

Unpacking Parkinson's Disease Psychosis

Rapid Detection and Management in Long-Term Care

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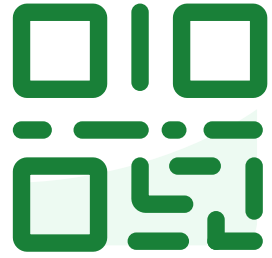
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Which of the following barriers to detecting Parkinson's Disease Psychosis (PDP) in patients who live in long-term care (LTC) are relevant for your practice? Select all that apply.

Today, We Will Learn That...

- Parkinson's disease psychosis (PDP) is common in long-term care (LTC) facilities, and it is associated with key symptoms and risk factors
- It is critical to rule out other potential causes of your patient's symptoms in order to provide the most effective care
- Optimal management of PDP requires a personalized approach tailored to each patient based on their unique needs and preferences

Parkinson's Disease Psychosis

Key Features, Risk Factors, and Burden of Disease



Burden of Parkinson's Disease Psychosis¹⁻⁵

Parkinson's disease psychosis (PDP) affects 50% to 70% of individuals with PD at some point in their disease course

Persistent, progressive, and associated with poor QOL and increased morbidity/mortality

Leading cause of care partner stress and burnout

- Care partners report increased fatigue, sleeplessness, irritability, anger, depression, social withdrawal, and inability to concentrate

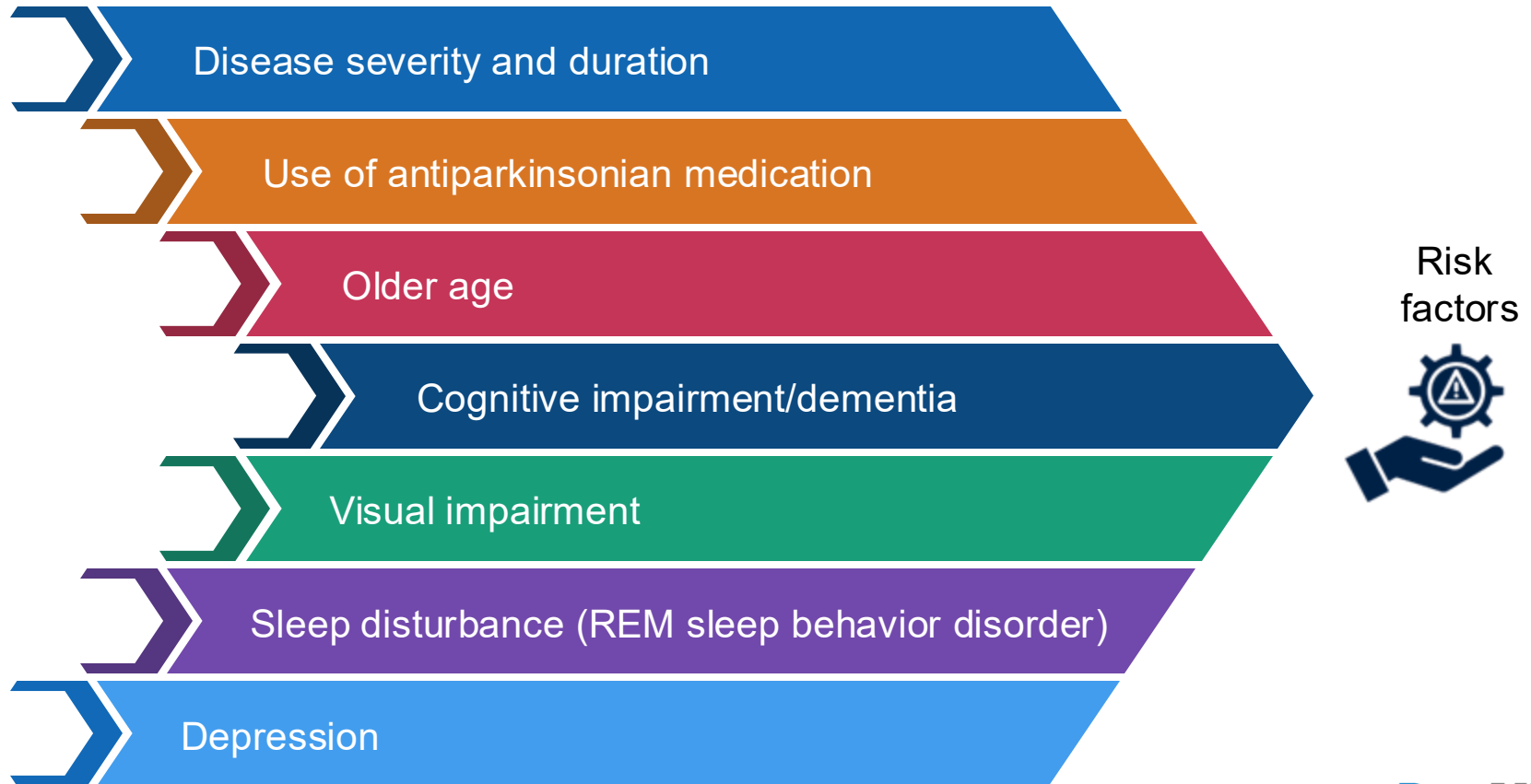
Significant risk factor for hospitalization and LTC facility placement

- Compared with patients with PD without psychosis, patients with PDP are 3x more likely to spend 100+ d in LTC



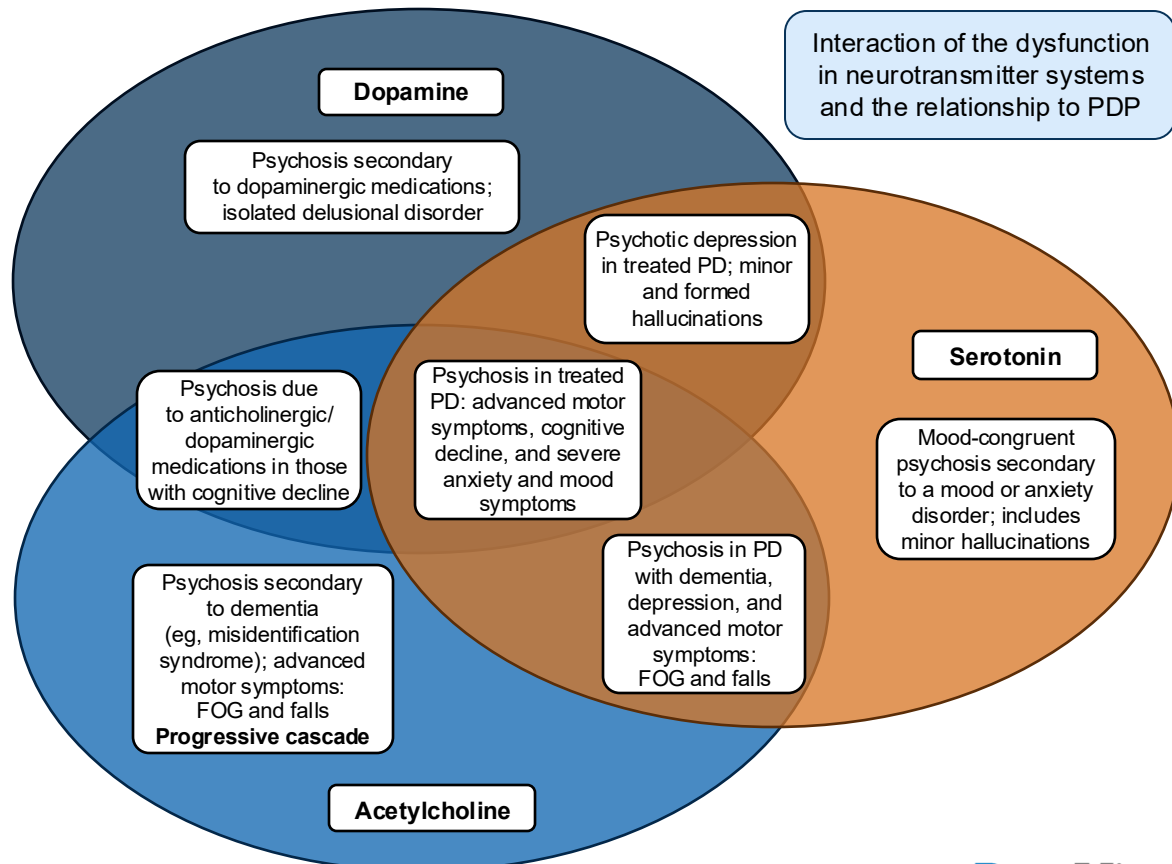
**Which of the following is
a risk factor for
Parkinson's disease
psychosis?**

Risk Factors for PDP¹⁻³



Possible Triggers of PDP¹⁻³

- Alterations/pathologies several areas of the brain, including
 - Visual processing areas
 - Hippocampus
 - Cholinergic brain structures
 - Brainstem
- Frontal cognitive dysfunction
- Sleep–wake cycle dysregulation



Kevin, a 79-Year-Old Man



- Diagnosed with Parkinson's disease 9 years ago
- Has a resting tremor in his left hand and uses a walker to move around
- Comorbid conditions include type 2 diabetes, urinary incontinence, and depression
- Medications include carbidopa/levodopa, pramipexole, metformin, oxybutynin, fluoxetine, and bupropion

- Moved into an assisted living facility about 9 months ago because he was finding it more difficult to perform his ADLs unassisted
- Wife visits him daily and reports that over the past 2 weeks, she feels like he has had worsening memory problems; he has been seeing their dog, who passed away 15 years ago, in his room at night

Differential Diagnosis of PDP



NINDS/NIMH Diagnostic Criteria for PD-Associated Psychosis¹

1

Presence of at least one of the following symptoms:

- Illusions
- False sense of presence
- Hallucinations
- Delusions

2

Primary diagnosis of PD according to UK Brain Bank criteria

3

Chronology of the onset of symptoms of psychosis:

- Symptoms in criterion 1 occur after onset of PD

4

Duration:

- Symptom(s) in criterion 1 recurrent or continuous for (at least) 1 mo

5

Exclusion of other causes:

- Symptoms in criterion 1 are not better explained by another cause of Parkinsonism (eg, dementia with Lewy bodies, psychiatric disorders, or a medical condition such as delirium)

6

Associated features (specify if associated):

- With/without insight
- With/without dementia
- With/without tx for PD (specify)

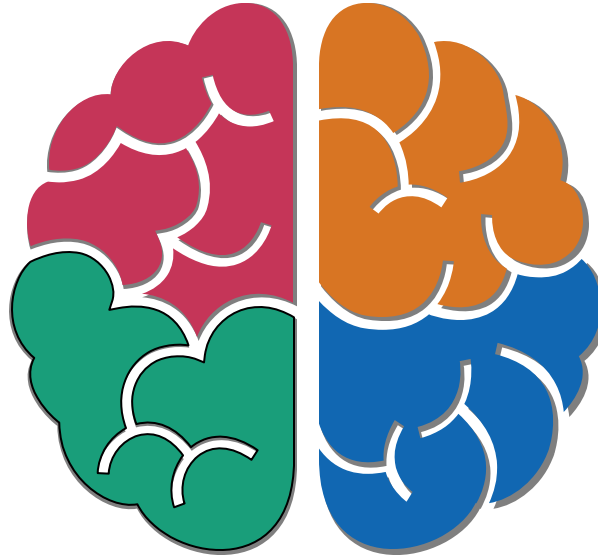


Which statement best describes illusions in the context of PDP?

Psychotic Symptoms of PDP¹

Hallucinations: perceptions without a physical stimulus, in any sensory modality, simple or complex

Illusions: misperceptions of real stimuli that are often visual in nature



Sense of presence: experience that someone is present when nobody is actually there

Delusions: false, fixed beliefs held despite contrary evidence; often involve paranoia (eg, infidelity, theft, or poisoning)

Hallucinations Associated With PDP¹⁻³

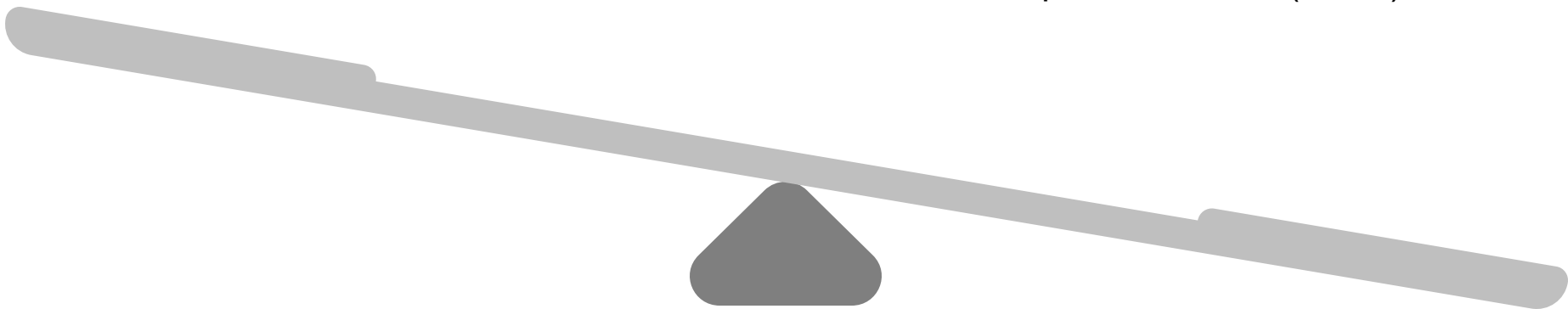


- Visual hallucinations are the most common type of psychotic symptom in PD
 - Occur in up to 70% of patients with advanced PD
 - Occur in up to 40% of PD patients treated with dopaminergic drugs
- Examples of visual hallucinations
 - Presence: perception of a shadow, person, or animal in close proximity
 - Passage: fleeting, passing, or moving images in peripheral vision
 - Simple: flashes of light, geometric patterns, and colors
- **Need to determine if the patient's insight is preserved**
 - Does the patient know that the person/thing they are perceiving is not there?

Rating Scales to Identify PDP¹⁻⁵

Scales that have been used to assess psychotic symptoms in PD include:

- Neuropsychiatric Inventory (NPI)
- Scale for Assessment of Positive Symptoms for PDP (SAPS-PD)
- Positive and Negative Syndrome Scale (PANSS)
- Brief Psychiatric Rating Scale (BPRS)
- Clinical Global Impression Scale (CGIS)



1. Cummings et al. *Neurology*. 1994;44:2308-2314. 2. Voss T et al. *Parkinsonism Relat Disord*. 2013;19:295-299. 3. Kay SR et al. *Schizophr Bull*. 1987;13:261-276. 4. Overall JE, Gorham DR. *Psychol Rep*. 1962;10:799-812. 5. Guy W. Clinical Global Impressions Scale. PsycTESTS Dataset. Published online January 1, 1976. <https://psycnet.apa.org/doiLanding?doi=10.1037%2Ft48216-000>.

Self-Administered Screening Questionnaire for Parkinson's Disease-Associated Psychosis (SASPAP)¹

Question 1

In the past month, have you misinterpreted something that you saw or heard; for example, thought a lamp was a person?

☐ Yes ☐ No ☐ Not now, but I have experienced this before

Question 2

In the past month, have you sensed that someone or something was around you, but nothing was actually there?

☐ Yes ☐ No ☐ Not now, but I have experienced this before

Question 3

In the past month, have you

☐ seen,
☐ heard,
☐ smelled, or
☐ physically felt things that you or other people around you did not think were real?

☐ Yes ☐ No ☐ Not now, but I have experienced this before

Question 4

In the past month, have you had thoughts or believed things that others did not think or believe to be true; for example, someone was cheating or harming you or being unfaithful to you?

☐ Yes ☐ No ☐ Not now, but I have experienced this before

Who completed this?

☐ Patient in person
☐ Patient via telemedicine
☐ Caregiver in person
☐ Caregiver via telemedicine

1. https://www.movementdisorders.org/MDS-Files/1/PDFs/Rating-Scales/SASPAP_Final.pdf.



Which of the following is a recommended best practice for screening PDP in long-term care settings?

Screening for PDP in LTC^{1,2}



Screen all incoming residents with PD for PDP



Regularly assess residents with PD for psychotic symptoms



Be aware that early detection of psychosis leads to better outcomes



Recognize that identifying PDP symptoms can be challenging because of under-reporting



Consider that patients may not always have a family member or advocate present



Monitor patient behavior for potential early signs of psychosis



Ensure nursing staff promptly report observed symptoms to the attending physician or medical director because they are often the first to notice in LTC settings

Interprofessional Team Members' Roles in Diagnosing PDP in LTC Settings^{1,2}

Certified Nursing Assistants (CNAs)/Direct Care Staff: crucial in identifying daily changes, monitoring for hallucinations or behavioral changes, and implementing care plans

- **Will probably be the first to notice PDP symptoms in LTC residents**

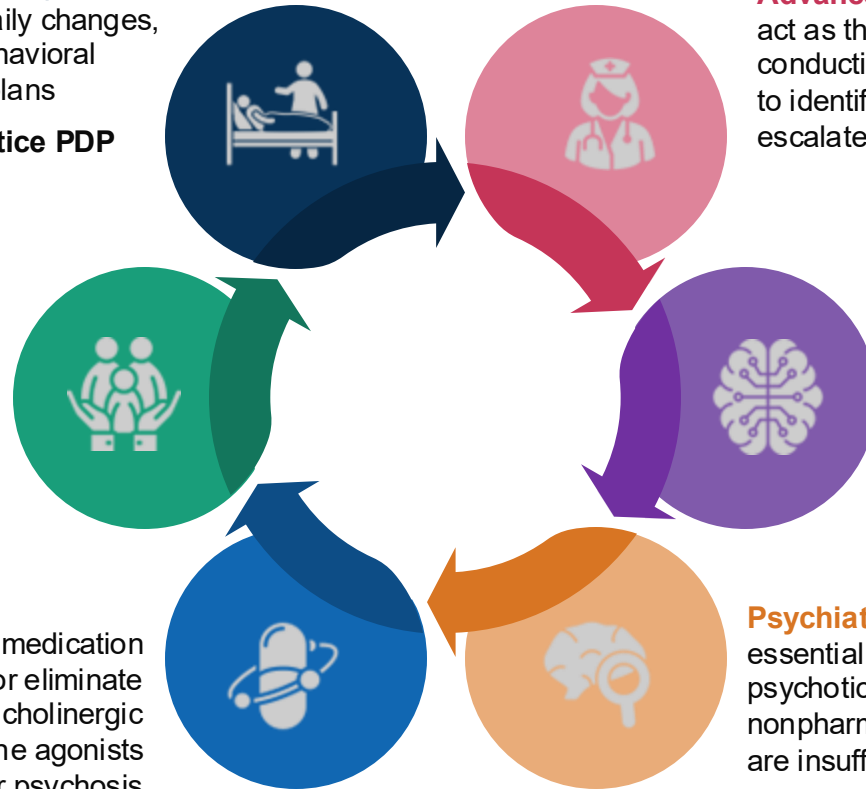
Social Workers: address the high care partner burden, facilitate family communication, and provide support for social isolation

Pharmacists: review medication regimens to reduce or eliminate drugs with anticholinergic properties or dopamine agonists that trigger psychosis

Advanced Practice Nurses (NPs/RNs): act as the core of care coordination, conducting comprehensive assessments to identify early symptoms before they escalate to crisis

Medical Director/Physician (PCP/Neurologist): diagnose PDP, including by talking to staff to determine changes in patients' behaviors

Psychiatrists/Mental Health Professionals: essential for diagnosing and managing psychotic symptoms when nonpharmacological interventions are insufficient



Differential Diagnosis¹



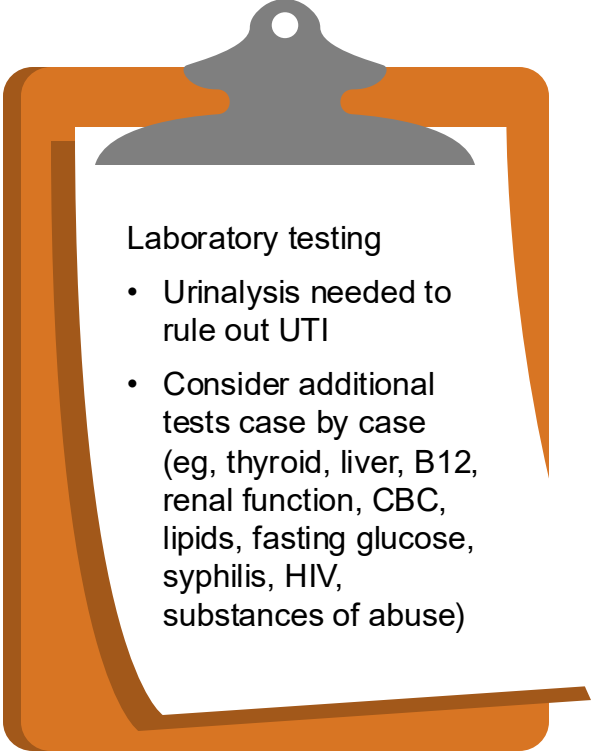
1. Greenland JC, Barker RA. Chapter 6: The Differential Diagnosis of Parkinson's Disease. In: Greenland JC, Barker RA, eds. *Parkinson's Disease: Pathogenesis and Clinical Aspects*. Codon Publications; 2018:109-128. <https://www.ncbi.nlm.nih.gov/books/NBK536715>.

Medical Evaluation¹

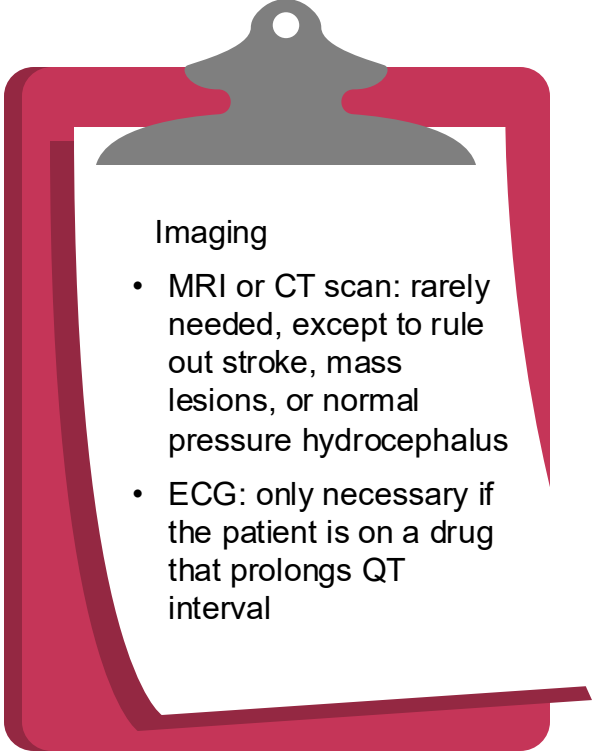


Review all current medications the patient is taking, and determine whether medication is being taken correctly

Laboratory testing

- 
- Urinalysis needed to rule out UTI
 - Consider additional tests case by case (eg, thyroid, liver, B12, renal function, CBC, lipids, fasting glucose, syphilis, HIV, substances of abuse)

Imaging

- 
- MRI or CT scan: rarely needed, except to rule out stroke, mass lesions, or normal pressure hydrocephalus
 - ECG: only necessary if the patient is on a drug that prolongs QT interval



- At admission to assisted living 9 months earlier, Kevin and his wife reported no psychotic symptoms
- After his wife noted he was seeing their deceased dog, NP conducted a brief assessment for visual hallucinations
- NP found that Kevin saw his deceased dog nightly, which upset Kevin because the dog watched from the corner and wouldn't come when called
 - Kevin's explanation indicated that he lacked insight that the dog was not really there
- He also developed suspicions that his wife was planning to leave him, despite visiting daily
- His sleep and appetite decreased considerably

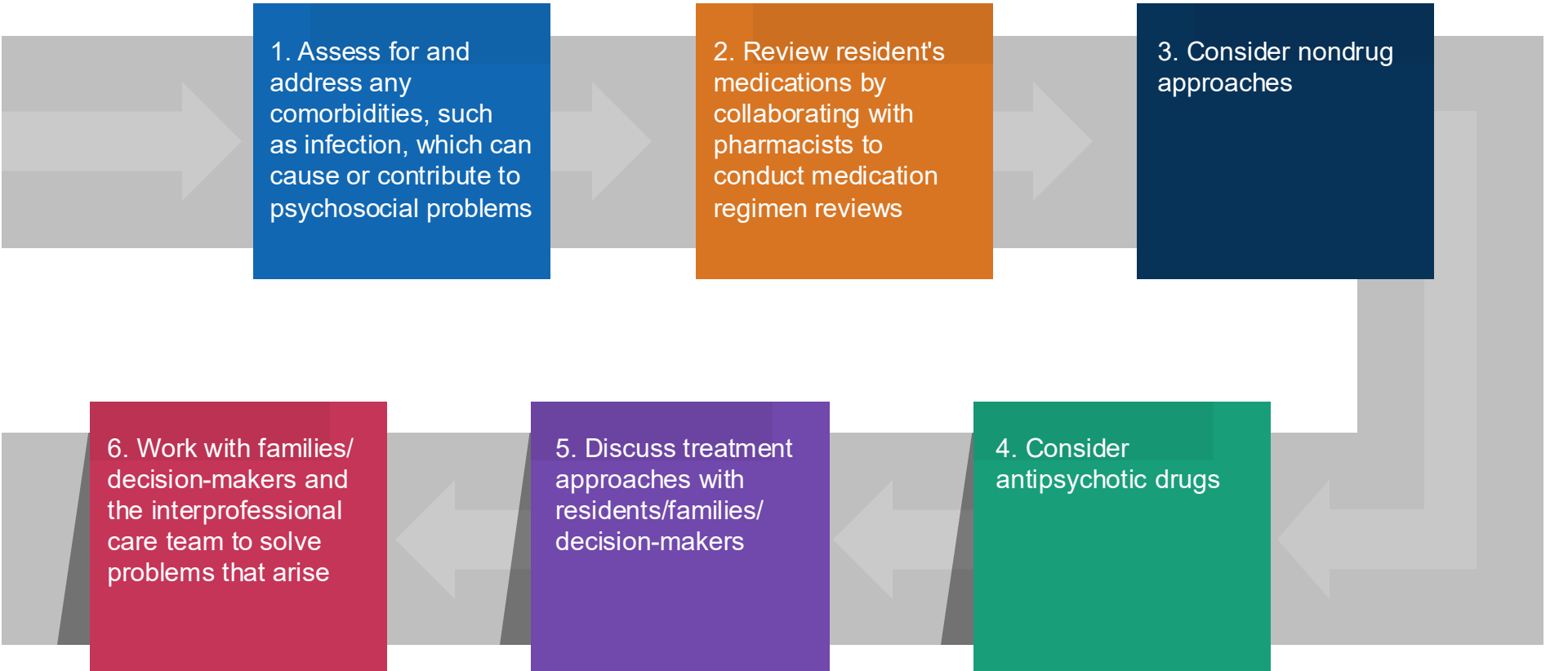
Patient-Centered Management of PDP





In the initial management of PDP in long-term care, which of the following is the recommended first step after ruling out other causes?

Managing PDP^{1,2}



```
graph LR; 1[1. Assess for and address any comorbidities, such as infection, which can cause or contribute to psychosocial problems] --> 2[2. Review resident's medications by collaborating with pharmacists to conduct medication regimen reviews]; 2 --> 3[3. Consider nondrug approaches]; 3 --> 4[4. Consider antipsychotic drugs]; 4 --> 5[5. Discuss treatment approaches with residents/families/decision-makers]; 5 --> 6[6. Work with families/decision-makers and the interprofessional care team to solve problems that arise];
```

1. Assess for and address any comorbidities, such as infection, which can cause or contribute to psychosocial problems

2. Review resident's medications by collaborating with pharmacists to conduct medication regimen reviews

3. Consider nondrug approaches

4. Consider antipsychotic drugs

5. Discuss treatment approaches with residents/families/decision-makers

6. Work with families/decision-makers and the interprofessional care team to solve problems that arise

Medication Management¹

Review all medications with the consultant pharmacist



On average, LTC residents receive approximately 7 to 10 prescriptions daily



Eliminate any nonessential medications (eg, anticholinergics, anticholinergics, anticholinergics, sedating drugs, narcotics, steroids)



Manage medications

- Stopping/weaning: anticholinergics, amantadine, MAO-B inhibitors, COMT inhibitors, dopamine agonists
- Levodopa: last medication to change in most cases
- Note: reducing PD medications may worsen parkinsonism

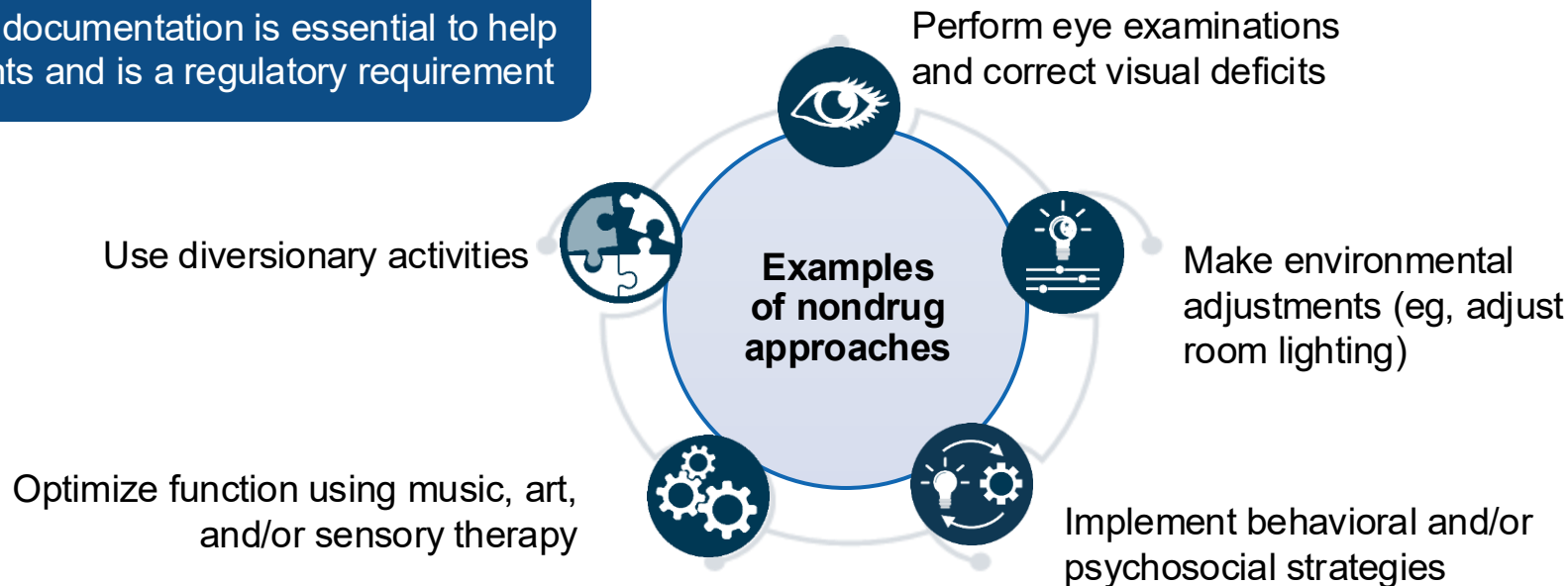


Consider Beers criteria for potentially inappropriate medication use in older adults

Nonpharmacological Approaches¹⁻⁴

Remember to document all interventions, including nondrug and ineffective interventions

Proper documentation is essential to help residents and is a regulatory requirement



Kevin's Case Continued



- Tapered off pramipexole (as slowly as possible) and oxybutynin
- Levodopa continued as previously
- Psychotic symptoms continued to worsen
- Became slower and had more trouble with mobility
- Family called in to discuss possible treatment with an antipsychotic

Pharmacologic Interventions for PDP¹⁻⁵

Consider antipsychotic medication when the patient is experiencing persistent psychotic symptoms that have a substantial effect on the patient and family

- Most antipsychotics are contraindicated for patients with PD because they worsen Parkinson's symptoms

Pimavanserin is the only FDA-approved treatment for hallucinations and delusions associated with PDP

- Selective 5-HT_{2A} inverse agonist without dopaminergic, adrenergic, histaminergic, or muscarinic affinity
- Taken orally once daily
- Approved for patients with PDP with and without dementia

Clozapine and quetiapine are used off label to treat PDP

- Lack of extrapyramidal symptoms is attributed to these agents' significantly lower occupancy of striatal dopamine D₂ receptors versus typical antipsychotic drugs

Evidence-Based Recommendations for the Use of Antipsychotics in the Management of PDP¹⁻⁸

- Pimavanserin was specifically developed to treat PDP by targeting serotonergic (5-HT_{2A}) pathways, allowing mitigation of hallucinations and delusions with minimal effect on motor function
- Clozapine is used off label to treat PDP, and a systematic review and network meta-analysis showed that clozapine also significantly improved symptoms without affecting motor function
- Quetiapine is also used off label to treat PDP, but it has been associated with significantly impaired cognition compared with placebo and should be avoided in patients with PDP and reduced cognitive abilities
- International Parkinson and Movement Disorder Society Evidence-Based Medicine Committee performed a systematic review of randomized controlled trials of interventions to treat psychosis in PD and found clozapine and pimavanserin to be efficacious and clinically useful, while there was insufficient evidence supporting clinical utility of quetiapine

1. Seppi K et al. *Movement Disorders*. 2019;34:180-198. 2. Parkinson Study Group. *N Engl J Med*. 1999;340:757-763. 3. French Clozapine Parkinson Study Group. *Lancet*. 1999;353:2041-2042. 4. Pollak P et al. *J Neurol Neurosurg Psychiatry*. 2004;75:689-695. 5. Sarva H, Henchcliffe C. *Ther Adv Neurol Disord*. 2016;9:462-473. 6. Berrio A et al. *Clin Park Relat Disord*. 2025;12:100342. 7. Abler V et al. *Front Neurol*. 2022;13:919778. 8. Yunusa I et al. *J Geriatr Psych Neurol*. 2023;36:417-432. 9. Dashtipour K et al. *Parkinsons Dis*. 2021;2021:2603641.

Safety of Pimavanserin, Clozapine, and Quetiapine¹⁻⁵

- In comparison with placebo, clozapine (SMD, -0.69; 95% CI, -1.35 to -0.02), pimavanserin (SMD, -0.01; 95% CI, -0.56 to 0.53), and quetiapine (SMD, 0; 95% CI, -0.68 to 0.69) did not impair motor function per UPDRS
- Based on Mini-Mental State Examination scale, quetiapine (SMD, 0.60; 95% CI, 0.07 to 1.14) significantly impaired cognition versus placebo
- MDS rated pimavanserin and quetiapine with acceptable risk without specialized monitoring and clozapine with acceptable risk with specialized monitoring

Clozapine

- **BOXED WARNING:** severe neutropenia, orthostatic hypertension, seizures, myocarditis, and increased risk of mortality in older adult patients with dementia-related psychosis (not approved for this indication)
- **Most common AEs:** sedation, dizziness, headache, tremor, tachycardia, hypotension, syncope, hypersalivation, sweating, dry mouth, visual disturbances, constipation, nausea, and fever

Quetiapine

- **Most common AEs in adults:** somnolence, dry mouth, constipation, dizziness, increased appetite, dyspepsia, weight gain, fatigue, dysarthria, and nasal congestion

Pimavanserin

- **Most common AEs:** peripheral edema, confusional state

1. Yunusa I et al. *J Geriatr Psych Neurol*. 2023;36:417-432. 2. Isaacson SH et al. *Expert Opin Pharmacother*. 2025;26:707-717. 3. Clozaril (clozapine) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/019758s107lbl.pdf. 4. Seroquel (quetiapine) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/020639s074lbl.pdf. 5. Nuplazid (pimavanserin) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/207318s014,210793s012lbl.pdf.

Black Box Warnings on Antipsychotic Use in Elderly Patients With Dementia¹⁻³

WARNING: INCREASED MORTALITY FOR ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSES

- Elderly patients with dementia-related psychoses treated with antipsychotic drugs are at an increased risk of death
- Antipsychotic drugs are not approved for the treatment of dementia-related psychosis



- Meta-analysis of 17 double-blind RCTs in elderly dementia patients found atypical antipsychotics associated with 1.6-1.7x greater risk of mortality compared with placebo
- Most deaths were from cardiac or infectious etiology, or stroke in some studies

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

See full prescribing information for complete boxed warning.

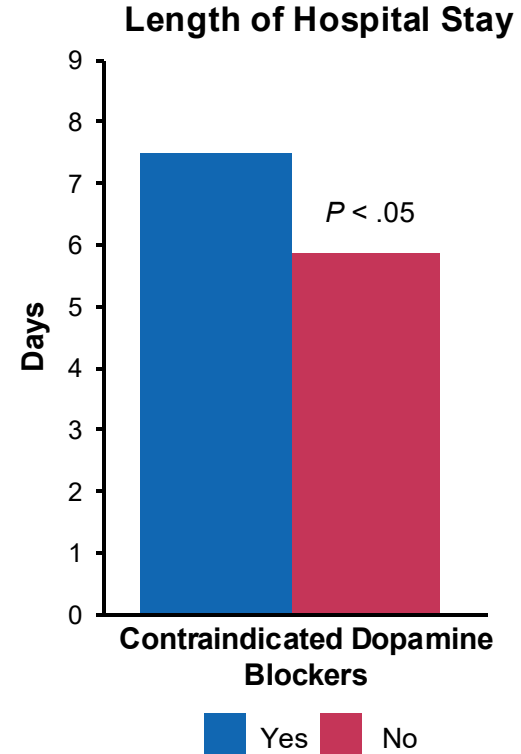
- Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death
- Pimavanserin is not approved for the treatment of patients with dementia who experience psychosis **unless their psychotic symptoms are related to Parkinson's disease**



- In 2024, the FDA updated pimavanserin label to clarify that it is approved for the treatment of PDP in patients **with or without dementia**
- Pimavanserin is not approved for the treatment of psychosis or dementia that is related to any other disease

Inappropriate Use of Antipsychotics Prolongs Length of Stay in Hospitalized Patients With PD¹

- Cross-sectional chart review of 339 consecutive hospital encounters from patients with PD
- Administration of any type of dopamine blocker occurred in 27.3% (90/330) of hospital encounters
 - 78.9% (71/ 90) of these were contraindicated dopamine blockers
 - Multiple or combinations of contraindicated dopamine-blocking drugs were used in 47.8% of these cases
 - Most common prescribed dopamine blockers were haloperidol in 54.4% (49/90) and olanzapine in 36.7% (33/90)
- Contraindicated dopamine-blocking agents were administered in 23% (71/339) of cases, and participants who received a contraindicated dopamine blocker stayed in the hospital longer (M 7.5 days, SD 9.1) than those who did not (M 5.9 days, SD 6.8)



Key Roles and Responsibilities of LTC Staff in Managing PDP¹

Medical Director



Ensure there is a facility-wide program for the management of PDP

Provide clinicians and others the education they need to manage PDP

Providers (Attending PCP/NP/PA)



Implement appropriate management

Review medication regimens, including those
for as-needed or standing anxiolytics

When psychotropic medication is indicated, document PDP diagnosis, clinical rationale, benefit–risk discussion with decision-maker, and reason for not attempting gradual dose reduction (if applicable)

Key Roles and Responsibilities of LTC Staff in Managing PDP¹

Director of Nursing



Partner with staff educator to ensure nursing and other staff understand PDP

Provide hands-on staff with specialized PDP care training

Develop care plans to address specific issues

Nursing/ Social Work/ Activities



Observe, document, and report changes in mood and behavior and their effect on the resident's physical and psychosocial health

Document person-centered, nonpharmacological interventions and their effectiveness

Pharmacist



Conduct drug regimen reviews monthly and more frequently when a change in a resident's mood and behavior is detected

Document gradual dose reductions and when they are clinically contraindicated



- **Began treatment with an antipsychotic medication**
- Over the next weeks, Kevin's psychotic symptoms improved
- Once psychosis was under control, neurologist was able to gently increase levodopa, and Kevin's motor symptoms returned to baseline
- More relaxed and began to interact with residents, nursing home staff, and family
- Self-care also improved, and he started eating more without support

Key Take-Home Points

- PDP is common and should be assessed in all patients with PD at intake to LTC and reassessed in residents with PD as needed
- It is important to rule out other causes of psychosis in residents with PD
- Try nonpharmacological approaches first
 - Simplify and optimize medications that may be contributing to PDP
- Pharmacotherapy is indicated if PDP symptoms persist and affect QOL
- Interprofessional team collaboration is key to early detection and management of PDP in the LTC setting



Audience Q&A

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Ask Your Questions Now!



- *What nonpharmacological interventions work best in your experience?*
- *How do you differentiate between dementia symptoms and psychotic symptoms?*
- *How long do you maintain antipsychotic medication before stopping?*
- *How does comorbid dementia affect treatment of psychosis in people with PD?*
- *In patients with PD and mild, nonbothersome psychotic symptoms, is it better to abstain from treatment until the symptoms become bothersome or treat them early to reduce the risk of worsening symptoms?*

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Abbreviations

AAP: atypical antipsychotic
AGS: American Geriatric Society
BPRS: Brief Psychiatric Rating Scale
CGIS: Clinical Global Impression Scale
CNA: certified nursing assistant
COMT: catechol-o-methyl-transferase
LTC: long-term care
M: median
MAO-B: monoamine oxidase-B
MDS: Movement Disorder Society
NP: nurse practitioner
NPI: Neuropsychiatric Inventory
OR: overall response
PA: physician's associate
PANSS: Positive and Negative Syndrome Scale
PD: Parkinson's disease
PDP: Parkinson's disease psychosis
REM: rapid eye movement

RN: registered nurse
SAPS-PD: Scale for Assessment of Positive
Symptoms for PDP
SASPAP: Self-Administered Screening Questionnaire
for Parkinson's Disease-Associated Psychosis
SMD: standardized mean difference
UK: United Kingdom
UPDRS: Unified Parkinson's Disease Rating Scale