MANAGING THE NEUROPSYCHIATRIC MANIFESTATIONS OF PD:

An Update for Pharmacists and Nurses

Complimentary Live Interactive Webcasts

Supported by an educational grant from Acadia Pharmaceuticals.

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Agenda

Activity Overview

Burden of Neuropsychiatric Symptoms in PD
Dawn M. Vanderhoef, PhD, DNP, PMHNP-BC, FAANP

Managing Neuropsychiatric Symptoms: *Current Treatment Landscape*
Jack J. Chen, PharmD, FASCP, FCCP, BCPS, BCGP

Role of Pharmacist and Nurse Neuropsychiatric Specialists
Jack J. Chen, PharmD, FASCP, FCCP, BCPS, BCGP, and Dawn M. Vanderhoef, PhD, DNP, PMHNP-BC, FAANP

Conclusions and Postassessment

Learning Objectives

- **RECOGNIZE** the prevalence of neuropsychiatric symptoms in PD and their impact on disease burden.
- **EVALUATE** current and novel treatment options for the various neuropsychiatric symptoms.
- **DISCUSS** the role of psychiatric nurses and pharmacists in managing the neuropsychiatric symptoms of PD.
- **ASSESS** strategies to minimize the impact adverse events and DDIs have on patient outcomes.

Continuing Education Credit

INTENDED AUDIENCE – This activity is designed to meet the educational needs of psychiatric nurses and pharmacists nationwide. No prerequisites required.

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Educational Grant

The College of Psychiatric and Neurologic Pharmacists and the American Psychiatric Nurses Association would like to acknowledge an educational grant from Acadia Pharmaceuticals which helped to make this activity possible.

Housekeeping

- Q&A
- Posttest, Evaluation, and Certification

MANAGING THE NEUROPSYCHIATRIC MANIFESTATIONS OF PD:

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Burden of Neuropsychiatric Symptoms in PD

Dawn M. Vanderhoef, PhD, DNP, PMHNP-BC, FAANP

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Burden of Neuropsychiatric Symptoms in PD

- Overview: neuropsychiatric symptoms in PD
  - Anxiety
  - Depression
  - Dementia
  - Psychosis
- Caregiver and disease burden
- Cost

PD = Parkinson's disease.

What Is PD?

- Recognized by James Parkinson in 1817
  - "An Essay on the Shaking Palsy"
    - "Paralysis agitans"
- PD clinical syndrome (TRAP)
  - Resting tremor
  - Rigidity
  - Bradykinesia (akinesia)
  - Postural instability
- Pathological findings
  - Depigmentation of the substantia nigra
    - Loss of melanin-laden dopaminergic neurons containing cytoplasmic inclusion

Goetz CG. *Cold Spring Harb Perspect Med.* 2011;1:a008862; Grover S et al. *J Neurosci Rural Pract.* 2015;6:65-76; Jankovic J. *J Neurol Neurosurg Psychiatry*. 2008;79:368-376.

Who Gets PD?

- Second most common neurodegenerative disorder
- Prevalence rate: 1.25%
  - Given aging population rates likely to increase
  - More common in men than women
  - Onset common in sixth decade of life
    - Increases with age
- Lower in Asian and African populations compared to Western countries

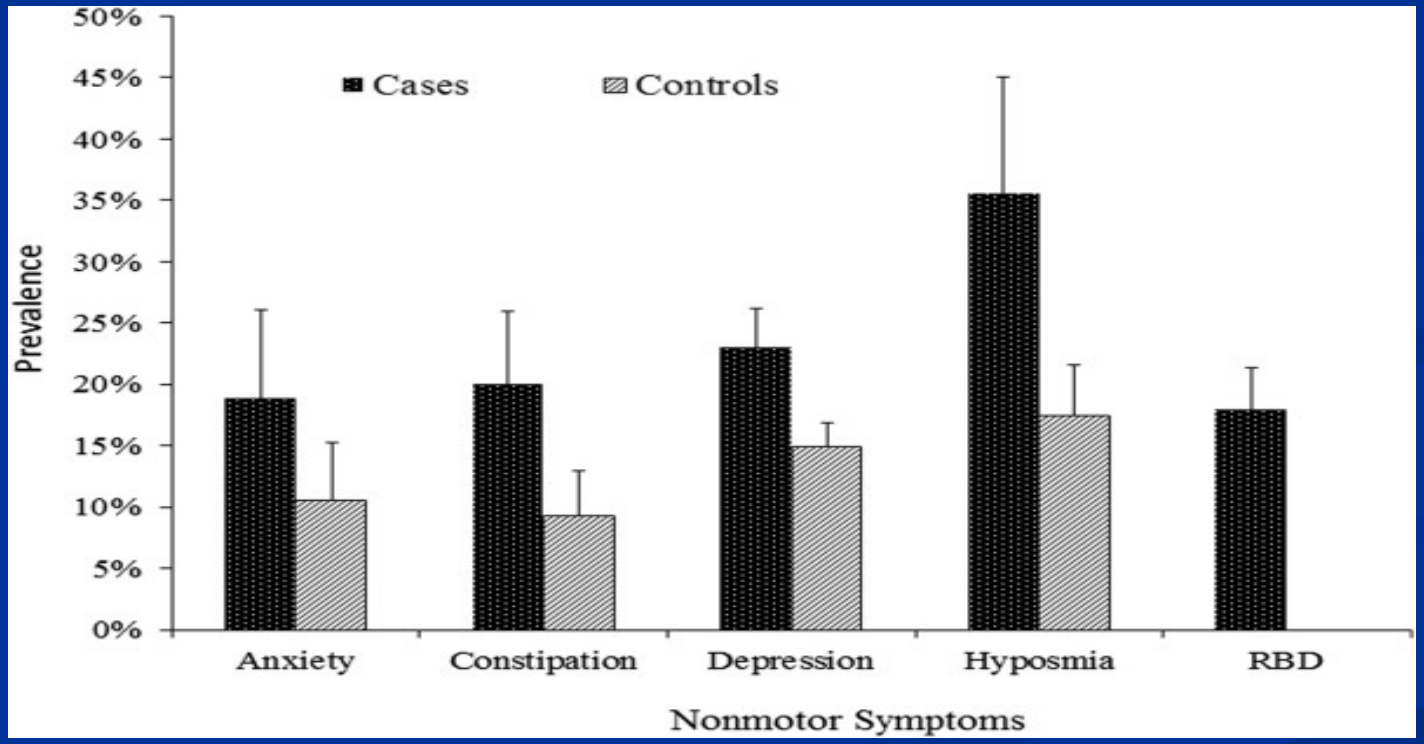
Grover S et al. *J Neurosci Rural Pract.* 2015;6:65-76; Berg D et al. *Mov Disord*. 2015;30:1600-1611.

What Are the Symptoms of PD?

- Motor
- Nonmotor
  - Autonomic dysfunction
    - Constipation is early feature even before diagnosis.
    - Dizziness
    - Urinary dysfunction
    - Hypotension
    - Hyposmia
  - Neuropsychiatric
    - Anxiety and depression
    - Psychosis/impulse-control problems/cognitive deficits
    - Rapid eye movement sleep behavior disorder (RBD)
      - Acting out dreams
    - Excessive daytime sleepiness (EDS)

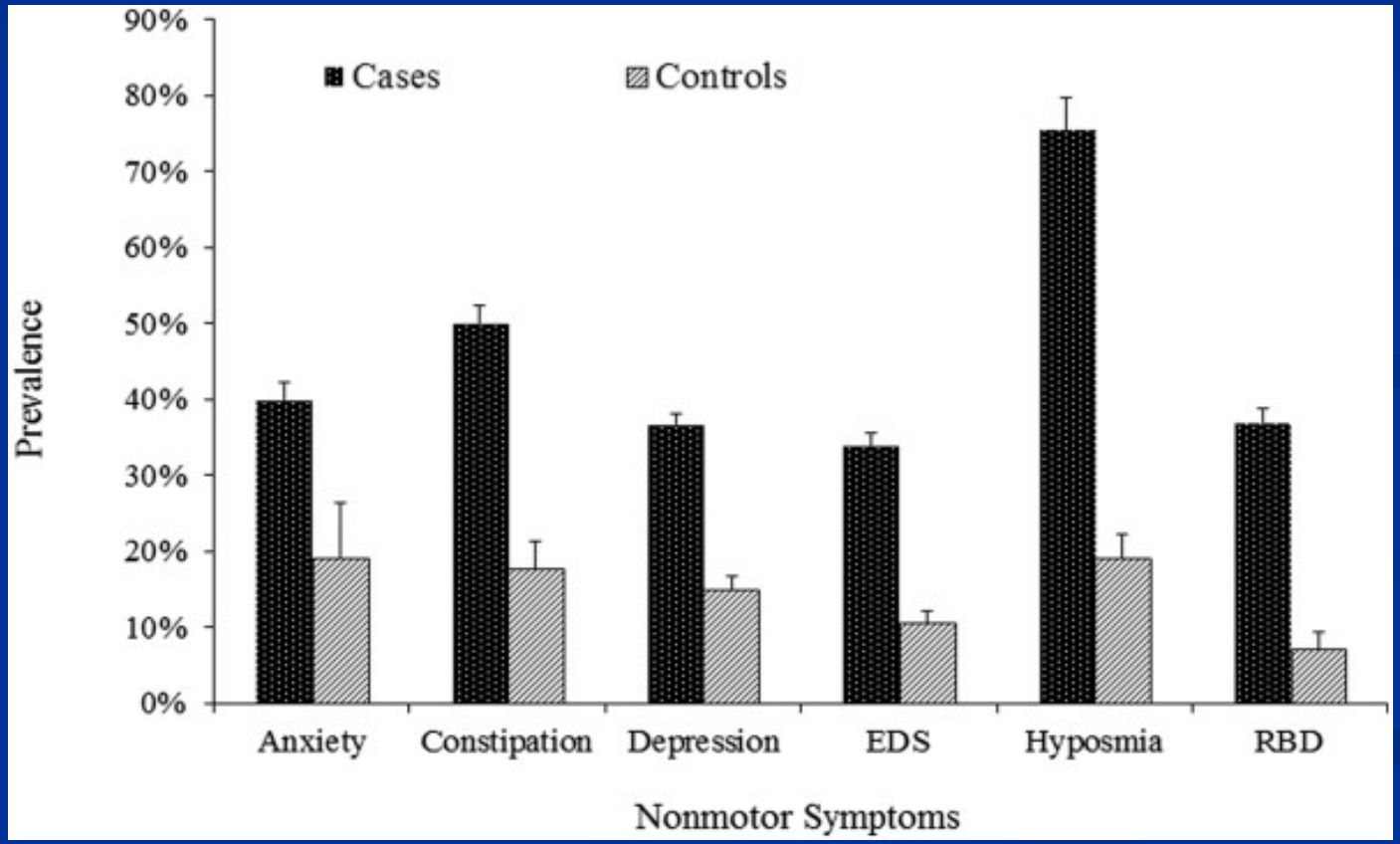
Berg D et al. *Mov Disord*. 2015;30:1600-1611; Chen H et al. *Transl Neurodegener*. 2015;4:1-8.

Prevalence of Nonmotor Symptoms Prior to PD Diagnosis



Chen H et al. *Transl Neurodegener*. 2015;4:1-8. For educational purposes only.

Prevalence of Nonmotor Symptoms After PD Diagnosis



Chen H et al. *Transl Neurodegener*. 2015;4:1-8. For educational purposes only.

What Are the Diagnostic Criteria for PD Dementia?

- **Major or mild neurocognitive disorder due to PD**
  - **The criteria are met for major or minor neurocognitive disorder.**
  - **The disturbance occurs in the setting of established PD.**
  - **There is insidious onset and gradual progression of impairment.**
  - **The neurocognitive disorder is not attributed to another medical condition and is not better explained by another mental disorder.**

Diagnostic and Statistical Manual, 5th ed; 2013.

Neuropsychiatric Symptoms in PD Dementia

- More severe symptoms associated with:
  - Younger age
  - Advanced stage of illness
  - Diagnosis of dementia with Lewy bodies

Pai-Yi C et al. *Plos ONE.* 2016;11:1-10.

The "Quintessential" Neuropsychiatric Illness: PD Dementia

- Depression
  - Anhedonia
  - Apathy
  - Suicide
- Anxiety
- Cognitive symptoms
- Impulse-control symptoms
- Psychosis

PD: Anxiety

- Prevalence rate: 31% with average 40%–70%
  - No indication that neurobiology is different than in those without PD
  - Anxiety in PD patients is worse.
  - Social anxiety, GAD, panic
    - Can make motor symptoms worse – tremor or dyskinesia and fear of falling
- Scales
  - Parkinson's Anxiety Scale (PAS)
  - Geriatric Anxiety Inventory (GAI)
  - Beck Anxiety Inventory (BAI)
  - Hamilton Anxiety Rating Scale

GAD = generalized anxiety disorder.

Grover S et al. *J Neurosci Rural Pract.* 2015;6:65-76; Pai-Yi C et al. *Plos ONE.* 2016;11:1-10; Chen JJ et al. *Ther Adv Neurol Disord.* 2014;7:52-59.

PD: Depression

- 3.24 times higher than in the general population
  - No indication that neurobiology is different than in those without PD
    - Anhedonia: rates 7%–45.7%
      - May be due to dysfunction of dopamine pathway
    - Apathy: rates 16.5%–70%
      - May be due to side effect of DBS
    - Suicide: rates 22.7%–30%
      - Risk factors: depression, anxiety, hopelessness, age of PD diagnosis, duration of illness, level of education, ICD
- Scales
  - Center for Epidemiologic Studies Depression Scale
  - Geriatric Depression Scale
  - Beck depression scale
  - PHQ-9

DBS = deep brain stimulation; ICD = impulse-control disorder; PHQ 9 = Patient Health Questionnaire-9.

Grover S et al. *J Neurosci Rural Pract.* 2015;6:65-76; Pai-Yi C et al. *Plos ONE.* 2016;11:1-10.

PD: Dementia

- **Average prevalence: 30%–40%**
  - **Point prevalence: 31.3%**
  - **Incidence rate is 4 to 6 times that compared to the general population**
- **Increased rates as disease progresses**
  - **Prevalence up to 75%**
  - **Mean time from onset of PD to dementia is approximately 10 years**
- **Higher dysfunction in the following domains:**
  - **Attention (lesser language and memory problems)**
  - **Executive and visuospatial functioning**
  - **Deficits may look like patients with frontal lobe damage**

Grover S et al. *J Neurosci Rural Pract.* 2015;6:65-76; Pai-Yi C et al. *Plos ONE.* 2016;11:1-10.

Assessment Tools

- Montreal Cognitive Assessment (MoCA)
  - Good for PD; not as language heavy compared to MMSE
- Mini Mental State Exam (MMSE)
  - Cognitive assessment
  - Brief, language/cultural bias
  - Not in public domain
- Saint Louis University Mental Status (SLUMS)
  - Studied in VA populations
  - Education cutoff
- Mini-Cog
  - Little to no education/race bias

VA = Veterans Affairs.

Cordell CB et al. *Alzheimers Dement*. 2013;9:141-150; Kansagara D et al. A systematic evidence review of the signs and symptoms of dementia and brief cognitive tests available in VA. US Department of Veteran's Affairs Web site. Available at: http://www.hsrd.research.va.gov/publications/esp/dementia.pdf. Published April 2010. Accessed January 2017; Sheehan B. *Ther Adv Neurol Disorders*. 2012;5:349-358.

Assessment Tools

Test	Time	Sensitivity	Specificity
MMSE	5–10 minutes	0.79	0.95
Mini-Cog	3 minutes	0.76	089
MoCA	10 minutes	1.00	0.87
SLUMS	10 minutes	1.0	0.9

Cordell CB et al. *Alzheimers Dement*. 2013;9:141-150; Kansagara D et al. A systematic evidence review of the signs and symptoms of dementia and brief cognitive tests available in VA. US Department of Veteran's Affairs Web site. Available at: http://www.hsrd.research.va.gov/publications/esp/dementia.pdf. Published April 2010. Accessed January 2017; Sheehan B. *Ther Adv Neurol Disorders*. 2012;5:349-358.

PD: Impulse-Control and Sleep Disorders

- Impulse-control disorders
  - Prevalence rate: 35.9%–60%
  - Gambling, hypersexuality, alcohol use
    - Higher in those on dopaminergic agents: direct D2/D3
- Sleep disorders
  - REM sleep disorder (RBD)
    - Prodromal for Lewy body disease
      - 90% conversion rate over 15 years
  - Excessive daytime sleepiness (EDS)
  - Nocturnal sleep disturbances
    - Restless leg syndrome
    - RBD

REM = rapid eye movement.

Grover S et al. *J Neurosci Rural Pract.* 2015;6:65-76; Pai-Yi C et al. *Plos ONE.* 2016;11:1-10.

PD: Psychosis

- Lifetime prevalence: 25%–60%
- Possible causes:
  - Underlying psychiatric illness
  - Medications
    - Levodopa, dopamine agonists, amantadine, anticholinergics
- Risk factors:
  - Advanced age
  - Longer PD diagnosis
  - Worse motor symptoms
  - Sleep disorder
  - Depression
  - Dementia

Goldman JG et al. *Curr Treat Options Neurol*. 2014;16:281.

PD: Psychosis

- **Symptoms:**
  - **Visual hallucinations (70% rate of reporting)**
  - **Nonvisual hallucinations less common**
  - **Illusions (17%–72% rate of reporting)**
  - **Delusions – themes of jealousy, abandonment, and infidelity**

Goldman JG et al. *Curr Treat Options Neurol*. 2014;16:281.

PD Psychosis: Rating Scales

Psychosis Scale	Time to Administer	Items Asked in a Structured Manner	Number of Items
Neuropsychiatric Inventory	15–30 minutes	Yes	12
Brief Psychiatric Rating Scale	15–30 minutes	No	18
Positive and Negative Syndrome Scale	>30 minutes	No	30
Schedule for Assessment of Positive Symptoms SAPS-PD	>30 minutes	Yes	35 items, 5 domains 9 items

Fernandez H et al. *Mov Disord*. 2007;23:484-500; Voss T et al. *Parkinsonism Relat Disord*. 2013;19:295-299.

Caregiver Burden

- Caregiver risk factors:
  - Prior depressive and anxiety symptoms
    - Implications: financial, social, occupational
- Patient characteristics increase burden:
  - Advanced stages
  - Neuropsychiatric symptoms
  - Increased need for care

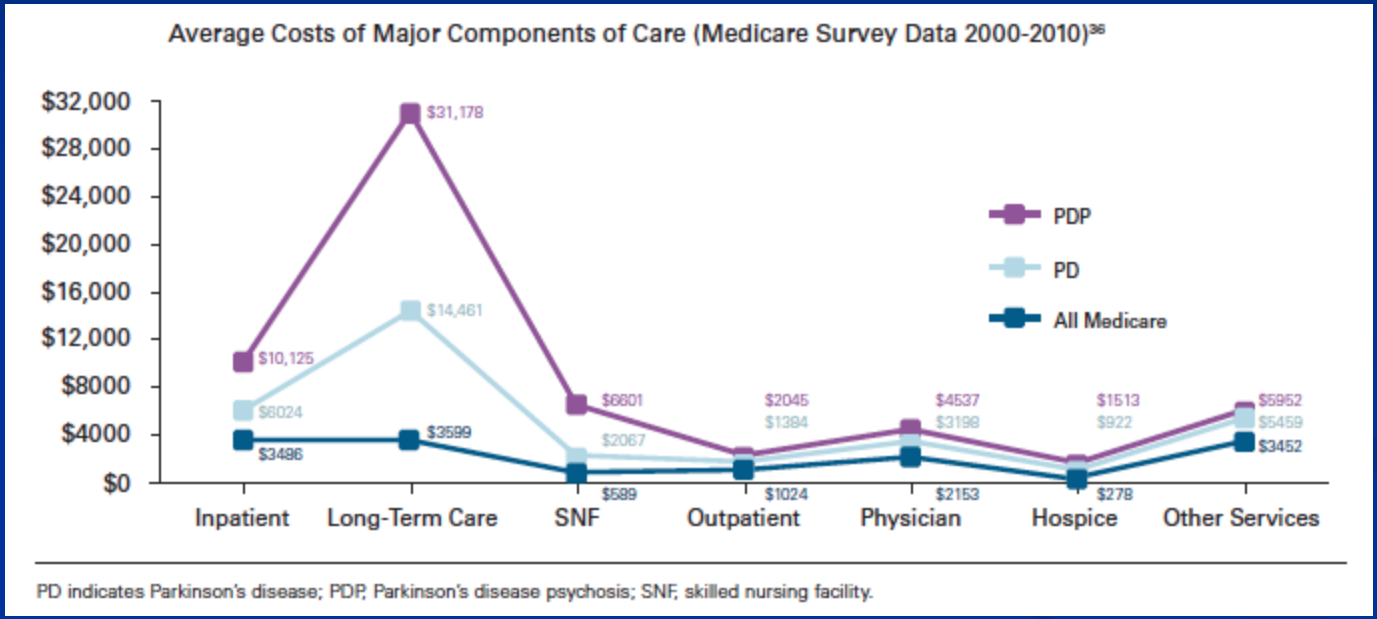
Oh Y et al. *J Mov Disorders*. 2015;8:26-32; Tew E et al. *Biomed Res Int*. 2013;151872.

Caregiver Burden and Cost

- Risk of nursing home placement
  - Hallucinations
  - Dementia
  - Higher scores on Hoehn and Yahr scale
    - Describe how symptoms of PD progress
- Cost of PD with psychosis is higher than PD alone

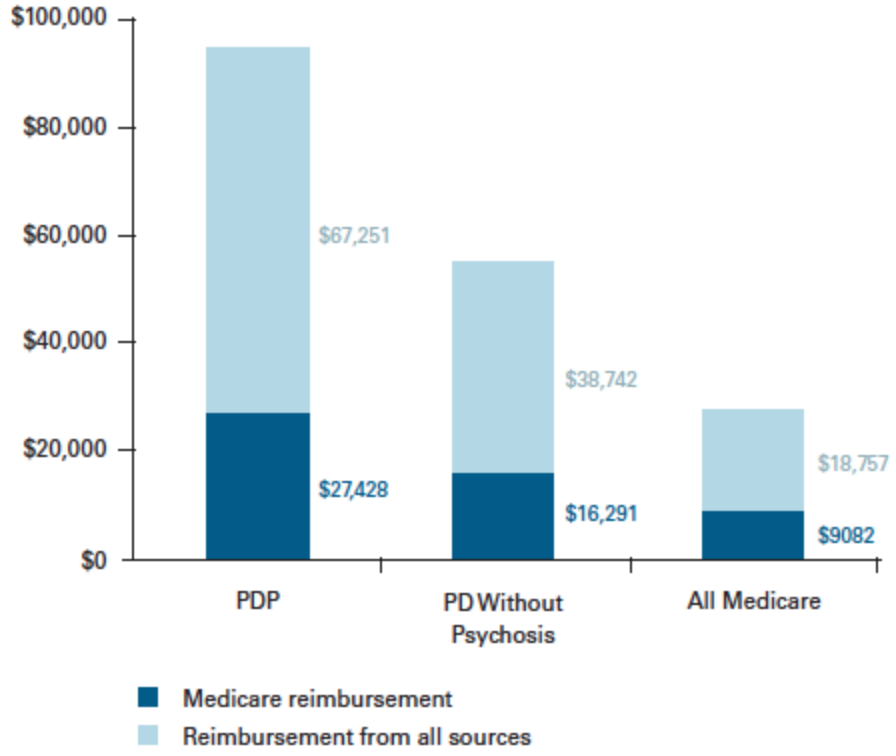
Hermanowicz N et al. *Am J Manag Care*. 2015:s199-s206.

Cost



Cost

Average Costs Across All Components of Care (Medicare Survey Data 2000-2010)[36]



PD indicates Parkinson's disease; PDP, Parkinson's disease psychosis.

Hermanowicz N et al. *Am J Manag Care*. 2015:s199-s206. For educational purposes only.

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9. Hermanowicz N, Edwards K. Parkinson's disease psychosis: symptoms, management, and economic burden. *Am J Manag Care*. 2015; 10 (suppl); s199-s206.

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13. Oh Y, Lee J, Lee P, et al. Neuropsychiatric symptoms in Parkinson's disease dementia are associated with increased caregiver burden. *J Mov Disorders*. 2015;8:26-32.
14. Pai-Yi C, Chun-Tang T, Ping-Kun C, et al. Neuropsychiatric symptoms in Parkinson's disease dementia are more similar to Alzheimer's disease than dementia with lewy bodies: a case-control study. *Plos ONE.* 2016;11:1-10.
15. Schrag A, Horsfall L. Walters K, et al. Prediagnosis presentations of Parkinson's disease in primary care: a case-control study. *Lancet Neurol*. 2014;14;57-64.
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Chair and Professor

Department of Pharmacy Practice
College of Pharmacy
Marshall B. Ketchum University
Fullerton, California

Managing Neuropsychiatric Symptoms: *Current Treatment Landscape*

- Available treatment options
  - Depression and anxiety
  - Psychosis
  - Dementia
- Efficacy and safety analysis
- Unmet needs in treatment and limitations
- Adverse events and DDIs

DDI = drug-drug interaction.

Question

Drugs with FDA-approved indications are available for PD-related:

A. Anxiety
B. Dementia
C. Depression
D. Psychosis

FDA = US Food and Drug Administration; PD = Parkinson's disease.

Anxiety in PD

- **Pharmacotherapy: insufficient evidence for specific treatment recommendations[1,2]**
- **Nonpharmacologic:**
  - **Cognitive and behavioral therapies[1]**
- **If correlated with motor fluctuations and frequency of freezing:**
  - **Adjust PD meds to minimize motor fluctuations.**

1. Chen JJ et al. *Ther Adv Neurol Disord*. 2014;7:52-59; 2. Zesiewicz TA et al. *Neurology*. 2010;74:924–931.

Anxiety in PD

- **Selective serotonin reuptake inhibitors (SSRIs)[1]**
  - **Citalopram, paroxetine, sertraline have been studied.**
    - **Citalopram: max dose of 20 mg/day if age >60 years (risk for QT prolongation).**
    - **Paroxetine: high anticholinergic burden[2]**
  - **SSRIs are generally well tolerated.**
    - **TEAEs: agitation, akathisia, loose stools, insomnia, nausea, somnolence. Occasionally, may worsen tremor.**
    - **Chronic use: risk of metabolic adverse effects (eg, bone fractures, hyponatremia, sexual dysfunction, weight gain).**
    - **Beers criteria recommends to avoid in patients with history of fall or fractures.**
    - **If discontinuation required: taper off to mitigate discontinuation syndrome (especially with short half-life agents [paroxetine]).**

TEAE = treatment-emergent adverse event.

1. Chen JJ et al. *Ther Adv Neurol Disord.* 2014;7:52-59; 2. http://www.agingbraincare.org/uploads/products/ACB_scale_-_legal_size.pdf.

Anxiety in PD

- **Tricyclic antidepressants (TCAs)**
  - **Associated with high anticholinergic burden[2]**
- **Benzodiazepines: use judiciously[1]**
  - **Use associated with unfavorable effects on alertness, cognition, gait, & fall risk[2]**
  - **Useful for comorbid insomnia or RBD**
- **Other agents: Beta-blockers, buspirone, gabapentin, hydroxyzine, lamotrigine, mirtazapine, nefazodone, pregabalin, quetiapine, trazodone**

RBD = Rapid eye movement (REM) sleep behavioral disorder.

1. http://www.agingbraincare.org/uploads/products/ACB_scale_-_legal_size.pdf 2. Chen JJ et al. *Ther Adv Neurol Disord.* 2014;7:52-59

Question

Which of the following statements is TRUE regarding SSRIs?

A. Citalopram maximum recommended dose in elderly is 20 mg/day.
B. Fluoxetine is a potent inhibitor of CYP450 2D6.
C. Paroxetine is on the 2015 Beers List of potentially inappropriate medications for use in older adults.
D. SSRIs are associated with increased risk of falls, fractures, and hyponatremia.

Depression in PD

- SSRIs
  - Commonly use but insufficient evidence for benefit (citalopram, fluoxetine, sertraline)[1-4]
  - Drug interactions: fluoxetine and paroxetine – potent CYP450 2D6 inhibitors
- TCAs
  - Likely efficacious (desipramine, nortriptyline)[1-4]
  - Anticholinergic burden and side effects limit sustained use.

PLM = periodic limb movements; RLS = restless legs syndrome.

1. Ferreira JJ et al. *Eur J Neurol*. 2013;20(1):5–15; 2. Seppi K et al. *Mov Disord*. 2011;26:s42-s80; 3. Miyasaki JM et al. *Neurology*. 2006;66(7):996-1002; 4. Chen JJ et al. *Pharmacotherapy*. 2013;33:972-983.

Depression in PD

- Dopamine agonists[1-3]
  - Pramipexole: antidepressant effect independent of motor effects
- Other agents: insufficient evidence[3-4]
  - Bupropion, duloxetine, milnacipran, mirtazapine, nefazodone, reboxetine, desipramine, des/venlafaxine, vilazodone, vortioxetine
- Psychotherapy (eg, CBT) and rTMS: warrant further study[1,4]
- Serial ECT effective: for severe medication-resistant depression, psychotic affective disorders[4]

CBT = cognitive behavioral therapy; ECT = electroconvulsive therapy; rTMS = repetitive transcranial magnetic stimulation.

1. Seppi K et al. *Mov Disord*. 2011;26:s42-s80; 2. Ferreira JJ et al. *Eur J Neurol*. 2013;20:5-15; 3. Miyasaki JM et al. *Neurology*. 2006;66:996-1002; 4. Chen JJ et al. *Pharmacotherapy*. 2013;33:972-983.

Parkinson's Disease Dementia[1-2]

- Assess for environmental or secondary causes of cognitive decline
  - Eg, delirium, depression, hypoxeemia, infection, electrolyte abnormalities, sleep apnea
- If possible, discontinue non-PD meds with potential harm on cognition
  - Antihistamines, benzodiazepines, bladder antispasmodics, muscle relaxants, sedative/hypnotics, TCAs
  - Review anticholinergic burden scale[3]
- Gradual and stepwise withdrawal of PD medications
  - Anticholinergic agents, amantadine, selegiline, and dopamine agonists
- Nonpharmacologic
  - Cognitive and behavioral therapies

1. Diagnosis and pharmacological management of Parkinson's disease: A national clinical guideline. Scottish Intercollegiate Guidelines Network; 2010;
2. Ferreira JJ et al. *Eur J Neurol*. 2013;20(1):5–15; 3. http://www.agingbraincare.org/uploads/products/ACB_scale_-_legal_size.pdf.

Parkinson's Disease Dementia

- **Cholinesterase inhibitors**
  - **Modest improvement in cognition[1-3]**
  - **Some benefit on anxiety, hallucinations, sleep, falls[4]**
  - **Rivastigmine: FDA-indicated for PDD**
    - **Capsule/Solution: initiate 1.5 mg bid, increase to 3, 4.5, 6 mg bid after 4 weeks at each previous dose**
    - **Patch: initiate 4.3 mg/24 hours, increase to 9.5 and 13.3 mg/24 hours after 4 weeks at each previous dose**
  - **Dose-limiting adverse effects: nausea, loose stools/diarrhea, vomiting**
- **Memantine: insufficient evidence[1,2]**

bid = twice a day; PDD = Parkinson's disease dementia.

1. Seppi K et al. *Mov Disord*. 2011;26:s42-s80; 2. Ferreira JJ et al. *Eur J Neurol*. 2013;20(1):5–15; 3. Miyasaki JM et al. *Neurology*. 2006;66(7):996-1002; 4. Henderson EJ. *Lancet Neurol*. 2016;15(3):249-258.

Parkinson's Disease Dementia

- Accompanying neuropsychiatric symptoms[1]
  - Agitation, aggression, anxiety, apathy, depression, dysphoria
  - Delusions, hallucinations, disinhibition, irritability, lability
  - Nighttime behaviors, wandering, rummaging
- Pharmacotherapy
  - Antiepileptics (eg, divalproex, carbamazepine): insufficient evidence
  - Antidepressants: SSRIs for agitation; avoid TCAs
  - Atypical antipsychotics: Worsening of parkinsonism with olanzapine & risperidone
  - Benzodiazepines: for acute crisis
  - Trazodone for sleep[2]

1. Kales HC et al. *BMJ*. 2015;350:369; 2. McCleery J et al. *Cochrane Database Syst Rev*. 2016;11:CD009178.

Question

Which of the following antipsychotics is associated with neutropenia?

A. Aripiprazole
B. Clozapine
C. Quetiapine
D. Olanzapine
E. Risperidone

Management of Hallucinosis and Psychosis in Parkinson's Disease[1]

1. Rule out secondary causes: environment, fluid/electrolyte disturbances, hypoxemia, infection, pain, medication toxidrome, brain lesion.[1-2]

2. Assess all medications and, if possible, discontinue offending meds (eg, anticholinergics, antihistamines, benzodiazepines, bladder antispasmodics, muscle relaxants, opioids, TCAs).[1,-]

3. Assess for overtreatment and simplify PD drug regimen as much as possible by stepwise discontinuation/dose reduction of meds with potential for psychosis induction.[1-2]

   a. Begin with: anticholinergics, monoamine oxidase-B inhibitors, amantadine.

   b. Attempt to reduce dose of dopamine agonist.

   c. Attempt to reduce dose of COMT inhibitor.

   d. Attempt to reduce dose of levodopa.

4. Add an atypical antipsychotic if disruptive symptoms persist:

   a. Pimavanserin 34 mg qd (FDA approved)

   b. Quetiapine (possibly useful): 12.5–25 mg at qhs; increase 25 mg each week until improvement or side effects[2]

   c. Clozapine (efficacious): 12.5–50 mg at qhs; increase 25 mg each week until improvement or side effects (requires REMS compliance)[2-4]

5. If atypical antipsychotic ineffective: consider adding a cholinesterase inhibitor.

COMT = catecholamine O-methyl transferase; qd = every day; qhs = every hour of sleep; REMS = risk evaluation and mitigation strategies.

1. Brandt et al. *Consult Pharm*. 2016;31:1-16; 2. Ferreira et al. *Eur J Neurol*. 2013;20:5-15; 3. Seppi et al. *Mov Disord*. 2011;26:s42-s80; 4. Miyasaki et al. *Neurology*. 2006;66:996-1002.

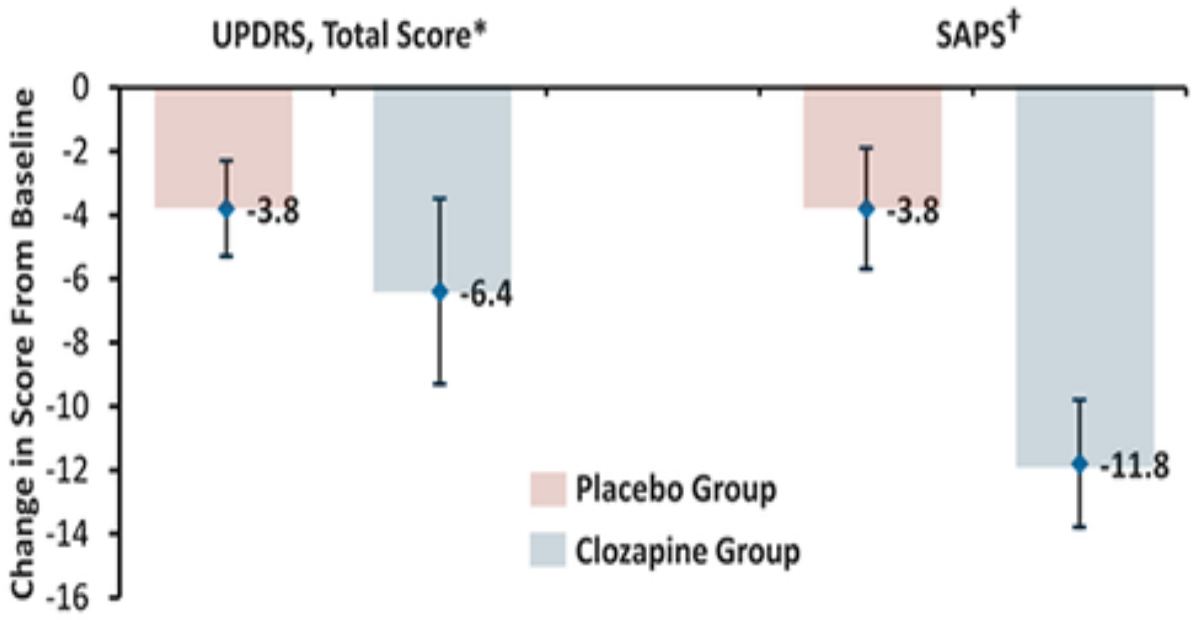
Other Atypical Antipsychotics

- **The following are not recommended for PDP due to lack of efficacy and/or unacceptable risk of motor deterioration (harmful):**
  - **Aripiprazole[1]**
  - **Olanzapine[1-3]**
  - **Risperidone[1]**

PDP = Parkinson's disease psychosis.

1. Ferreira JJ et al. *Eur J Neurol*. 2013;20(1):5–15; 2. Miyasaki JM et al. *Neurology*. 2006;66(7):996-1002; 3. Seppi K et al. *Mov Disord*. 2011;26:s42-s80.

Clozapine: Efficacy



*P = .36; †P = .01.

SAPS = Scale for the Assessment of Positive Symptoms; UPDRS = Unified Parkinson's Disease Rating Scale.

Parkinson Study Group. *New Engl J Med*. 1999; 340:757-763. For educational use only.

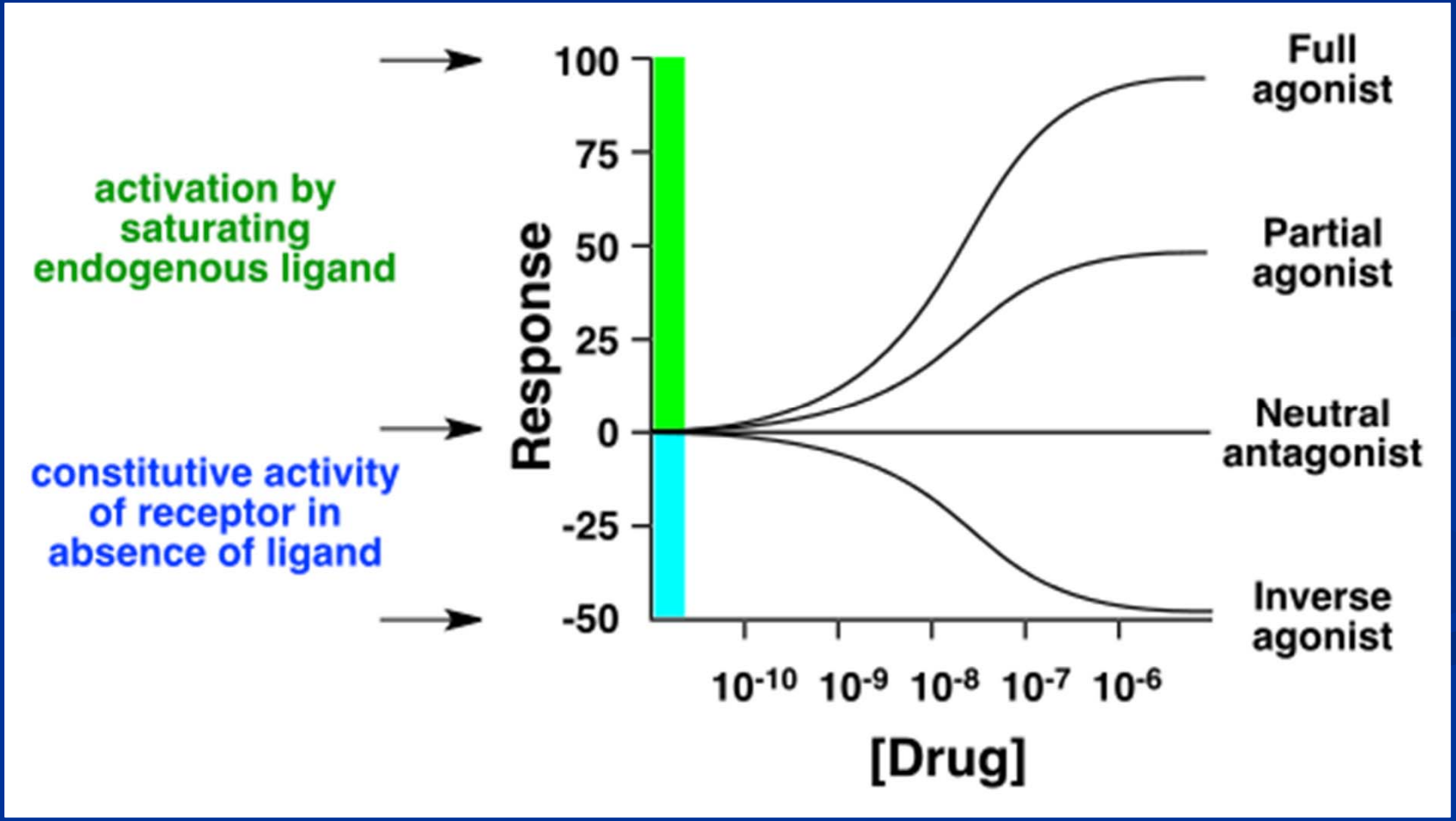
Quetiapine

Fernandez et al, 2009 **Quetiapine vs placebo** **Double-blind**	**PDP**	***N* = 16** **4 weeks**	**Quetiapine effective.** **CGI-S improvement > placebo.** Mean dose 58.3 mg/day.	**4 quetiapine and 1 placebo dropped out due to AEs.**
Shotbolt et al, 2009 **Quetiapine vs placebo** **Double-blind**	**PDP**	***N* = 24** **12 weeks**	**Not different vs placebo in time to drop out due to lack of efficacy.** Mean dose 73 mg/day.	**Only 36% quetiapine and 31% placebo completed 12 weeks.**
Kurlan et al, 2007 **Quetiapine vs placebo** **Double-blind**	**PDP and dementia**	***N* = 40** **10 weeks**	**Not different vs placebo on change in total BPRS.**	**Dropout rates:** **35% for placebo; 15% for quetiapine**
Rabey et al, 2007 **Quetiapine vs placebo** **Double-blind**	**PDP;** **50% with dementia**	***N* = 58** **12 weeks**	**Not different vs placebo on change in total BPRS.** Mean dose 119 mg/day.	**Treatment discontinued in 50% quetiapine and 36% placebo groups.**
Ondo et al, 2004 **Quetiapine vs placebo** **Double-blind**	**PDP**	***N* = 31** **12 weeks**	**Not different vs placebo on change in total BPRS or Baylor PD Hallucination Questionnaire.** Quetiapine up to 200 mg/day.	**84% of subjects completed study.** **No quetiapine dropouts due to AEs.**
Merims et al, 2007 **Quetiapine vs clozapine** **Double-blind**	**PDP**	***N* = 27** **22 weeks**	**Both similarly improved CGI-C.** Mean doses: quetiapine 91 mg/day; clozapine 13 mg/day.	**Clozapine: 1 patient neutropenia; 2 borderline leukopenia.** **50% clozapine and 69% quetiapine completed the full 22 weeks.**
Morgante et al, 2004 **Quetiapine vs clozapine** **Rater-blinded**	**PDP**	***N* = 27** **12 weeks**	**Both similarly improved BPRS and CGI-S.** Mean doses: quetiapine 91 mg/day; clozapine: 26 mg/day.	**3 clozapine dropped out due to AEs; no leukopenia reported.** **2 quetiapine dropped out due to AEs.**

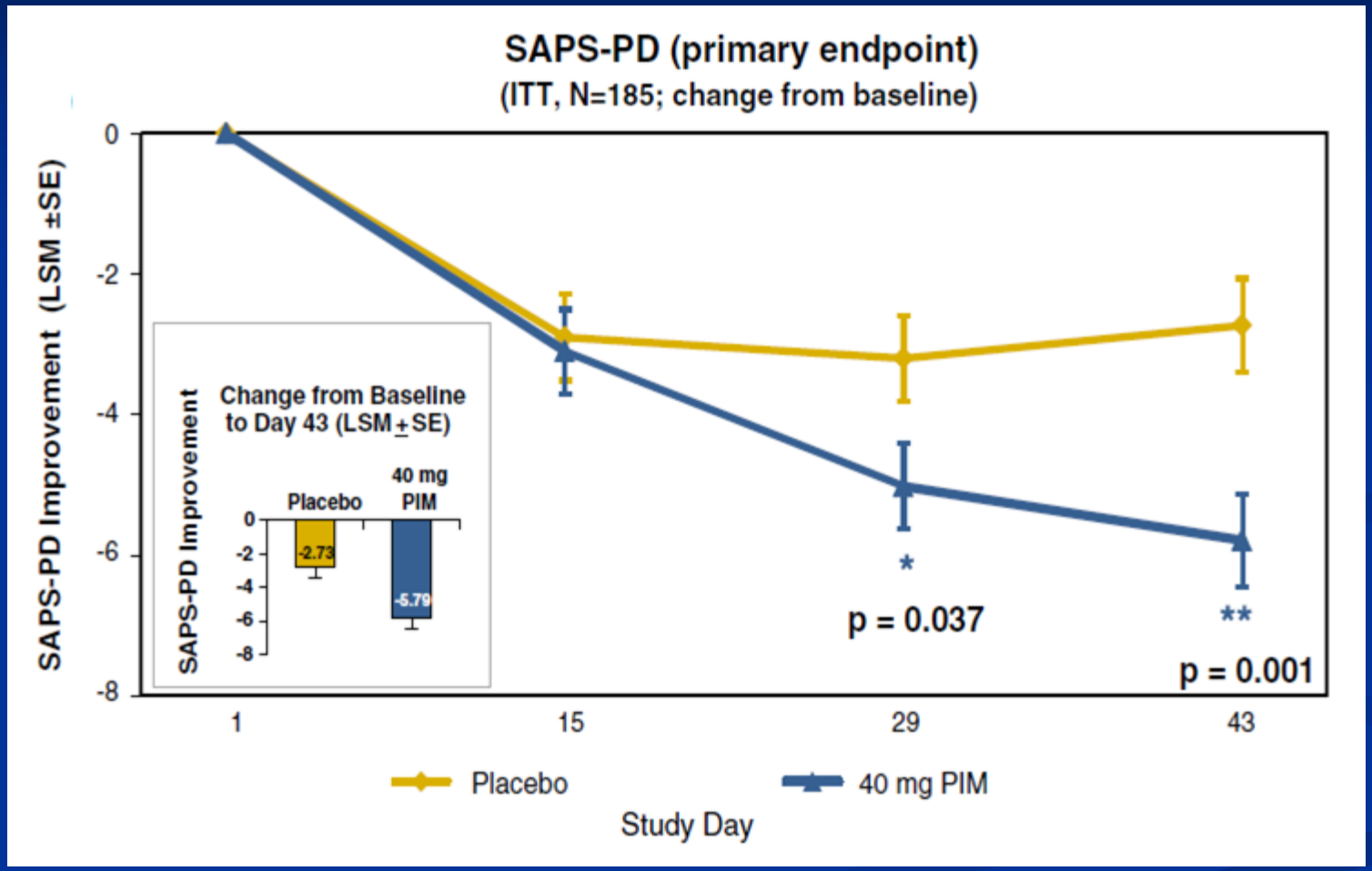
AE = adverse effect; BPRS = Brief Psychiatric Rating Scale; CGI-C = Clinical Global Impression of Change; CGI-I = Clinical Global Impression of Improvement; CGI-S = Clinical Global Impression of Severity.

Dashtipour et al. *Mov Disord* .2016;31:s694.

Pimavanserin: Inverse Agonist Shifts 5-HT_{2A} Receptor to Inactive State



Pimavanserin: Efficacy in PDP



LSM = least squares mean; PIM = pimavanserin; SE = standard error.

Hacksell U et al. *Neurochem Res*. 2014;39:2008-2017. For educational purposes only.

Pimavanserin: Adverse Effects

	Placebo (*n* = 94)	Pimavanserin 40 mg (*n* = 104)
Nausea	6 (6%)	6 (6%)
Peripheral edema	3 (3%)	7 (7%)
UTI	11 (12%)	14 (13%)
Fall	8 (9%)	11 (11%)
Confusional state	3 (3%)	6 (6%)
Headache	5 (5%)	1 (1%)
Hallucination (including visual)	4 (4%)	7 (7%)

40 mg pimavanserin tartrate = 34 mg pimavanserin (free base).

UTI = urinary tract infection.

Cummings et al. *Lancet.* 2014;383:533-540.

PDP Treatment Options

Drug		Dosing	Adverse Effects
Clozapine	Off-label; REMS monitoring	Initial: 6.25 mg/day; maintenance: 10–50 mg/day	Dizziness, drowsiness, constipation, seizures, hypersalivation, agranulocytosis, arrhythmias
Quetiapine	Off-label	Initial: 12.5 mg/day; maintenance: 25–200 mg/day	Dizziness, drowsiness, orthostatic hypotension, weight gain, xerostomia
Pimavanserin	FDA-indicated; specialty pharmacy	Initial & maintenance: 34 mg/day	Confusion, constipation, nausea, peripheral edema

Summary: Managing Neuropsychiatric Symptoms of PD

- **Anxiety:**
  - **SSRIs: insufficient evidence**
  - **Benzodiazepines and TCAs: use limited by side effects**
- **Depression:**
  - **SSRIs (despite modest evidence)**
  - **TCAs: use limited by side effects**
- **Dementia:**
  - **Rivastigmine – FDA indicated**
  - **Management of associated neuropsychiatric symptoms**
- **Hallucinations/Delusions:**
  - **Pimavanserin – FDA indicated**
  - **Clozapine**
  - **Quetiapine**

MANAGING THE NEUROPSYCHIATRIC MANIFESTATIONS OF PD:

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Supported by an educational grant from Acadia Pharmaceuticals.

Role of Nurse and Pharmacist Neuropsychiatric Specialists

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Role of the Psychiatric Nurse

- Front line providers to identify symptoms early
- Assist in accessing treatment
  - Neurology
  - Psychiatry
- Providing interventions to decrease disability
  - Groups
  - Movement interventions
  - Psychoeducation
  - Case management and care coordination

Role of the Advanced Practice Psychiatric Mental Health Nurse

- Identification of symptoms
  - Those who are at risk for or who have symptoms of PD in the psychiatric setting
- Referral and coordination with interdisciplinary team
  - Neurology/primary care
  - Pharmacy
  - Home care/case management
- Measurement based care
  - Scales
- Access to evidence-based treatment
  - Direct care provider

PD = Parkinson's Disease.

Role of the Neuropsychiatric Pharmacist

- Collaborative, front-line providers focus on neuropsychiatric pharmacotherapy management
- Expanded scope of practice to provide patient care
  - State-specific legislative code
  - Provision of comprehensive medication management
- Patient-centered focus on optimizing drug treatment
  - Recommending appropriate evidence-based drug therapy
  - Longitudinal monitoring for sustained optimal response
  - Monitoring age, comorbidities, and organ function for pharmacokinetic and pharmacodynamic optimization
  - Recognizing/managing drug-induced problems
  - Educating patients, caregivers, healthcare team

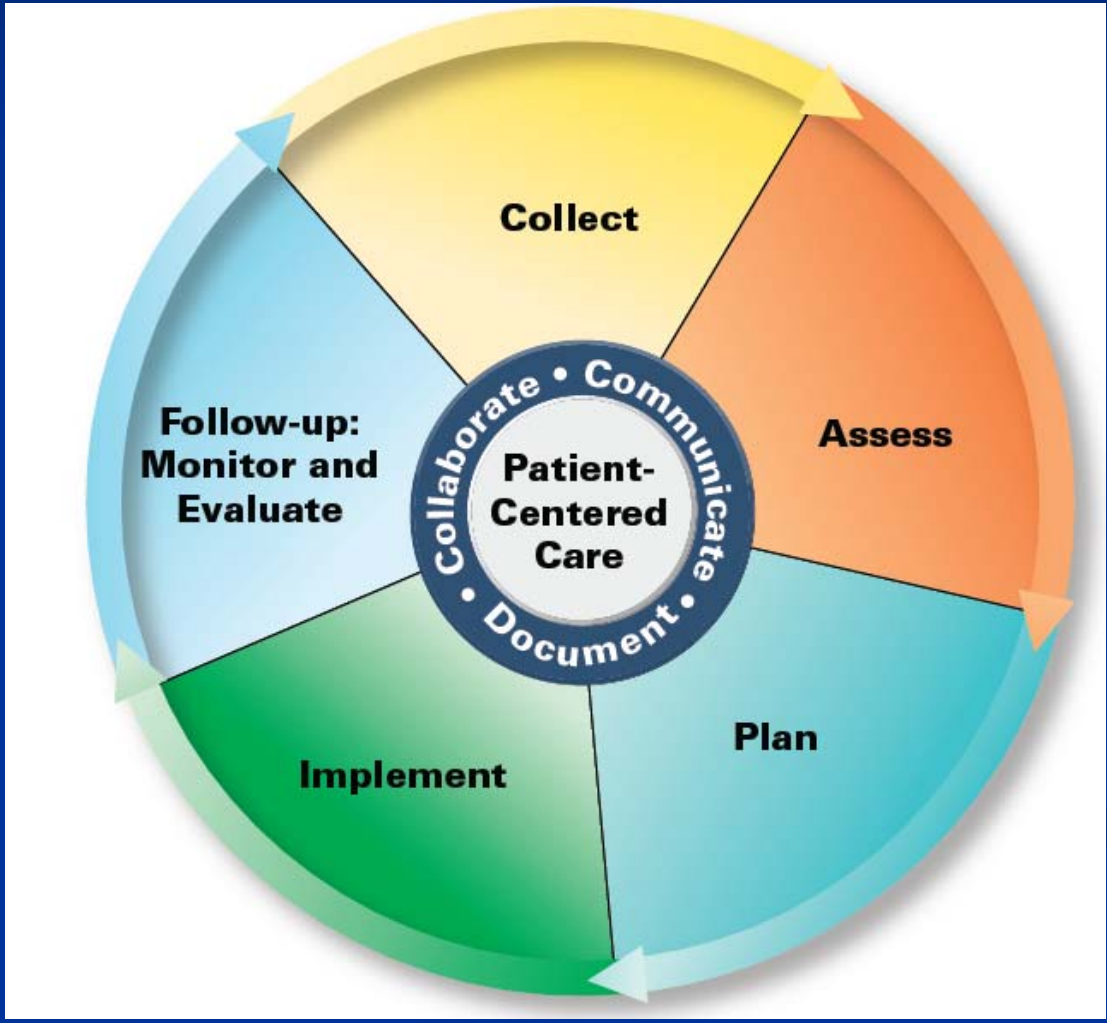
Role of the Neuropsychiatric Pharmacist

- **Assist with regulatory compliance, medication safety, and screening:**
  - **Beers Criteria[1]**
  - **STOPP (Screening Tool of Older Person's potentially inappropriate Prescriptions)[2]**
  - **START (Screening Tool of Alert doctors to the Right Treatment)[2]**
- **Provision of transitions of care and medication reconciliation across continuum of care**
  - **Assist with medication access**
  - **Prevent disruptions in maintenance drug therapy and symptom relapse**
  - **Medication alignment with the patient's home medications and prescriber's admission, transfer, and/or discharge orders**

1. Fick DM et al; American Geriatrics Society 2015 Beers Criteria Update Expert Panel. *J Am Geriatr Soc*. 2015;63:2227-2246; 2. O'Mahony D, et al. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. *Age Ageing*. 2015;44:213–218.

Role of the Pharmacist in Patient-Centered Care

- **Pharmacists' Patient Care Process[1]**



1. Joint Commission of Pharmacy Practitioners. *Pharmacists' Patient Care Process*. JCPP.net Web site. Available at: http://jcpp.net/patient-care-process/. Published May 29, 2014. For educational purposes only.

Patient Case

Bill, a 73-year-old, married, right-handed male was diagnosed with PD 10 years ago. He has a history of levodopa-induced dyskinesias, orthostatic hypotension, visual hallucinations, paranoid delusions, insomnia, and weight loss. Bill's wife, Mary, reports he is having increasing difficulty with performing activities independently not solely due to his movements; he falls frequently and is more forgetful and confused. She also reports difficulty in caring for him as he has episodes of delusional behavior and is often argumentative. On a few occasions, Bill has threatened Mary with his walking cane. He believes that she is having an affair with a man who lives somewhere in the house and that they spy on him. He believes Mary is "hiding" the man from him. He also has visual hallucinations of 4 men who loiter on the backyard patio and believes these "patio people" are conspiring with a television news anchor who is spying on him.

Current Medications:

- **Pramipexole 1.5 mg twice daily**
- **Carbidopa/levodopa 25/100 mg 4 times daily (0800-1200-1600-2000)**
- **Amantadine 100 mg 3 times daily**
- **Amitriptyline 25 mg at bedtime**
- **Risperidone M-Tab 1 mg at bedtime as needed for agitation**
- **Lorazepam 1 mg as needed for anxiety**
- **Neurological examination: Mild resting tremor and moderate rigidity and bradykinesia of both upper extremities.**
- **MMSE is 24.**
- **After a clinical evaluation, he was diagnosed with PD psychosis and possible dementia.**

What are the roles of the nurse and the pharmacist in caring for Bill?

- Assessment
- Diagnosis
- Planning
- Implementation
- Evaluation

Assessment

Nursing

- Physical health condition
  - Coordination with PCP and neurology
    - Rule out delirium
      - Physical health
      - Tricyclic and benzodiazepine
- Co-morbid mental health disorders
  - Screening
    - Geriatric Depression Scale
    - Montreal Cognitive Assessment
    - SAPS-PD
    - Sleep assessment
- Safety
  - Coordination with wife
- Caregiver burden
  - Assess care giver needs both mental and physical
- Resources
  - Support groups
  - Respite

Pharmacy

- Medications and physical health
  - Triggers for delirium, memory impairment, cerebral hypoperfusion
    - Anticholinergic burden
    - TCA and benzodiazepine
    - PD medications
- Medication history and reconciliation
  - To identify hidden delirium triggers including dietary supplements and OTCs
- Screening
  - Beer's list, START, STOPP
  - Laboratory tests
    - Renally eliminated drugs and CrCl
  - Current drug-drug and drug-disease interactions
  - Effect of current medications on:
    - Cognitive impairment
    - Parkinsonism
    - Orthostatic hypotension
  - Unmet treatment needs
    - Orthostatic hypotension
    - Falls
- Medication access and barriers
- Medication treatment goals
- Immunization and preventative health status

CrCl = creatinine clearance; OTC = over the counter; PCP = primary care physician; SAPS = Scale for the Assessment of Positive Symptoms; TCA = tricyclic antidepressant.

Diagnosis

Nursing

- Medically induced symptoms
- Psychiatric
  - Depression
  - Pseudo-dementia
  - Sleep disorder
  - Dementia

Pharmacy

- Rule out medication toxicity
- Rule out comorbid harm due to medications effects on:
  - Parkinsonism
  - Cognitive impairment
  - Orthostatic hypotension
  - Falls

Planning

Nursing

- Psychopharmacologic interventions
  - Coordination with PCP/neurology and pharmacy
- Non-pharmaceutical/ psychosocial interventions
  - Investigate/review evidence-based practices
- Referrals
  - Explore local resources

Pharmacy

- Psychopharmacologic interventions
  - Coordination with PCP, neurology, psychiatry
    - Goals of pharmacotherapy
    - Investigate/review evidence-based practices and new therapeutic agents
    - Priorities and step-wise approach
    - Pharmaceutical care continuity
- Medication access
- Transitions of care
- Medication education and self-management

Implementation

Nursing

- Psychopharmacological
  - Discontinuation of TCA and atypical antipsychotic
  - Taper benzodiazepine
  - Initiate pimavanserin
    - Consider alternatives
      - SNRI/SSRI/AA
      - Acetylcholinesterase inhibitor
- Non-pharmaceutical/psychosocial interventions
  - Sleep hygiene
  - Supportive therapy
  - PT/OT
  - Dietary education
- Caregiver intervention/resources
  - Linkage based on need
    - Home health
    - Support group/individual therapy

Pharmacy

- Coordinate with PCP/neurology
  - Discuss priorities and step-wise approach
  - Discontinuation of TCAs
    - Consider alternatives
      - Trazadone
  - Taper benzodiazepine
  - Reduce dose of dopamine agonist
  - Discontinue risperidone
  - Initiate pimavanserin
    - Consider quetiapine
- Discuss approach for unmet needs
  - Falls, orthostatic hypotension, concurrent neuropsychiatric conditions
- Caregiver intervention
  - Provide medication education and management strategies to patient/caregiver

PT = physical therapy; OT = occupational therapy; SNRI = serotonin norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor.

Evaluation

Nursing

- Medical
  - Laboratory results
  - Physical examination
- Psychiatric
  - Response to psychopharmacologic medication changes
  - Measurement based evaluation
- Psychosocial
  - Response to evidence base interventions
  - Communication with members of the healthcare team
- Caregiver burden
  - Based on resource utilization and level of engagement

Pharmacy

- Medical
  - Ongoing monitoring/evaluating of laboratory results
    - Electrolytes, CrCl, LFTs
- Psychiatric
  - Response to psychopharmacologic medication changes
  - Adherence, side effects
  - Communication with members of the healthcare team
- Medication access
- Caregiver
  - Refer to appropriate resource
    - EG, social worker, home healthcare worker, PCP

LFT = liver function tests.

Q&A

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