Parkinson disease primer, part 2: management of motor and nonmotor symptoms

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Abstract

Objective To provide family physicians with an approach to the management of motor and nonmotor symptoms of Parkinson disease (PD).

Sources of information Published guidelines on the management of PD were reviewed. Database searches were conducted to retrieve relevant research articles published between 2011 and 2021. Evidence levels ranged from I to III.

Main message Family physicians can play an important role in identifying and treating motor and nonmotor symptoms of PD. Family physicians should initiate levodopa treatment for motor symptoms if they affect function and if specialist wait times are long, and they should be aware of basic titration approaches and possible side effects of dopaminergic therapies. Abrupt withdrawal of dopaminergic agents should be avoided. Nonmotor symptoms are common and underrecognized and are a major factor in disability, quality of life, and risk of hospitalization and poor outcomes for patients. Family physicians can manage common autonomic symptoms such as orthostatic hypotension and constipation. Family physicians can treat common neuropsychiatric symptoms such as depression and sleep disorders, and they can help recognize and treat psychosis and PD dementia. Referrals to physiotherapy, occupational therapy, speech language therapy, and exercise groups are recommended to help preserve function.

Conclusion Patients with PD present with complex combinations of motor and nonmotor symptoms. Family physicians should have basic knowledge of dopaminergic treatments and their side effects. Family physicians can play important roles in management of motor symptoms and particularly nonmotor symptoms and can have a positive impact on patients' quality of life. An interdisciplinary approach involving specialty clinics and allied health experts is an important part of management.

Family physicians have a substantial role to play in the management of Parkinson disease (PD), in both early recognition of symptoms and ongoing management. Family physicians may need to diagnose PD and initiate treatment, especially when there are prolonged wait times for specialist care, as reviewed in part 1 of this series.[1]

While traditional management focuses on motor symptoms, nonmotor symptoms are highly prevalent in PD, with a dominant impact on patients' quality of life and function.[2,3] Family physicians, through longitudinal therapeutic relationships with patients with PD, are well positioned to identify and manage patients' nonmotor symptoms.

This paper aims to empower family physicians in basic management of patients' motor symptoms and to help with recognition and management of common nonmotor symptoms.

Case description

Maria is a 65-year-old retired teacher. She presents to your office with a complaint of a rest tremor in her left hand for the past 6 months. She reports

Editor's key points

- Parkinson disease (PD) presents a challenging array of motor and nonmotor symptoms that requires collaboration between family physicians, PD specialists, and allied health professionals.
- Levodopa is the most effective medication for the treatment of motor symptoms in patients with PD. A trial of levodopa may be considered while awaiting assessment by other specialists.
- Although common, nonmotor symptoms are often underrecognized and undertreated in patients with PD. This can negatively affect patients' function and quality of life, and it can increase hospitalization risk and caregiver burden.

having had more difficulty buttoning her shirts recently and complains of slowing down in general. It takes her longer to perform grooming tasks than previously and, when asked, she says she has had difficulty turning over in bed. She also has noticed some shuffling in her gait but no falls. Her husband says she has yelled and moved about in her sleep, as if acting out dreams, for 10 years. She reports slowing of her bowels over the past year. After identifying parkinsonism and ruling out features to suggest an alternative diagnosis (see part 1 of this series),[1] you focus on management of Parkinson disease.

Sources of information

Search strategies looked for research articles or guidelines related to PD management published between 2011 and 2021. Canadian guidelines published in 2019 were used to inform evidence-based suggestions in this paper.[4] Evidence levels ranged from I to III.

Main message

Motor symptoms. Motor symptoms of PD include the hallmark features bradykinesia and rest tremor or rigidity. Substantial postural impairment early in the disease is considered atypical.[5] Medications, supported by physiotherapy and exercise, improve function and quality of life.[4]

Levodopa is the most effective medication for patients with PD and has a safer side-effect profile compared with other agents, particularly for older adults.[4,6] A trial of levodopa may be considered to treat functionally limiting symptoms while awaiting specialist assessment.[1]

Levodopa is used to treat symptoms, is neither neurotoxic nor neuroprotective, and should be initiated if function is affected. Delaying levodopa initiation until severe symptoms develop worsens disability.[4,7,8] Dyskinesias (involuntary movements, often choreiform) are a more common motor complication in younger patients with PD and result from disease progression, not only from levodopa exposure.[9]

Oral levodopa preparations include combinations with carbidopa or benserazide. Levodopa should be initiated at low dose, titrating to the minimum effective dose with caution regarding adverse effects in older adults. A sample titration schedule is provided in **Box 1**.

Gastrointestinal issues such as constipation can affect levodopa absorption. Levodopa is best administered 30 to 60 minutes before meals for optimal absorption and efficacy.[10,11] Patients experiencing nausea could administer levodopa at meals with carbohydrates, as concurrent protein can interfere with levodopa response.[11,12]

Physicians should monitor patients for side effects such as nausea, orthostatic hypotension (OH), confusion, and hallucinations. Patients often develop motor fluctuations such as *wearing off* (when levodopa effects diminish toward the end of dosing periods) and dyskinesias. These should be managed in collaboration with other specialists and may necessitate adjunctive agents or advanced therapies (such as deep brain stimulation or intestinal levodopa administration).[9]

Box 1. Initial titration of levodopa and carbidopa

Week 1: Half a tablet of 100 mg levodopa and 25 mg carbidopa taken orally 3 times daily, 30 minutes before meals

Week 2: One tablet of 100 mg levodopa and 25 mg carbidopa taken orally 30 minutes before breakfast, and half a tablet taken 30 minutes before lunch and before supper

Week 3: One tablet of 100 mg levodopa and 25 mg carbidopa taken orally 30 minutes before breakfast and before lunch, and half a tablet taken 30 minutes before supper

Week 4: One tablet of 100 mg levodopa and 25 mg carbidopa taken orally 3 times daily, 30 minutes before meals. Note: Doses for ongoing treatment may be as high as 1000 mg levodopa per day or higher. Bedtime doses may be considered, especially if there are troublesome symptoms overnight

Adjunctive agents for wearing off include dopamine agonists, catechol-O-methyltransferase inhibitors, and monoamine oxidase B inhibitors.[9] Current guidelines caution against use of dopamine agonists in patients older than 70 years, given potential side effects.[4] While adjunctive agents are typically initiated and titrated in specialist clinics, family physicians should be aware of potential side effects, including impulse control disorders, hallucinations, peripheral edema, sleep attacks, and OH.[9]

Where side effects are experienced, especially psychosis and impulsivity, medications may need to be reduced judiciously (information related to psychosis is provided later in this article). Medications for PD should not be stopped abruptly, as this can precipitate neuroleptic malignant syndrome.[4] Amantadine and dopamine agonists need to be tapered owing to risks of amantadine withdrawal syndrome and dopamine agonist withdrawal syndrome, respectively.[13,14]

Early referral to support and exercise groups, physiotherapy, occupational therapy, and speech language therapy is recommended.[4]

Nonmotor symptoms. Nonmotor symptoms, although present in 70% of patients with PD, are often underrecognized and undertreated and have a substantial impact on patient function and quality of life.[2,15-17] Patients with PD are at increased risk of hospitalization, prolonged hospital stays, and functional decline while hospitalized.[18-20] Nonmotor symptoms, polypharmacy, comorbidities, and caregiver burden increase hospitalization risk.[18,20,21] Nonmotor symptoms can broadly be classified into autonomic dysfunction or sleep disorders and neuropsychiatric symptoms.

Autonomic dysfunction: Autonomic dysfunction includes cardiovascular (OH, supine hypertension),

gastrointestinal (constipation, delayed gastric emptying, gastroesophageal reflux), urogenital (urinary retention, bladder urgency), and thermoregulatory problems.[4]

Sleep disorders and neuropsychiatric symptoms: Sleep disorders and neuropsychiatric symptoms of PD include fatigue, daytime sleepiness, rapid eye movement sleep behaviour disorder (RBD), restless legs syndrome (RLS), depression, anxiety, psychosis, cognitive impairment, and dementia.[4]

Diagnosis and management of select nonmotor symptoms. *Gastrointestinal:* More than 70% of patients with PD experience sialorrhea,[22] while more than 80% develop dysphagia during the course of disease.[23] Patients should be screened for dysphagia (common in advanced disease) and referred to speech language therapy. Botulinum toxin A injections into the salivary glands are highly effective for the treatment of sialorrhea.[4] While evidence for other treatments is mixed,[22] given the low risk of adverse effects we also recommend chewing gum (or sucking candy) and trialing 0.03% (21 µg) ipratropium bromide nasal spray, with 2 sprays by mouth up to 4 times daily.

Constipation is a common and treatable symptom in PD. Pathologic changes can be found in the gastrointestinal tract up to 20 years in the premotor stage.[24] Constipation can contribute to poor levodopa absorption, urinary retention, urinary tract infections, abdominal pain, and poor oral intake.[25] Poor fluid intake exacerbates OH and further compounds the issue of constipation.[4,25] Constipation is underrecognized in PD, but abnormal colonic transit time is seen in 80% of patients with PD.[24,26]

Gastrointestinal motility, adequate stool consistency (measured by the Bristol Stool Scale[27]), and core strength are important factors in constipation. Stool charting with the goal of stool types 3 or 4 on the Bristol Stool Scale daily is encouraged.[27,28]

General measures include increasing fibre, fluids, and physical activity and discontinuing exacerbating medications (eg, opioids, antipsychotics, anticholinergics, and amantadine).[4] Available evidence supports use of polyethylene glycol.[4] We suggest regular use of polyethylene glycol, even at low doses, to improve stool consistency and prevent cycles of constipation and diarrhea. Other osmotic laxatives such as lactulose can be considered, especially for patients for whom medication coverage issues exist.[4]

Stimulant laxatives, such as sennosides and bisacodyl, should be used in select patients, preferably on a short-term or as-needed basis.[4] We recommend stimulant laxatives at bedtime if the patient has not had an adequate bowel movement. Stimulant laxatives can be prescribed more regularly for patients with limited gastrointestinal motility from immobility or medications. Psyllium, although discussed in some guidelines,[4] is often less effective owing to poor fluid intake and gastrointestinal motility, especially in older patients with PD. Probiotics for treatment of constipation in PD have shown positive results in 2 randomized controlled trials.[29,30]

Other autonomic symptoms: Orthostatic hypotension, defined as a drop in systolic blood pressure of 20 mm Hg or diastolic blood pressure of 10 mm Hg or more within 3 minutes of standing or head-up tilt, is common and often underrecognized in patients with PD.[31,32] A lack of adequate compensatory heart rate increase with blood pressure drop (<10 to 15 beats per minute) is suggestive of neurogenic OH.[33]

Orthostatic hypotension is associated with falls,[34] increased risk of cognitive dysfunction,[35] and morbidity and mortality.[36] Orthostatic hypotension in patients with PD is caused by sympathetic denervation, but it can be exacerbated by hypovolemia and medications (dopaminergic agents, antihypertensives, α-blockers, and antidepressants, especially tricyclic antidepressants).[37-39]

We recommend screening for symptoms and measuring orthostatic vitals as part of routine visits for patients with PD. Supine blood pressure should be measured to screen for supine hypertension.[39] Patients could be encouraged to self-monitor for OH at home. Medication review with particular attention to reduction of antihypertensives and other culprits is recommended (see **Table 1** for a summary of medication considerations and other management issues in PD).[4,31,37,39,40]

Having patients learn about OH triggers (eg, large meals, hot baths, alcohol, dehydration), increase fluid and salt intake, elevate the heads of their beds, and pump their legs before slowly getting up are first steps.[4,31,41] Abdominal binders are effective for OH by compressing splanchnic circulation,[31,42] while compression stockings, although often recommended, have limited benefit and poor acceptability.[43]

If nonpharmacologic measures are insufficient, medications should be considered. Domperidone, although recommended in some guidelines, lacks good evidence.[4] We recommend the following:

- Midodrine has good efficacy and could be started at low dose (eg, 2.5 mg to 5 mg spaced 3.5 to 4 hours apart; eg, 8:00 AM, 12:00 PM, 4:00 PM), with the last dose taken at least 4 hours before bedtime owing to the risk of supine hypertension. Patients should wait 4 hours after a dose before lying down flat.[44]
- Fludrocortisone is less effective than midodrine as monotherapy[4] and could cause hypokalemia and peripheral edema and exacerbate supine hypertension.[45]
- Pyridostigmine provides modest benefit in OH without exacerbating supine hypertension,[46] with limiting side effects of diarrhea, nausea, and sialorrhea.[47] We recommend a dose of 30 mg to 60 mg 3 times daily.

Urinary symptoms including urgency, nocturia, and incontinence are common.[4] Although these symptoms are primarily due to autonomic dysfunction, it should be noted that constipation worsens urinary

Table 1. Summary of management issues in PD

MANAGEMENT ISSUE	CONSIDERATIONS
Symptoms	Motor symptoms • Tremor, rigidity (and associated pain), bradykinesia, falls • Later, motor complications and fluctuations (dyskinesias, wearing off) Nonmotor symptoms • Neuropsychiatric: sleep disorders (eg, RBD, RLS, daytime sleepiness), depression, anxiety, psychosis, cognitive impairment • Cardiovascular: postural dizziness (unexplained falls) • Genitourinary: retention, overactive bladder • Gastrointestinal: dysphagia, reflux, constipation, early satiety or dyspepsia Antiparkinsonian medication side effects • Gastrointestinal symptoms, confusion, hallucinations, nightmares, impulse control disorders
Physical monitoring	• Orthostatic vital signs (blood pressure, heart rate) • Assessment of gait and motor symptoms • Cognitive testing, depression screening tools • Bowels
Investigations and referrals	• Consider referral to speech language pathology (for problems with communication, swallowing, or saliva), physiotherapy (for balance or motor problems), and occupational therapy (for challenges with activities of daily living)[4] • Consider bloodwork to rule out iron deficiency as reversible cause of RLS[4]
Education and counseling	• Physical exercise for both motor and nonmotor symptoms[4] • Fluid encouragement for motor symptoms and orthostatic hypotension[4] • Sleep hygiene for any sleep disturbance[4] • Trigger avoidance, abdominal binders for orthostatic hypotension[31,39] • Behavioural management for urinary incontinence[40] • Diet modification for constipation, gastrointestinal symptoms, or dysphagia • Bed safety for sleep disorders • Advance care planning[4]
Medications	Deprescribing medications that may worsen OH[37] • Antihypertensives • Anticholinergics (may also worsen constipation) • Antidepressants (may also worsen RLS) Review anti-dopamine medications, including antiemetics (may worsen RLS and motor symptoms) Prescribing • Levodopa for motor symptoms[4] • Favour osmotic laxatives over stimulant laxatives for constipation[4] • Domperidone, midodrine, or fludrocortisone for OH[4] • Overactive bladder treatment[4] • Dual-action or timed-release melatonin, clonazepam for RBD[4] • Gabapentinoids for RLS[4]

OH—orthostatic hypotension, PD—Parkinson disease, RBD—rapid eye movement sleep behaviour disorder, RLS—restless legs syndrome.

symptoms by causing incomplete emptying or retention.[40] Management approaches are similar to those used with other patient populations.[40]

Sleep disorders and neuropsychiatric symptoms: Sleep disorders in PD include RBD, RLS, insomnia, and daytime sleepiness. A sleep history and sleep hygiene counseling are recommended as a starting point to evaluation and management.[4]

With RBD, loss of large muscle atonia during rapid eye movement sleep (eg, acting out dreams, punching, kicking, yelling, and falling out of bed) is common in PD and can predate motor symptoms by years.[48] Bed safety should be advised with removal of potentially injurious objects; bed partners may be advised to sleep separately. Antidepressants may exacerbate RBD[49,50]; morning administration may be of help. Clonazepam (0.25 mg to 1 mg) and melatonin taken at bedtime have been effective in trials and are endorsed by guidelines.[37] Clonazepam has more adverse effects and should be reserved as second-line therapy. Dual-action or extended-release melatonin may be suggested over the immediate-release formula as most RBD events occur in early morning hours, during the latter part of the sleep period.

Restless legs syndrome is experienced as subjective sensations of restlessness, discomfort, and paresthesia

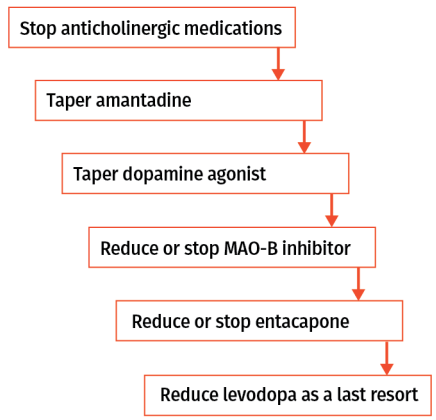
while resting, accompanied by the urge to move and relieved by movement. Patients should be screened for iron deficiency,[4] and medications known to worsen RLS (antipsychotics, antidepressants) should be minimized.[51] Optimizing nocturnal dopaminergic therapies is recommended, as RLS may be a wearing-off symptom. Gabapentinoids, such as pregabalin, can be considered.[4]

Depression occurs in about 35% of patients with PD[52] and anxiety in about 25%.[53] Guidelines recommend having a low threshold for diagnosis of depression and tailoring therapy to each patient.[4] A trial of selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors, such as escitalopram, sertraline, or duloxetine, with breakfast or lunch may be considered, while taking mirtazapine at bedtime is known to exacerbate RBD.[6]

Psychotic symptoms can emerge owing to medication side effects or disease progression to cognitive impairment or dementia. Psychosis should always prompt a thorough evaluation and treatment of reversible causes. Reduction of PD medications is sometimes necessary but is better done with support from experienced collaborators.[4] The general principle is to decrease or stop medications with greater potential for psychosis first (**Figure 1**).[4] Monitoring for motor worsening whi le balancing the impact of psychosis on function and quality of life is advised. In general, reduction of medications with high risk of psychosis should be attempted before, or at least concurrently as, antipsychotic medication is initiated for distressing symptoms.

Quetiapine and clozapine are those antipsychotic medications least likely to worsen motor symptoms in PD.[4] In older patients with PD, quetiapine should be started at 12.5 mg to 25 mg taken at bedtime and then increased as tolerated while monitoring for risks, including hypotension, constipation, and QT prolongation. Clozapine is reserved for refractory cases owing to risk of agranulocytosis and need for monitoring. Other antipsychotics should be strictly avoided.

Figure 1. How to reduce polypharmacy in patients with PD and psychosis



MAO-B—monoamine oxidase B, PD—Parkinson disease.
Data from Grimes et al.[4]

Cognitive assessment is recommended in patients with cognitive or functional decline or psychosis. If PD dementia is diagnosed a trial of cholinesterase inhibitor (rivastigmine or donepezil) should be offered, except where contraindicated.[4] Cognitive impairment, motor disability, and daytime sleepiness necessitate consideration of driving safety and cessation.[4]

Case resolution

For Maria, you initiate half a tablet of 100 mg levodopa and 25 mg carbidopa taken orally 3 times daily, 30 minutes before meals, to be titrated over 3 weeks up to 1 tablet taken 3 times daily. Maria notices an immediate response to the medication, finding she is walking faster and smoother and is better able to fasten buttons. When you examine her, you find she can tap her fingers and toes more quickly than at your previous assessment.

At your next follow-up visit with Maria, you check her orthostatic vital signs. Her blood pressure is 128/74 mm Hg and heart rate is 78 beats per minute while supine. After 1 minute standing, her blood pressure is 112/71 mm Hg and heart rate is 81 beats per minute. Maria agrees to discontinue amlodipine and monitor her blood pressure at home, which will be reviewed at future appointments. You also screen for nonmotor symptoms of PD. Maria denies urinary frequency and speech or swallowing concerns but reports bothersome constipation, for which you discuss a trial of osmotic laxatives. As her husband continues to report Maria is acting out her dreams, you prescribe 5 mg of dual-action or timed-release melatonin taken at bedtime and provide information on bed safety.

At subsequent follow-up visits with Maria, you plan to reassess these issues and screen for neuropsychiatric symptoms, including depression and cognitive decline.

Conclusion

Parkinson disease presents a challenging array of motor and nonmotor symptoms that necessitates collaboration between family physicians, PD specialists, and allied health professionals. Family physicians could have an important impact in management of PD through early recognition and treatment of motor symptoms, management of common nonmotor symptoms, and care planning in progressive disease, including referrals to allied health professionals and supportive services.

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Contributors
All authors contributed to the literature review and interpretation and to preparing the manuscript for submission.

Competing interests
None declared

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References

1. Frank C, Chiu R, Lee J. Parkinson disease primer, part 1: diagnosis. *Can Fam Physician* 2023;69:20-4 (Eng), e8-13 (Fr).
2. Hu M, Cooper J, Beamish R, Jones E, Butterworth R, Catterall L, et al. How well do we recognise non-motor symptoms in a British Parkinson's disease population? *J Neurol* 2011;258(8):1513-7. Epub 2011 Mar 11.
3. Weintraub D, Moberg PJ, Duda JE, Katz IR, Stern MB. Effect of psychiatric and other nonmotor symptoms on disability in Parkinson's disease. *J Am Geriatr Soc* 2004;52(5):784-8.
4. Grimes D, Fitzpatrick M, Gordon J, Miyasaki J, Fon EA, Schlossmacher M, et al. Canadian guideline for Parkinson disease. *CMAJ* 2019;191(36):E989-1004.
5. Postuma RB, Berg D, Stern M, Poewe W, Olanow CW, Oertel W, et al. MDS clinical diagnostic criteria for Parkinson's disease. *Mov Disord* 2015;30(12):1591-601.
6. Klietz M, Greten S, Wegner F, Höglinger GU. Safety and tolerability of pharmacotherapies for Parkinson's disease in geriatric patients. *Drugs Aging* 2019;36(6):511-30.
7. PD Med Collaborative Group; Gray R, Ives N, Rick C, Patel S, Gray A, et al. Long-term effectiveness of dopamine agonists and monoamine oxidase B inhibitors compared with levodopa as initial treatment for Parkinson's disease (PD MED): a large, open-label, pragmatic randomised trial. *Lancet* 2014;384(9949):1196-205. Epub 2014 Jun 11. Erratum in: *Lancet* 2014;384(9949):1186.
8. Verschuur CVM, Suwijn SR, Boel JA, Post B, Bloem BR, van Hilten JJ, et al. Randomized delayed-start trial of levodopa in Parkinson's disease. *N Engl J Med* 2019;380(4):315-24.
9. Fox SH, Katzenschlager R, Lim SY, Barton B, de Bie RMA, Seppi K, et al. International Parkinson and Movement Disorder Society evidence-based medicine review: update on treatments for the motor symptoms of Parkinson's disease. *Mov Disord* 2018;33(8):1248-66. Epub 2018 Mar 23. Erratum in: *Mov Disord* 2018;33(12):1992. Epub 2018 Oct 30.
10. Espay AJ, Lang AE. Common myths in the use of levodopa in Parkinson disease: when clinical trials misinform clinical practice. *JAMA Neurol* 2017;74(6):633-4.
11. DrugDex evaluations [database]. *Carbidopa and levodopa*. Armonk, NY: IBM Micromedex 2.0. Available from: **https://www.micromedexsolutions.com/**. Accessed 2022 Oct 4.
12. Virmani T, Tazan S, Mazzoni P, Ford B, Greene PE. Motor fluctuations due to interaction between dietary protein and levodopa in Parkinson's disease. *J Clin Mov Disord* 2016;3:8.
13. Murray JP, Kerins A. Amantadine withdrawal syndrome masquerading as COVID-19 encephalopathy: a case report and review of the literature. *Oxf Med Case Reports* 2021;2021(2):omaa133.
14. Nirenberg MJ. Dopamine agonist withdrawal syndrome: implications for patient care. *Drugs Aging* 2013;30(8):587-92.
15. Barone P, Antonini A, Colosimo C, Marconi R, Morgante L, Avarello TP, et al. The PRIAMO study: a multicenter assessment of nonmotor symptoms and their impact on quality of life in Parkinson's disease. *Mov Disord* 2009;24(11):1641-9.
16. Katunina E, Titova N. The epidemiology of nonmotor symptoms in Parkinson's disease (cohort and other studies). *Int Rev Neurobiol* 2017;133:91-110. Epub 2017 Jun 27.
17. Zhang TM, Yu SY, Guo P, Du Y, Hu Y, Piao YS, et al. Nonmotor symptoms in patients with Parkinson disease: a cross-sectional observational study. *Medicine* (Baltimore) 2016;95(50):e5400.
18. Hassan A, Wu SS, Schmidt P, Dai Y, Simuni T, Giladi N, et al. High rates and the risk factors for emergency room visits and hospitalization in Parkinson's disease. *Parkinsonism Relat Disord* 2013;19(11):949-54. Epub 2013 Jul 5.
19. Shahgholi L, De Jesus S, Wu S, Pei Q, Hassan A, Schmidt P, et al. The profile of the hospitalized and re-hospitalized Parkinson disease patient: 5 year data from the National Parkinson Foundation (S48.006). *Neurology* 2015;84(Suppl 14):S48.006.
20. Shahgholi L, De Jesus S, Wu SS, Pei Q, Hassan A, Armstrong MJ, et al. Hospitalization and rehospitalization in Parkinson disease patients: data from the National Parkinson Foundation centers of excellence. *PLoS One* 2017;12(7):e0180425.
21. Woodford H, Walker R. Emergency hospital admissions in idiopathic Parkinson's disease. *Mov Disord* 2005;20(9):1104-8.
22. Chou KL, Evatt M, Hinson V, Kompoliti K. Sialorrhea in Parkinson's disease: a review. *Mov Disord* 2007;22(16):2306-13.
23. Suttrup I, Warnecke T. Dysphagia in Parkinson's disease. *Dysphagia* 2016;31(1):24-32. Epub 2015 Nov 21.
24. Knudsen K, Krogh K, Østergaard K, Borghammer P. Constipation in Parkinson's disease: subjective symptoms, objective markers, and new perspectives. *Mov Disord* 2017;32(1):94-105. Epub 2016 Nov 22.
25. Lubomski M, Davis RL, Sue CM. Gastrointestinal dysfunction in Parkinson's disease. *J Neurol* 2020;267(5):1377-88. Epub 2020 Jan 27.
26. Knudsen K, Fedorova TD, Bekker AC, Iversen P, Østergaard K, Krogh K, et al. Objective colonic dysfunction is far more prevalent than subjective constipation in Parkinson's disease: a colon transit and volume study. *J Parkinsons Dis* 2017;7(2):359-67.
27. Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. *Scand J Gastroenterol* 1997;32(9):920-4.
28. Schuster BG, Kosar L, Kamrul R. Constipation in older adults. Stepwise approach to keep things moving. *Can Fam Physician* 2015;61:152-8.
29. Tan AH, Lim SY, Chong KK, Manap MAAA, Hor JW, Lim JL, et al. Probiotics for constipation in Parkinson disease: a randomized placebo-controlled study. *Neurology* 2021;96(5):e772-82. Epub 2020 Oct 12.
30. Barichella M, Pacchetti C, Bolliri C, Cassani E, Iorio L, Pusani C, et al. Probiotics and prebiotic fiber for constipation associated with Parkinson disease: an RCT. *Neurology* 2016;87(12):1274-80. Epub 2016 Aug 19.
31. Freeman R, Abuzinadah AR, Gibbons C, Jones P, Miglis MG, Sinn DI. Orthostatic hypotension: JACC state-of-the-art review. *J Am Coll Cardiol* 2018;72(11):1294-309.
32. Velseboer DC, de Haan RJ, Wieling W, Goldstein DS, de Bie RMA. Prevalence of orthostatic hypotension in Parkinson's disease: a systematic review and meta-analysis. *Parkinsonism Relat Disord* 2011;17(10):724-9. Epub 2011 May 14.
33. Lamarre-Cliche M, Cusson J. The fainting patient: value of the head-upright tilt-table test in adult patients with orthostatic intolerance. *CMAJ* 2001;164(3):372-6.
34. LeWitt PA, Kymes S, Hauser RA. Parkinson disease and orthostatic hypotension in the elderly: recognition and management of risk factors for falls. *Aging Dis* 2020;11(3):679-91.
35. Udow SJ, Robertson AD, MacIntosh BJ, Espay AJ, Rowe JB, Lang AE, et al. 'Under pressure': Is there a link between orthostatic hypotension and cognitive impairment in α-synucleinopathies? *J Neurol Neurosurg Psychiatry* 2016;87(12):1311-21. Epub 2016 Sep 9.
36. Robertson AD, Messner MA, Shirzadi Z, Kleiner-Fisman G, Lee J, Hopyan J, et al. Orthostatic hypotension, cerebral hypoperfusion, and visuospatial deficits in Lewy body disorders. *Parkinsonism Relat Disord* 2016;22:80-6. Epub 2015 Nov 23.
37. *Parkinson's disease in adults: diagnosis and management. NICE guideline, no. 71.* London, UK: National Institute for Health and Care Excellence; 2017. Available from: **https://www.ncbi.nlm.nih.gov/books/NBK447153/**. Accessed 2023 Jan 15.
38. Farrell MC, Shibao CA. Morbidity and mortality in orthostatic hypotension. *Auton Neurosci* 2020;229:102717. Epub 2020 Aug 17.
39. Fanciulli A, Leys F, Falup-Pecurariu C, Thijs R, Wenning GK. Management of orthostatic hypotension in Parkinson's disease. *J Parkinsons Dis* 2020;10(s1):S57-64.
40. Frank C, Szlanta A. Office management of urinary incontinence among older patients. *Can Fam Physician* 2010;56:1115-20.
41. Molnar F, Frank CC. Determining the causes of postural hypotension. *Can Fam Physician* 2018;64:40.
42. Fanciulli A, Goebel G, Metzler B, Sprenger F, Poewe W, Wenning GK, et al. Elastic abdominal binders attenuate orthostatic hypotension in Parkinson's disease. *Mov Disord Clin Pract* 2015;3(2):156-60.
43. Newton JL, Frith J. The efficacy of nonpharmacologic intervention for orthostatic hypotension associated with aging. *Neurology* 2018;91(7):e652-6. Epub 2018 Jul 13.
44. DrugDex evaluations [database]. *Midodrine*. Armonk, NY: IBM Micromedex 2.0. Available from: **https://www.micromedexsolutions.com/**. Accessed 2022 Oct 4.
45. Veazie S, Peterson K, Ansari Y, Chung KA, Gibbons CH, Raj SR, et al. Fludrocortisone for orthostatic hypotension. *Cochrane Database Syst Rev* 2021;(5):CD012868.
46. Limwatthana C. A randomized controlled trial comparing the efficacy and safety of pyridostigmine versus midodrine for the treatment of orthostatic hypotension in Parkinson's disease patients [abstract]. *Mov Disord* 2022;37(Suppl 1). Available from: **https://www.mdsabstracts.org/abstract/a-randomized-controlled-trial-comparing-the-efficacy-and-safety-of-pyridostigmine-versus-midodrine-for-the-treatment-of-orthostatic-hypotension-in-parkinsons-disease-patients/#:~:text=Conclusion%3A%20Pyridostigmine%2**. Accessed 2023 Jan 15.
47. MedlinePlus [website]. *Pyridostigmine*. Bethesda, MD: National Library of Medicine; 2020. Available from: **https://medlineplus.gov/druginfo/meds/a682229.html**. Accessed 2023 Jan 15.
48. Postuma RB, Iranzo A, Hogl B, Arnulf I, Ferini-Strambi L, Manni R, et al. Risk factors for neurodegeneration in idiopathic rapid eye movement sleep behavior disorder: a multicenter study. *Ann Neurol* 2015;77(5):830-9. Epub 2015 Mar 13.
49. McCarter SJ, St Louis EK, Sandness DJ, Arndt K, Erickson M, Tabatabai G, et al. Antidepressants increase REM sleep muscle tone in patients with and without REM sleep behavior disorder. *Sleep* 2015;38(6):907-17.
50. Stefani A, Högl B. Sleep in Parkinson's disease. *Neuropsychopharmacology* 2020;45(1):121-8. Epub 2019 Jun 24.
51. Patatanian E, Claborn MK. Drug-induced restless legs syndrome. *Ann Pharmacother* 2018;52(7):662-72. Epub 2018 Feb 26.
52. Aarsland D, Påhlhagen S, Ballard CG, Ehrt U, Svenningsson P. Depression in Parkinson disease—epidemiology, mechanisms and management. *Nat Rev Neurol* 2011;8(1):35-47.
53. Broen MPG, Narayen NE, Kuijf ML, Dissanayaka NNW, Leentjens AFG. Prevalence of anxiety in Parkinson's disease: a systematic review and meta-analysis. *Mov Disord* 2016;31(8):1125-33. Epub 2016 Apr 29.

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