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Parkinson's disease medication adjustments based on wearable device information compared to other methods: randomized clinical trial

Alejandro Rodríguez-Molinero[1] ✉, Carlos Pérez-López[1], Nuria Caballol[2], Mariateresa Buongiorno[3], María Asunción Ávila Rivera[2], Núria López Ariztegui[4], Lydia López-Manzanares[5], Jorge Hernández-Vara[3,6], Àngels Bayes-Rusiñol[7], Alexandre Gironell Carreró[8], María Álvarez Saúco[9], Elisabet Franquet Gomez[10], David A. Pérez-Martínez[11], Sonia Escalante Arroyo[12], Silvia Martí-Martínez[13], Pablo Mir[14,15,16], José Mª Salom Juan[17], Juan Carlos Martínez-Castrillo[18] & Cristian Tebé[19] On behalf of the MoMoPa-EC Research Group*

Parkinson's disease (PD) is characterized by motor fluctuations, with alternating periods of good ("ON") and poor ("OFF") motor function. Monitoring these fluctuations is crucial for optimizing treatment, yet traditional methods rely on subjective patient reports. This multicenter, single-blind, cluster-randomized trial evaluated the effectiveness of three monitoring approaches in real-world clinical practice. Neurologists from 35 centers were randomized into three groups: one using clinical visit data alone, another incorporating Hauser diary entries, and a third integrating Parkinson's Holter (STAT-ON®) reports. A total of 156 patients were recruited. Changes in 'OFF time' from baseline to 26 weeks were minimal and non-significant across groups. Secondary outcomes, including 'ON time,' dyskinesia, and quality-of-life scores, showed no significant differences. These findings suggest that the choice of motor fluctuation monitoring method may not significantly impact clinical outcomes, underscoring the need for a broader understanding of how these monitoring tools are integrated and utilized in real-world settings. Trial registration: NCT04176302 (November 21, 2019 - ClinicalTrials.gov).

Parkinson's disease (PD) is a progressive neurological disorder characterized by the loss of dopamine-producing neurons in the brain's substantia nigra, leading to motor and non-motor symptoms that affect movement control and daily activities[1]. The disease manifests with motor symptoms, such as bradykinesia, tremor, rigidity, and impaired gait, alongside several non-motor symptoms, encompassing cognitive impairment, psychiatric disorders, and sensory disturbances[2,3]. According to the World Health Organization (WHO), the global prevalence of PD has doubled in the last 25 years, with more than 8.5 million individuals worldwide living with the disease in 2019[4]. Disability and mortality rates due to PD are increasing faster than for any other neurological disorder, with PD causing 5.8 million disability-adjusted life years in 2019 (an 81% increase since 2000) and 329,000 deaths (over 100% increase since 2000[4].

PD treatment aims to alleviate symptoms using medications that restore dopamine levels in the striatum[5]. While patients typically respond well to dopaminergic drugs in the early PD stages, their effectiveness diminishes as PD advances, requiring frequent adjustments to control motor symptoms adequately[6]. Approximately 90% of PD patients experience motor fluctuations after ten years, characterized by alternating periods of apparent medication ineffectiveness and reappearance of parkinsonian features (OFF periods) and periods of symptom relief (ON periods)[7,8]. The intensity and unpredictable nature of OFF periods significantly impact the quality of life (QoL) of individuals with PD[9]. Therefore, the identification and management of OFF-period symptoms are of utmost importance. However, managing the various motor complications is challenging due to their variable appearance and fluctuating nature[10]. A temporal profile of

A full list of affiliations appears at the end of the paper. *A list of authors and their affiliations appears at the end of the paper
✉e-mail: arodriguez@csapg.cat

symptom appearance may increase the accuracy of therapeutic adjustments, but the availability of precise information for neurologists is limited, as they have limited time during consultation, leading to difficulties in achieving satisfactory medication outcomes. Moreover, patients do not always accurately recognize or report the different motor symptoms.

Currently, motor fluctuation assessment is conducted in two ways: retrospectively during clinical consultations, where information is gathered by questioning the patient, or through patient-maintained written diaries, such as the Hauser diary, in which patients record their motor state at regular intervals (e.g., every 30 min). However, both methods have significant limitations. Patients often struggle to recognize, recall, and accurately report their motor symptoms, and adherence to diary-keeping is generally low, restricting its use to short periods[11,12].

To overcome these limitations, wearable sensors have been developed to automatically track patients' motor manifestations over extended periods when needed. The Parkinson's Holter (PH) (STAT-ON®) is a wearable sensor, that can be comfortably worn on the waist and records data automatically without requiring any action from the user. This sensor has demonstrated the ability to accurately identify different motor states when compared with patient diaries and effectively monitor the various motor manifestations of the disease[13–23].

The MoMoPa-EC (NCT04176302) trial aimed to compare the effectiveness, measured as 'OFF time', of medication adjustments prescribed by neurologists using three different sources of information to assess motor fluctuations[13,23]: (1) PH (STAT-ON®) reports plus clinical information, (2) patient diaries (Hauser diary, the gold-standard method) plus clinical information, and (3) clinical information collected during routine consultations. Secondary objectives included assessing associations between the information source and other variables, measured using PH and the Hauser diary. Other secondary outcomes were the overall effectiveness of the interventions, including their impact on QoL and activities of daily living.

Results

Characteristics of study patients

A total of 38 neurologists participated in the study: 13 were allocated to the VG arm, 11 to the DG arm, and 14 to the SG arm. They recruited 156 patients of which none were lost to follow-up, and all were valid for analysis (Fig. 1). The study population was divided into three arms: VG ($n = 55$), DG ($n = 51$), and SG ($n = 50$), based on the allocation group of their neurologists. Detailed sociodemographic characteristics for each group are provided in Table 1.

Mean (SD) age for VG, DG, and SG patients was 62.5 (9.05), 65.8 (10.9), and 65.9 (8.85) years, respectively. Gender distribution across groups varied, with VG having a larger percentage of men (67.3%), whereas it was more balanced in DG and SG (56.9% and 54.0% of men, respectively). Most participants in all three groups were married (Table 1).

Regarding baseline clinical variables (Table 1), DG patients appeared to experience a marginally elevated symptom burden in specific domains, including 'OFF time' (as recorded in the Hauser diary) and UPDRS-II, -III, and -IV scores.

Thirty-nine (25%) patients did not have any changes in medication throughout the study.

Primary outcome

Table 2 illustrates changes in the 'OFF time' as recorded in the Hauser diary throughout this study. The mean (SD) 'OFF time' did not show statistically

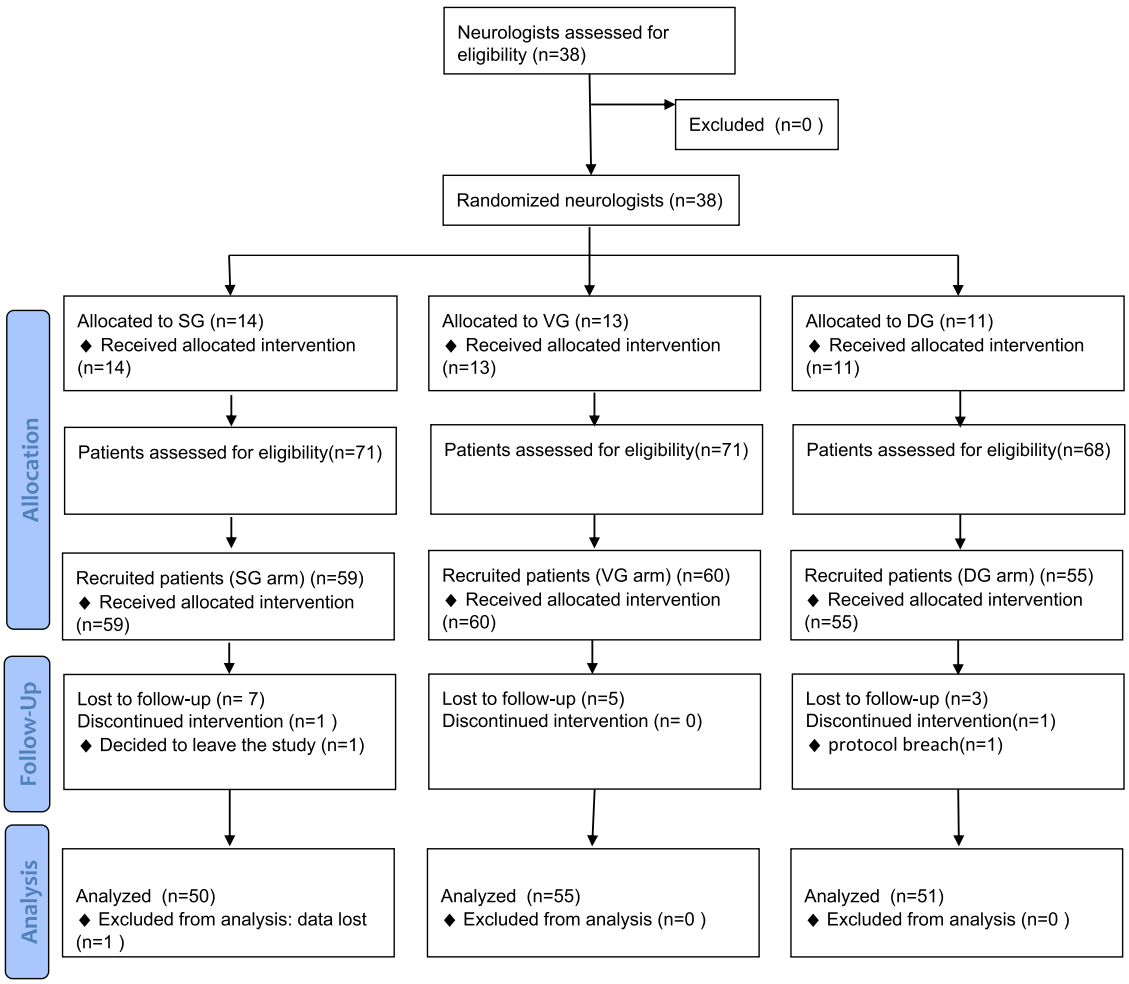

Fig. 1 | Flowchart of participating neurologists and study patients.

significant changes from baseline to the end of the study in any of the groups. DG patients had the most notable mean reduction by 3.5%, followed by SG, with a mean decrease of 2.3%, whereas G had a minimal change, with a slight mean reduction of 0.2%. Comparison of both DG and SG methods to the non-monitoring approach (VG) using a multivariate regression model did not yield significant differences in changes in 'OFF time' (DG vs. VG: $p = 0.085$; SG vs. VG: $p = 0.689$) (Table 2).

Secondary outcomes

Hauser Diary Variables: Throughout the study, DG experienced the largest mean increase in percentage of 'ON time' by 6.0%, followed by SG (5.2%), while in VG the mean percentage of 'ON time' decreased (−2.3%) (Table 3). DG's increase was statistically significant compared to VG ($p = 0.004$). Dyskinesia increased in both DG and VG and slightly decreased in SG, but none of the changes were statistically significant in a multivariate regression model when compared to VG (Table 3).

Parkinson Holter Variables: Table 4 shows data measured via PH throughout the study. The 'OFF time' varied slightly across all groups, whereas the 'ON time' increased by approximately a mean of 6% in DG, with only a modest increase in SG. 'Dyskinesia' levels underwent slight shifts in all groups as the study progressed. FOG-Q remained unchanged across the board. Similarly, minimal changes were observed in 'SMA' and 'Stride fluidity'. Nevertheless, none of the changes in all the examined variables showed statistical significance in a multivariate regression model when compared to VG (Table 4).

Questionnaire Variables: The FOG-Q, PDQ-39, and UPDRS-II, -III, and -IV questionnaire scores showed small changes throughout the study and among study groups (Table 5). However, changes in DG and SG compared to VG did not reach statistical significance in a multivariate regression model.

Table 1 | Baseline sociodemographic and clinical characteristics of the study population

	Visit Group, $n = 55$	Diary Group, $n = 51$	Sensor Group, $n = 50$
Sociodemographic characteristics			
Age, mean (SD), years	62.5 (9.05)	65.8 (10.9)	65.9 (8.85)
Age upon completing education, mean (SD), years	16.9 (4.51)	17.4 (5.60)	18.1 (6.63)
Gender, *n* (%)			
Men	37 (67.3)	29 (56.9)	27 (54.0)
Women	18 (32.7)	22 (43.1)	23 (46.0)
Marital status, *n* (%)			
Unmarried	13 (23.6)	5 (9.80)	13 (26.0)
Married	35 (63.6)	43 (84.3)	35 (70.0)
Widower	7 (12.7)	3 (5.88)	2 (4.00)
Clinical characteristics			
Years of disease, mean (SD)	8.76 (4.55)	8.20 (4.64)	10.2 (5.46)
Need for assistance, *n* (%)	5 (9.09%)	13 (25.5%)	5 (10.0%)
Hoehn & Yahr, mean (SD)	2.36 (0.52)	2.52 (0.40)	2.51 (0.47)
Percentage of OFF time, mean (SD)	29.3 (12.2)	26.9 (13.3)	31.7 (14.0)
FOG-Q (%), mean (SD)	10.1 (6.08)	10.8 (6.73)	10.8 (6.28)
PDQ-39 summary index, mean (SD)	30.7 (15.4)	36.1 (18.4)	30.5 (16.4)
UPDRS-II, mean (SD)	10.2 (5.28)	12.9 (6.65)	12.7 (5.70)
UPDRS-III, mean (SD)	18.0 (10.4)	22.9 (12.4)	22.2 (10.0)
UPDRS-IV, mean (SD)	1.55 (1.76)	1.22 (1.76)	1.78 (1.81)

FOG-Q Freezing of Gait Questionnaire, *PDQ-39* the 39-item PD Questionnaire, *SD* standard deviation, *UPDRS* Unified PD Rating Scale.

Discussion

The results from this cluster-randomized clinical trial showed that the three different follow-up methods to assess PD motor symptoms—a regular consultation (Visit Group, VG), Hauser diary follow-up (Diary Group, DG), and a PH follow-up (Sensor Group, SG)—yielded no significant differences in clinical outcomes (i.e., motor fluctuations) for patients with PD. Specifically, no differences were observed in the primary outcome ('OFF time') or in secondary outcomes, encompassing both Hauser diary variables ('ON time', dyskinesia), PH variables ('OFF time', 'ON time', dyskinesia, FOG-Q, SMA, and stride fluidity), and questionnaire scores (FOG-Q, PDQ-39, UPDRS-II, -II, and -IV).

The results from our study showed no differences among the different methods used to assess motor fluctuations. One possible explanation for these results is that the complexity of PD management goes beyond motor symptom monitoring[24]. While motor fluctuations and their patterns play an instrumental role in therapeutic adjustments, they represent only a fraction of the entire clinical picture. The presence and characteristics of motor fluctuations, including 'ON-OFF' phenomena and dyskinesias, may reflect how the disease responds to medication over time[25]. Therefore, neurologists primarily consider the range and severity of motor symptoms, such as tremors, bradykinesia, and rigidity, to gauge the baseline symptomatology[26]. However, besides the obvious motor symptoms, neurologists base medication adjustments on other non-motor symptoms, including sleep issues, cognitive shifts, mood disorders, daily activities, lifestyle, and the impact of symptoms on QoL[27,28]. Finally, the treatment plan is influenced by concomitant medications due to potential drug interactions and their overall effect, as well as the patient's preferences and concerns[29,30]. Thus, the numerous parameters guiding medication adjustments may have masked the impact of motor fluctuations, measured using different methods, on these adjustments and consequently, clinical outcomes.

Another possible explanation for the lack of differences is that neurologists might not accurately integrate the data obtained from the Hauser diary or the PH into their clinical decision-making processes. Instead, they might prioritize information gathered from patients' verbal accounts and

Table 2 | Changes in 'OFF' time measured with the Hauser diary according to study group

		Visit Group $n = 55$	Diary Group $n = 51$	Sensor Group $n = 50$	Regression analysis			
					Comparison	Estimate	CI	*p*-value
Percentage OFF time, Mean (SD)	Baseline	29.3 (12.2)	26.9 (13.3)	31.7 (14.0)	DG vs. VG[a]	−5.91	−12.63 to 0.82	0.085
	Final	29.1 (19.3)	23.4 (15.2)	29.4 (17.4)	SG vs. VG[a]	−1.36	−8.03 to 5.32	0.689
p-value (Baseline vs. Final)		0.962	0.227	0.4707				

CI confidence interval, *DG* Diary Group, *SD* standard deviation, *SG* Sensor Group, *VG* Visit Group.
[a]Observations = 148, R2/R2 adjusted=0.181/0.146, AIC = 1259.514.
Model adjusted by equivalent dopaminergic dose, UPRS-II, UPDRS-III, and 'OFF time' at baseline.

Table 3 | Changes in ON time and dyskinesia measured with the Hauser diary throughout the study

Variable		Visit Group $n = 55$	Diary Group $n = 51$	Sensor Group $n = 50$	Regression analysis			
					Comparison	Estimate	CI	*p*-value
Percentage ON time, Mean (SD)	Baseline	64.0 (11.9)	63.8 (17.1)	58.7 (14.8)	DG vs. VG[a]	10.50	3.38 to 17.63	**0.004**
	Final	61.7 (20.4)	69.8 (16.9)	63.9 (17.8)	SG vs. VG[a]	5.26	−1.91 to 12.43	0.149
p-value (Baseline vs. Final)		0.4695	0.0762	0.1143				
Dyskinesia (%), Mean (SD)	Baseline	7.04 (12.9)	9.51 (17.8)	9.21 (12.1)	DG vs.VG[b]	2.17	−4.66 to 9.00	0.532
	Final	8.82 (19.2)	11.4 (21.0)	8.94 (11.5)	SG vs. VG[b]	−0.55	−7.36 to 6.26	0.873
p-value (Baseline vs. Final)		0.5693	0.622	0.9092				

CI Confidence interval, *DG* Diary Group, *SD* standard deviation, *SG* Sensor Group, *VG* Visit Group.
[a]Observations = 148, R2/R2 adjusted=0.172/0.137, AIC = 1278.082.
[b]Observations = 148, R2/R2 adjusted=0.148/0.112, AIC = 1265.541.
Model adjusted by equivalent dopaminergic dose, UPRS-II, UPDRS-III, and 'ON time' at baseline.

their own observations during visits, available to all three neurologists' groups. The integration of new technological tools and patient-recorded data requires a learning curve and a shift in traditional clinical practice. Despite the availability of comprehensive data for motor fluctuations obtained from monitoring instruments, neurologists may still rely on traditional methods. Moreover, there may be a level of skepticism or uncertainty about the validity or reliability of the data collected through these tools. Additionally, time constraints during consultations, as well as a potential lack of training or familiarity with the technology, could further limit the degree to which this data is considered. In essence, while tools like PH present an innovative approach to capture the motor manifestation of PD, integrating this data into the routine clinical practice may not be seamless, and could explain the absence of differences observed within the three groups with respect to medical adjustments.

Moreover, the lack of differences between monitoring methods may be explained by the neurologists' caution when adjusting medication. For instance, higher doses of PD medications may cause dyskinesias related to levodopa[31]. It is likely that neurologists perceive that changes in medication, especially frequent adjustments, could lead to a greater destabilization in the patient's condition[31], and therefore, might be reluctant to changes. Hence, even when faced with motor fluctuations or other symptoms, neurologists may prefer stability and predictability over introducing potential uncertainties by changing the medication. In this regard, 25% of study patients in each group did not have any medication adjustments throughout the six-month follow-up period, which may explain, at least in part, the lack of significant changes in motor fluctuations across study groups.

Finally, the study's infrequent visit schedule (one visit every three months) may contribute to the observed lack of impact on 'OFF time.' Given that medication effects occur within hours[32], more frequent visits may be necessary to implement and assess changes effectively. However, although neurologists were allowed to schedule consultations as needed in this study, they completed only two, the minimum required to complete the study. An explanation for this could be the hesitancy to modify medication regimens despite the presence of motor fluctuations; therefore, neurologists might not need additional consultations with patients. Another possible explanation is that neurologists have a high workload that may not allow scheduling more visits. This draws attention to the real-world challenges faced by neurologists in balancing optimal patient care with resource limitations, shedding light on potential barriers to achieving desired clinical outcomes in the context of PD management.

One of the key contributions of this study is that it successfully integrated the studied technology into real-world neurology consultations in hospital settings. This demonstrates that wearable sensors can be incorporated into routine clinical practice. However, their impact on symptom management did not meet expectations, likely due, at least in part, to the previously discussed barriers.

Although these technologies may not provide significant advantages within the current clinical practice model, they enable a potential shift in care delivery—allowing for more frequent, and not necessarily in-person, patient assessments, which could lead to a more efficient use of time. This new approach could reveal their true value in improving disease management. Therefore, an important avenue for future research in the field of wearables for Parkinson's disease is exploring how these devices can be effectively integrated into different healthcare models to maximize their potential benefits.

The results from this study should be interpreted considering certain limitations associated with sample size and follow-up. The sample size for this study was initially calculated with the assumption of a 1.25-h reduction in 'OFF time' as an outcome, likely representing an unrealistic clinical benefit. However, increasing the sample size would unlikely alter the overall results and conclusions of the study.

Additionally, this study lacked a quality control mechanism to assess how neurologists interpreted and utilized the data from both the sensors and the Hauser diary. While objective measurements of motor fluctuations were provided to the neurologists in the Sensor and Diary groups, the study did

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Table 4 | Changes in OFF/ON time, dyskinesia, FOG-Q, SMA, and fluency measured with the Parkinson Holter throughout the study

Variable		Visit Group, *n* = 50	Diary Group, *n* = 47	Sensor Group, *n* = 44	Regression analysis			
					Comparison	Estimate	CI	*p*-value
Percentage OFF time, Mean (SD)	Baseline	15.2 (9.55)	17.4 (9.09)	19.0 (9.20)	DG vs. VG[a]	−1.36	−4.59 to 1.87	0.407
	Final	15.6 (9.26)	15.3 (9.62)	18.7 (9.99)	SG vs. VG[a]	0.92	−2.46 to 4.30	0.591
p-value (Baseline vs. Final)		0.9538	0.4968	0.763				
Percentage ON time, Mean (SD)	Baseline	43.8 (17.4)	36.9 (15.6)	39.3 (16.5)	DG vs. VG[b]	4.83	−0.66 to 10.32	0.084
	Final	43.3 (17.8)	42.9 (17.3)	40.2 (15.0)	SG vs. VG[b]	2.05	−3.60 to 7.69	0.474
p-value (Baseline vs. Final)		0.9697	0.0852	0.9359				
Dyskinesia (%), Mean (SD)	Baseline	17.4 (17.5)	15.3 (14.3)	18.1 (14.9)	DG vs. VG[c]	4.45	−0.75 to 9.65	0.092
	Final	17.6 (16.1)	19.7 (16.2)	19.5 (16.4)	SG vs. VG[c]	4.74	−0.63 to 10.11	0.083
p-value (Baseline vs. Final)		0.9001	0.2559	0.5873				
FOG-Q (%), Mean (SD)	Baseline	0.38 (0.69)	0.21 (0.28)	0.34 (0.61)	DG vs. VG[d]	0.06	−0.12 to 0.23	0.535
	Final	0.37 (0.89)	0.25 (0.36)	0.35 (0.68)	SG vs. VG[d]	0.01	−0.17 to 0.19	0.905
p-value (Baseline vs. Final)		0.9361	0.6591	0.9654				
SMA (m/s^2), Mean (SD)	Baseline	0.43 (0.15)	0.35 (0.11)	0.38 (0.10)	DG vs. VG[e]	0.01	−0.02 to 0.05	0.368
	Final	0.41 (0.14)	0.37 (0.12)	0.39 (0.12)	SG vs. VG[e]	−0.00	−0.04 to 0.03	0.818
p-value (Baseline vs. Final)		0.5646	0.313	0.9593				
Stride fluidity (m/s^2), Mean (SD)	Baseline	8.65 (1.44)	7.30 (1.47)	7.69 (1.29)	DG vs. VG[f]	0.22	−0.11 to 0.55	0.183
	Final	8.56 (1.59)	7.63 (1.58)	7.78 (1.40)	SG vs. VG[f]	−0.16	−0.48 to 0.17	0.340
p-value (Baseline vs. Final)		0.7579	0.2955	0.7513				

CI Confidence interval, *DG* Diary Group, *FOG-Q* Freezing of Gait Questionnaire, *SG* Sensor Group, *SMA* Signal magnitude area, *VG* Visit Group.

[a]Observations = 119, R2/R2 adjusted=0.497/0.470, AIC = 815.654.

[b]Observations = 119, R2/R2 adjusted=0.506/0.480, AIC = 940.408.

[c]Observations = 119, R2/R2 adjusted=0.512/0.486, AIC = 929.521.

[d]Observations = 119, R2/R2 adjusted=0.714/0.698, AIC = 123.830.

[e]Observations = 119, R2/R2 adjusted=0.744/0.730, AIC = -291.272.

[f]Observations = 119, R2/R2 adjusted=0.811/0.801, AIC = 260.373.

Model adjusted by the equivalent dopaminergic dose, UPRS-II, UPDRS-III, and the corresponding variable at baseline.

Table 5 | Changes in FOG-Q, PDQ 39, and UPDRS scores throughout the study

Variable		Visit Group, *n* = 54	Diary Group, *n* = 50	Sensor Group, *n* = 50	Regression analysis			
					Comparison	Estimate	CI	*p*-value
FOG-Q scores, Mean (SD)	Baseline	10.1 (6.08)	10.8 (6.73)	10.8 (6.28)	DG vs. VG[a]	−1.20	−2.72 to 0.33	0.123
	Final	11.3 (6.12)	10.9 (6.63)	11.0 (5.62)	SG vs. VG[a]	−1.13	−2.64 to 0.38	0.140
p-value (Baseline vs. Final)		0.3701	0.9269	0.9992				
PDQ-39 scores, Mean (SD)	Baseline	30.7 (15.4)	36.1 (18.4)	30.5 (16.4)	DG vs. VG[b]	−2.94	−7.09 to 1.21	0.163
	Final	30.4 (17.8)	31.5 (17.5)	29.9 (14.8)	SG vs. VG[b]	0.02	−4.07 to 4.10	0.993
p-value (Baseline vs. Final)		0.9168	0.2111	0.8641				
UPDRS-II scores, Mean (SD)	Baseline	10.2 (5.28)	12.9 (6.65)	12.7 (5.70)	DG vs. VG[c]	−0.74	−2.50 to 1.01	0.403
	Final	9.74 (6.11)	11.2 (7.47)	13.0 (6.00)	SG vs. VG[c]	0.93	−0.82 to 2.68	0.295
p-value (Baseline vs. Final)		0.6606	0.2493	0.7983				
UPDRS-III scores, Mean (SD)	Baseline	18.0 (10.4)	22.9 (12.4)	22.2 (10.0)	DG vs. VG[d]	0.70	−2.33 to 3.73	0.647
	Final	16.4 (11.1)	21.5 (13.9)	22.1 (10.9)	SG vs. VG[d]	2.16	−0.86 to 5.18	0.159
p-value (Baseline vs. Final)		0.4456	0.6122	0.962				
UPDRS-IV scores, Mean (SD)	Baseline	1.55 (1.76)	1.22 (1.76)	1.78 (1.81)	DG vs. VG[e]	0.01	−0.56 to 0.59	0.963
	Final	1.36 (1.67)	1.25 (1.57)	1.80 (2.02)	SG vs. VG[e]	0.22	−0.35 to 0.79	0.441
p-value (Baseline vs. Final)		0.5798	0.9058	0.9585				

CI confidence interval, *DG* Diary Group, *FOG-Q* Freezing of Gait Questionnaire, *PDQ39* the 39-item PD Questionnaire, *SG* Sensor Group, *UPDRS* unified PD rating scale, *VG* Visit Group.
[a]Observations = 142, R2/R2 adjusted=0.646/0.630, AIC = 782.103.
[b]Observations = 141, R2/R2 adjusted=0.622/0.605, AIC = 1054.381.
[c]Observations = 146, R2/R2 adjusted=0.604/0.590, AIC = 848.489.
[d]Observations = 147, R2/R2 adjusted=0.633/0.620, AIC = 1016.022.
[e]Observations = 148, R2/R2 adjusted=0.350/0.322, AIC = 530.809.
Model adjusted by equivalent dopaminergic dose, UPRS-II, UPDRS-III, and the corresponding variable at baseline, where applicable.

not track to what extent this information influenced their clinical decision-making. Neurologists may have prioritized subjective patient reports and their own clinical assessment over these objective data sources, which could have diluted the potential impact of these monitoring tools on treatment adjustments. A longer study with more frequent visits could have provided neurologists with additional time to familiarize themselves with the technology and progressively integrate it into their decision-making process. This learning curve could be critical in determining the real impact of objective monitoring on clinical outcomes, as adaptation to new tools often requires sustained exposure and iterative feedback. Future studies should explore whether extended follow-up periods and structured training programs enhance the adoption and clinical utility of wearable monitoring devices in Parkinson's disease management.

In conclusion, while our study suggests that the method of monitoring PD may not significantly influence its clinical outcomes, it also underscores the importance of understanding the broader context in which these tools are employed. Future research should delve deeper into the barriers preventing the effective integration of these monitoring tools into clinical practice and explore how they can be effectively combined with other clinical indicators to enhance patient outcomes.

Methods

Trial design

The MoMoPa-EC trial was a multicenter, single-blind, cluster-randomized, controlled clinical trial, including patients with moderate-to-severe PD. Patients were consecutively recruited between November 2019 and December 2021 during routine visits to participating neurologists at the 44 participating centers (listed in Supplementary Table 1). Patients' motor fluctuations were assessed using three different methods: a wearable device (Parkinson's Holter, PH), a patient diary (Hauser diary), and during routine patient visits. Neurologists participating in the study were randomly assigned to one of the three groups, each receiving different sets of data for review: clinical information from patient visits along with PH readings (Sensor Group, SG), data from patient visits along with Hauser diary entries (Diary Group, DG), and data from patient visits alone (Visit Group, VG). Consequently, the neurologists' clinical decisions were informed by the specific data set available to each group. A detailed description of this clinical trial protocol has been previously published[13].

The study protocol received approval from the independent research ethics committee of Bellvitge Hospital (Hospitalet de Llobregat, Spain) under reference AC012/19. This study's conduct adhered to the principles outlined in the Helsinki Declaration and complied with the EU General Data Protection Regulation (GDPR). As per GDPR guidelines, all personal data were appropriately anonymized and kept separate from the research results.

Participating Neurologists and Patients

Participating neurologists were required to visit at least 10 patients with PD per month and have the potential to recruit patients with difficult-to-control motor fluctuations during the recruitment period. All investigators and collaborators at the study sites attended a one-day training session on study procedures and instruments before recruitment started.

Patients' inclusion criteria were an idiopathic PD diagnosis based on the UK Brain Bank's PD Society criteria[33], hard-to-control motor fluctuations, a Hoehn & Yahr score between 2 and 5 (excluding 5)[34], and motor challenges, including daily 'OFF time' or dyskinesia. Exclusion criteria were inability to walk independently, participation in other clinical trials, acute intercurrent diseases, presence of psychiatric or cognitive disorders hindering participation (Mini-Mental State Examination score <24), and difficulty understanding the study processes (including proper completion of the Hauser diary). Additionally, those whose baseline Hauser diaries recorded less than 2 h of OFF-period state daily were excluded[13]. All patients provided written informed consent.

Interventions

Patients were classified into three groups based on the allocation of the corresponding neurologist into one of three study arms: (1) the Sensor Group (SG), including neurologists with access to data from PH (STAT-ON®) in addition to information collected during the regular consultation; (2) the Diary Group (DG), including neurologists with access to data from a motor fluctuations diary (i.e., the Hauser diary) in addition to information collected

during the regular consultation; and (3) the Visit Group (VG), including neurologists with access only to information collected during the regular consultation. The diary version used in this study, along with an example of the sensor recording, can be found in the study protocol publication[13].

Neurologists were randomly allocated to one of three designated groups and assessed patient eligibility during an inclusion visit. Patients meeting the inclusion criteria were invited to participate in the study and those who accepted were scheduled for the baseline visit. Neurologists were allowed to schedule follow-up visits as needed according to their criteria.

Throughout the study, all participants received standardized guidelines from neurologists on Hauser diary completion, enriched with instructional videos showcasing motor fluctuation examples. A dedicated research team thoroughly examined the baseline Hauser diaries, and entries with incomplete details, ambiguous data, or discrepancies were omitted.

Data collection and visits

Study data were collected during three visits: a baseline visit, a follow-up visit at week 12 (± 2 weeks) after the baseline visit, and a final visit at week 26 (± 2 weeks) after the baseline visit. All patients used the diary for seven days before the baseline and final visits and the PH for seven days before the three visits. DG patients additionally used the Hauser diary before the follow-up visits. However, SG and VG patients were not provided with the diary in the intermediate visits to prevent bias originated from the use of a recording instrument (the diary), which may have improved symptoms' self-perception and possibly enhanced the accuracy of the information provided to neurologists.

Outcomes and variables

The primary outcome of this study was to compare the changes in daily 'OFF time', measured as a percentage of hours in 'OFF' using the Hauser diary, from baseline to the final visit among the three study groups. The Hauser diary allows reporting of four motor phases (OFF, ON minus dyskinesias, On with non-troublesome dyskinesias, and ON with troublesome dyskinesias). For each patient, the daily time percentages in each motor phase were calculated by dividing the total daily time (hours) in the phase by the total day's tracking time. An average daily percentage of 'OFF time', 'ON time', and dyskinesia were calculated.

For the secondary objectives, we analyzed 'ON time' and dyskinesia measured with the Hauser diary and parameters obtained by the PH, including 'OFF time,' 'ON time,' and dyskinesia, expressed as daily time percentages. Additional PH parameters considered were the frequency of freezing of gait (FOG), expressed as the number of FOGs over the total monitoring time in hours, stride fluidity (m/s^2), and the accelerometer signal magnitude area (SMA) (m/s^2), calculated as previously described[14,35–37]. Stride fluidity is derived from a hierarchical algorithm that analyzes the patient's walking[14], while SMA is an algorithm that estimates calorie expenditure during physical activities[35,36].

Furthermore, we assessed the changes in the scores of the Freezing of Gait Questionnaire (FOG-Q), the 39-item PD Questionnaire (PDQ-39), self-administered by the patients or their caregivers, and the Unified PD Rating Scale (UPDRS), parts II, III, and IV (dyskinesia items), administered by the neurologists. FOG-Q was designed as a 6-item questionnaire to quantify FOG, a common parkinsonian symptom interfering with daily functioning and QoL[38]. Higher FOG-Q scores indicate a greater severity of freezing of gait. PDQ-39 measures the frequency of challenges encountered by patients in eight daily living dimensions and is the predominant disease-specific, patient self-administered rating scale in PD research[39,40]. Higher PDQ-39 scores indicate a more significant impact of PD on daily living. UPDRS is a widely used instrument that monitors PD-related disability and impairment[41]. Of the four components included in the scale[41], the 'Activities of Daily Living' (part II), 'Motor' (part III), and 'Complications' (part IV - dyskinesia items) were used in the present study. Higher UPDRS scores indicate more severe impairment or disability.

Dopaminergic drug dose data were also collected during the study and were expressed as levodopa equivalent dose[42]. Sociodemographic variables considered at baseline included age, gender, marital status, and years of education age upon completing education.

Sample size

To determine the sample size, we assumed an average reduction of 75 min (SD 130) in daily OFF time between Group A and Group C. Based on this assumption, a sample size of 49 patients per group was calculated to achieve 80% power at a significance level of $\alpha = 5\%$ (two-tailed). To compensate for potential dropouts and non-evaluable patients, the sample size was increased by 10%, resulting in a total of 162 patients (54 per group). To complete the study, it was estimated that 30 to 40 neurologists would be needed, with each expected to recruit an average of four patients.

Randomization and blinding

Neurologists, and by extension all their patients, were randomly assigned to one of the three study arms. The randomization sequence was generated by the coordinating team using a balanced block design. The team responsible for implementing the allocation was blinded to the composition and size of the randomization blocks. This team received patient data and, before each consultation, securely sent the corresponding neurologist the information they were assigned to access based on their randomization group: Holter data, diary data, or no additional information.

The neurologists were blinded to the outcomes self-administered by patients, the data analysts were blinded to the interventions, and patients were blinded to the allocation group.

Statistical methods

Categorical variables were presented in terms of frequencies and percentages, while continuous variables were expressed using the mean and standard deviation (SD).

The primary outcome of the study was OFF time at the final visit. To compare this outcome across the different study groups, a linear regression model was fitted, with OFF time at the final visit as the dependent variable. The study arm and OFF time at the baseline visit were included as covariates. Additionally, the model was adjusted for UPDRS-II and UPDRS-III scores, as well as the levodopa equivalent dose at baseline, calculated as previously described[42]. The study group coefficients for study group were reported with a 95% confidence interval and p-value. For all tests, a two-sided alpha of less than 0.05 was considered significant. Statistical evaluations were conducted using the R 4.1.2 software.

This clinical trial was registered at ClinicalTrials.gov on November 21, 2019 (NCT04176302).

Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Author contributions

Conceptualization, Alejandro Rodríguez-Molinero and Carlos Pérez-López; Investigation, Nuria Caballol, Mariateresa Buongiorno, María Asunción Ávila Rivera, Núria López Ariztegui, Lydia López-Manzanares, Jorge Hernández-Vara, Àngels Bayes Rusiñol, Alexandre Gironell Carreró, María Álvarez Saúco, Elisabet Franquet Gomez, David A Pérez-Martínez, Sonia Escalante Arroyo, Silvia Martí Martínez, Pablo Mir, José Mª Salom Juan and Juan Carlos Martínez-Castrillo; Methodology, Jorge Hernández-Vara, Àngels Bayes Rusiñol, David A Pérez-Martínez, Juan Carlos Martínez-Castrillo; Formal analysis, Cristian Tebé; Project administration, Alejandro Rodríguez-Molinero; Software, Carlos Pérez-López; Validation, Carlos Pérez-López; Writing–review, All authors.

Competing interests

C.P.L., A.R.M., J.H.V., and A.B. are shareholders of Sense4Care the company that markets the tested device. The remaining declare that they have no competing interests.

Additional information

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Correspondence and requests for materials should be addressed to Alejandro Rodríguez-Molinero.

[1]Àrea de Recerca, Consorci Sanitari de l'Alt Penedès i Garraf, Vilafranca del Penedès, Spain. [2]Department of Neurology, Complex Hospitalari Universitari Moisès Broggi, Barcelona, Spain. [3]Department of Neurology , Hospital Universitari Vall d'Hebron, Barcelona, Spain. [4]Department of Neurology, Hospital Universitario de Toledo, Toledo, Spain. [5]Department of Neurology, Hospital Universitario de la Princesa, Madrid, Spain. [6] Neurodegenerative Diseases Research Group. , Vall D´Hebron Institut de Recerca (VHIR), Barcelona, Spain. [7]Parkinson's and Movement Disorders Unit, Hospital Quirón-Teknon, Barcelona, Spain. [8]Department of Neurology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain. [9]Department of Neurology, Hospital general de Elche, Alicante, Spain. [10]Department of Neurology, Hospital Sant Camil. Sant Pere de Ribes, Barcelona, Spain. [11]Department of Neurology, Hospital Universitario 12 de Octubre, Madrid, Spain. [12]Department of Neurology, Hospital de Tortosa Verge de la Cinta, Tarragona, Spain. [13]Department of Neurology, Hospital General de Alicante, Alicante, Spain. [14]Unidad de Trastornos del Movimiento, Servicio de Neurología, Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Sevilla, Spain. [15]Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Instituto de Salud Carlos III, Madrid, Spain. [16]Departamento de Medicina, Facultad de Medicina, Universidad de Sevilla, Sevilla, Spain. [17]Department of Neurology, Hospital Clínico de Valencia, Valencia, Spain. [18]Movement Disorders and Neurodegenerative Diseases Unit, IRYCIS, Hospital Ramón y Cajal, Madrid, Spain. [19]Biostatistics Support and Research Unit, Germans Trias I Pujol Research Institute and Hospital (IGTP), Barcelona, Badalona, Spain. ✉e-mail: arodriguez@csapg.cat

On behalf of the MoMoPa-EC Research Group

Anna Planas-Ballvé[2], Pau Pastor[20], Ignacio Alvarez[21], Mª Isabel Morales Casado[4], Sara Lucas del Pozo[3,6], Anna Prats[7,20], Álvaro Sánchez-Ferro[11], Antonio Méndez Guerrero[11], Carlos Leiva Santana[13], Laura Muñoz-Delgado[14,15], Daniel Macías-García[14,15], Silvia Jesús[14,15], Astrid Adarmes-Gómez[14,15], Antonio Salvador Aliaga[17], Gema Sánchez[18], Esther Cubo[22], Lourdes Ispierto González[20], Ramiro Álvarez-Ramo[20], Dolores Vilas Rolan[20], Antonio Koukoulis Fernández[23], Mª Gema Alonso Losada[23], Jon Infante[24,25], María Sierra Peña[24,25], Isabel González Aramburu[24,25], Mª Victoria Sánchez Peláez[24,25], Marina Mata Álvarez-Santullano[26,27], Carmen Borrúe Fernández[26], Mª Concepción Jimeno Montero[26], Lydia Vela Desojo[28], Berta Solano Vila[29], Anna Cots Foraster[29], Daniel López Domínguez[29], Esteban Peña Llamas[30], Pilar Sánchez Alonso[31], Elisa Gamo Gonzalez[31], Sabela Novo Ponte[31], Alfredo López López[32], Mª José Gómez Heredia[33], Francisco Pérez Errazquin[33], Mª Pilar Solís Pérez[34], Esther Blanco Vicente[35], Rafael García Ruiz[35], Ana Rita Santos Pinto[35], Marta Recio-Bermejo[35], Ernest Balaguer[36], Antonio Hernández Vidal[36], Rocío García-Ramos[37], Eva López Valdés[37], Rubén Alonso Redondo[38], Jessica González Ardura[38], Teresa Muñoz Ruiz[39], Lucía Flores García[39], Javier Ruiz Martínez[40], Ana Vinagre Aragón[40], Ioana Croitoru[40], Esther Catena Ruiz[41], Victor Puente[42], Irene Navalpotro Gómez[42] & Antonio Miñarro[43]

[20]Unit of Neurodegenerative diseases, Department of Neurology, Hospital Germans Trias i Pujol, Badalona, Spain. [21]Department of Neurology, Hospital Universitari Mútua Terrassa, Terrassa, Barcelona, Spain. [22]Department of Neurology, Hospital Universitario de Burgos, Burgos, Spain. [23]Hospital Álvaro Cunqueiro, Vigo, Spain. [24]Servicio de Neurología, Hospital Universitario Marqués de Valdecilla-IDIVAL, Universidad de Cantabria., Santander, Spain. [25] Centro de Investigación Biomédica en Red Enfermedades Neurodegenerativas (CIBERNED), Instituto de Salud Carlos III, Madrid, , Spain. [26]Hospital Universitario Infanta Sofía, Madrid, Spain. [27]Departamento de Medicina, Facultad de Medicina, Salud y Deportes, Universidad Europea de Madrid, Madrid, Spain. [28]Hospital Universitario Fundación Alcorcón, Madrid, Spain. [29]Hospital Universitari de Girona Doctor Josep Trueta, Girona, Spain. [30]Hospital Moraleja, Madrid, Spain. [31]Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain. [32]Hospital Royo Villanova, Zaragoza, Spain. [33]Clínico Virgen de la Victoria, Málaga, Spain. [34]Hospital Arnau de Vilanova-Llíria, Llíria, Spain. [35]Hospital Alcázar de San Juan, Alcázar de San Juan, Spain. [36]Hospital Universitari General de Catalunya, Barcelona, Spain. [37]Hospital Clínico San Carlos, Madrid, Spain. [38]Hospital Univ Lucus Augusti, Lugo, Spain. [39]Hospital Regional de Málaga, Málaga, Spain. [40]Hospital Universitario Donostia, Donostia, Spain. [41]Hospital Comarcal de l'Alt Penedès, Barcelona, Spain. [42]Hospital del Mar, Barcelona, Spain. [43]Department of Genetics, Microbiology and Statistics, Faculty of Biology, Universitat de Barcelona, Barcelona, Spain.