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**Research Article**

# Association of Levodopa Exposure With Impulse-Control Behaviors, Depression, Anxiety, and Medication Adherence Among Adults With Parkinson's Disease: A Cross-Sectional Study

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## Abstract

**Background:**
Levodopa remains the cornerstone of symptomatic pharmacotherapy in Parkinson's disease (PD). However, prolonged or high-dose levodopa exposure is increasingly recognized to modulate mesocorticolimbic dopaminergic pathways, potentially predisposing patients to impulse-control behaviors (ICBs), mood disturbances, and erratic medication adherence.

**Objective:**
To evaluate the association between levodopa equivalent daily dose (LEDD) exposure, the presence of impulse-control behaviors, symptoms of depression and anxiety, and overall medication adherence among adult patients with Parkinson's disease.

**Methods:**
This hospital-based cross-sectional study evaluated 160 adult patients with idiopathic Parkinson's disease attending outpatient neurology clinics at Fatima Memorial College of Medicine and Dentistry. Cumulative levodopa exposure was quantified using LEDD. Impulse-control behaviors were evaluated using the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP-RS). Depression and anxiety severity were assessed using the Hospital Anxiety and Depression Scale (HADS-D and HADS-A), while medication adherence was measured via the 8-item Morisky Medication Adherence Scale (MMAS-8). Bivariate correlations and multivariable linear/logistic regression models were constructed to evaluate independent associations.

**Results:**
Among 160 participants (mean age 64.2 ± 8.6 years; 58.8% male; mean disease duration 7.1 ± 4.2 years), the mean LEDD was 685.4 ± 245.2 mg/day. Screening for ICBs was positive in 31.3% ($n = 50$) of patients, with compulsive shopping (14.4%) and hypersexuality (11.9%) being most prevalent. High LEDD exposure ($> 800$ mg/day) was independently associated with a higher odds of ICBs (adjusted OR = 3.84, 95% CI: 1.82–8.11, $p < 0.001$). Patients with high LEDD also demonstrated significantly higher anxiety scores ($p = 0.002$) and lower medication adherence ($p = 0.012$). Multivariable regression confirmed that ICB severity and elevated LEDD were significant independent predictors of suboptimal medication adherence ($p < 0.001$).

**Conclusion:**
Higher levodopa exposure is significantly associated with impulse-control behaviors, elevated anxiety levels, and compromised medication adherence in patients with Parkinson's disease. Comprehensive neuropsychiatric screening and LEDD optimization should be routinely incorporated into movement disorder management to improve therapeutic adherence and quality of life.

**Keywords:** Parkinson's disease; Levodopa equivalent daily dose; Impulse-control behaviors; Depression; Anxiety; Medication adherence; Neuropsychiatry.

## 1. Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the loss of dopaminergic neurons in the substantia nigra pars compacta, leading to cardinal motor manifestations including bradykinesia, resting tremor, rigidity, and postural instability [1, 2]. Levodopa, administered in combination with a peripheral dopa-decarboxylase inhibitor, remains the most efficacious symptomatic therapy for restoring motor function in PD [2, 3]. However, long-term pharmacological management is complicated by non-motor symptoms (NMS) and treatment-related neuropsychiatric adverse events [3, 4].

While exogenous levodopa effectively replenishes depleted dopamine within the motor striatum (dorsal striatum), it simultaneously floods the relatively preserved ventral striatum and mesocorticolimbic pathways [5, 6]. This unbalanced stimulation of dopamine $D_2$ and $D_3$ receptors can disrupt incentive salience and reward processing, giving rise to impulse-control behaviors (ICBs)—including pathological gambling, compulsive buying, hypersexuality, and binge eating—as well as dopamine dysregulation syndrome (DDS) [6, 7].

Furthermore, affective disturbances such as depression and anxiety are prevalent non-motor manifestations, affecting up to 40–50% of PD patients across disease stages [8, 9]. These mood disorders stem from both neurodegenerative damage to serotonergic and noradrenergic networks and fluctuating central dopamine concentrations [9, 10]. Uncontrolled anxiety and depression, combined with cognitive rigidity or compulsive medication-seeking behaviors induced by elevated levodopa exposure, severely impair medication adherence [11, 12].

Suboptimal medication adherence in PD leads to motor fluctuations, dyskinesias, increased emergency room visits, and accelerated functional decline [12, 13]. Despite the clear clinical implications, the complex interplay between total levodopa

equivalent daily dose (LEDD), ICB manifestation, affective symptoms, and patient-reported medication adherence remains incompletely characterized in clinical practice [14, 15].

Therefore, this cross-sectional study was undertaken to evaluate the associations between levodopa exposure, impulse-control behaviors, depression, anxiety, and medication adherence among adult patients with Parkinson's disease.

## 2. Rationale of the Study

Optimizing pharmacotherapy in Parkinson's disease requires balancing motor benefit against neuropsychiatric adverse effects [3, 4]. While dopamine agonists are classically linked to ICBs, high total levodopa exposure (alone or in combination) also contributes to mesolimbic reward dysregulation, anxiety fluctuations, and erratic medication compliance [6, 11]. Evaluating these interconnected behavioral, affective, and pharmacological parameters in a structured observational setting provides essential clinical insights to guide individualized dosage titration, early risk screening, and adherence interventions.

## 3. Objectives

### Primary Objective

- To examine the association between total levodopa exposure (LEDD) and the presence and severity of impulse-control behaviors (ICBs) in adults with Parkinson's disease.

### Secondary Objectives

1. To evaluate the relationship between LEDD exposure and symptoms of depression (HADS-D) and anxiety (HADS-A).
2. To assess the impact of levodopa exposure and ICB status on medication adherence (MMAS-8).
3. To identify independent clinical and pharmacological predictors of poor medication adherence in patients with PD using multivariable regression modeling.

## 4. Materials and Methods

### 4.1 Study Design and Setting

A hospital-based cross-sectional study was conducted at Fatima Memorial College of Medicine and Dentistry.

### 4.2 Study Duration

The study was conducted over a six-month period, encompassing patient recruitment, standardized neurological and psychiatric clinical assessments, medication regimen verification, and data processing.

### 4.3 Study Population

Adult men and women aged 40 years or older with a established diagnosis of idiopathic Parkinson's disease according to the Movement Disorder Society (MDS) clinical diagnostic criteria [1].

### 4.4 Sample Size

A total sample size of 160 participants with Parkinson's disease was evaluated. The sample size was calculated to detect a correlation coefficient ($r \geq 0.25$) between LEDD and behavioral/adherence scale scores with an alpha level of 0.05 and a statistical power of 85%.

### 4.5 Inclusion Criteria

1. Diagnosis of idiopathic Parkinson's disease established for at least 1 year.

2. Treatment with levodopa-containing regimens for a minimum of 6 consecutive months.

3. Hoehn and Yahr (H&Y) clinical stage I to IV.

4. Cognitive capacity to complete self-report questionnaires (Mini-Mental State Examination [MMSE] score $\geq$ 24).

5. Provision of written informed consent.

**4.6 Exclusion Criteria**

1. Diagnosis of atypical or secondary parkinsonism (e.g., progressive supranuclear palsy, multiple system atrophy, drug-induced parkinsonism).

2. Advanced dementia (MMSE $<$ 24) impairing accurate self-reporting.

3. History of major psychotic disorders or substance use disorder pre-dating the diagnosis of PD.

4. Recent deep brain stimulation (DBS) or duodenal levodopa infusion therapy.

**4.7 Clinical Evaluation and Levodopa Equivalent Daily Dose (LEDD)**

Patient demographics, disease duration, and motor severity (Hoehn and Yahr stage; UPDRS Part III) were systematically documented. Complete pharmacological profiles—including levodopa formulations, dopamine agonists, COMT inhibitors, MAO-B inhibitors, and amantadine—were recorded.

Total Levodopa Equivalent Daily Dose (LEDD, mg/day) was calculated according to standardized theoretical conversion factors proposed by Tomlinson et al. [15]:

$$\begin{aligned}&\text{LEDD (mg/day)}\\&= \text{Immediate-release Levodopa (mg)} \times 1.0\\&+ \text{Controlled-release Levodopa (mg)} \times 0.75\\&+ \text{Pramipexole (mg)} \times 100\\&+ \text{Ropinirole (mg)} \times 20 + \cdots\end{aligned}$$

Patients were categorized into LEDD exposure tiers: Low/Moderate ($\leq$ 800 mg/day) and High ($>$ 800 mg/day).

**4.8 Assessment of Impulse-Control Behaviors (ICBs)**

Screening for ICBs (gambling, hypersexuality, compulsive buying, and compulsive eating) and related behaviors (punding, hobbyism, and dopamine dysregulation) was performed using the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease Rating Scale (QUIP-RS) [7]. Total and domain-specific scores were derived, with pre-specified clinical cutoffs used to establish ICB positivity.

**4.9 Assessment of Affective Symptoms and Medication Adherence**

- **Depression and Anxiety:** Measured using the Hospital Anxiety and Depression Scale (HADS), containing separate subscales for anxiety (HADS-A) and depression (HADS-D), each scored from 0 to 21 [8].

- **Medication Adherence:** Evaluated using the 8-item Morisky Medication Adherence Scale (MMAS-8) [13]. Scores were categorized as High adherence ($=$ 8), Moderate adherence (6 to $<$ 8), and Low adherence ($<$ 6).

**4.10 Statistical Analysis**

Data were analyzed using SPSS version 26.0. Continuous variables were presented as mean ± standard deviation (SD) or median (interquartile range, IQR). Categorical variables were expressed as frequencies and percentages (n, %).

Inter-group comparisons between LEDD strata were conducted using Student's t-test or Mann-Whitney U test for continuous parameters and Chi-square test for categorical variables. Bivariate correlation analysis (Pearson/Spearman) assessed relationships between LEDD, QUIP-RS, HADS, and MMAS-8 scores. Multivariable binary logistic regression evaluated factors associated with ICB presence, while multivariable linear regression identified independent determinants of MMAS-8 adherence scores. A two-sided p-value $< 0.05$ was considered statistically significant.

## 5. Results

### 5.1 Demographic and Baseline Clinical Characteristics

The study included 160 PD patients (mean age $64.2 \pm 8.6$ years; 58.8% male). The mean disease duration was $7.1 \pm 4.2$ years, with an average MMSE score of $26.8 \pm 1.9$. The mean total LEDD across the cohort was $685.4 \pm 245.2$ mg/day. Concomitant dopamine agonist therapy was prescribed in 41.3% ($n = 66$) of patients.

| Variable | Low/Moderate LEDD (≤800 mg/day) (n = 104) | High LEDD (>800 mg/day) (n = 56) | Total Cohort (n = 160) | p-value |
|---|---|---|---|---|
| Age, years | 65.1 ± 8.4 | 62.5 ± 8.8 | 64.2 ± 8.6 | 0.071 |
| Male sex, n (%) | 59 (56.7) | 35 (62.5) | 94 (58.8) | 0.478 |
| Female sex, n (%) | 45 (43.3) | 21 (37.5) | 66 (41.2) | 0.478 |
| Disease duration, years | 5.8 ± 3.2 | 9.5 ± 4.8 | 7.1 ± 4.2 | <0.001 |
| Hoehn and Yahr Stage, median (IQR) | 2.0 (1.5–2.5) | 3.0 (2.5–3.5) | 2.5 (2.0–3.0) | <0.001 |

| Variable | Low/Moderate LEDD (≤800 mg/day) (n = 104) | High LEDD (>800 mg/day) (n = 56) | Total Cohort (n = 160) | p-value |
|---|---|---|---|---|
| Total LEDD, mg/day | 524.1 ± 142.6 | 984.8 ± 182.3 | 685.4 ± 245.2 | <0.001 |
| Dopamine Agonist Use, n (%) | 34 (32.7) | 32 (57.1) | 66 (41.3) | 0.003 |

**Table 1: Baseline demographic and clinical characteristics of participants stratified by LEDD exposure.**

### 5.2 Prevalence and Spectrum of Impulse-Control Behaviors

Overall, positive screening for at least one ICB on the QUIP-RS was identified in 31.3% ($n = 50$) of the total cohort. Compulsive buying (14.4%) and hypersexuality (11.9%) were the most common specific behaviors. Patients in the high LEDD group exhibited a significantly higher total ICB prevalence compared to the low/moderate LEDD group (48.2% vs. 22.1%, $p = 0.001$).

| ICB Domain (QUIP-RS Positive) | Low/Moderate LEDD (n = 104) | High LEDD (n = 56) | Total Cohort (n = 160) | p-value |
|---|---|---|---|---|
| Pathological Gambling, n (%) | 4 (3.8) | 8 (14.3) | 12 (7.5) | 0.016 |
| Hypersexuality, n (%) | 7 (6.7) | 12 (21.4) | 19 (11.9) | 0.006 |

| ICB Domain (QUIP-RS Positive) | Low/Moderate LEDD (n = 104) | High LEDD (n = 56) | Total Cohort (n = 160) | p-value |
|---|---|---|---|---|
| Compulsive Buying, n (%) | 10 (9.6) | 13 (23.2) | 23 (14.4) | 0.021 |
| Compulsive Eating, n (%) | 8 (7.7) | 10 (17.9) | 18 (11.3) | 0.052 |
| Any ICB (Overall), n (%) | 23 (22.1) | 27 (48.2) | 50 (31.3) | 0.001 |
| Dopamine Dysregulation / Punding, n (%) | 5 (4.8) | 11 (19.6) | 16 (10.0) | 0.003 |

**Table 2: Prevalence of impulse-control behaviors stratified by levodopa equivalent daily dose.**

### 5.3 Affective Symptoms and Medication Adherence Profiles

Patients in the high LEDD group demonstrated significantly higher mean anxiety scores on the HADS-A ($9.4 \pm 3.8$ vs. $7.2 \pm 3.1$, $p = 0.002$) and significantly lower medication adherence scores on the MMAS-8 ($5.8 \pm 1.6$ vs. $6.6 \pm 1.4$, $p = 0.002$). Low medication adherence (MMAS-8 $< 6$) was present in 41.1% of the high LEDD group compared to 20.2% of the low/moderate LEDD group ($p = 0.006$).

| Outcome Parameter | Low/Moderate LEDD (n = 104) | High LEDD (n = 56) | Total Cohort (n = 160) | p-value |
|---|---|---|---|---|
| HADS-Depression Score (0–21) | 7.4 ± 3.5 | 8.6 ± 4.1 | 7.8 ± 3.8 | 0.054 |
| HADS-Anxiety Score (0–21) | 7.2 ± 3.1 | 9.4 ± 3.8 | 8.0 ± 3.5 | 0.002 |
| MMAS-8 Adherence Score (0–8) | 6.6 ± 1.4 | 5.8 ± 1.6 | 6.3 ± 1.5 | 0.002 |
| High Adherence (MMAS-8 = 8), n (%) | 31 (29.8) | 9 (16.1) | 40 (25.0) | 0.058 |
| Moderate Adherence (MMAS-8 6 to <8), n (%) | 52 (50.0) | 24 (42.9) | 76 (47.5) | 0.384 |
| Low Adherence (MMAS-8 < 6), n (%) | 21 (20.2) | 23 (41.1) | 44 (27.5) | 0.006 |

**Table 3: Comparison of mood scores and medication adherence levels across LEDD categories.**

### 5.4 Correlation Analysis

Bivariate correlation analysis revealed significant positive correlations between total LEDD and QUIP-RS score ($r = 0.38, p < 0.001$) as well as HADS-Anxiety ($r = 0.31, p < 0.001$). MMAS-8 adherence score demonstrated significant inverse correlations with LEDD ($r = -0.33, p < 0.001$), QUIP-RS score ($r = -0.42, p < 0.001$), and HADS-Depression ($r = -0.36, p < 0.001$).

| Parameter Pair | Correlation Coefficient (r) | p-value |
|---|---|---|
| LEDD vs QUIP-RS Total Score | 0.38 | <0.001 |
| LEDD vs HADS-Anxiety | 0.31 | <0.001 |
| LEDD vs MMAS-8 Adherence Score | -0.33 | <0.001 |
| QUIP-RS Score vs MMAS-8 Adherence Score | -0.42 | <0.001 |
| HADS-Depression vs MMAS-8 Adherence Score | -0.36 | <0.001 |
| HADS-Anxiety vs MMAS-8 Adherence Score | -0.28 | <0.001 |

**Table 4: Bivariate correlations among LEDD, neuropsychiatric scores, and medication adherence.**

### 5.5 Multivariable Regression Analysis for Predictors of Suboptimal Medication Adherence

In multivariable linear regression with MMAS-8 score as the continuous dependent variable, elevated QUIP-RS score ($\beta = -0.32, p < 0.001$), higher LEDD ($\beta = -0.24, p = 0.003$), and HADS-Depression score ($\beta = -0.22, p = 0.006$) were identified as independent predictors of lower medication adherence.

| Predictor Variable | Unstandardized β | Standard Error | Standardized β | p-value |
|---|---|---|---|---|
| QUIP-RS Total Score | -0.08 | 0.02 | -0.32 | <0.001 |

| Predictor Variable | Unstandardized β | Standard Error | Standardized β | p-value |
|---|---|---|---|---|
| Total LEDD (per 100 mg increase) | -0.15 | 0.05 | -0.24 | 0.003 |
| HADS-Depression Score | -0.09 | 0.03 | -0.22 | 0.006 |
| HADS-Anxiety Score | -0.04 | 0.03 | -0.10 | 0.182 |
| Disease Duration (years) | -0.03 | 0.03 | -0.08 | 0.314 |

**Table 5: Multivariable linear regression modeling determinants of MMAS-8 medication adherence** score.

## 6. Discussion

This cross-sectional study evaluated the associations between total levodopa exposure (LEDD), impulse-control behaviors, affective symptoms, and medication adherence in patients with Parkinson's disease. The results demonstrate that elevated LEDD ($> 800$ mg/day) is significantly linked to higher ICB prevalence, increased anxiety, and suboptimal medication adherence [6, 7, 11].

### 6.1 Levodopa Exposure and Impulse-Control Behaviors

While dopamine receptor agonists are well-established primary risk factors for ICBs, our findings reinforce growing evidence that cumulative levodopa load also plays a major role in mesolimbic pathway dysregulation [5, 6]. Pulsatile stimulation of $D_2/D_3$ receptors in the nucleus accumbens by high-dose levodopa impairs reward-learning dynamics, predisposing vulnerable patients to compulsive behaviors such as buying, gambling, and hypersexuality [6, 7]. The 31.3% overall ICB prevalence observed in our cohort aligns with international literature reporting ICB rates of 14–35% in treated PD populations [7, 14].

### 6.2 Impact on Affective Symptoms and Mood Dynamics

Elevated LEDD exposure was also associated with significantly higher anxiety levels. In PD, anxiety frequently manifests alongside motor fluctuations (e.g., "off-period" anxiety) [9, 10]. Rapid cycling of central dopamine levels following high-dose

levodopa dosing can induce emotional instability and panic symptoms during end-of-dose wearing-off phases [9]. Conversely, depressive symptoms were strongly linked to lower medication adherence, highlighting the compounding impact of negative mood states on self-management behaviors [8, 12].

### 6.3 Determinants of Suboptimal Medication Adherence

Medication non-adherence in PD is multifactorial, stemming from complex dosing schedules, cognitive changes, and mood disturbances [12, 13]. Our multivariable model demonstrated that elevated ICB severity and high LEDD independently predicted poor adherence [11, 14]. Patients with compulsive behaviors or dopamine dysregulation syndrome often exhibit erratic dosing patterns—either compulsively overusing levodopa to avoid mild motor off-states or missing doses due to disorganized behavioral routines [6, 12].

### 6.4 Clinical Implications

These findings underscore the necessity of routine neuropsychiatric screening in outpatient movement disorder clinics [4, 7]. Clinicians should proactively screen for ICBs using validated tools like the QUIP-RS before and during dose escalations of levodopa or dopamine agonists [7]. When ICBs or severe anxiety are detected, treatment strategies may include gradual LEDD optimization, tapering dopamine agonists, utilizing continuous delivery systems, or adding targeted behavioral/psychiatric interventions [2, 6, 12].

### 6.5 Limitations

Several study limitations should be considered. First, the cross-sectional design precludes establishing temporal causality between LEDD escalation, ICB onset, and adherence decline. Second, medication adherence was measured via a self-report scale (MMAS-8), which may be susceptible to recall bias compared to electronic pill-cap monitoring [13]. Third, genetic vulnerabilities (such as dopamine transporter or receptor gene polymorphisms) were not evaluated in this cohort [6].

## 7. Conclusion

High levodopa equivalent daily dose exposure in adult patients with Parkinson's disease is significantly associated with an increased prevalence of impulse-control behaviors, heightened anxiety symptoms, and reduced medication adherence. Impulse-control behaviors and depressive symptoms independently contribute to compromised treatment adherence. Routine neuropsychiatric monitoring and tailored pharmacotherapy balancing motor control against behavioral risks are essential to optimize long-term outcomes in Parkinson's disease.

## 8. Recommendations

1. Implement routine screening for impulse-control behaviors using validated tools (e.g., QUIP-RS) prior to and during levodopa or dopamine agonist dose escalations.

2. Monitor medication adherence closely in patients requiring high levodopa equivalent daily doses (> 800 mg/day).

3. Assess and treat comorbid anxiety and depressive symptoms systematically to improve overall patient quality of life and treatment compliance.

4. Utilize simplified dosing schedules or continuous dopaminergic delivery strategies

when motor fluctuations drive compulsive medication overuse.

5. Conduct prospective longitudinal studies to clarify the temporal relationships between levodopa titration, mesolimbic sensitization, and medication adherence trajectories.

**9. References**


1. Postuma RB, Berg D, Stern M, et al. MDS clinical diagnostic criteria for Parkinson's disease. Mov Disord. 2015;30(12):1591–1601. doi:10.1002/mds.26424.

2. Armstrong MJ, Okun MS. Diagnosis and treatment of Parkinson disease: A review. JAMA. 2020;323(6):548–560. doi:10.1001/jama.2019.22360.

3. Connolly BS, Lang AE. Pharmacological treatment of Parkinson disease: A review. JAMA. 2014;311(16):1670–1683. doi:10.1001/jama.2014.3654.

4. Schapira AHV, Chaudhuri KR, Jenner P. Non-motor symptoms of Parkinson disease in clinical practice. Nat Rev Neurol. 2017;13(2):85–98. doi:10.1038/nrneurol.2016.178.

5. Kish SJ, Shannak K, Hornykiewicz O. Unequal vulnerability of striatal dopamine subregions in Parkinson's disease. N Engl J Med. 1988;318(14):876–880. doi:10.1056/NEJM198804073181402.

6. Weintraub D, David AS, Evans AH, et al. Clinical spectrum of impulse control disorders in Parkinson's disease. Mov Disord. 2015;30(2):121–127. doi:10.1002/mds.26016.

7. Weintraub D, Mamikonyan E, Papay K, et al. Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale. Mov Disord. 2012;27(2):242–247. doi:10.1002/mds.24023.

8. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand. 1983;67(6):361–370. doi:10.1111/j.1600-0447.1983.tb09716.x.

9. Reijnders JS, Ehrt U, Weber WE, et al. A systematic review of prevalence studies of depression in Parkinson's disease. Mov Disord. 2008;23(2):183–189. doi:10.1002/mds.21803.

10. Dissanayaka NN, Sellbach A, Matheson S, et al. Anxiety disorders in Parkinson's disease: prevalence and risk factors. Mov Disord. 2010;25(7):838–845. doi:10.1002/mds.22833.

11. Corvol JC, Artaud F, Cormier-Dequaire F, et al. Longitudinal analysis of impulse control disorders in Parkinson disease. Neurology. 2018;91(3):e189–e201. doi:10.1212/WNL.0000000000005816.

12. Straka I, Minár M, Skorvanek M, et al. Adherence to pharmacotherapy in patients with Parkinson's disease. Front Neurol. 2019;10:604. doi:10.3389/fneur.2019.00604.

13. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. J Clin Hypertens (Greenwich). 2008;10(5):348–354. doi:10.1111/j.1751-7176.2008.07572.x.

14. Garcia-Ruiz PJ, Martinez Castrillo JC, Alonso-Canovas A, et al. Impulse control disorders in Parkinson's disease in clinic practice. J Neurol Sci. 2014;345(1-2):242–245. doi:10.1016/j.jns.2014.07.039.

15. Tomlinson CL, Stowe R, Patel S, et al. Systematic review of levodopa equivalent

dose conversion factors in Parkinson's disease. Mov Disord. 2010;25(15):2649–2653. doi:10.1002/mds.23428.

16. Chaudhuri KR, Schapira AH. Non-motor symptoms of Parkinson's disease: dopaminergic pathophysiology and treatment. Lancet Neurol. 2009;8(5):464–474. doi:10.1016/S1474-4422(09)70068-7.

17. Voon V, Napier TC, Bhattacharyya S, et al. Impulse control disorders and levodopa-induced dyskinesias in Parkinson's disease: an update. Lancet Neurol. 2017;16(3):238–250. doi:10.1016/S1474-4422(17)30004-2.

18. Daley DJ, Myint PK, Gray RJ, Deane KH. Systematic review on factors associated with medication non-adherence in Parkinson's disease. Parkinsonism Relat Disord. 2012;18(10):1053–1061. doi:10.1016/j.parkreldis.2012.09.004.

19. Evans AH, Katzenschlager R, Pavese N, et al. Punding in Parkinson's disease: relationship to men, levodopa dose, and dopamine dysregulation syndrome. Mov Disord. 2004;19(4):397–404. doi:10.1002/mds.10665.

20. Bloem BR, Okun MS, Klein C. Parkinson's disease. Lancet. 2021;397(10291):2284–2303. doi:10.1016/S0140-6736(21)00218-