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Personalized DAT Selection in Advanced Parkinson's Disease: A Milestone-Guided, Phenotype-Aligned Framework.

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Abstract:

Oral medication frequently fails in advanced Parkinson's disease (PD), necessitating a prompt switch to device-aided therapies (DAT) such as DBS, LCIG, or CSAI. Current DAT initiation techniques, however, continue to be non-individualized, reactive, and delayed. We offer a useful, phenotype-aligned, milestone-driven model to help choose therapies based on the unique paths of each patient. We created a decision framework and scoring checklist based on patient subtypes and clinical milestones by incorporating ideas from important literature. Three primary PD phenotypes: tremor-dominant, PIGD, and cognitive decline - are correlated with five milestone-based clinical indicators. Our structured model allows for more accurate and timely DAT initiation by striking a balance between treatment efficacy, invasiveness, and contraindications. A decision tree and scoring matrix provide a visual summary of the framework, maximizing its practicality. This framework supports multidisciplinary collaboration and shared decision-making, enhancing patient outcomes by providing structured yet flexible approach to advanced PD management.

Keywords: Parkinson's disease, Device-aided therapy, Framework.

Introduction:

Parkinson's Disease (PD) is a clinically heterogeneous neurodegenerative disease characterized by progressive motor and non-motor symptoms, requiring equally nuanced treatment, especially in advanced stages of the disease, where standardized oral dopamine replacement therapy starts proving to be insufficient. That's when, advanced treatment options like Device Assisted Therapies (DAT) including levodopa/carbidopa intestinal gel (LCIG), and continuous subcutaneous apomorphine infusion (CSAI), Deep Brain Stimulation (DBS) offer significant symptomatic relief in advanced stages. However, the therapeutic success of DAT has been poorly optimized from the standpoint of timely initiation and patient experience, potentially due to traditional selection criteria for DAT, failing to

fully account for disease variations across different patient phenotypes. Requiring an urgent need for a clinically actionable framework for timely, personalized DAT decision making. (1)

We aim to create a structured framework that utilizes critical dimensions of PD management like clinical disease progression, timely initiation of DATs, and tailored therapy profiles. By tracking key disease milestones, this model seeks to systematically match advanced DATs to patients most likely to benefit.

Methods

We conducted a literature review using PubMed, with integrative synthesis of four high impact studies, which are Schröter et al. (2) , Dijk et al. (3), Mouchaileh et al. (4), Antonini et al. (5). Search terms included "Parkinson's Disease", "Device Assisted Therapy", "Advanced PD", "Deep Brain Stimulation", and "Phenotypic Subtypes".

Studies were included based on relevance, methodological rigor, and insights into therapeutic indications, patient subtyping, and timing of DAT initiation. Data were extracted and integrated into a unified decision-making framework based on milestones, subtype vulnerability, and treatment profiles. Additionally, A scoring prototype was also developed to align different patient features with optimal DAT options (6).

Results:

Five clinical milestones were identified as the most actionable triggers for DAT: disabling motor fluctuations, refractory tremor, moderate-to-severe dyskinesia, >2 hours OFF time/day and intolerance to oral therapy. These were matched into four core PD phenotypes: tremor dominant, postural instability and gait disorder (PIGD), cognitive decline prone and mixed or intermediate. This highlights cumulative disease burden rather than isolated clinical markers. (5)

Our integrated model is an algorithm balancing efficacy, contraindications, invasiveness, and patient phenotype. It proposes a milestone cluster approach, guiding DAT selection based on patient trajectory and disease phenotype. DBS was favored for cognitively intact, tremor dominant patients. LCIG/CSAI for those with cognitive burden or frailty. We also embedded key findings from Antonini et al. (5), to refine therapeutic matching based on clinical judgment and real-world treatment dynamics. (Figure 1).

A flexible scoring checklist was developed, factoring levodopa responsiveness, age, neuropsychiatric profile and treatment preferences. The proposed algorithm allows dynamic, phenotype-aligned approach of advanced therapies, supporting early, personalized intervention across multidisciplinary PD centers. (Figure 2).

Discussion:

The transition to DAT in advanced PD care is often delayed because of uncertainty about timing and inappropriate patient selection. This milestone-guided, phenotype-aligned framework addresses these gaps by providing a structured and adaptable model. Unlike conventional algorithms that link isolated symptoms to treatments, this algorithm emphasizes cluster-based milestone interpretation and phenotype differentiation. Allowing for a multidimensional understanding of the patient's trajectory and customizes intervention accordingly. For example, while both tremor dominant and PIGD patients may have dyskinesia, their broader clinical context guides whether DBS or LCIG is preferred. This model aligns with current expert consensus and real-world treatment data, while enhancing precision.

A simple method of striking a balance between patient characteristics and clinical indicators is provided by the structured scoring matrix. A patient with severe cognitive decline, moderate OFF time, high levodopa responsiveness, and incapacitating dyskinesias, for instance, would benefit more from LCIG or CSAI than DBS. On the other hand, a patient who scores highly on the matrix and is tremor-dominant, strong, and cognitively intact would be a perfect candidate for DBS.

By combining objective scoring with patient preferences and practical considerations like invasiveness and tolerance, this model facilitates shared decision-making. Crucially, it permits flexibility; with the right amount of prudence, multidisciplinary input, and follow-up, patients who score in the intermediate zone (11–15) can still be considered for DAT. (7)

The decision-making flowchart's (Figure 1) visual format makes it easier to use in standard clinical settings. By providing a quantitative tool that can be improved upon in future electronic decision-support systems, the scoring checklist (Figure 2) further improves accuracy.

Despite its innovation, this model has some limitations. It is derived from literature review synthesis and requires prospective validation in clinical settings. Future directions include integration of this framework into clinical trials testing effectiveness of timely and personalized DAT selection and creation of app-based decision support tools. (7)

Conclusion

This milestone-guided subtype-informed individualized framework offers a shift in management of advanced PD, moving from delayed and reactive escalation to timely, strategic intervention. By unifying phenotypic and clinical milestones with real world clinical guidance, our model looks forward to enhancing therapeutic precision, improving patient outcomes and streamlining decision making in complex PD care pathways. Future research on prospective validation of the milestone-based scoring system in clinical settings and integration of the algorithm into clinical decision support tools could enable real-time, personalized therapy selection during routine consultations.

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Supplementary Material:

Figure 1. Decision Making Framework for initiating DATs.

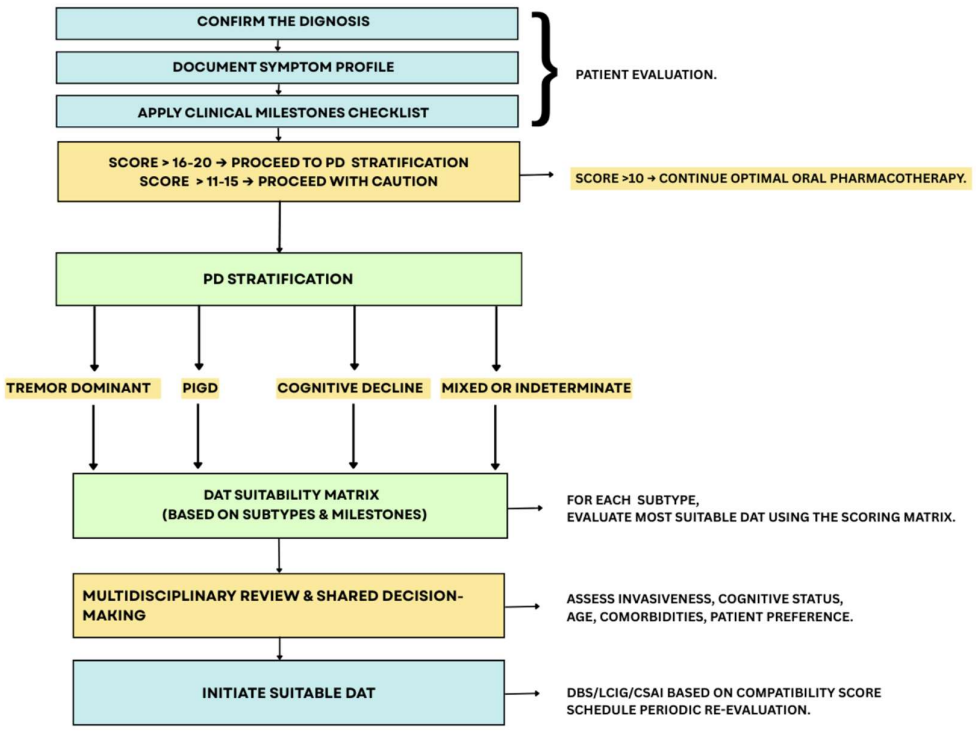

Figure 2. Scoring Checklist based on Clinical Milestones.

Milestone-Based DAT Scoring Matrix for Advanced PD Personalization

Patient Feature	Score Range	DBS score	LCIG SCORE	CSAI SCORE
Tremor Dominant Subtype	0–2			
PIGD Subtype	0–2			
Cognitive Impairment	0–2			
Age	<65 = 2, 65–75 = 1, >75 = 0			
Levodopa Responsiveness	Poor = 0, Mod = 1, Good = 2			
>2 Hours OFF Time Daily	No = 0, Yes = 2			
Refractory Dyskinesia	No = 0, Yes = 2			
Willingness for Invasive Treatment	No = 0, Yes = 1			
Frailty	Robust = 2, Mild = 1, Frail = 0			
Neuropsychiatric Burden (e.g. hallucinations)	Low = 2, Mod = 1, High = 0			

Total Score Interpretation for Each DAT:

Score Range	Interpretation
16–20	Strong candidate
11–15	Consider with caution
<10	Generally not suitable