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Advancing Parkinson's Disease Management: From Dopaminergic Therapy to Deep Brain Stimulation and Beyond

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Abstract

Parkinson's Disease (PD) is a progressive neurodegenerative disorder characterized by the degeneration of dopaminergic neurons in the substantia nigra, leading to motor and non-motor dysfunction that significantly impacts quality of life. Although current treatments provide substantial symptomatic relief, long-term disease management remains limited by medication-related complications, high economic burden, and the absence of widely implemented early diagnostic strategies. This narrative review synthesizes current pharmacologic therapies, neurosurgical interventions such as deep brain stimulation (DBS), and emerging diagnostic technologies within a broader biological, economic, and psychosocial framework. Dopamine replacement therapy, particularly levodopa combined with carbidopa, remains the cornerstone of treatment but is constrained by a narrowing therapeutic window and progressive motor complications. DBS offers significant motor improvement in selected patients but raises important considerations regarding cognitive outcomes, accessibility, and cost-effectiveness. Beyond symptom control, PD imposes substantial indirect costs related to caregiver burden, productivity loss, and long-term care needs. Emerging biomarker-based blood and cerebrospinal fluid assays, along with advanced imaging and artificial intelligence-supported diagnostics, hold promise for earlier detection and individualized intervention. This review highlights the need for an integrated, multimodal approach that combines pharmacologic, surgical, diagnostic, and economic considerations to improve long-term outcomes and support sustainable, patient-centered PD care.

Keywords: PD; Dopamine replacement therapy; Levodopa; Deep brain stimulation; Neurodegeneration; Biomarkers; Precision medicine

1. Introduction

PD is one of the most prevalent neurological disorders worldwide, with incidence increasing with age. In 2021, the global incidence rate was 79.68 cases per 100,000 population among middle-aged adults (40–64 years) and 477.50 cases per 100,000 population among older adults (≥65 years), respectively (Zhang et al., 2025). Although aging is a major risk factor, PD can also arise due to certain genetic mutations like on the PARK7 gene, and also from environmental influences like exposure to pesticides and other herbicides, leading to early-onset cases in younger individuals (Blauwendraat et al., 2020).

Dopamine is a neurotransmitter that plays a crucial role in the brain's reward system, motivation, and movement control. It acts as a chemical messenger, allowing nerve cells to communicate and regulate various functions, including mood, learning, and decision-making. In the basal ganglia, dopamine is essential for smooth and controlled movements. The basal ganglia is a group of structures deep within the brain that plays a key role in controlling movement, learning, and habits, working closely with the motor cortex to help start, stop, and smooth out voluntary movements. The basal ganglia rely on dopamine to function properly, ensuring that when dopamine levels are balanced, movements are fluid and coordinated, and the brain can efficiently manage voluntary actions (Fahn, 2008).

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The basal ganglia controls movement through two main pathways: the direct and indirect pathways. These pathways help start and stop voluntary movements. In the direct pathway, dopamine activates certain receptors (called D1) in the striatum, which leads to less inhibition of the thalamus (DRD1 (Human)). Since the thalamus sends signals to the motor cortex, this allows movement to happen more easily. In the indirect pathway, dopamine blocks other receptors (called D2), which normally help stop movements (Bhatia et al., 2025). This pathway involves the external and internal parts of the globus pallidus (GPe and GPi) and the subthalamic nucleus (STN). When dopamine is low, like in PD, the direct pathway becomes weaker, and the indirect pathway becomes stronger. This leads to too much inhibition of the thalamus, making it harder for the brain to start movements, hence why people with PD often move slowly or have trouble moving at all.

Besides movement, the basal ganglia also influence emotions and decision-making, making them an essential part of how we think and act. Dopamine is synthesized primarily in the substantia nigra and plays a central role in regulating motor control through basal ganglia circuits. In PD, degeneration of dopaminergic neurons reduces dopamine availability, disrupting normal signaling and contributing to both motor and non-motor symptoms (Latif et al., 2021).

PD (PD) is a progressive neurodegenerative disorder primarily affecting the basal ganglia. The disease is characterized by the degeneration of dopaminergic neurons in the substantia nigra, overall decreasing dopamine production. As dopamine levels decline, patients experience hallmark motor symptoms such as bradykinesia (slowness of movement), muscle rigidity, postural instability, and resting tremors. Beyond motor dysfunction, PD also contributes to cognitive decline, affecting memory, executive function, and overall quality of life.

Histopathologically, PD is marked by the presence of Lewy bodies, which are abnormal intracellular aggregates composed primarily of the misfolded protein alpha-synuclein. These inclusions are typically found in the cytoplasm of neurons, particularly within the substantia nigra and other regions of the brain. Alpha-synuclein is a presynaptic neuronal protein that plays a role in synaptic transmission, but in PD, it undergoes pathological conformational changes that promote aggregation and neurotoxicity. The accumulation of alpha-synuclein disrupts cellular homeostasis, impairs mitochondrial function, and activates neuroinflammatory pathways, all contributing to progressive neuronal death. The spread of Lewy body pathology through the brain is also believed to underlie the non-motor symptoms of PD, including cognitive impairment, mood disorders, and autonomic dysfunction (Morris et al., 2024).

1.1 Rationale and Unique Contribution of This Review

Although PD has been extensively reviewed in the literature, many existing reviews focus narrowly on either pharmacologic therapy, surgical intervention, or molecular pathogenesis in isolation. Fewer analyses integrate biological mechanisms, clinical treatment strategies, economic burden, and psychosocial consequences within a single framework. Additionally, the long-term cost-effectiveness of advanced therapies and the role of emerging diagnostic technologies are often underemphasized. This review aims to address these gaps by synthesizing established and emerging treatment paradigms alongside economic and systems-level considerations. By integrating pharmacologic management, deep brain stimulation, caregiver burden, and early diagnostic innovation, this article offers a comprehensive, multimodal perspective on PD management that extends beyond descriptive summaries and emphasizes long-term clinical and societal impact.

1.2 Scope and Methodology

This article is a narrative literature review rather than an experimental or systematic review. Sources were identified through targeted searches of PubMed and other peer-reviewed biomedical databases, with emphasis on clinical trials, meta-analyses, epidemiologic studies, economic evaluations, and translational research published primarily between 2000 and 2025. Articles were selected to represent established standards of care, emerging therapeutic strategies, and evolving diagnostic approaches in PD. Economic and psychosocial studies were included to capture both direct and indirect disease burden. Non–peer-reviewed sources were limited to regulatory or organizational references where appropriate. The goal of this review is to synthesize findings across disciplines rather

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than exhaustively catalog all available studies.

2. Current Treatment Paradigms: Dopamine Replacement Therapy

PD is primarily characterized by the degeneration of dopaminergic neurons in the substantia nigra pars compacta, leading to a significant depletion of dopamine in the striatum. This dopamine deficiency is responsible for hallmark motor symptoms such as bradykinesia, rigidity, and tremors. Consequently, the current foundation of PD treatment revolves around dopamine replacement therapy.

Although directly administering dopamine might seem like a logical approach, it is not viable. Dopamine itself cannot cross the blood-brain barrier (BBB) due to its polarity and the lack of a suitable transport mechanism. Additionally, systemic administration of dopamine would activate peripheral dopamine receptors, causing significant cardiovascular and gastrointestinal side effects such as increased heart rate, hypertension, nausea, and vomiting. (Sonne et al., 2025) Instead, the primary strategy involves using dopamine precursors, the most effective being levodopa (L-DOPA). Unlike dopamine, levodopa can cross the BBB via the large neutral amino acid transporter (LAT-1). Once inside the brain, it is converted into dopamine by the enzyme aromatic L-amino acid decarboxylase (AADC) within dopaminergic neurons (Church, 2021; Tambasco et al., 2018). However, a major challenge is that a significant portion of levodopa undergoes peripheral metabolism before reaching the brain, reducing its efficacy and increasing systemic side effects.

To counter this, levodopa is co-administered with carbidopa, forming the combination drug Sinemet. Carbidopa is a peripheral AADC inhibitor that prevents the premature conversion of levodopa outside the brain, thereby increasing the amount that reaches the central nervous system while minimizing peripheral side effects. Sinemet remains the gold standard for PD treatment, but its dosing is highly individualized and also frequently requires regular redosing (Rodnitzky, 1992). Each patient requires a tailored regimen based on disease progression, symptom severity, and response to treatment. The complexity of Sinemet dosing arises from the narrow therapeutic window, which is the range in which the drug provides benefits without causing intolerable side effects (Leyden & Tadi, 2025). In early PD, this window is relatively broad, allowing for effective symptom control. During this period, the amount of variance allowed in dosing is significantly higher without either inadequately managing symptoms or incurring adverse effects. However, as the disease progresses, the window narrows, necessitating frequent dose adjustments. Higher or more frequent doses can lead to motor complications, including dyskinesias (involuntary movements) and motor fluctuations. Non-motor side effects such as hallucinations, orthostatic hypotension, and nausea further complicate treatment.

To optimize symptom control, adjunct medications are often employed (Tan et al., 2021). Monoamine oxidase-B inhibitors (MAO-B inhibitors), such as selegiline and rasagiline, work by preventing dopamine breakdown, thereby prolonging its action in the brain. Dopamine agonists like ropinirole and pramipexole mimic dopamine's effects by directly stimulating dopamine receptors, which can be useful for delaying levodopa initiation in early disease stages (Rewane et al., 2025) (Singh & Parmar, 2025). Amantadine, an NMDA receptor antagonist, is thought to reduce glutamatergic overactivity and increase dopamine release, offering benefits for both motor symptoms and levodopa-induced dyskinesias. While memantine, also an NMDA receptor antagonist primarily used in Alzheimer's disease, has a similar mechanism, it has been explored for its potential neuroprotective effects and possible benefits on cognitive and motor function in PD (Chang & Ramphul, 2025) (Kuns et al., 2025).

As patients require multiple medications, the risk of polypharmacy increases. PD treatment involves complex drug interactions that require careful management. For instance, combining MAO-B inhibitors with certain antidepressants can lead to serotonin syndrome, while dopamine agonists can exacerbate impulse control disorders. Given the progressive nature of PD, treatment strategies must be continuously reassessed to balance symptom relief with medication-related complications. In advanced stages, when medications alone become insufficient, interventions such as deep brain stimulation (DBS) or even potentially continuous levodopa infusion may be considered to maintain function and quality of life (Dovjak, 2022) (Bhagavathula et al., 2022).

Figure 1 provides an overview of FDA-approved pharmacologic therapies for PD, organized by mechanism of action and clinical role. The figure illustrates how treatment strategies evolve as disease severity progresses and

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highlights the complementary roles of dopaminergic replacement, enzymatic inhibition, and adjunctive therapies.

3. Adjunctive and Alternative Approaches: Deep Brain Stimulation

Deep brain stimulation (DBS) is a neurosurgical therapy that delivers targeted electrical stimulation to specific brain regions to modulate abnormal neural activity. In PD (PD), DBS is most commonly used to improve motor symptoms such as rigidity, bradykinesia, and resting tremor, particularly in patients whose symptoms are no longer adequately controlled with medication alone. While DBS does not halt disease progression, it can significantly improve quality of life and reduce reliance on dopaminergic pharmacotherapy.

FDA-Approved Parkinson's Disease Treatments

Drug Name (Brand/Generic)	Drug Class / Mechanism	Delivery Method	Indication / Stage
Sinemet (carbidopa/levodopa)	Dopamine precursor	Oral tablet	First-line for motor symptoms
Stalevo (carbidopa/levodopa/entacapone)	Dopamine precursor + COMT inhibitor	Oral tablet	Advanced PD with motor fluctuations
Vyalev (fos carbidopa/fos levodopa)	Levodopa prodrugs	24-hour subcutaneous infusion	Advanced PD with motor fluctuations
Onapgo (apomorphine)	Dopamine agonist	Continuous subcutaneous infusion	Advanced PD "off" episodes
Neupro (rotigotine)	Dopamine agonist	Transdermal patch	Early-stage PD
Requip (ropinirole)	Dopamine agonist	Oral tablet	Early to mid-stage PD
Mirapex (pramipexole)	Dopamine agonist	Oral tablet	Early to mid-stage PD
Xadago (safinamide)	MAO-B inhibitor	Oral tablet	Add-on for "off" episodes
Azilect (rasagiline)	MAO-B inhibitor	Oral tablet	Monotherapy or adjunct
Eldepryl (selegiline)	MAO-B inhibitor	Oral tablet	Early-stage PD
Inbrija (levodopa inhalation powder)	Dopamine precursor	Inhalation	Intermittent "off" episodes
Amantadine (Gocovri)	NMDA receptor antagonist	Oral tablet	Dyskinesia in advanced PD
Nuplazid (pimavanserin)	Atypical antipsychotic	Oral tablet	Parkinson's disease psychosis
Exelon (rivastigmine)	Cholinesterase inhibitor	Oral capsule / transdermal patch	Parkinson's disease dementia
Northera (droxidopa)	Norepinephrine precursor	Oral capsule	Neurogenic orthostatic hypotension
Myobloc (rimabotulinumtoxinB)	Neurotoxin	Injection	Sialorrhea (drooling) in PD
Trihexyphenidyl (Artane)	Anticholinergic	Oral tablet	Tremor in young patients
Benztropine	Cogentin	Injection	Dry mouth and eyes, constipation, urinary retention, memory impairment, confusion, depression, hallucinations
Deep Brain Stimulation (DBS)	Surgical intervention	Implanted device	Advanced PD with motor complications

Figure 1. FDA-approved pharmacologic treatments for PD, categorized by mechanism of action and stage of clinical use.

In PD, DBS is typically applied to either the subthalamic nucleus (STN) or the globus pallidus internus (GPi). Both targets have demonstrated efficacy in improving motor symptoms, though patient characteristics often guide target selection. GPi stimulation may be preferred in individuals with preexisting cognitive or psychiatric vulnerability, while STN stimulation is frequently associated with greater medication reduction. Careful preoperative evaluation, including neuropsychological assessment and confirmation of levodopa responsiveness, is essential to optimize outcomes and minimize adverse effects.

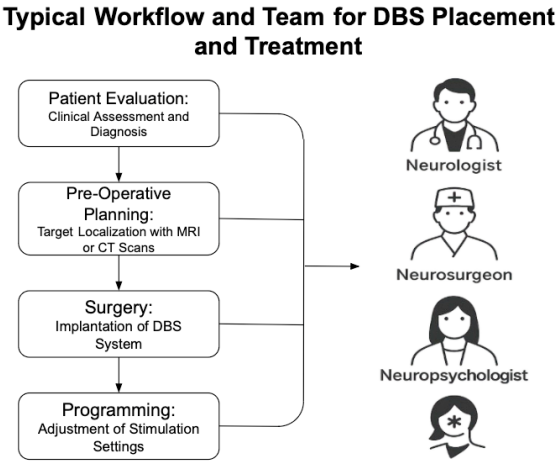

Figure 2. Multidisciplinary evaluation and management pathway for deep brain stimulation in PD.

Long-term benefits of DBS depend not only on surgical implantation but also on postoperative programming, multidisciplinary follow-up, and ongoing symptom monitoring. Although stimulation can produce side effects related to unintended activation of nearby neural structures, most adverse effects are manageable through programming adjustments. Overall, DBS has demonstrated sustained motor improvement and enhanced daily functioning in appropriately selected patients.

As a surgical intervention requiring specialized care and long-term follow-up, DBS involves substantial medical costs. Surgical implantation accounts for approximately 20% of total first-year DBS-related expenses, with additional costs arising from postoperative programming, outpatient care, and eventual implantable pulse generator replacement. Despite these costs, DBS has been shown to reduce disability, lower long-term

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medication burden, and decrease caregiver dependence, supporting its role as a cornerstone therapy in advanced PD management.

Figure 2 illustrates the multidisciplinary framework required for deep brain stimulation, emphasizing the coordinated roles of neurology, neurosurgery, neuropsychology, and long-term follow-up care. This model underscores that successful DBS outcomes depend on comprehensive evaluation and ongoing management rather than surgical implantation alone.

4. Long-Term Economic and Social Impact of PD

Beyond immediate symptom relief, the long-term economic and quality-of-life considerations for PD (PD) treatment are critical for treatment planning and health policy. While levodopa remains a cornerstone of PD treatment, its long-term use is linked with motor complications like dyskinesias and fluctuations, prompting emergence and increasing exploration of combination therapies and surgical options such as deep brain stimulation (DBS) (Gandhi & Saadabadi, 2025). DBS, although effective in select patients, carries high upfront costs and is not universally accessible, creating disparities in care. In the real world, Medicare data shows that treatment patterns for PD (PD) vary widely. Among newly diagnosed patients, 51.1% started with levodopa and 5.9% with dopamine agonists (DAs), with levodopa being the most common first-line therapy. The median time to start treatment was 2.0 months, and patients stayed on levodopa longer (median 18.7 months) than on DAs (9.5 months). Over time, more patients used DAs and other therapies. Both PD symptoms, especially severe motor symptoms, and treatment-related side effects were linked to significantly higher healthcare use and costs. This highlights the need for better-tolerated treatments to reduce the burden on patients and the healthcare system. (Song et al., 2023)

Additionally, a more generalized scope of view extends beyond direct medical costs to include significant indirect costs such as caregiver labor, productivity loss, and long-term care services. Unfortunately, most economic assessments fail to include or accurately assess these indirect costs or measure outcomes using quality-adjusted life years, limiting capacity to perform robust cost-effectiveness comparisons between historical benchmarks such as standard-of-care dopamine replacement therapy with newer interventions like surgery, advanced drug therapy, and emerging biologics. (Yang et al., 2020) One solution would be to perform a true assessment of the long-term impact of multimodal care on PD healthcare delivery, including additional prospective trials like the PD Outcomes Project or integrated care initiatives such as ParkinsonNet. To be effective, these trials must include robust data collection spanning clinical outcomes, patient-reported quality of life, caregiver burden, and comprehensive economic metrics including both direct and indirect costs. If such data were to become available, we could use this to guide plans of action by developing cost-effectiveness models that more accurately reflect the holistic burden of PD and support evidence-based policy decisions regarding treatment reimbursement, resource allocation, and healthcare infrastructure planning (Bloem et al., 2020). For example, cost-effectiveness analyses commonly use the incremental cost-effectiveness ratio (ICER), measured as cost per quality-adjusted life year (QALY) gained. Prior economic modeling studies have evaluated DBS using ICER thresholds to determine whether the additional upfront cost is justified by long-term improvements in motor function and quality of life. Incorporating both direct medical costs and indirect societal costs into such models would allow for more comprehensive comparisons between pharmacologic management alone and multimodal approaches that include surgical intervention.

Alongside advancements in motor symptom management, increasing attention is being given to the non-motor and psychosocial dimensions of PD. Factors such as depression, caregiver burden, and loss of functional independence are key contributors to declining quality of life but are often overlooked in economic evaluations. While the financial impact of depression secondary to PD (PD) is challenging to quantify, its psychological toll, marked by a reported prevalence of 40% to 50% among PD patients, poses a major barrier to improving patient well-being, especially as it significantly exacerbates disability and reduces quality of life independent of motor symptoms. Depression in PD is also associated with greater caregiver burden and increased healthcare utilization, including longer hospital stays and higher readmission rates, compounding the already considerable clinical and economic challenges of managing the disease. (Baquero & Martin, 2015) In addition to the direct effects on individuals, PD imposes a substantial burden on caregivers, particularly in later stages, where patients may require near-constant supervision and assistance.

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Beyond the emotional strain, physical disability itself can initiate a cascade of secondary physiological declines, particularly in the absence of robust caregiver support. Reduced mobility in PD can lead to deconditioning, muscle atrophy, increased risk of falls, pressure ulcers, urinary tract infections, and pulmonary complications such as aspiration pneumonia. These complications often stem from prolonged immobility and diminished capacity to perform activities of daily living. Without consistent assistance from caregivers to promote movement, ensure proper nutrition, and manage hygiene and medications, these risks are significantly amplified. Furthermore, the physiological consequences of chronic stress, both for patients experiencing disability and for overburdened caregivers, can exacerbate cardiovascular, immune, and metabolic dysregulation, further complicating disease management. In this way, PD-related disability does not only limit motor function but can also accelerate systemic health deterioration, creating a vicious cycle of declining health outcomes and increasing care needs. (Aamodt, 2023)

Educational programs and personalized care plans have shown promise in improving quality of life (QoL) among individuals with PD by promoting self-management, enhancing patient understanding of disease progression, and facilitating proactive symptom management. (van Halteren et al., 2020) These interventions can also empower caregivers, reduce anxiety, and support adherence to treatment regimens. Tailored care plans, when designed in collaboration with patients and multidisciplinary teams, address the specific motor and non-motor symptoms that impact daily functioning and well-being.

A comprehensive healthcare approach to PD may involve a scheme similar to that described in Figure 3, where following early diagnosis with developing radiographic and molecular adjuncts to clinical assessment, systems-based approaches to multimodal care, such as ParkinsonNet, personalized care planning, and telemedicine-supported specialist networks, may augment advancing biological and surgical treatment approaches to further improve long-term PD outcomes. Integrating indirect costs and long-term impacts, both medical and societal, is essential for identifying sustainable strategies in the face of a growing global PD burden (Bloem et al., 2020).

5. Emerging Technology and Approaches for PD Diagnostics and Treatment

Innovative approaches are now targeting the disease earlier in its course, with some researchers advocating for widespread adoption of biomarker-based screening. Although imaging techniques like PET scans can identify early dopaminergic deficits, their high cost makes them impractical for population-wide screening. This cost burden arises from several interrelated factors. First, PET imaging requires highly specialized facilities equipped with cyclotrons and radiochemistry labs to produce short-lived radioactive tracers, which are expensive to build and maintain. Second, the procedures are labor-intensive, relying on highly trained nuclear medicine technologists, radiologists, and support staff, all of whom contribute to significant operational costs. Third, advanced training is necessary for both the acquisition and interpretation of neuroimaging data, further raising the barrier to scaling these technologies. Fourth, the throughput of PET scanning is relatively low compared to other diagnostic modalities, limiting efficiency and inflating per-patient costs. Finally, the radiotracers and reagents themselves are costly and have a short half-life, necessitating frequent synthesis and immediate use, which introduces logistical constraints and further increases overall expenditure.

However, further technological developments—such as the emergence of longer-lasting and more stable radiotracers, the miniaturization of PET hardware, and the integration of AI-based image analysis tools—may reduce costs over time by improving efficiency and reducing the need for highly specialized interpretation. Additionally, as these technologies become more widely validated and accepted within the medical community, increased government and private-sector funding may help subsidize infrastructure and training, ultimately improving accessibility and feasibility for earlier detection of PD at scale. Importantly, competition within the biomedical technology market may also play a critical role in driving down costs. For example, if a company develops a novel imaging platform or biomarker tool under patent protection, the eventual expiration of that patent could open the market to competitors, stimulating innovation and price reductions through market forces. This dynamic, found common in pharmaceutical and diagnostic technology sectors, could help dismantle monopolistic pricing and improve affordability over time (Balaji et al., 2024)

Blood-based biomarkers are being actively explored as a potentially scalable and cost-effective solution for early

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PD diagnosis. These biomarkers include proteins (e.g., α-synuclein, Apolipoprotein A-I), inflammatory cytokines, and metabolites linked to oxidative stress, lipid metabolism, and neurodegeneration (Khan & Ali, 2018). One promising candidate is Apolipoprotein A-I (ApoA-I), a plasma protein involved in lipid transport and neuroprotection, which has been consistently found to be downregulated in multiple patient cohorts (Georgila et al., 2019). While blood-based assays offer the advantage of accessibility and reduced invasiveness, cerebrospinal fluid (CSF) remains a gold standard in many neurodegenerative diagnostic protocols due to its close proximity to the brain and higher concentrations of central nervous system (CNS)-derived biomarkers. For example, CSF levels of total and phosphorylated α-synuclein, tau proteins, and neurofilament light chain (NfL) have shown potential for distinguishing PD from other parkinsonian syndromes. Although CSF sampling via lumbar puncture is more invasive than blood draws, it may offer greater diagnostic sensitivity and specificity in certain contexts. Future research should focus on comparing the diagnostic performance and practicality of blood- versus CSF-based biomarker panels in early-stage PD detection.

Monoamine metabolites, such as L-DOPA and sphingomyelins, have also been studied in individuals with prodromal symptoms. In a landmark study, patients at risk for PD showed decreased blood levels of L-DOPA, suggesting early degeneration of catecholaminergic neurons, and increased sphingomyelins, reflecting neurodegenerative processes like synucleinopathy and apoptosis. (Wichit et al., 2021) Additionally, Urate, a natural antioxidant, is another promising biomarker. Multiple studies have shown that individuals with higher serum uric acid levels have a lower risk of developing PD and may experience slower disease progression. In particular, research by Schwarzschild and colleagues found that serum urate levels could predict clinical progression in PD, making it a valuable prognostic indicator. (Cipriani et al., 2010)

Figure 3 presents a conceptual model for integrated PD management, demonstrating how early diagnostics, individualized pharmacologic therapy, neuromodulation, and economic considerations may converge to optimize long-term outcomes.

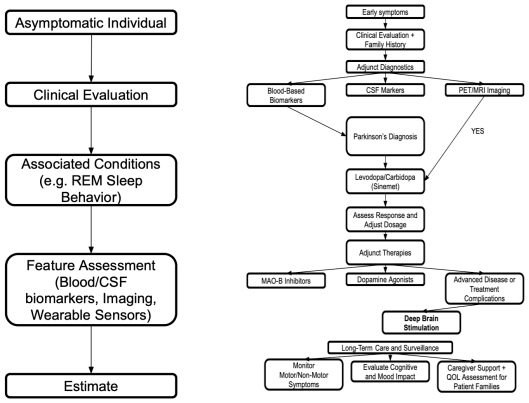

Figure 3. Putative Multimodal Care Pathway. Hypothesized care approaches for de-novo diagnosis (left) and symptomatic validation (right) of PD using emerging technologies and treatment approaches.

6. Conclusion

PD (PD) presents a multifaceted challenge marked by progressive motor and non-motor symptoms rooted in dopaminergic neuron degeneration. While dopamine replacement therapy, particularly levodopa in combination with carbidopa, remains the cornerstone of treatment, its long-term use is limited by a narrowing therapeutic window and complex side effects. Adjunctive pharmacologic options and surgical interventions like deep brain stimulation (DBS) offer symptomatic relief but are not curative. DBS, especially when targeted to the subthalamic nucleus or globus pallidus internus, significantly improves motor function and quality of life, though its accessibility and cost-effectiveness remain areas of concern. Emerging diagnostic innovations, including biomarker development and imaging technologies, promise earlier detection and potentially earlier intervention. Furthermore, integrating holistic care approaches that address psychosocial, economic, and caregiver burdens is critical to improving long-term outcomes. Future strategies should focus on advancing disease-modifying treatments, reducing disparities in care access, and implementing comprehensive cost-effectiveness models to inform sustainable healthcare planning. By embracing a multimodal, patient-centered approach to PD, we can better address the complexity of this neurodegenerative disorder and improve both functional outcomes and quality of life longitudinally.

References

Aamodt, W. (2023). Caregiver Burden in Parkinson Disease: A Scoping Review of the Literature from 2017-2022. *Journal of Geriatric Psychiatry and Neurology*. https://pubmed.ncbi.nlm.nih.gov/37551798/

Vol. 2026 (7) 578 – 587
ISSN 2688-3651 [online]

Anderson, V. C., et al. (2005). Pallidal vs subthalamic nucleus deep brain stimulation in Parkinson disease. *Archives of Neurology*, *62*(4), 554–560. https://doi.org/10.1001/archneur.62.4.554

Approved Medications | American Parkinson Disease Assoc. (n.d.). Retrieved July 7, 2025, from https://www.apdaparkinson.org/living-with-parkinsons-disease/treatment-medication/medication/

Balaji, V., et al. (2024). Artificial Intelligence for PET and SPECT Image Enhancement. *Journal of Nuclear Medicine*, *65*(1), 4–12. https://doi.org/10.2967/jnumed.122.265000

Baquero, M., & Martín, N. (2015). Depressive symptoms in neurodegenerative diseases. *World Journal of Clinical Cases : WJCC*, *3*(8), 682–693. https://doi.org/10.12998/wjcc.v3.i8.682

Bhagavathula, A. S., et al. (2022). Polypharmacy and Hyperpolypharmacy in Older Individuals with PD: A Systematic Review and Meta-Analysis. *Gerontology*, *68*(10), 1081–1090. https://doi.org/10.1159/000521214

Bhatia, A., Lenchner, J. R., & Saadabadi, A. (2025). Biochemistry, Dopamine Receptors. In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK538242/

Blauwendraat, C., Nalls, M. A., & Singleton, A. B. (2020). The genetic architecture of PD. *The Lancet. Neurology*, *19*(2), 170–178. https://doi.org/10.1016/S1474-4422(19)30287-X

Bloem, B. R., et al. (2020). Integrated and patient-centred management of PD: A network model for reshaping chronic neurological care. *The Lancet. Neurology*, *19*(7), 623–634. https://doi.org/10.1016/S1474-4422(20)30064-8

Chang, C., & Ramphul, K. (2025). Amantadine. In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK499953/

Church, F. C. (2021). Treatment Options for Motor and Non-Motor Symptoms of PD. *Biomolecules*, *11*(4), 612. https://doi.org/10.3390/biom11040612

Cipriani, S., Chen, X., & Schwarzschild, M. A. (2010). Urate: A novel biomarker of PD risk, diagnosis and prognosis. *Biomarkers in Medicine*, *4*(5), 701–712. https://doi.org/10.2217/bmm.10.94

Deep Brain Stimulation Reported Costs. (2018). In *Pharmacoeconomic Review Report: Levodopa/Carbidopa (Duodopa): (Abbvie Corporation): Indication: For the treatment of patients with advanced levodopa-responsive PD who do not have satisfactory control of severe, debilitating motor fluctuations and hyper-/dyskinesia despite optimized treatment with available combinations of PD medicinal products, and, for whom the benefits of this treatment may outweigh the risks associated with the insertion and long-term use of the percutaneous endoscopic gastrostomy-jejunostomy (PEG-J) tube required for administration [Internet]*. Canadian Agency for Drugs and Technologies in Health. https://www.ncbi.nlm.nih.gov/books/NBK539446/

Dovjak, P. (2022). Polypharmacy in elderly people. *Wiener Medizinische Wochenschrift (1946)*, *172*(5–6), 109–113. https://doi.org/10.1007/s10354-021-00903-0

Fahn, S. (2008). The history of dopamine and levodopa in the treatment of PD. *Movement Disorders: Official Journal of the Movement Disorder Society*, *23 Suppl 3*, S497-508. https://doi.org/10.1002/mds.22028

Follett, K. A., & Torres-Russotto, D. (2012). Deep brain stimulation of globus pallidus interna, subthalamic nucleus, and pedunculopontine nucleus for PD: Which target? *Parkinsonism & Related Disorders*, *18 Suppl 1*, S165-167. https://doi.org/10.1016/S1353-8020(11)70051-7

Gandhi, K. R., & Saadabadi, A. (2025). Levodopa (L-Dopa). In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK482140/

Georgila, K., Vyrla, D., & Drakos, E. (2019). Apolipoprotein A-I (ApoA-I), Immunity, Inflammation and Cancer. *Cancers*, *11*(8), 1097. https://doi.org/10.3390/cancers11081097

Vol. 2026 (7) 578 – 587
ISSN 2688-3651 [online]

Horn, A., et al. (2017). Probabilistic conversion of neurosurgical DBS electrode coordinates into MNI space. *NeuroImage*, *150*, 395–404. https://doi.org/10.1016/j.neuroimage.2017.02.004

How Do Dopamine Precursors Work? Uses, Side Effects, Drug Names. (n.d.). RxList. Retrieved July 7, 2025, from https://www.rxlist.com/how_do_dopamine_precursors_work/drug-class.htm

Khan, Z., & Ali, S. A. (2018). Oxidative stress-related biomarkers in PD: A systematic review and meta-analysis. *Iranian Journal of Neurology*, *17*(3), 137–144.

Kuns, B., et al. (2025). Memantine. In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK500025/

Latif, S., et al. (2021). Dopamine in PD. *Clinica Chimica Acta; International Journal of Clinical Chemistry*, *522*, 114–126. https://doi.org/10.1016/j.cca.2021.08.009

Leyden, E., & Tadi, P. (2025). Carbidopa. In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK554552/

Li, W. Y., et al. (2024). DBS in the restoration of motor functional recovery following spinal cord injury. *Frontiers in Neurology*, *15*, 1442281. https://doi.org/10.3389/fneur.2024.1442281

Malek, N. (2019). Deep Brain Stimulation in PD. *Neurology India*, *67*(4), 968–978. https://doi.org/10.4103/0028-3886.266268

Mansouri, A., et al. (2018). Deep brain stimulation for PD: Meta-analysis of results of randomized trials at varying lengths of follow-up. *Journal of Neurosurgery*, *128*(4), 1199–1213. https://doi.org/10.3171/2016.11.JNS16715

Moro, E., et al. (2010). Long-term results of a multicenter study on subthalamic and pallidal stimulation in PD. *Movement Disorders: Official Journal of the Movement Disorder Society*, *25*(5), 578–586. https://doi.org/10.1002/mds.22735

Morris, H. R., et al. (2024). The pathogenesis of PD. *Lancet (London, England)*, *403*(10423), 293–304. https://doi.org/10.1016/S0140-6736(23)01478-2

Obeso, J. A., Rodríguez, M. C., Gorospe, A., Guridi, J., Alvarez, L., & Macias, R. (1997). Surgical treatment of PD. *Bailliere's Clinical Neurology*, *6*(1), 125–145.

Odekerken, V. J. J., et al. (2013). Subthalamic nucleus versus globus pallidus bilateral deep brain stimulation for advanced PD (NSTAPS study): A randomised controlled trial. *The Lancet. Neurology*, *12*(1), 37–44. https://doi.org/10.1016/S1474-4422(12)70264-8

Olanow, C. W., Brin, M. F., & Obeso, J. A. (2000). The role of deep brain stimulation as a surgical treatment for PD. *Neurology*, *55*(12 Suppl 6), S60-66.

Perlmutter, J. S., & Mink, J. W. (2006). Deep brain stimulation. *Annual Review of Neuroscience*, *29*, 229–257. https://doi.org/10.1146/annurev.neuro.29.051605.112824

PubChem. (n.d.). *DRD1—Dopamine receptor D1 (human)*. Retrieved July 7, 2025, from https://pubchem.ncbi.nlm.nih.gov/gene/DRD1/human

Rewane, A., Patel, P., & Nagalli, S. (2025). Ropinirole. In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK554532/

Rodnitzky, R. L. (1992). The use of Sinemet CR in the management of mild to moderate PD. *Neurology*, *42*(1 Suppl 1), 44–50; discussion 57-60.

Vol. 2026 (7) 578 – 587
ISSN 2688-3651 [online]

Sasidharan, A., Bagepally, B. S., & Kumar, S. S. (2024). Cost Effectiveness of Deep Brain Stimulation for PD: A Systematic Review. *Applied Health Economics and Health Policy*, *22*(2), 181–192. https://doi.org/10.1007/s40258-023-00848-y

Sedrak, M., et al. (2010). Diffusion tensor imaging (DTI) and colored fractional anisotropy (FA) mapping of the subthalamic nucleus (STN) and the globus pallidus interna (GPi). *Acta Neurochirurgica*, *152*(12), 2079–2084. https://doi.org/10.1007/s00701-010-0813-4

Singh, R., & Parmar, M. (2025). Pramipexole. In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK557539/

Song, Y., et al. (2023). Treatment Patterns and Healthcare Resource Use in Medicare Beneficiaries with PD. *ClinicoEconomics and Outcomes Research: CEOR*, *15*, 631–643. https://doi.org/10.2147/CEOR.S422023

Sonne, J., Goyal, A., & Lopez-Ojeda, W. (2025). Dopamine. In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK535451/

Tambasco, N., Romoli, M., & Calabresi, P. (2018). Levodopa in PD: Current Status and Future Developments. *Current Neuropharmacology*, *16*(8), 1239–1252. https://doi.org/10.2174/1570159X15666170510143821

Tan, Y.-Y., Jenner, P., & Chen, S.-D. (2021). Monoamine Oxidase-B Inhibitors for the Treatment of PD: Past, Present, and Future. *Journal of PD*, *12*(2), 477–493. https://doi.org/10.3233/JPD-212976

van Halteren, A. D., et al. (2020). Personalized Care Management for Persons with PD. *Journal of PD*, *10*(Suppl 1), S11–S20. https://doi.org/10.3233/JPD-202126

Wichit, P., et al. (2021). Monoamine Levels and PD Progression: Evidence From a High-Performance Liquid Chromatography Study. *Frontiers in Neuroscience*, *15*, 605887. https://doi.org/10.3389/fnins.2021.605887

Yang, W., et al. (2020). Current and projected future economic burden of PD in the U.S. *NPJ PD*, *6*, 15. https://doi.org/10.1038/s41531-020-0117-1

Zhang, J., et al. (2025). Global, regional and national temporal trends in PD incidence, disability-adjusted life year rates in middle-aged and older adults: A cross-national inequality analysis and Bayesian age-period-cohort analysis based on the global burden of disease 2021. *Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, *46*(4), 1647–1660. https://doi.org/10.1007/s10072-024-07941-7