

# Incorporating Lifestyle Medicine Into Parkinson Disease Care

# Evidence and Guidance for Clinical Practice

Lifestyle medicine strategies play an important role in managing Parkinson disease and empowering patients and their care partners.

Rachel Dolhun, MD, DipABLM, and Jennifer G. Goldman, MD, MS



Parkinson disease (PD) affects ~10 million people worldwide, with anticipated increases in frequency, health care costs, and PD-related disability.<sup>12</sup> Medical and surgical treatments can ease

symptoms, but proven therapies to slow or stop disease progression are lacking.

Lifestyle medicine (LM) is an evidence-based branch of conventional medicine that leverages daily activities as the primary treatment modality to prevent, treat, and reverse chronic disease. The pillars of LM are physical activity (PA); a whole-food, plant-predominant diet; restorative sleep; stress management; positive social connections; and avoidance of risky substances<sup>3</sup> (Figure 1). For people with PD, LM can amplify medication and surgical benefits, lessen symptoms, improve quality of life, and enhance empowerment.<sup>4</sup> LM may be helpful at all stages of PD, from mild to advanced disease, and may provide ways to delay or prevent disease onset.<sup>5-8</sup> Although long-term, randomized, controlled trials for LM for PD are limited, evidence for use in patient care is growing.<sup>9,10</sup> This article describes how LM applies to PD and offers recommendations for incorporating LM into clinical practice.

#### **Physical Activity and Exercise**

PA refers to any movement resulting in energy expenditure.<sup>11</sup> Although often used interchangeably with physical



Figure 1. The pillars of lifestyle medicine.

exercise, PA includes not only planned and structured exercise, but also movement-related activities performed during leisure time, work, or household chores. In PD, physical activity and exercise are often diminished because of motor, cognitive, and mood changes; apathy; fatigue; autonomic dysfunction; or comorbidities.<sup>12</sup> One study found that lack of time, fear of falling, and low expectations of outcomes were perceived barriers to exercising in PD.<sup>13</sup>

Both PA and exercise can improve PD motor and nonmotor symptoms (eg, sleep, mood, cognition), as well as quality of life.<sup>14,15</sup> Numerous types of exercise have been studied in PD, including ones incorporating dual-task motorcognitive training (eg, boxing), cross-body movement patterns (eg, boxing, Nordic walking), and socialization (eg, group classes).



### **EXERCISES FOR PEOPLE LIVING WITH PARKINSON DISEASE**

_	Aerobic	Strength	Flexibility	Balance
What does it do?	Supports heart, lung, brain and whole-body health	Builds muscle and strengthens bones	Allows joints and muscles to move more freely	Boosts stability
What are the benefits?	Better health and well- being, mood, memory, digestion, etc.	Improved movement and overall health, less risk of breaking bones	Healthier joints, less pain and injury risk	Smoother walking and less falling
What might it look like?	<ul> <li>Brisk walking</li> <li>Nordic walking, also called Urban Poling</li> <li>Hiking</li> <li>Jogging or running</li> <li>Biking</li> <li>Swimming or water aerobics</li> <li>Martial arts</li> <li>Skiing</li> <li>Canoeing</li> <li>Skating</li> <li>Playing basketball, tennis, pickleball or other sports</li> </ul>	<ul> <li>Lifting weights</li> <li>Working with resistance bands</li> <li>Bodyweight exercises, like squats, push-ups or sit-ups</li> <li>Heavy gardening, with digging and shoveling</li> </ul>	<ul> <li>+ Yoga</li> <li>+ Pilates</li> <li>+ Targeted stretching of upper body (neck, back, chest, trunk, arms)</li> <li>+ Targeted stretching of lower body (hips, knees, ankles, feet)</li> </ul>	<ul> <li>+ Dance</li> <li>+ Tai chi</li> <li>+ Non-contact boxing</li> <li>+ Ping-pong</li> <li>+ Kayaking</li> <li>+ Yoga</li> <li>+ Pilates</li> </ul>
How often should I do this?*	At least 3 days per week 30 to 40 minutes per session Moderate to vigorous intensity (See page 20)	At least 2 to 3 non- consecutive days per week 30 to 60 minutes per session	At least 2 to 3 days per week (daily, if possible) For major muscle groups, hold 30 seconds and repeat 2 times	At least 2 to 3 times per week (the more, the better) 30 to 60 minutes per session

\*Adapted from the American Physical Therapy Association and the

American College of Sports Medicine exercise guidelines for Parkinson's.

Figure 2. Parkinson disease exercise recommendations.

Adapted from The Michael J. Fox Foundation for Parkinson's Research's Make Your Move: Exercise for brain health and life with Parkinson's 2024 (michaeljfox.org/exerciseguide).



PA recommendations for people with PD are based on American Heart Association guidelines,<sup>16</sup> but also may incorporate flexibility, balance, agility, and multitasking (Figure 2). Unanswered questions remain regarding the best type, frequency, and setting of exercise for people with PD. PA and exercise can be performed in many ways: individually or in groups, with guidance from trained professionals, ambulatory or seated, in person or virtually, and with or without equipment. People with PD should be encouraged to focus on activities that are enjoyable and safe and incorporate motor and cognitive aspects.

Exercise may have both symptomatic and disease-modifying effects on PD.<sup>17</sup> A longitudinal study found that regular exercisers at baseline had not only better quality of life and physical function, but also less disease progression, cognitive decline, and caregiver burden 1 year later.<sup>18</sup> In a populationbased cohort study, PA, along with a healthy diet, was associated with a lower rate of all-cause mortality among people with PD.<sup>19</sup>

Exercise benefits may relate to increased dopamine or neurotrophic factors (eg, brain-derived neurotrophic factor [BDNF]), improved neuroplasticity, or targeted neurovascular or neuroinflammatory mechanisms.<sup>20,21</sup> Imaging studies in PD reveal brain changes with exercise; in one study, after a 6-month exercise program, the expected decrease in dopamine transporter availability and neuromelanin content on imaging was reversed in participants with early PD.<sup>22,23</sup> In addition, PA and exercise may play a role in disease prevention. Greater total daily PA in older adults was associated with reduced risk of parkinsonism and slower progression in one study; in another study comparing people with incident PD and controls, those who consistently engaged in high levels of PA had a 51% lower PD risk than those with low levels of PA.<sup>24,25</sup>

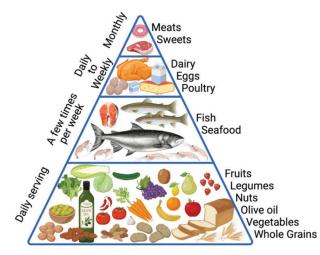


Figure 3. Mediterranean diet.

Adapted from Bisaglia M. Mediterranean diet and Parkinson's disease. Int J Mol Sci. 2022;24(1):42.27

BRAIN HEALTHY MEAL PLAN RECOMMENDATION



#### THE **MIND** DIET

15 dietary components: 10 brain-healthy foods to focus on; 5 food groups to limit

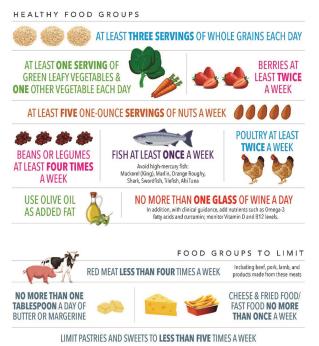


Figure 4. Mediterranean–Dietary Approaches to Stop Hypertension Intervention for Neurodegenerative Delay (MIND) diet. Used with permission from Pacific Neuroscience Institute.

#### Whole-Food, Plant-Predominant Diet

Diet refers to an individual's pattern of eating, or the foods regularly consumed. Diet can shape the gut microbiome, which includes bacteria, fungi, and viruses in the gastrointestinal tract that contribute to immune health, vitamin synthesis, metabolism, and other processes. The gut microbiome composition and function differ in people with PD compared with those without PD. In people with PD, there is evidence of reduced numbers of microbes producing shortchain fatty acids, which have anti-inflammatory properties and help maintain gut epithelial lining, and thus, a shift toward a proinflammatory state in PD.

The Mediterranean diet and the Mediterranean– Dietary Approaches to Stop Hypertension Intervention for Neurodegenerative Delay (MIND) diet are associated with improved gut microbiome, enhanced medication benefit, reduced symptom severity, and potentially slower PD progression.<sup>27</sup> Both diets focus on whole, unprocessed or minimally processed foods, including vegetables, fruits, whole grains, and legumes. The diets allow fish and red wine in moderation, but limit sweets, red meat, and dairy (Figures 3 and 4). In small, short-term randomized controlled trials, the



Educate about dietary protein and medication interactions, discussing plant sources of protein (e.g., quinoa, beans, smoothies). Many people equate protein with only animal meat. Recognize the importance of protein for muscle and bone health, especially with aging and PD. Data does not support diets that are low in total daily protein for PD. Ask your patient to keep a log for a few days, noting when and what they eat, when they take their PD medications, when medication kicks in, and how long the medication lasts.

Recommend taking PD medication (e.g., levodopa) approximately 30-60 minutes before or after a meal or, if necessary, e.g., due to nausea, by taking medications with meals containing little or no protein. If motor fluctuations occur, consider a protein redistribution diet in which people consume the recommended daily amount of protein, but eat higher protein meals in the evening (when generally less active) and lower protein meals during the day, when medication benefit may be most needed.

#### Figure 5. Addressing dietary protein and levodopa interactions in Parkinson disease.

Mediterranean diet led to decreased constipation<sup>28</sup> and improved cognition<sup>29</sup> in people with PD. In observational studies evaluating outcomes reported by people with PD, an association was shown between both diets and slowed PD progression,<sup>30</sup> with one study suggesting greater improvement with the MIND diet over the Mediterranean diet.<sup>31</sup> For people at risk of PD, observational studies have linked these diets to lower rates of PD diagnoses and later age at onset.<sup>32,33</sup> Potential mechanisms of action include antioxidant and antiinflammatory effects, downregulation of metabolic disease pathways, and positive gut microbiome changes.<sup>27</sup>

Few data are available on the contribution of specific food sources to PD. One observational study noted an association between intake of dairy products (eg, yogurt, ice cream) and faster disease progression<sup>30</sup>; another found a link between frequent low- or no-fat milk intake and PD diagnosis.<sup>34</sup>

The Mediterranean and MIND diets can be modified, with the help of speech language pathologists or dietitians, to address symptoms such as dysphagia, smell loss, "off" time, or motor fluctuations. Interactions between dietary protein and levodopa may contribute to the latter, necessitating separation of medications from meal times (Figure 5).

#### **Restorative Sleep**

Sleep dysfunction in PD, which is frequent across all disease stages, includes disturbances of sleep (eg, insomnia, sleep-related movement disorders, sleep-disordered breathing, parasomnias, rapid eye movement sleep behavior disorder [RBD]), wakefulness (eg, excessive daytime sleepiness), and circadian rhythms.<sup>35</sup> Sleep disruption in PD is multifactorial, including neurodegeneration in sleep-regulatory pathways, dysregulation of key neurotransmitters and clock genes, motor and nonmotor symptoms, drug side effects, and primary sleep disorders. Environmental effects (eg, light-dark cycles) may contribute to sleep dysfunction, given circadian system neurodegeneration, dysfunction in hypothalamic suprachiasmatic nuclei and retinal dopaminergiccontaining cells, and altered melatonin levels.<sup>36</sup>

Poor sleep in PD may worsen cognitive, emotional, and functional performance; impair driving and activities; predispose to falls and safety risks; and decrease quality of life for individuals and caregivers.<sup>37</sup> However, some people with PD experience sleep benefit, in which they awaken in the morning or after naps with improved motor function, hypothesized to relate to increased dopamine release during sleep or certain genetic mutations, such as Parkin or PINK1.<sup>38</sup>

Management of sleep disturbances depends on the problem being experienced, and referral to a sleep specialist may be helpful. Addressing sleep hygiene is essential. Incorporating lifestyle modifications highlights the interconnectedness of sleep with one's environment, nutrition, exercise, and stress management (Figure 6). Exercise can improve sleep time, phase, and quality, with potential mechanisms involving toxin clearance, increased neurotrophic factors (eg, BDNF), or reduced neuroinflammation.<sup>36</sup> Cognitive behavioral therapy for insomnia, based on changing dysfunctional behaviors and thinking patterns contributing to sleep disruption, has been used successfully in the general population but has not been well studied in PD. Two small studies have revealed improved sleep measures with cognitive behavioral therapy.<sup>39</sup> Other treatments may include medications (eg, for nighttime PD symptoms, restless legs symptoms, RBD, insomnia, daytime



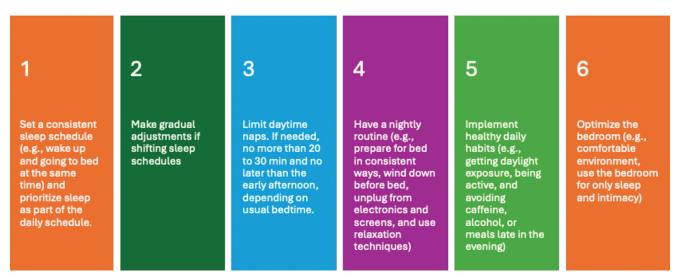


Figure 6. Improving sleep hygiene. Data from Suni E, Rosen D. Mastering sleep hygiene: your path to quality sleep. Updated March 4, 2024. https://www.sleepfoundation.org/sleep-hygiene.<sup>40</sup>

sleepiness) or positive-airway pressure devices for sleep apnea. Although the Sleep Foundation recommends that adults sleep for at least 7 hours each night, the optimal length can vary with age, personal needs, and sleep quality.<sup>40</sup>

RBD can precede synucleinopathies, including PD. However, whether sleep disturbances in the general population are linked to increased risk of PD is not clear. Some population-based studies suggest that worse sleep quality and shorter sleep duration may be associated with a higher risk of developing parkinsonism.<sup>41</sup> Whether disease-modifying therapies, including lifestyle modifications, in people with RBD could prevent neurodegenerative disease or slow progression is unclear.

#### **Stress Management**

In one survey, people with PD reported a higher level of stress (ie, a state of worry or mental tension) than people without PD, and higher stress level was linked to a lower quality of life.<sup>42</sup> Acute stress can worsen motor and nonmotor symptoms, especially tremor, freezing of gait, dyskinesia, sleep problems, and depression. Stress also may reduce dopaminergic medication effects.<sup>43</sup> Chronic stress is associated with anxiety and depression in PD.<sup>42</sup> Chronic stress can elevate glucocorticoid levels, which may decrease BDNF and increase inflammatory factors, causing hippocampal and amygdala structural changes and striatal dopaminergic dysfunction. These changes could increase psychologic distress and contribute to disease progression.<sup>44-46</sup>

In the aforementioned survey, >80% of people with PD used physical exercise to manage stress. Nearly 40% used mindfulness (ie, nonjudgmental awareness of the moment) and reported symptom improvement.<sup>42</sup> One meta-analysis of mindfulness

and meditation trials in PD showed improved motor symptoms and cognitive function<sup>47</sup>; another analysis suggested decreased levels of anxiety and depression.<sup>46</sup> The mechanisms of the mindfulness benefit are unclear but may include BDNF increases or remodeling of neural networks involved in PD.<sup>48,49</sup>

Mindfulness allows an individual to self-manage and adapt to PD symptoms and other stressors. There are many ways to practice mindfulness, including meditation, yoga, journaling, prayer, reading, or engaging with creative endeavors. Additional methods to decrease stress levels include exercise, mental health counseling and treatment (including medications for anxiety or depression), or talking with loved or trusted ones.

#### **Positive Social Connections**

Meaningful social connections can raise resilience to stress,<sup>50</sup> mitigate loneliness, and potentially reduce dementia risk in the general population.<sup>51</sup> Loneliness—the feeling of being socially disconnected even in the presence of others or in relationships—is associated with an increased risk of PD.<sup>52</sup> In addition, having PD is associated with an increased risk of loneliness.<sup>53</sup> Loneliness can occur through all PD stages, but may increase for both people living with PD and their loved ones around the time of diagnosis and with disease progression. Loneliness is associated with greater individualreported symptom severity and poorer quality of life.<sup>54</sup>

Stigma regarding PD motor and nonmotor symptoms can lead to social withdrawal. For example, tremor, drooling, and slowness may cause social embarrassment, and speech and cognitive changes along with masked facies can affect communication. PD symptoms can affect relationships and lead to early workforce departure.<sup>55</sup> Furthermore, psychological stress associated with loneliness can negatively affect lifestyle



# SOCIAL CONNECTION NETWORK MAP

## AMERICAN COLLEGE OF Lifestyle Medicine

Building and maintaining relationships requires effort, but even small steps can lead to significant gains over time; as the landmark, Harvard Grant Study notes, "How happy we are in our relationships has a powerful influence on our health.[1]" This map is designed to help individuals identify their social resources and assess the quality of their relationships. It can be used to set goals for improving social connections. Discussing each connection category (circles) on the map with a mental health professional can provide valuable insights to help one better understand their resources and offer strategies to enhance communication, manage conflicts, and cultivate healthier and more fulfilling relationships.



- Significant others, close friends, family
- People that an individual relies on for protection, support, and help during a need or crisis
- Strongest mutual bonds that require the most time and energy
- Close friends can move from the inner to the middle circle if less time is spent with them
- People spend over half of their time in their inner circle.

#### Middle Circle -Occasional Companions

- Former classmates, extended family members
- They are not our closest confidants but will likely assist, especially when requested.
- Less strong connections have the potential to grow stronger.
- These acquaintances tend to change more often.
- This circle becomes more challenging to maintain as people age, with limited time for socializing

#### Circles of Connection[2]

- In the inner circle, write up to 5 people with whom you are most closely connected.
- In the middle circle, write up to 5 occasional companions (past/present school/work friends, distant relatives).
- In the outer circle, write up to 5 places you regularly visit and see people familiar to them but not close with.
   (e.g., grocery store, gym or yoga class, places of worship, school/work).

Network Map adapted from Columbia School of Social Work https://ssnm.ctl. columbia.edu/map/tutorial/

#### Outer Circle – Coworkers and Acquaintances

- Support from organizations like work/school, grocery stores, places of worship, etc.
- These are friendly relationships that exist on the edges of our lives.
- Less intimate connections, but they still contribute to a feeling of belonging.
- Spending time expanding the outer circle supports building inner circles.

#### Figure 7. Mapping social connections.

The American College of Lifestyle Medicine offers a toolkit to help evaluate and maximize connections. Create a free account and download the kit at https://connect.lifestylemedicine.org/resources/resource-landing-page



choices (eg, reduced physical activity, poor nutrition).

Maintaining social connections invokes 3 spheres: intimate (eg, marriage, emotional partner, close confidant), relational (eg, a close friendship), and collective (eg, belonging to a group with a shared purpose or interest). Many people with PD and their care partners create positive connections within the PD community through activities such as support groups, online chat forums, exercise classes, research participation, fundraising, or advocacy. Others may connect with their local community through volunteer work, social hobbies (eg, book club) or faith-based activities.

People with PD and their care partners should be encouraged to build personal support networks as part of the care plan, emphasizing quality of connections over quantity (Figure 7). Social prescribing (ie, providing referrals to resources and community activities that foster connection) may leverage expertise from social workers, occupational therapists, recreational therapists, and others.<sup>56, 57</sup>

#### **Avoidance of Risky Substances**

In LM, avoidance of risky substances typically focuses on cigarette smoking, alcohol, and illicit drugs. Whereas cigarette smoking remains a leading cause of morbidity and mortality, epidemiologic studies support an inverse association between cigarette smoking and PD risk, with current and former smokers having lower risks of developing PD compared with nonsmokers.<sup>58,59</sup> Whether nicotine or other chemicals in cigarette smoke affect neurodegeneration requires further study, although the health risks associated with cigarette smoking and use of nicotine products are well known.

Regarding alcohol consumption in PD, a systematic review revealed an overrepresentation of never drinkers among people with PD, and most studies do not support an association between alcohol consumption and PD risk.<sup>60</sup> Drugs of abuse such as amphetamine have been associated with increased PD risk and may act by means of neurotoxic effects on the nigrostriatal system.<sup>61</sup> Conversely, phytocannabinoids may have a neuroprotective role in PD, and the endocannabinoid system is involved in central nervous system development and synaptic plasticity. Additional research is needed regarding use of cannabis products in PD. In one survey, 73% of respondents reported medicinal use; improvements in pain, anxiety, agitation, and sleep were reported, as were side effects of dry mouth, dizziness, and cognitive changes.<sup>62</sup> Caffeine—one of the most frequently consumed psychoactive substances-may have a neuroprotective effect in PD, acting potentially through adenosine A2A receptor blockade and related genetic polymorphisms.<sup>63</sup> As such, coffee drinking has been found to confer a lower risk of PD in cohort and case-control studies, with a meta-analysis suggesting a 30% reduction in risk.<sup>64</sup>

water, air pollution, metal ions) are also potential risk factors for PD, with possible effects on dopaminergic neurons, oxidative stress, mitochondrial dysfunction, and neuroinflammation.<sup>4</sup> Studying LM modifications for environmental exposures should be considered for PD risk reduction.

#### **Future Directions**

LM strategies play an important role in managing PD and empowering patients and their care partners. Greater understanding of the effects of lifestyle modifications on the symptoms and pathobiology of PD, optimal ways to implement LM activities, and potential contributions of LM to reducing PD risk or slowing progression are needed. Enhancing resources and support systems devoted to LM will enhance benefit and implementation.

#### Select Resources

#### **Lifestyle Medicine**

- Lifestyle medicine: 6 ways to take control of your health: lifestylemedicine.org/wp-content/uploads/2023/06/ Pillar-Booklet.pdf
- · American College of Lifestyle Medicine: lifestylemedicine.org

#### **Physical Activity and Exercise**

- · Make your move: Exercise of brain health and life with Parkinson's: michaeljfox.org/exerciseguide
- Parkinson's Foundation: parkinson.org/sites/default/ files/documents/professional-exercise-guidelines.pdf
- Physical activity: cdc.gov/physicalactivity
- Guide to overcoming exercise barriers in Parkinson's 2024: parkinsonseurope.org/app/uploads/2024/05/Guide-toovercoming-exercise-barriers-in-Parkinsons-2.pdf
- American Heart Association recommendations for physical activity in adults and kids: heart.org/en/ healthy-living/fitness/fitness-basics/aha-recs-for-physical-activity-in-adults

#### Diet

Brain food: Eating well if you have Parkinson's (or worry you might get it): michaelifox.org/dietguide

#### Sleep

Sleep Foundation: sleepfoundation.org

#### Stress

PD health @ home: parkinson.org/resources-support/ online-education/pdhealth

#### **Social Connections**

• Parkinson's buddy network: parkinsonsbuddynetwork. michaeljfox.org

<sup>1.</sup> Dorsey ER, Sherer T, Okun MS, Bloem BR. The emerging evidence of the Parkinson pandemic. J Parkinsons Dis.

 <sup>2018;8(</sup>s1):S3-S8. doi:10.233/JPD-181474
 2018;8(s1):S3-S8. doi:10.233/JPD-181474
 2. Yang W, Hamilton JL, Kopil C, et al. Current and projected future economic burden of Parkinson's disease in the U.S. NPJ Parkinsons Dis. 2020;6:15. doi:10.1038/s41531-020-0117-1

Lippman D, Stump M, Veazey E, et al. Foundations of lifestyle medicine and its evolution. Mayo Clin Proc Innov Qual Outcomes. 2024;8(1):97–111. doi:10.1016/j.mayocpiqo.2023.11.004

<sup>4.</sup> Reichmann H, Csoti I, Koschel J, et al. Life style and Parkinson's disease. J Neural Transm (Vienna). 2022;129(9):1235-



1245. doi:10.1007/s00702-022-02509-1

- 5. Kola S, Subramanian I. Updates in Parkinson's disease integrative therapies: an evidence-based review. Curr Neurol Neurosci Rep. 2023;23(11):717-726. doi:10.1007/s11910-023-01312-z
- McDaniels B, Pontone GM, Keener AM, Subramanian I. A prescription for wellness in early PD: just what the doctor ordered. J Geriatr Psychiatry Neurol. 2023;36(6):461–469. doi:10.1177/08919887231164358
- 7. Oh S, Kim E, Shoda J. Editorial: Lifestyle modification strategies as first line of chronic disease management. Front Physiol. 2023;14:1204581. doi:10.3389/fphys.2023.1204581
- Paul KC, Chuang YH, Shih IF, et al. The association between lifestyle factors and Parkinson's disease progression and mortality. Mov Disord. 2019;34(1):58–66. doi:10.1002/mds.27577
- 9. Nag N, Jelinek GA. More research is needed on lifestyle behaviors that influence progression of Parkinson's disease. Front Neurol. 2019;10:452. doi:10.3389/fneur.2019.00452
- 10. Vodovotz Y, Barnard N, Hu FB, et al. Prioritized research for the prevention, treatment, and reversal of chronic disease: recommendations from the Lifestyle Medicine Research Summit. Front Med (Lausanne). 2020;7:585744. doi:10.3389/ fmed.2020.585744
- 11. World Health Organization. Physical activity. Published June 26, 2024. https://www.who.int/news-room/fact-sheets/
- detail/physical-activity 12. van Nimwegen M, Speelman AD, Hofman-van Rossum EJ, et al. Physical inactivity in Parkinson's disease. J Neurol. 2011;258(12):2214-2221. doi:10.1007/s00415-011-6097-7
- 13. Ellis T, Boudreau JK, DeAngelis TR, et al. Barriers to exercise in people with Parkinson disease. Phys Ther. 2013;93(5):628-636. doi:10.2522/ptj.20120279
- 14. Bispo D, Lins C, Hawkes KL, Tripp S, Khoo TK. The positive effects of physical activity on quality of life in Parkinson's disease: a systematic review. Geriatrics (Basel). 2024;9(4). doi:10.3390/geriatrics9040094 15. Ernst M, Folkerts AK, Gollan R, et al. Physical exercise for people with Parkinson's disease: a systematic review and
- network meta-analysis. Cochrane Database Syst Rev. 2024;4(4):CD013856. doi:10.1002/14651858.CD013856.pub3 16. American Heart Association. American Heart Association recommendations for physical activity in adults and kids. Last
- reviewed January 19, 2024. https://www.heart.org/en/healthy-living/fitness/fitness-basics/aha-recs-for-physicalactivity-in-adults
- 17. Langeskov-Christensen M, Franzen E, Grondahl Hvid L, Dalgas U. Exercise as medicine in Parkinson's disease. J Neurol Neurosurg Psychiatry. Published online February 28, 2024. doi:10.1136/jnnp-2023-332974
- 18. Oguh O, Eisenstein Á, Kwasny M, Simuni T. Back to the basics: regular exercise matters in Parkinson's disease: results from the National Parkinson Foundation QII registry study. Parkinsonism Relat Disord. 2014;20(11):1221–1225. doi:10.1016/j.parkreldis.2014.09.008
- 19. Zhang X, Molsberry SA, Schwarzschild MA, Ascherio A, Gao X. Association of diet and physical activity with all-cause mortality among adults with Parkinson disease. JAMA Netw Open. 2022;5(8):e2227738. doi:10.1001/jamanetworkopén.2022.27738
- 20. Gronek P, Haas AN, Czarny W, et al. The mechanism of physical activity-induced amelioration of Parkinson's disease: a downer, Frada XH, Carli Y, et al. The international opposited activity-induced antennation of Farahinous usease narrative review. Aging Dis 2021;72(1):22-202. doi:10.14336/AD.2020.0407
   Hirsch MA, van Wegen EEH, Newman MA, Heyn PC. Exercise-induced increase in brain-derived neurotrophic factor
- in human Parkinson's disease: a systematic review and meta-analysis. Transl Neurodegener. 2018;7:7. doi:10.1186/ \$40035-018-0112-1
- 22. de Laat B, Hoye J, Stanley G, et al. Intense exercise increases dopamine transporter and neuromelanin concentrations in the substantia nigra in Parkinson's disease. NPJ Parkinsons Dis. 2024;10(1):34. doi:10.1038/s41531-024-00641-1
- 23. Li J, Guo J, Sun W, et al. Effects of exercise on Parkinson's disease: a meta-analysis of brain imaging studies. Front Hum Neurosci. 2022;16:796712. doi:10.3389/fnhum.2022.796712 24. Oveisgharan S, Yu L, Dawe RJ, Bennett DA, Buchman AS. Total daily physical activity and the risk of parkinsonism in
- community-dwelling older adults. J Gerontol A Biol Sci Med Sci. 2020;75(4):702–711. doi:10.1093/gerona/glz111
- 25. Shih IF, Liew Z, Krause N, Ritz B. Lifetime occupational and leisure time physical activity and risk of Parkinson's disease. Parkinsonism Relat Disord. 2016;28:112-117. doi:10.1016/j.parkreldis.2016.05.007
- The Michael J. Fox Foundation for Parkinson's Research. Make your move: Exercise for brain health and life with Parkinson's 2024. https://viewer.joomag.com/exercise-guide/0272799001706805200
   Bisaglia M. Mediterranean diet and Parkinson's disease. Int J Mol Sci. 2022;24(1):42. doi:10.3390/ijms24010042
- 28. Rusch C, Beke M, Tucciarone L, et al. Mediterranean diet adherence in people with Parkinson's disease reduces constipation symptoms and changes fecal microbiota after a 5-week single-arm pilot study. Front Neurol. 2021;12:794640. doi:10.3389/fneur.2021.794640
- 29. Paknahad Z, Sheklabadi E, Derakhshan Y, Bagherniya M, Chitsaz A. The effect of the Mediterranean diet on cognitive function in patients with Parkinson's disease: a randomized clinical controlled trial. Complement Ther Med 2020;50:102366. doi:10.1016/j.ctim.2020.102366
- Mischley LK, Lau RC, Bennett RD. Role of diet and nutritional supplements in Parkinson's disease progression. Oxid Med Cell Longev. 2017;2017:6405278. doi:10.1155/2017/6405278
- 31. Fox DJ, Park SJ, Mischley LK. Comparison of associations between MIND and Mediterranean diet scores with patientreported outcomes in Parkinson's disease. Nutrients. 2022;14(23):5185. doi:10.3390/nu14235185 32. Agarwal P, Wang Y, Buchman AS, Holland TM, Bennett DA, Morris MC. MIND diet associated with reduced incidence
- and delayed progression of parkinsonism in old age. J Nutr Health Aging. 2018;22(10):1211-1215. doi:10.1007/ s12603-018-1094-5
- 33. Yin W, Lof M, Pedersen NL, Sandin S, Fang F. Mediterranean dietary pattern at middle age and risk of Parkinson's disease: a Swedish cohort study. Mov Disord. 2021;36(1):255-260. doi:10.1002/mds.28314
- Hughes KC, Gao X, Kim IV, et al. Intake of dairy foods and risk of Parkinson disease. Neurology. 2017;89(1):46-52. doi:10.1212/WNL.000000000004057
- 35. Iranzo A, Cochen De Cock V, Fantini ML, Perez-Carbonell L, Trotti LM. Sleep and sleep disorders in people with Parkinson's disease. Lancet Neurol. 2024;23(9):925-937. doi:10.1016/S1474-4422(24)00170-4
- Gros P, Videnovic A. Overview of sleep and circadian rhythm disorders in Parkinson disease. Clin Geriatr Med. 2020;36(1):119–130. doi:10.1016/j.cqer.2019.09.005
- 37. Mahmood Z, Van Patten R, Nakhla MZ, Twamley EW, Filoteo JV, Schiehser DM. REM sleep behavior disorder in Parkinson's disease: effects on cognitive, psychiatric, and functional outcomes. J Int Neuropsychol Soc. 2020;26(9):894-905. doi:10.1017/S1355617720000430
- Wang RF, Li YP, Zhang HY, et al. Sleep benefit in patients with Parkinson's disease is associated with the dopamine transporter expression in putamen. Brain Res. 2023;1802:148173. doi:10.1016/j.brainres.2022.148173
- 39. Schutz L, Sixel-Doring F, Hermann W. Management of sleep disturbances in Parkinson's disease. J Parkinsons Dis. 2022;12(7):2029-2058. doi:10.3233/JPD-212749
- 40. Suni E, Rosen D. Mastering sleep hygiene: your path to quality sleep. Updated March 4, 2024. https://www.sleepfoundation.org/sleep-hygiene 41. Lysen TS, Darweesh SKL, Ikram MK, Luik AI, Ikram MA. Sleep and risk of parkinsonism and Parkinson's disease: a
- population-based study. Brain. 2019;142(7):2013-2022. doi:10.1093/brain/awz11
- van der Heide A, Speckens AEM, Meinders MJ, Rosenthal LS, Bloem BR, Helmich RC. Stress and mindfulness in Parkinson's disease: a survey in 5000 patients. NPJ Parkinsons Dis. 2021;7(1):7. doi:10.1038/s41531-020-00152-9
   Zach H, Dirkx MF, Pasman JW, Bloem BR, Helmich RC. Cognitive stress reduces the effect of levodopa on Parkinson's
- resting tremor. CNS Neurosci Ther. 2017;23(3):209-215. doi:10.1111/cns.12670 44. Burtscher J, Copin JC, Rodrigues J, et al. Chronic corticosterone aggravates behavioral and neuronal symptomatology
- in a mouse model of alpha-synuclein pathology. Neurobiol Aging. 2019;83:11-20. doi:10.1016/j.neurobiolag-

ing.2019.08.007

- 45. Hemmerle AM, Dickerson JW, Herman JP, Seroogy KB. Stress exacerbates experimental Parkinson's disease. Mol Psychiatry. 2014;19(6):638-640. doi:10.1038/mp.2013.108
- van der Heide A, Meinders MJ, Speckens AEM, Peerbolte IF, Bloem BR, Helmich RC. Stress and mindfulness in Parkinson's disease: clinical effects and potential underlying mechanisms. Mov Disord. 2021;36(1):64–70. doi:10.1002/ mds.28345
- 47. Liu X, Lu H. Mindfulness or meditation therapy for Parkinson's disease: a systematic review and meta-analysis of randomized controlled trials. Eur J Neurol. 2023;30(12):3982-3983. doi:10.1111/ene.16004
- 48. You T. Ogawa EF. Effects of meditation and mind-body exercise on brain-derived neurotrophic factor: a literature review of human experimental studies. Sports Med Health Sci. 2020;2(1):7-9. doi:10.1016/j.smhs.2020.03.001
- 49. Pickut BA, Van Hecke W, Kerckhofs E, et al. Mindfulness based intervention in Parkinson's disease leads to structural brain changes on MRI: a randomized controlled longitudinal trial. Clin Neurol Neurosurg. 2013;115(12):2419-2425. doi:10.1016/j.clineuro.2013.10.002
- 50. van der Heide A, Dommershuijsen LJ, Puhlmann LMC, et al. Predictors of stress resilience in Parkinson's disease and associations with symptom progression. NPJ Parkinsons Dis. 2024;10(1):81. doi:10.1038/s41531-024-00692-4
- 51. Livingston G, Huntley J, Liu KY, et al. Dementia prevention, intervention, and care: 2024 report of the Lancet standing
- Campisoli V, Indred Z. 204404 (10452):572–628. doi:10.1016/S0140-6736(24)01296-0
   Terracciano A, Luchetti M, Karakose S, Stephan Y, Sutin AR. Loneliness and risk of Parkinson disease. JAMA Neurol. 2023;80(11):1138–1144. doi:10.1001/jamaneurol.2023.3382
- 53. Prell T, Schonenberg A, Heimrich KG. The impact of loneliness on quality of life in people with Parkinson's disease: results from the Survey of Health, Ageing and Retirement in Europe. Front Med (Lausanne). 2023;10:1183289.
- doi:10.3389/fmed.2023.1183289
   Subramanian I, Farahnik J, Mischley LK. Synergy of pandemics—social isolation is associated with worsened Parkinson severity and quality of life. NPJ Parkinsons Dis. 2020;6:28. doi:10.1038/s41531-020-00128-9
- Perepezko K, Hinkle JT, Shepard MD, et al. Social role functioning in Parkinson's disease: a mixed-methods systematic review. Int J Geriatr Psychiatry. 2019;34(8):1128-1138. doi:10.1002/gps.5137
   Prenger MTM, Madray R, Van Hedger K, Anello M, MacDonald PA. Social symptoms of Parkinson's disease. Parkinsons
- Dis. 2020;2020:8846544. doi:10.1155/2020/8846544
- 57. Roland M, Everington S, Marshall M. Social prescribing: transforming the relationship between physicians and their
- patients. N Engl J Med. 2020;383(2):97-99. doi:10.1056/NEJMp1917060 58. di Biase L, Pecoraro PM, Carbone SP, Alessi F, Di Lazzaro V. Smoking exposure and Parkinson's disease: a UK Brain Bank pathology-validated case-control study. Parkinsonism Relat Disord. 2024;125:107022. doi:10.1016/j.parkreldis.2024.107022
- 59. Gallo V, Vineis P, Cancellieri M, et al. Exploring causality of the association between smoking and Parkinson's disease. Int Guido Y, Micca Y, Guichard MY, et al. Departing decample of the association section of the section
- Parkinsons Dis. 2022;12(8):2369-2381. doi:10.3233/JPD-223522
- 61. Ferreira C, Almeida C, Tenreiro S, Quintas A. Neuroprotection or neurotoxicity of illicit drugs on Parkinson's disease. Life (Basel). 2020;10(6). doi:10.3390/life10060086
- Lodden SJ, Doemo H, Slida S, Lu Y, Leehey MA. Higher risk, higher reward? Self-reported effects of real-world cannabis use in Parkinson's disease. Mov Disord Clin Pract. 2022;9(3):340–350. doi:10.1002/mdc3.13414
- 63. Popat RA, Van Den Eeden SK, Tanner CM, et al. Coffee, ADORA2A, and CYP1A2: the caffeine connection in Parkinson's disease. Eur J Neurol. 2011;18(5):756-765. doi:10.1111/j.1468-1331.2011.03353.x
- Hernan MA, Takkouche B, Caamano-Isorna F, Gestal-Otero JJ. A meta-analysis of coffee drinking, cigarette smoking, and the risk of Parkinson's disease. Ann Neurol. 2002;52(3):276-284. doi:10.1002/ana.10277

#### Rachel Dolhun, MD, DipABLM

Principal Medical Advisor

The Michael J. Fox Foundation for Parkinson's Research New York, NY

#### Jennifer G. Goldman, MD, MS

JPG Enterprises LLC Chicago, IL

Adjunct Professor **Barrow Neurological Institute** Phoenix, AZ

#### **Disclosures**

Dr. Dolhun is an employee of The Michael J. Fox Foundation for Parkinson's Research.

Dr. Goldman has received research support from Acadia, the Lewy Body Dementia Association, and The Michael J. Fox Foundation for Parkinson's Research; consulting fees from CervoMed, GE Healthcare, InMuneBio, KeifeRx, the Lewy Body Dementia Association, the Parkinson's Foundation, PaxMedica, Roche, and SAGE; and honoraria from the International Parkinson and Movement Disorder Society, the Lewy Body Dementia Association, the Parkinson Study Group, and the Parkinson's Foundation.