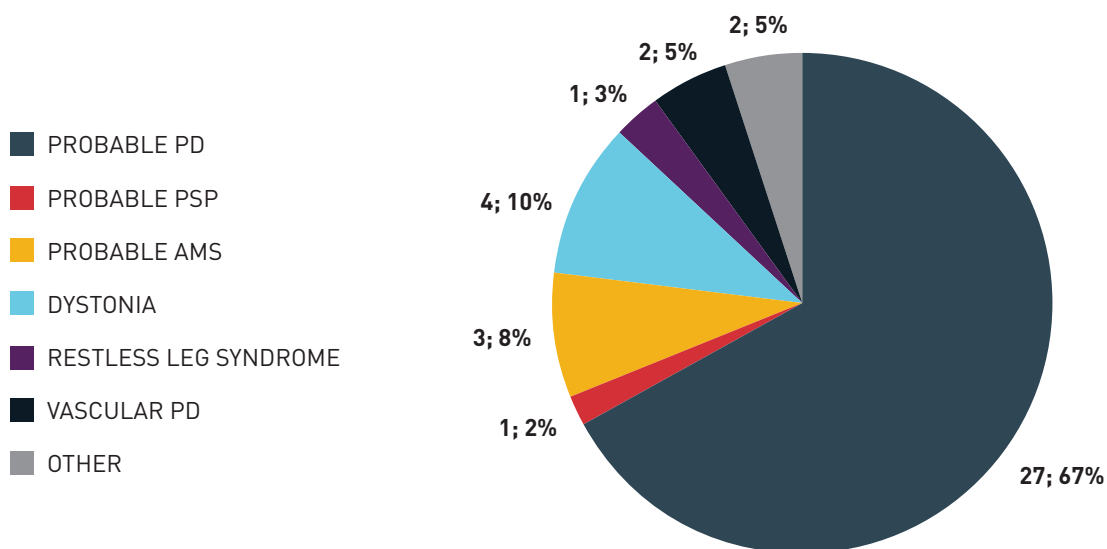
M. Cesarini, J.L. Etcheverry, N. Gonzalez Rojas, G. Da Prat, V. Parisi, G. Rojas, G. Persi, E. Gatto (Buenos Aires, Argentina)

SUMMARY BY DR. JULIUS ANANG

Data is scarce on the safety and efficacy of cannabis oil for use in patients with movement disorders. Yet, the use of this alternative medicine is on the rise in this population. This study set out to gain a better understanding of patient responses to illegal or nonstandardized manufactured cannabis oil (CBDo). This descriptive, cross-sectional single site study captured the effect of “artisanal” formulations of CBDo in patients with a variable spectrum of movement disorders. The retrospective case series relied on the spontaneous reports of cannabis consumption by patients from June 2016 to June 2018.

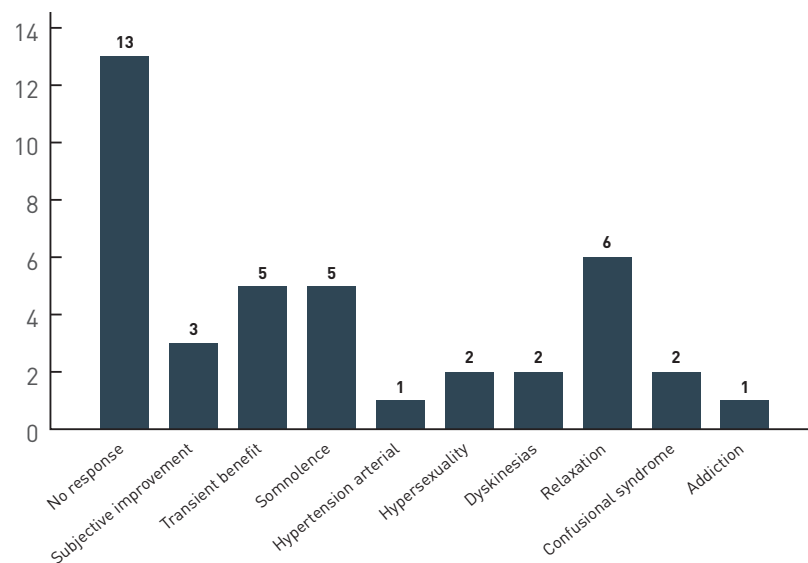
In all, 40 patients aged 21 years and older who self-administered CBDo, cannabis tincture, and smoked marijuana were included in the analysis. Patients were mostly male (27) with a mean age of  $64.08 \pm 14.07$  years and a median disease duration of 5.5 years. Most patients had Parkinson’s disease (PD) (Figure 1). The demographic data, comorbidities, and clinical characteristics that were analyzed included cannabis preparation, subjective patient response (SPR), and symptoms associated with use (SAU), which encompassed motor and nonmotor symptoms and side effects. Median cannabis consumption duration was 34.5 days, which consisted of 1 administration of smoked marijuana, 2 of cannabis tincture and 37 of CBDo.

**FIGURE 1: Movement disorder spectrum for study participants**



Adapted with permission from Cesarini et al. *Mov Disord.* 2018; 33 [suppl 2], abstract 185

When patient response to cannabis was examined, nonclinical improvement was reported in 84% of patients (n=28), while clinical subjective and transient improvement occurred in 12% (n=4). The most commonly reported side effect was sedation (n=6) (Figure 2).


**FIGURE 2: SPR and SAU observed after cannabis consumption**


Adapted with permission from Cesarini et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 185.

The number of patients with PD reporting subjective symptom improvement with use of cannabis products was relatively low (26%), but almost half of the participants reported symptoms associated with use (adverse effects) (Table 1).

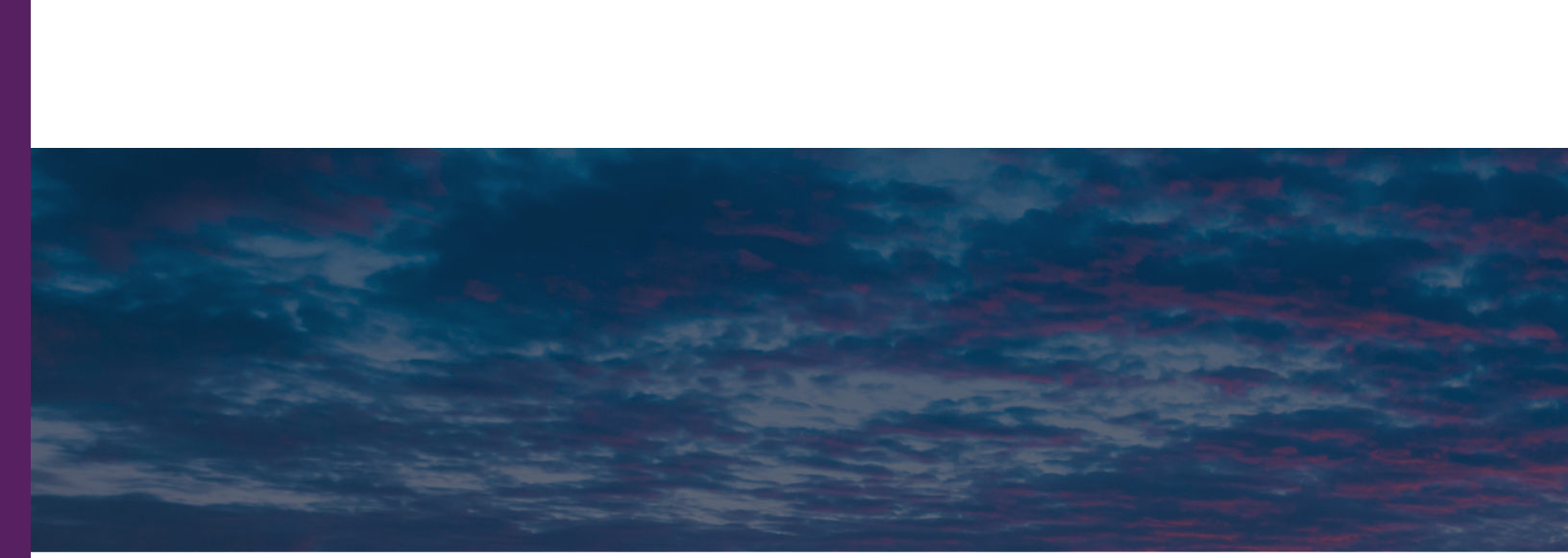
**TABLE 1: Comparative analysis between subjective improvement and SAU**

	PD diagnosis N=27	P	Non PD (N=13)	P
<b>Subjective response to NS/P:</b>				
Improvement % (n)	26 (7)	0.18	7 (1)	0.18
No improvement % (n)	22 (6)	0.62	23 (3)	0.64
<b>SAU % (n)</b>	49 (14)	0.33	61.5 (8)	0.33

References: NS/P Non Standardized Cannabis formulation. PD: Probable Parkinson's Disease. SAU: Symptoms associated to use. N/A: Non applicable. \* Comparative analysis between subjective improvement and SAU

Adapted with permission from Cesarini et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 185.





The authors concluded that randomized clinical trials are needed on standardized cannabis formulations to provide a better understanding of the pharmacological profile, benefits, impact on quality of life (QOL), and any potential neuroprotective effects it may have on patients with movement disorders. Given the lack of strong scientific evidence for use, they also suggest informing patients of the potential risk of cannabis consumption, especially older patients with polypharmacy.

## EXPERT TAKEAWAY

This is a relatively small cross-sectional study and the reported subjective response rate might not be generalizable. It also does not really address the question of efficacy in managing any specific symptoms of PD, such as tremor, insomnia or pain. The study supports the need to exercise caution with the use of cannabis in movement disorders until stronger evidence is available and indications for treatment are established.

## POTENTIAL FUTURE IMPACT

This is a very relevant study in light of the recent legalization of recreational marijuana in Canada. It is likely that cannabis products could prove beneficial for PD. As such, this could be a treatment adjunct to mitigate some motor and nonmotor symptoms in selected patients. However, without any objective assessment of PD symptoms, any reported benefits cannot be confirmed. Placebo-controlled, randomized studies on the use of standardized cannabis formulations are needed to inform clinical decisions in PD patient care.

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## ALTERNATIVE MEDICINE

### Long-term intake of *Mucuna pruriens* in drug-naïve Parkinson's disease in sub-Saharan Africa: A multicenter, non-inferiority, randomized, controlled clinical trial

R. Cilia, F. Del Sorbo, F.S. Sarfo, M Cham, A. Akpalu, S. Caronni, E. Cassani, N.A. Boafoa, S. Adamu, K. Oppon, P. Akorsu, R. Laryea, G. Owusu, D. Adjorlolo, M. Barichella, S. Fahn and G. Pezzoli (Ghana, Italy, USA)

#### SUMMARY BY DR. JULIUS ANANG

Access to levodopa is limited in low-income countries for patients with Parkinson's disease (PD). As a consequence, these patients are often undertreated and their quality of life (QOL) is often severely limited. This study sought to provide insights on the feasibility of self-cultivation of the *Mucuna pruriens* (MP) plant to treat PD (Figure 1). The researchers compared the long-term efficacy and tolerability of MP powder to levodopa (LD) plus a dopa decarboxylase inhibitor (DDCI) in levodopa-naïve PD patients. The study also sought to capture any MP responsive symptoms typically considered levodopa nonresponsive (i.e. postural instability, dysphagia) in patients with PD.

**FIGURE 1: *Mucuna pruriens* plant and *Mucuna pruriens* powder**



Figure courtesy of Cilia et al. *International Congress of Parkinson's Disease and Movement Disorders*, 2018; LBA 16.

This Phase II noninferiority, prospective study is being conducted at three Ghanaian hospitals. The aim is to recruit 90 patients with PD who will be randomized to either receive MP or LD-DDCI. Ghanaian MP powder contains 6.3% of levodopa due to a lack of DDCI in MP. Thus, in calculating the individual daily dosage, a five-fold conversion factor was needed. The dose equivalent worked out to be 8 g of MP powder for 100 mg of LD-DDCI.

After 3 months, a total of 26 patients with a mean age of  $61.3 \pm 8.3$  years and a mean disease duration of 5.7 years (range: 1–14 years) have been recruited. These patients have been randomized to receive a daily dose of MP powder ( $43.0 \pm 6.0$  g) or LD-DDCI ( $620 \pm 205$  mg). The preliminary results show overall tolerability among patients and a progressive shortening of "on" time has been reported in a few participants. At the time this data was presented, two treatment-naïve patients had shown improvement in severe postural instability. Thus far, there are no withdrawals reported due to adverse events. The authors are hopeful that MP could be an alternative source of levodopa in the long-term for PD patients worldwide who cannot afford levodopa-based medications.



## EXPERT TAKEAWAY

Both the sample size and observation time remain limited at the preliminary stage of this study. The report at the 2018 Congress did not provide data on the side effects or adverse event frequency for PD patients on MP. In terms of the preliminary outcome, it is impossible to exclude a similar response of improvement in postural instability and dysphagia with levodopa in the reported cases, as these were all drug-naïve patients randomized to MP. The dopaminergic response is also described to progressively shorten with MP. Thus, for those with severe disease fluctuations, this would result in more frequent daily and higher doses of MP than would be needed with LD-DDCI, potentially resulting in more side effects.

## POTENTIAL FUTURE IMPACT

This study is not yet complete, but preliminary data shows promise that MP could be used as a substitute for patients in developing countries or remote regions where levodopa formulations are not affordable or available. Self-cultivation of MP appears feasible but without information on the price of MP powder outside of the study setting, it isn't possible to determine if this option would be more affordable for those that might not be able to self-cultivate MP.

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## DISEASE BURDEN AND STANDARDS OF CARE

### Economic burden of advanced Parkinson's disease in a national sample of elderly US Medicare beneficiaries: A prevalence-based estimate

N. DAHODWALA, P. LI, J. JAHNKE, V. LADAGE, P. KANDUKURI, J. ZAMUDIO, Y. BAO, Y. JALUNDHWALA, J. DOSHI  
(PHILADELPHIA, PA, USA)

SUMMARY BY DR. TIAGO A. MESTRE

As Parkinson's disease (PD) progresses, the symptom burden and risk of complications also increases for patients. Using a prevalence-based cost-of-illness approach, this study measures the incremental cost of advanced PD (APD) compared to the cost associated with mild to moderate PD. From Medicare claims in 2013, a total of 144,703 patients with PD aged 65 years and older were assessed. Based on diagnostic codes for the initial sample size, the following subgroups were identified and analyzed for cost: all-cause (any diagnosis), PD-related (primary PD diagnosis) and probably PD-related (primary or secondary PD diagnosis). Total costs, medical costs, and pharmaceutical costs were calculated for all groups. From the large initial sample, 20% (n=28,974) had APD. The proxy used to denote APD was any pharmacy claims of a 30-day average levodopa equivalent dose of >1000 mg/day.

Risk adjustments to the total cost of APD vs. mild to moderate PD were made using generalized linear models for age, sex, race/ethnicity, region of residence, comorbidity/risk score, and neurological visits (Yes/No). When compared to mild to moderate PD, the risk-adjusted incremental cost for APD was \$5,110 USD for all-cause, \$3,201 USD for PD-related APD, and \$5,347 USD for probable PD-related APD ( $p < 0.001$  for all values).

The authors note that this is the first study to estimate the direct cost burden of APD in a national sample of US patients on Medicare. The study results provide policymakers and practitioners with a better understanding of the economic burden of APD. The authors propose that this information could help guide the better use of resources to improve patient outcomes.

### EXPERT TAKEAWAY

This study shows that APD has a much higher economic impact on healthcare compared to mild to moderate PD. The results of this study, however, must be viewed in context of the chosen methodology. Using a medication-based proxy and a Medicare database presents some validation issues, as there is poor clinical characterization of participants. It was also difficult to translate the results into clear actions that can be applied to practice.

### POTENTIAL FUTURE IMPACT

This study makes a case for adjusting policy and clinical practice accordingly to ensure this patient population receives adequate care and allocated resources. However, there needs to be further validation of the algorithm and methodology used here, as well as more concrete interpretations as to how the results could translate to better policy and practice.



# DISEASE BURDEN AND STANDARDS OF CARE

## Efficacy of multidisciplinary care in people with Parkinson's disease: A systematic review and meta-analysis

S. Balakrishnan, D. Tan (Singapore)

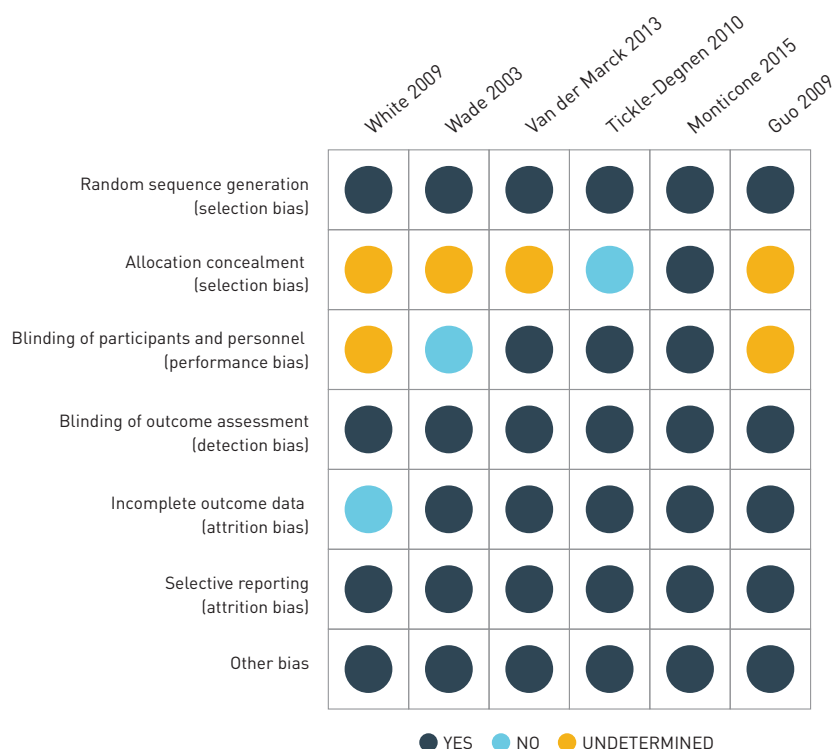
SUMMARY BY DR. TIAGO A. MESTRE

The efficacy of a multidisciplinary approach to care in Parkinson's disease (PD) has not been widely evaluated. Although this strategy is advocated, there is scarce data to show if it works in the long term. The current study is a systematic review that sought to evaluate the impact of multidisciplinary care in PD on physical and quality of life (QOL) outcomes.

A systematic search for randomized controlled trials (RCTs) published until June 2016 was done on Cochrane, PsychInfo, Scopus, Embase, and CINAHL databases. The Cochrane "risk of bias" tool was used to ensure methodological quality. Only studies that were RCTs, featured a multidisciplinary team, and had certain specific outcome measures (assessed impairment, functional outcomes, falls, balance, fear of falling, and QOL) were included in the study. Standardized mean differences (SMD) were calculated to determine effect size for the final meta-analyses.

Of the 1,616 titles and abstracts vetted, six studies met the inclusion criteria. A total of 637 participants with early to advanced PD were followed across all six studies, which were evaluated for potential bias (Figure 1).

**FIGURE 1: Potential bias for the studies included in meta-analysis**



Adapted with permission from Balakrishnan et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 1047.



This systematic review found that a multidisciplinary care approach for PD is effective at improving QOL measures and parkinsonian disability in PD patients compared to a nonmultidisciplinary approach ( $p=0.01$ ) (Table 1). However, depression and caregiver burden did not appear to benefit from this approach.

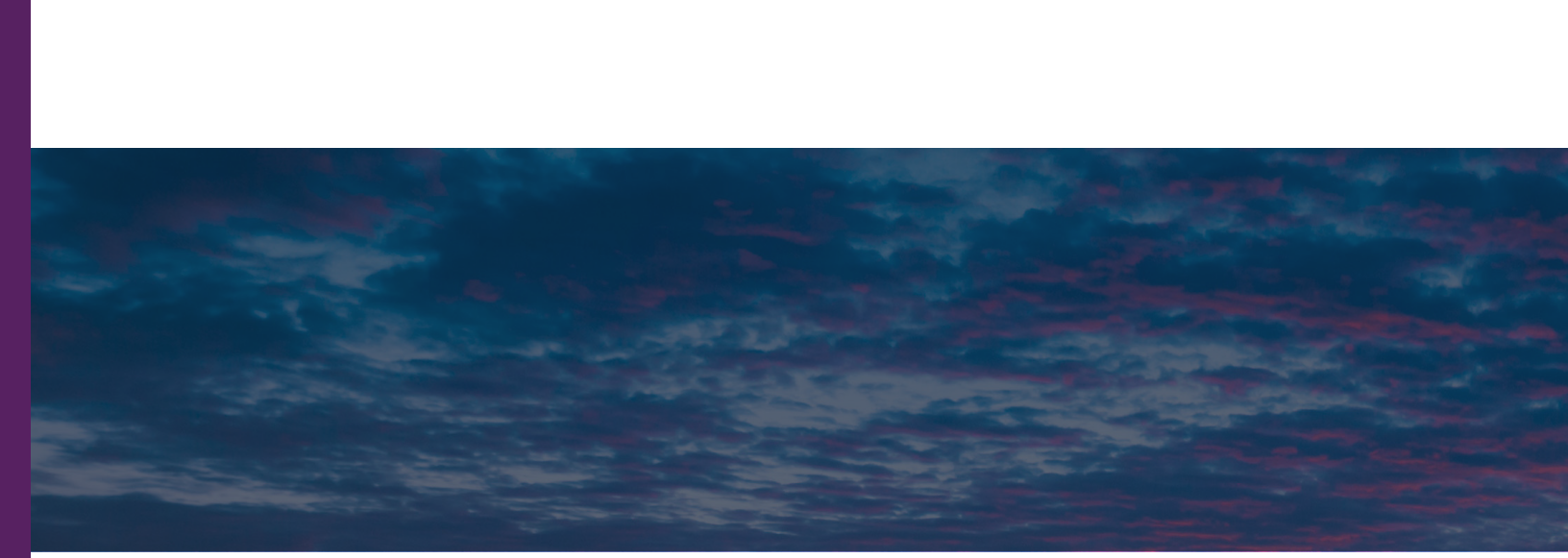
**TABLE 1: Outcome measures for multidisciplinary care**

Study	MDT Programme	Control	QOL (PDQ 39)		Motor (UPDRS/2MWT/AM)		Mood (PMS/MADRS/HADS)		Caregiver (CMS/Euroqol-5d)	
			MDC	Control	MDC	Control	MDC	Control	MDC	Control
<b>Guo et al 2009 (n=44)</b>	<b>8 weeks intervention:</b> (1) group lectures (2) information on website (3) interviews and consultations (4) caregivers own activities (5) customized rehabilitation	No specific intervention	↑*	=	↑	↑	↑	=	↑	=
<b>Monticone et al 2015 (n=64)</b>	<b>8 weeks inpatient intervention:</b> (1) PT motor training (2) OT	PT general	↑*	=	↑*	↑*	×	×	×	×
<b>Tickle-Degnen et al 2010 (n=117)</b>	<b>6 weeks intervention:</b> (1) group rehab + attention control social sessions (2) group rehab + rehab into home & community routines	Medication only	↑	=	×	×	×	×	×	×
<b>Van der Marck et al 2013 (n=100)</b>	<b>6 months intervention:</b> (1) care from a movement disorders specialist (PD nurses and social worker)	Care from general neurologist	↑	↓	↑	↓	↑*	=	=	=
<b>Wade et al 2003 (n=144)</b>	<b>6 weeks intervention:</b> (1) group educational activities & individual rehab from a MDT	No active intervention	=	=	=	=	=	=	↓	↑
<b>White et al 2009 (n=104)</b>	<b>6 weeks intervention:</b> (1) clinic based rehab & social activity (2) clinic & home rehab	No active rehab	×	×	×	=	×	×	×	×

**LEGEND:** ↑ improved    ↑\* significantly improved    = no significant improvement    ↓ deteriorated    ↓\* significantly deteriorated    × not measured

Global patient's mood status (PMS), Caregiver's mood status (CMS), Parkinson's Disease Questionnaire (PDQ-39), Montgomery-Asburg Depression Scale (MADRS), Caregiver Strain Index (CS), 25 item self-assessment Parkinsons disease disability questionnaire (Euroqol-5d), two-minute walk test (2MWT), Activity monitor (AM)

Adapted with permission from Balakrishnan et al. *Mov Disord.* 2018; 33 (suppl 2), abstract 1047.



Although this study shows benefit for a multidisciplinary approach to PD care, the authors admit the small sample sizes and existence of biases in the studies included in the analysis are problematic.

## EXPERT TAKEAWAY

Although the study did show a positive impact for a multidisciplinary approach in improving QOL for patients, a similar benefit was not found for depression or to alleviate caregiver burden. By limiting the inclusion criteria to only RCTs, the selection process used here may have missed some key studies of very good methodological quality that could have informed on the efficacy of this strategy in practice – for instance, the 2013 IMPACT study (Integrated multidisciplinary care in Parkinson’s disease: a nonrandomized, controlled trial).

## POTENTIAL FUTURE IMPACT

This is an important field of study as it evaluates an approach to PD care that is widely viewed to have a great impact and is welcomed by patients. There is a place for multidisciplinary care in PD but determining the most effective components of this strategy is fundamental. Further, evaluation of the safety data and cost-effectiveness of this approach should be investigated. Larger high-quality studies would be warranted to gain a better understanding of how best to implement this care strategy to obtain the most benefits.

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# CLINICAL QUESTIONS

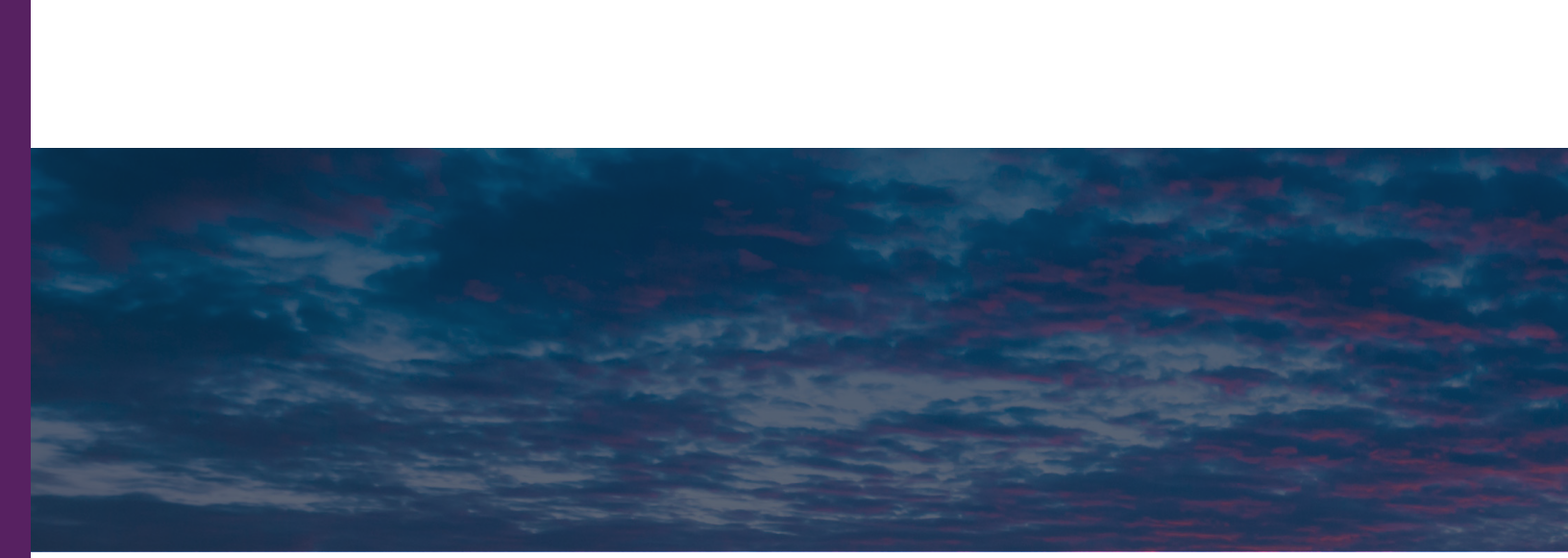
## PHARMACOLOGICAL MANAGEMENT

1. In the study on weight variations found in patients on levodopa-carbidopa intestinal gel (LCIG) treatment, most weight loss occurred:
  - a. In the first 3 months on LCIG
  - b. Gradually over the 12 months of the study
  - c. Within the first 6 months on LCIG
  - d. In the group on deep brain stimulation (DBS)
  - e. In the control group
2. After 12 months of therapy, the Bulgarian study investigating the association of LCIG and vitamin levels in advanced Parkinson's disease (PD) found that patients on LCIG had:
  - a. Elevated folate levels
  - b. Low vitamin B12 levels
  - c. Elevated homocysteine levels
  - d. b and c
  - e. a, b and c
3. In the ADEQUA study, patients on LCIG therapy showed statistically significant improvement after 6 months in these quality of life (QOL) measures (PDQ-39 scores):
  - a. Mobility
  - b. Social support
  - c. Emotional well-being
  - d. a, b and c
  - e. a and c

## NEUROSURGICAL THERAPY

4. In the small study (n=12) showing that gamma knife radiosurgery could improve tremor in elderly patients, the following side effect was *not* reported:
  - a. Transient hand paresthesia
  - b. Postradiation necrosis
  - c. Cognitive disturbance
  - d. Depression



- 
5. The trial to reduce habituation to chronic DBS found that:
    - a. Alternating DBS programming weekly could prolong tremor control
    - b. Patients on fixed DBS programming performed better than those on alternating programming
    - c. Both patients on weekly alternating and fixed DBS programming exhibited similar tremor control after 12 weeks
    - d. Neither standard nor alternating DBS programming sustained tremor control after 12 weeks
  6. In the Italian study evaluating factors that may contribute to poorer outcomes in patients who underwent subthalamic nucleus deep brain stimulation (STN-DBS), poor DBS-responders after 1 year had:
    - a. Worse UPDRS II scores
    - b. Unchanged Schwab England scores
    - c. Worse UPDRS axial scores
    - d. a and c
    - e. a, b and c

## ASSESSING DISEASE SEVERITY

7. In the OBSERVE-PD subanalysis that compared Delphi consensus criteria and physician judgment to identify PD patients with advanced disease, the main reason that eligible patients did not receive device-aided treatment (DAT) was:
  - a. Motor function related issues
  - b. Patient refusal
  - c. Patients needed more time to decide
  - d. Lack of caregiver/family support
  - e. None of the above
8. The study investigating the relationship between low body weight and functional status found that PD patients with lower body weight had poorer:
  - a. Functional status
  - b. Motor function
  - c. QOL
  - d. a and b
  - e. a, b and c



9. The retrospective analysis of the OBSERVE-PD study found that the following diagnostic markers of advanced Parkinson's disease (APD) performed the best *except*:
- a. Having moderate/severe troublesome motor fluctuations
  - b. Having "off" time at least every 4 hours
  - c. Having  $\geq 2$  hours of troublesome dyskinesia/day
  - d. Having moderate/severe limitations with ADL
  - e. Having NMS fluctuations

## NOVEL TECHNOLOGIES

10. When symptom severity was assessed using wearable sensors, the Digital Biomarker Challenge study found that data was easiest to extract on which parameter(s)?
- a. Bradykinesia
  - b. Dyskinesia
  - c. Tremor
  - d. a and c
  - e. b and c
11. In the study evaluating a smartphone app to assess gait in PD:
- a. Mean stride time (ST) and ST variability (STV) were found to be correlated across participants
  - b. Patients with more severe disease had longer ST
  - c. Patients with shorter ST in dual tasking had better UPDRS III scores
  - d. Higher STV was found to be correlated with poorer cognitive function
  - e. All of the above
12. When the efficacy of proprioceptive focal stimulation to improve gait quality was evaluated in PD patients, the study found this nanotechnological device improved:
- a. Stride velocity, stride length, and double support stance
  - b. Stride length and velocity
  - c. Double support stance only
  - d. UPDRS II scores
  - e. b and d



## ALTERNATIVE MEDICINE

- 13.** In the study capturing the impact of cannabis use in patients with movement disorders:
- a. Nonclinical improvement was reported in the majority of patients (84%)
  - b. A small sample size of mostly male patients was evaluated
  - c. Impact on tremor, insomnia, and pain was not captured
  - d. The most common side effect reported was sedation
  - e. All of the above
- 14.** In the preliminary report on the noninferiority study of *Mucuna pruriens* powder compared to levodopa to treat PD:
- a. Worsening of severe postural instability was found in patients on *M. pruriens* powder
  - b. Ninety patients had been recruited for the study
  - c. Overall tolerability and a shortening of “on” time was reported in patients on *M. pruriens* powder
  - d. Recruited patients had a mean disease duration of 8.3 years
  - e. Patients were randomized to receive *M. pruriens* or LCIG therapy

## DISEASE BURDEN AND STANDARDS OF CARE

- 15.** A systematic review and meta-analysis assessing the efficacy of a multidisciplinary care approach in PD found that:
- a. This strategy improved QOL measures and parkinsonian disability
  - b. Depression as well as caregiver burden were improved with this approach
  - c. The sample sizes of the studies included were adequate
  - d. The studies analyzed showed minimal bias
  - e. a and b



# CLINICAL QUESTIONS- ANSWER KEY

## PHARMACOLOGICAL MANAGEMENT

1. In the study on weight variations found in patients on levodopa-carbidopa intestinal gel (LCIG) treatment, most weight loss occurred:
  - a. In the first 3 months on LCIG
  - b. Gradually over the 12 months of the study
  - c. Within the first 6 months on LCIG**
  - d. In the group on deep brain stimulation (DBS)
  - e. In the control group

**Explanation:** The study by Fernández-Rodríguez et al. assessed the BMI measurements of patients at baseline, at 6 months and at 12 months (Figure 1). The results showed that the majority of weight loss happened within 6 months of therapy for patients on LCIG compared to those on DBS and those in the control group.

2. After 12 months of therapy, the Bulgarian study investigating the association of LCIG and vitamin levels in advanced Parkinson's disease (PD) found that patients on LCIG had:
  - a. Elevated folate levels
  - b. Low vitamin B12 levels
  - c. Elevated homocysteine levels
  - d. b and c**
  - e. a, b and c

**Explanation:** In the study by Chorbazhieva, when patients were evaluated for vitamin levels, cobalamin (vitamin B12) levels were found to be low after 12 months of LCIG therapy. Meanwhile, homocysteine levels were higher in these patients at 12 months compared to Day 1. Folate levels, however, were lower at 12 months compared to Day 1.

3. In the ADEQUA study, patients on LCIG therapy showed statistically significant improvement after 6 months in these quality of life (QOL) measures (PDQ-39 scores):
  - a. Mobility
  - b. Social support
  - c. Emotional well-being
  - d. a, b and c
  - e. a and c**

**Explanation:** In the study by Valldeoriola et al., patients who were evaluated after 6 months of therapy with LCIG showed statistically significant improvement in the PDQ-39 domains of mobility and emotional well-being. The social support domain also showed improvement – but it was not statistically significant.





## NEUROSURGICAL THERAPY

4. In the small study (n=12) showing that gamma knife radiosurgery could improve tremor in elderly patients, the following side effect was *not* reported:
- a. Transient hand paresthesia
  - b. Postradiation necrosis**
  - c. Cognitive disturbance
  - d. Depression

**Explanation:** In the study by Perez-Sanchez et al., patients were followed for a minimum of 12 months after gamma knife radiosurgery. Among the side effects that were reported were transient hand paresthesia, cognitive disturbance and depression. Postradiation necrosis is a typical concern with radiation but was surprisingly not a side effect reported in this study.

5. The trial to reduce habituation to chronic DBS found that:
- a. Alternating DBS programming weekly could prolong tremor control**
  - b. Patients on fixed DBS programming performed better than those on alternating programming
  - c. Both patients on weekly alternating and fixed DBS programming exhibited similar tremor control after 12 weeks
  - d. Neither standard nor alternating DBS programming sustained tremor control after 12 weeks

**Explanation:** In the study by Seier et al. that investigated DBS programming methods to sustain tremor control, alternating programming weekly was found to help sustain the benefits of DBS at 12 weeks when compared to fixed or standard programming.

6. In the Italian study evaluating factors that may contribute to poorer outcomes in patients who underwent subthalamic nucleus deep brain stimulation (STN-DBS), poor DBS-responders after 1 year had:
- a. Worse UPDRS II scores
  - b. Unchanged Schwab England scores
  - c. Worse UPDRS axial scores
  - d. a and c
  - e. a, b and c**

**Explanation:** The study by Zibetti et al. evaluated patients who have undergone STN-DBS. At the 1-year follow up, patients who were poor DBS responders had worse UPDRS II and UPDRS axial scores – the latter score was not statistically significant. The Schwab England scores, however, remained unchanged in poor responders. Meanwhile, good DBS responders had significantly better UPDRS II and UPDRS axial scores as well as better Schwab England scores.



## ASSESSING DISEASE SEVERITY

7. In the OBSERVE-PD subanalysis that compared Delphi consensus criteria and physician judgment to identify PD patients with advanced disease, the main reason that eligible patients did not receive device-aided treatment (DAT) was:
- a. Motor function related issues
  - b. Patient refusal**
  - c. Patients needed more time to decide
  - d. Lack of caregiver/family support
  - e. None of the above

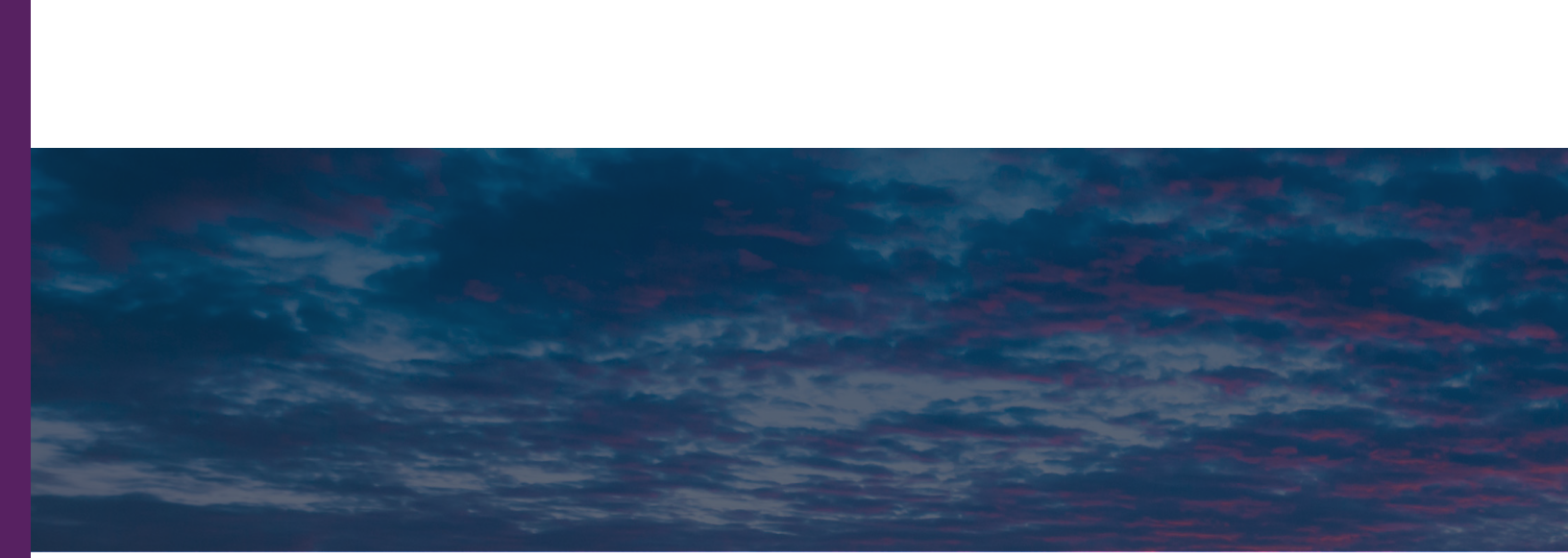
**Explanation:** In the study by Djaldetti et al., even though DAT was recommended for 57.1% of patients with advanced disease and 12% of patients who did not have advanced disease, only 40% of patients received DAT. On further investigation, “patient refusal” was the main reason found for this treatment gap.

8. The study investigating the relationship between low body weight and functional status found that PD patients with lower body weight had poorer:
- a. Functional status
  - b. Motor function
  - c. QOL
  - d. a and b**
  - e. a, b and c

**Explanation:** This study by Chan et al. investigated if poor nutrition and low body weight was associated with poorer function. The study found that PD patients with low body weight had significantly poorer functional status and motor function compared to average weight patients. There was no significant difference in QoL between both groups.

9. The retrospective analysis of the OBSERVE-PD study found that the following diagnostic markers of advanced Parkinson’s disease (APD) performed the best *except*:
- a. Having moderate/severe troublesome motor fluctuations
  - b. Having “off” time at least every 4 hours**
  - c. Having  $\geq 2$  hours of troublesome dyskinesia/day
  - d. Having moderate/severe limitations with ADL
  - e. Having NMS fluctuations

**Explanation:** According to the study by Odin et al. that assessed the diagnostic value of clinical markers of APD, the following markers performed the best: having moderate/severe limitations with ADL; having moderate/severe troublesome motor fluctuations; taking oral levodopa  $\geq 5$  times/day; having “off” symptoms for  $\geq 2$  hours of the waking day; having NMS fluctuations;



having “off” time at least every 3 hours; and having  $\geq 2$  hours of troublesome dyskinesias/day (Table 1).

## NOVEL TECHNOLOGIES

**10.** When symptom severity was assessed using wearable sensors, the Digital Biomarker Challenge study found that data was easiest to extract on which parameter(s)?

- a. Bradykinesia
- b. Dyskinesia
- c. Tremor**
- d. a and c
- e. b and c

**Explanation:** In the study by Daneault et al., wearable sensors were used to record continuous data on patients. After recording data in the clinic and in the home environment, data on tremor was found to be the easiest to extract when compared to bradykinesia and dyskinesia.

**11.** In the study evaluating a smartphone app to assess gait in PD:

- a. Mean stride time (ST) and ST variability (STV) were found to be correlated across participants
- b. Patients with more severe disease had longer ST
- c. Patients with shorter ST in dual tasking had better UPDRS III scores
- d. Higher STV was found to be correlated with poorer cognitive function**
- e. All of the above

**Explanation:** The study by Su et al. evaluated a smartphone app to assess gait at home and investigated if the metrics captured by the phone app correlated with actual clinical symptoms and functional performance of PD patients. The study found that ST and STV were not correlated across participants, patients with more severe disease had shorter ST, patients with shorter ST in dual tasking had worse UPDRS III scores and that higher STV correlated with poorer cognitive function.

**12.** When the efficacy of proprioceptive focal stimulation to improve gait quality was evaluated in PD patients, the study found this nanotechnological device improved:

- a. Stride velocity, stride length, and double support stance**
- b. Stride length and velocity
- c. Double support stance only
- d. UPDRS II scores
- e. b and d



**Explanation:** In the study by Peppe et al., the efficacy of Equistasi (a device that provides proprioceptive focal stimulation) to improve gait was assessed. The study found that the device significantly improved stride velocity (Figure 1), stride length and double support stance (Figure 2) in patients.

## ALTERNATIVE MEDICINE

**13.** In the study capturing the impact of cannabis use in patients with movement disorders:

- a. Nonclinical improvement was reported in the majority of patients (84%)
- b. A small sample size of mostly male patients was evaluated
- c. Impact on tremor, insomnia, and pain was not captured
- d. The most common side effect reported was sedation
- e. All of the above**

**Explanation:** In the study by Cesarini et al. assessing patient responses to illegal or nonstandardized manufactured cannabis oil, a sample of 12 patients (majority male) were included. In the study, nonclinical improvement was reported in 84% of patients and the most common side effect found was sedation. However, the impact of cannabis on tremor, insomnia and pain were not assessed.

**14.** In the preliminary report on the noninferiority study of *Mucuna pruriens* powder compared to levodopa to treat PD:

- a. Worsening of severe postural instability was found in patients on *M. pruriens* powder
- b. Ninety patients had been recruited for the study
- c. Overall tolerability and a shortening of “on” time was reported in patients on *M. pruriens* powder**
- d. Recruited patients had a mean disease duration of 8.3 years
- e. Patients were randomized to receive *M. pruriens* or LCIG therapy

**Explanation:** The study by Cilia et al. evaluated the efficacy of *M. pruriens* powder compared to levodopa to improve symptoms in PD patients. After 3 months, the preliminary results showed overall tolerability among patients and a progressive shortening of “on” time reported in a few participants.





## DISEASE BURDEN AND STANDARDS OF CARE

**15.** A systematic review and meta-analysis assessing the efficacy of a multidisciplinary care approach in PD found that:

- a. This strategy improved QOL measures and parkinsonian disability**
- b. Depression as well as caregiver burden were improved with this approach
- c. The sample sizes of the studies included were adequate
- d. The studies analyzed showed minimal bias
- e. a and b

**Explanation:** The systematic review by Balakrishnan and Tan sought to evaluate the impact of the widely advocated multidisciplinary approach to PD care. The study found that QoL measures and parkinsonian disability improved with this approach. However, depression and caregiver burden did not appear to benefit from this approach. Overall, the sample sizes of the studies included in the meta-analysis were deemed inadequate and many had biases that were found to be problematic.

# NOTES

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