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DEEP BRAIN STIMULATION WITHIN THE ADVANCED THERAPY PATHWAY FOR PARKINSON'S DISEASE: A STRUCTURED NARRATIVE REVIEW

Neurology

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ABSTRACT

Background: Deep brain stimulation (DBS) is a symptomatic therapy that is used with selected people with Parkinson's disease (PD), particularly those with levodopa-responsive motor complications, disabling dyskinesia or medication-refractory tremor. It is usually delivered together with medication and should be considered within an advanced-therapy pathway that also incorporates optimized medical therapy, levodopa-carbidopa intestinal gel (LCIG), continuous subcutaneous apomorphine infusion (CSAI), continuous subcutaneous foslevodopa-foscarbidopa and emerging sensing-enabled DBS.**Aim:** To synthesize contemporary evidence on DBS in advanced PD, with emphasis on candidate selection, target choice, device-aided alternatives, safety, adaptive DBS and multidisciplinary care.**Methods:** A structured narrative review was undertaken. English-language literature from January 2016 to 1 July 2026 was prioritized, while foundational pre-2016 trials and consensus papers were retained where clinically indispensable. Direct randomized and systematic-review evidence was attributed greatest significance; indirect network meta-analyses were used for pathway framing; and adaptive DBS studies were interpreted separately from mature conventional DBS evidence.Findings and **Conclusion:** The strongest evidence supports DBS plus optimized medical therapy over medical therapy alone for selected motor and PD-specific quality-of-life outcomes. Evidence against LCIG, CSAI and foslevodopa-foscarbidopa is less direct and should not be used to claim universal superiority. Treatment choice should be individualized around levodopa responsiveness, symptom priorities, cognitive and psychiatric risk, patient values, caregiver support, programming capacity and long-term multidisciplinary follow-up.

KEYWORDS

Parkinson's Disease; Deep Brain Stimulation; Device-aided Therapy; LCIG; Apomorphine Infusion; Foslevodopa-foscarbidopa; Adaptive Dbs; Multidisciplinary Care.

INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by bradykinesia, rigidity, tremor and postural instability, often presenting with non-motor manifestations including pain, fatigue, autonomic dysfunction, sleep disturbance, depression, anxiety and cognitive decline (Bloem et al., 2021). The global burden of neurological disease is on the rise, and PD contributes in a predominant way to disability, care dependence and health-system pressure (Steinmetz et al., 2024). Levodopa remains the central symptomatic treatment, but long-term use is frequently complicated by wearing-off, unpredictable motor fluctuations and levodopa-induced dyskinesias. When these complications persist (even when careful oral and transdermal optimization is employed), advanced therapies may be considered.

DBS involves stereotactic implantation of electrodes into targets such as the subthalamic nucleus (STN), globus pallidus internus (GPi) or, in narrower tremor-dominant cases, the ventral intermediate thalamic nucleus (VIM). It is a symptomatic intervention. While it can reduce tremors, rigidity, bradykinesia, OFF time and dyskinesia in selected patients, it needs to be made clear that it does not cure PD or stop neurodegeneration. The central question is therefore not whether DBS is simply better than medication. DBS is usually adjunctive to medication, and advanced PD pathways now include DBS, LCIG, CSAI and continuous subcutaneous foslevodopa-foscarbidopa (NICE, 2017/2024, 2023). A clinically useful review must ask how DBS should be positioned, which patients are likely to benefit, how target choice should be made, and how harms, expectations and follow-up capacity influence real-world outcomes.

Methods and evidence weighting

This article was conducted as a structured narrative review. Searches were structured around PubMed/MEDLINE, the Cochrane Library, guideline repositories and targeted backward/forward citation chaining from major trials, systematic reviews and consensus papers. The search window was 1 January 2016 to 1 July 2026. Foundational pre-2016 sources were retained where necessary to interpret efficacy, timing, target choice or neuropsychological safety. Search concepts combined Parkinson disease, deep brain stimulation, STN, GPi, VIM, best medical therapy, LCIG, CSAI, foslevodopa, foscarbidopa, adaptive DBS, closed-loop stimulation, PDQ-39, UPDRS/MDS-UPDRS, OFF time, dyskinesia, cognition, mood, adverse events, nursing and multidisciplinary care. SANRA informed the narrative-review approach, and PRISMA 2020/PRISMA-S informed transparency expectations, although this was not a registered systematic review and no new meta-analysis was undertaken (Baethge et al., 2019; Page et al., 2021; Rethlefsen et al., 2021).

Evidence was weighted hierarchically. Direct comparative randomized trials and systematic reviews were given greatest weight for efficacy claims. Head-to-head target-comparison studies and evidence-based guidelines were used for STN-GPi interpretation. Network meta-analyses informed pathway framing but not categorical superiority claims. Feasibility studies, biomarker papers and adaptive DBS reports were treated as exploratory or early implementation evidence. This distinction is important because conventional DBS, infusion therapies and adaptive DBS do not have the same evidential maturity.

Table 1. Evidence hierarchy used to calibrate claims

Tier	Study type	What it can support	What it cannot support alone
1	Direct RCTs; consistent systematic reviews; major guidelines	DBS plus best medical therapy improves selected motor and PD-specific quality-of-life outcomes versus medical therapy alone.	Superiority over all device-aided therapies.
2	STN-GPi trials and target-selection guidelines	Domain-specific target trade-offs: medication reduction, dyskinesia, cognition and mood.	A universal target hierarchy.
3	Network meta-analyses and indirect comparisons	Pathway framing across DBS, LCIG, CSAI and best medical therapy.	Definitive clinical ranking across all patients.
4	Feasibility, sensing and adaptive DBS studies	Plausibility, implementation lessons and future directions.	Equivalence to mature conventional DBS evidence.

DBS plus medical therapy

The strongest comparative claim is that, in carefully selected patients, DBS plus best medical therapy improves several motor and PD-specific quality-of-life outcomes more than had medical therapy to be administered alone. This rests primarily on direct randomized trial evidence. Deuschl et al. (2006), Weaver et al. (2009) and the PD SURG trial (Williams et al., 2010) all support benefit from DBS added to medical therapy, while also showing that surgery introduces adverse-event and follow-up burdens. EARLYSTIM extended the discussion by showing benefit in selected patients with earlier motor complications, but its results should not be merged uncritically with late-stage advanced PD cohorts (Schuepbach et al., 2013). Timing is a referral question, not merely a disease-duration threshold.

Recent review-level evidence reinforces DBS efficacy while also cautioning against overconfidence. Petersen et al. (2024) concluded that DBS may reduce several PD-specific symptoms but also pointed out methodological limitations and the need for careful harms assessment. The conclusion should therefore remain calibrated in the

sense that while DBS is likely to be effective for selected levodopa-responsive motor outcomes in selected patients, all the same, evidence strength varies by outcome, comparator, target, surgical era and follow-up duration.

Device-aided pharmacological alternatives

DBS should not be framed as a replacement for pharmacological therapy. Patients usually continue medication after implantation, although doses, timing and formulation may change. STN DBS may permit levodopa equivalent daily dose reduction, but rapid or excessive dopaminergic tapering can contribute to apathy, depression or dopamine-withdrawal phenomena., thereby having an adverse influence on patients' quality of life. GPi DBS may provide dyskinesia control while allowing more conservative medication adjustment.

Comparative advanced therapy literature is more indirect than the DBS-versus-medical-therapy literature. Network meta-analyses place DBS alongside LCIG, CSAI and best medical therapy and support DBS and LCIG as major options for OFF time and quality of life (Antonini et al., 2022; Rajan et al., 2022). However, indirect comparisons cannot establish universal superiority because populations, eligibility criteria and follow-up periods differ. LCIG may suit patients who prefer to avoid intracranial surgery or whose pathway can sustain pump management, but it carries PEG-J/tube, infection and caregiver burdens. CSAI can reduce OFF time in responders, but tolerability may be limited by infusion-site reactions, nausea, hypotension or neuropsychiatric vulnerability. Foslevodopa-foscarbidopa has expanded the continuous levodopa landscape. NICE positions it for selected adults with advanced levodopa-responsive PD when available medicines are insufficient and apomorphine or DBS cannot be used or no longer control symptoms (NICE, 2023). Its inclusion changes pathway choice, but it does not displace DBS evidence.

Table 2. Practical advanced-therapy comparison

Option	Main role	Key strengths	Main cautions
DBS-STN	Levodopa-responsive fluctuations, dyskinesia or tremors, especially where medication reduction is a goal.	Mature direct evidence versus best medical therapy; adjustable stimulation.	Surgical risk, programming burden, verbal fluency, mood/apathy and medication-withdrawal concerns.
DBS-GPi	Dyskinesia control or cases needing medication flexibility.	Robust dyskinesia suppression; may be preferable in some vulnerable neuropsychiatric profiles.	Same surgical pathway; usually less medication reduction than STN.
LCIG	Continuous levodopa delivery when surgery is unsuitable or not preferred.	Avoids intracranial surgery; can improve OFF time and QoL.	PEG-J/tube complications, infection, pump and caregiver burden.
CSAI	Selected OFF-period management in apomorphine responders.	Less invasive than DBS/LCIG.	Infusion-site reactions, nausea, hypotension, hallucinations and psychiatric caution.
Foslevodopa-foscarbidopa	Newer continuous subcutaneous levodopa pathway.	Avoids intracranial surgery and intestinal tubing.	Infusion-site reactions, access, cost and long-term comparative uncertainty.
Adaptive DBS	Emerging refinement of DBS in selected centres.	Potential personalisation using sensed signals.	Small samples, biomarker instability, artefacts and programming workload.

Candidate selection and target choice

Candidate selection is the central determinant of DBS outcome. Levodopa responsiveness remains important because DBS most reliably improves dopaminergic motor symptoms, but it is necessary rather than sufficient. Candidacy also depends on the disabling symptom profile, disease duration, age and frailty, cognitive profile, psychiatric stability, imaging suitability, surgical risk, caregiver support, ability to attend programming visits and realistic expectations (Bronstein et al., 2011; Hariz et al., 2022). Prominent levodopa-unresponsive gait freezing, falls in the best ON state, advanced dementia, unstable psychiatric illness, severe frailty or inability to engage with follow-up may reduce suitability.

STN and GPi are both established targets. Randomized target-comparison trials and guideline synthesis indicate broadly comparable motor improvement, but different trade-offs (Follett et al., 2010; Odekerken et al., 2013; Rughani et al., 2018). STN is often chosen when medication reduction and OFF-time control are central goals, while GPi may be favored when dyskinesia suppression, medication flexibility or cognitive/psychiatric vulnerability are prominent. VIM has a narrower role in medication-refractory tremors. Target choice should therefore be domain-specific and patient-specific rather than a universal STN-versus-GPi hierarchy (Lachenmayer et al., 2021).

Non-motor outcomes, safety and multidisciplinary care

DBS evaluation should not be motor-centric. Quality-of-life improvement does not follow automatically from motor improvement because cognition, mood, sleep, pain, autonomy, social participation, caregiver support and expectations also shape outcome. Systematic-review evidence suggests that quality of life after STN DBS is influenced by baseline motor and non-motor profiles, age and preoperative quality of life (Geraedts et al., 2020). Global cognition is often preserved in carefully selected patients without dementia, but verbal fluency and some executive or language domains may decline, especially after STN DBS (Bucur & Papagno, 2023; Witt et al., 2008). Mood outcomes are heterogeneous, and include apathy, depression, impulse-control changes and dopamine-withdrawal states that are likely to require active monitoring (Cartmill et al., 2021; Zoon et al., 2021).

DBS is generally safe in experienced centers but should not be described as low risk without qualification. Harms include peri-operative hemorrhage, infection, seizure or confusion; hardware migration, fracture, battery depletion or revision; programming-related dysarthria, paresthesia, gait worsening or dyskinesia; and neuropsychiatric complications in vulnerable patients. Consent should cover realistic benefits, alternatives, ongoing programming demands, medication adjustment, caregiver implications and the fact that disease progression may continue despite better motor fluctuation control.

The DBS pathway is multidisciplinary from referral to long-term review. Movement-disorder specialists, neurosurgeons, neuropsychologists, psychiatrists, specialist nurses, therapists and community teams all contribute to whether trial efficacy becomes patient-centered benefit. Nursing input is particularly important for expectation management, medication diaries, wound surveillance, infection awareness, medication reconciliation, recognition of mood/cognitive change and coordination of follow-up.

Adaptive DBS and implementation

Sensing- enabled and adaptive DBS are important recent developments, but they must be separated from mature conventional DBS evidence. Directional leads, rechargeable generators and sensing devices can support more individualized programming. Subthalamic beta activity is a plausible feedback signal, yet it is context-sensitive and not a universal surrogate for clinical benefit (Little & Brown, 2020; Neumann et al., 2023). Oehrn et al. (2024) reported a blinded randomized feasibility trial in four male patients showing improved motor symptoms and quality of life with personalized adaptive stimulation compared with clinically optimized conventional stimulation. This is a significant proof of concept, however it does not assert definitive superiority.

Commercial and regulatory movement has made adaptive DBS more practically relevant, while newer continuous infusion options have expanded non-surgical choice. Nevertheless, adaptive DBS remains lower-certainty evidence relative to conventional STN/GPi trials. Unresolved issues include patient selection, biomarker stability, artefact handling, programming workload, clinician training, cybersecurity, reimbursement and equitable access. Health-system interpretation should therefore compare full care pathways rather than devices alone: DBS requires functional neurosurgery and programming infrastructure; LCIG, CSAI and foslevodopa-

foscarbidopa require pump training, troubleshooting and community support; all require caregiver capacity and continuity of specialist care.

Limitations and conclusion

This review is a narrative review which does not provide duplicate screening, formal risk-of-bias tables, GRADE certainty ratings or new pooled estimates. Its conclusions should therefore be read as a structured, evidence-weighted narrative synthesis rather than a definitive comparative-effectiveness estimate. A final journal submission would be strengthened by rerunning database searches in the author's institutional environment, recording retrieval counts and exporting a complete search log.

The highest-certainty conclusion is that DBS plus optimized medical therapy has stronger direct comparative evidence than medical therapy alone for selected motor and PD-specific quality-of-life outcomes in carefully selected levodopa-responsive patients. That conclusion should not be extended to universal superiority over LCIG, CSAI or foslevodopa-foscarbidopa because cross-therapy evidence is often indirect and pathway-dependent. STN, GPi and VIM target choice should be individualized around medication goals, dyskinesia, cognition, mood, tremor dominance and local expertise. Adaptive DBS is promising and increasingly relevant, but remains developmental relative to conventional DBS. For clinicians, nurses, patients and families, the central task is shared decision-making grounded in realistic expectations, transparent risk discussion, neuropsychological and psychiatric screening, staged medication adjustment and long-term multidisciplinary follow-up.

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