Improving Detection and Treatment of

PARKINSON'S DISEASE PSYCHOSIS



1.1 MILLION AMERICANS are living with **Parkinson's Disease (PD).**

40%-70% will develop PD Psychosis (PDP).

Diagnostic Criteria

Presence of **one or more of the following**, if recurrent or continuous for **at least one month** in a patient with **confirmed primary PD**, is diagnostic for PDP.

Hallucinations
Seeing or hearing something that is not there.

False Sense of Presence
Feeling someone nearby who is not actually there.

Delusions
Firmly believing something that is untrue (e.g., paranoia).

Illusions
Mistaking something real (e.g., a coat rack) for something else (e.g., a person).

Validated Screening Tools

CLINICIAN AWARENESS IS KEY!

Tool	Completed by	Length	Primary Focus	Practical Use
SASPAP	Patient	4 Questions	Rapid identification of possible PDP.	Brief screening at intake or during a visit.
SAPS-PD	Clinician	9 Questions	Hallucinations and delusions.	Evaluating symptoms and treatment response.
PPQ	Patient/ Caregiver	14 Items	Sleep, hallucinations, delusions and disorientation.	Characterizing symptom severity and frequency.
Psych-Q	Patient	20 Items	Psychosis/hallucinations and sleep/attention.	Assessing symptom severity and frequency across two domains.
PPRS	Clinician	6 Items	Severity of psychosis symptoms.	Brief symptom rating; less sensitive for early PDP.

SASPAP: Self-Administered Screening Questionnaire for PD-Associated Psychosis; **SAPS-PD**: Scale for Assessment of Positive Symptoms-PD; **PPQ**: Parkinson's Psychosis Questionnaire; **Psych-Q**: Psychosis and Hallucinations Questionnaire; **PPRS**: Parkinson's Psychosis Rating Scale.

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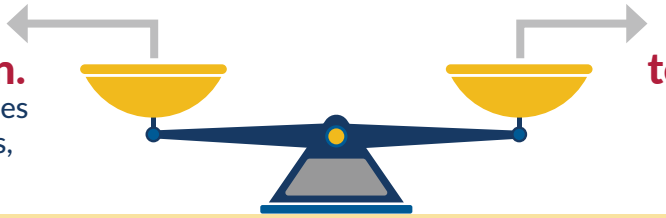
Managing PDP: Dopamine-Serotonin Balancing Act

PD comes from dopamine dysfunction.
Traditional antipsychotic therapies antagonize dopamine receptors, which **exacerbates PD**.



PDP is rooted in too much serotonin.
Overactivation of serotonergic signaling pathways underpin PDP.

The ideal PDP antipsychotic: **inhibits serotonin signaling while sparing dopamine.**

Differentiate From Other Etiologies.

- Infections (i.e., UTI, pneumonia).
- Metabolic imbalance or other systemic causes (i.e., thyroid, renal or hepatic dysfunction).
- Sleep disorders can be causative or simply comorbid.
- Other psychiatric or neurodegenerative disease states (i.e., LBD, schizophrenia, Alzheimer's disease).

Discontinue Offending Meds.

- Start with anticholinergics. Common examples include: diphenhydramine, oxybutynin, tiotropium and benztropine.
- If no improvement, consider taper of dopaminergic medications. Generally, core PD medications (i.e., carbidopa/levodopa) should be tapered as a last resort.

Pharmacologic Intervention: Review of the Options

	CLOZAPINE	QUETIAPINE	PIMAVANSERIN
FDA Status	Off-Label.	Off-Label.	**FDA-Approved for PDP.**
MoA	D_2 and 5-HT_2A receptor antagonist.	D_2 and 5-HT_2A receptor antagonist.	5-HT_2A antagonist and inverse agonist. **No D_2 affinity.**
Evidence in PDP	**Robust efficacy** in placebo-controlled studies.	Efficacy inconclusive; **no significant benefit** versus placebo demonstrated.	Significant improvement in PDP symptoms; durable benefit reported.
Motor Effects	No or minimal worsening.	Generally does not worsen.	No worsening demonstrated.
Clinical Pearls	**Severe neutropenia** and other serious risks; REMS removed in 2025, but neutropenia risk remains.	Generally **well tolerated**; commonly used in practice despite limited efficacy evidence.	Increased-mortality boxed warning for **older adults with dementia-related psychosis**; postmarketing review found no new safety risks.

Sources: Ballanger B, et al. Arch Neurol. 2010; Ballard C, et al. Parkinsonism Relat Disord. 2020; Brandstaedter D, et al. J Neurol. 2005; Chang A, et al. Drugs. 2016; Chen J. Ment Health Clin. 2018; Cummings J, et al. Lancet. 2014; FDA Prescribing Information; Forsaa E, et al. Arch Neurol. 2010; Friedman J. Mov Disord Clin Pract. 2022; Huot P, et al. Mov Disord. 2010; Isaacson S, et al. Expert Opin Drug Saf. 2022; Isaacson S, et al. J Parkinsons Dis. 2020; Isaacson S, et al. Parkinsonism Relat Disord. 2021; Joutsa J, et al. J Nucl Med. 2015; Koneru V, et al. Mov Disord. 2023; Kurlan R, et al. Neurology. 2007; Layton J, et al. Drug Saf. 2023; Longardner K, et al. PLoS One. 2023; Meltzer H, et al. Neuropsychopharmacology. 2010; Mijovic A, et al. Ann Hematol. 2020; Mosholder A, et al. Am J Psychiatry. 2022; Muller A, et al. Mov Disord Clin Pract. 2018; NIH NINDS website. 2025; Parkinson Study Group. N Engl J Med. 1999; Parkinson's Foundation. Statistics. 2026; Pawha R, et al. Neurol Ther. 2022; Pollak P, et al. J Neurol Neurosurg Psychiatry. 2004; Rao S, et al. Drug Saf. 2025; Ravina B, et al. Mov Disord. 2007; Samudra N, et al. Drugs Aging. 2016; Schleisman A, et al. US Pharm. 2016; Shotbolt P, et al. Neuropsychiatr Dis Treat. 2009; Shotbolt P, et al. Ther Adv Neurol Disord. 2010; Stang C, et al. J Parkinsons Dis. 2022; Voss T, et al. Parkinsonism Relat Disord. 2013.

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