



# Conceptualizing an economic model structure for Parkinson's Disease

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## Background

- Parkinson's Disease (PD) is a **progressive neurodegenerative disorder** with **motor and non-motor symptoms (NMS)** that substantially reduce health-related **quality of life (HRQoL)** and impose a **significant caregiver burden**.<sup>1</sup>
- While current treatments address PD symptoms, there is a substantial unmet need for **disease-modifying therapies (DMTs)** that can **slow progression and delay loss of independence**.
- A systematic literature review (2010 - 2022) of economic evaluations of PD treatments found 20 publications. The majority of them used the **Markov cohort structure** to assess the disease progression in terms of **motor symptoms** (e.g., using the Hoehn and Yahr (H&Y) scale and ‘OFF’ time) in patients with **advanced PD** from a narrow **payer perspective**. Such evaluations neglected the significant impact of NMS on costs and HRQoL for patients, family, and caregivers.<sup>2</sup>
- To capture the **economic value of a DMT, new modelling approaches are needed** that balance clinical relevance and transparency with credible long-term extrapolations while avoiding unnecessary complexity.

**Objective** To develop an evidence-based conceptual framework for a robust and holistic economic model capable of analysing the economic evaluation (EE) of DMTs for PD.

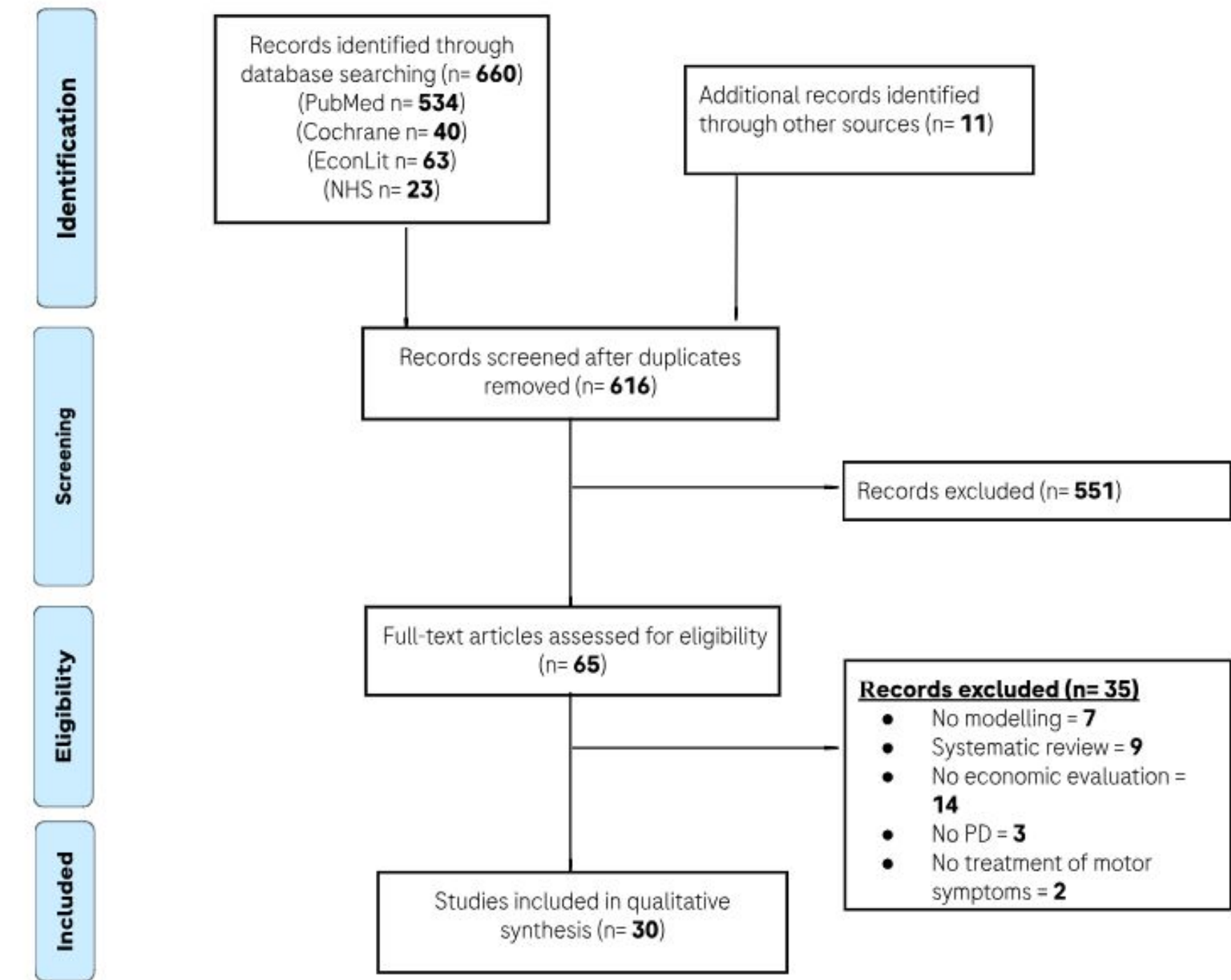
## Methods

### Systematic Literature Review (SLR) Update

We updated the Dams et al. (2023) systematic review of economic evaluations in PD using an artificial intelligence (AI)-assisted, human-in-the-loop protocol.

- **Databases:** Systematic searches were conducted across key databases (PubMed, EconLit, Cochrane, DARE, NHS EED, HTA) from July 2022 onward.
- **Supplementary searches:** Conference abstracts (Embase) were reviewed; bibliographic searches and searches using advanced keywords (PubMed, Google, Google Scholar) were also conducted.
- **Appraisal:** Studies were assessed for inclusion using the same PICOS criteria applied in the previous Dams (2023) SLR<sup>2</sup>. The quality of the included economic evaluations was critically appraised using Drummond's checklist.<sup>3</sup>

Figure 1: PRISMA flow diagram of included studies



Dams (2023)<sup>2</sup> + Current update  
NHS: National Health Service; PD: Parkinson's Disease; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

The resulting **key components and gaps for future holistic economic evaluations** were then reviewed and summarised.

## References

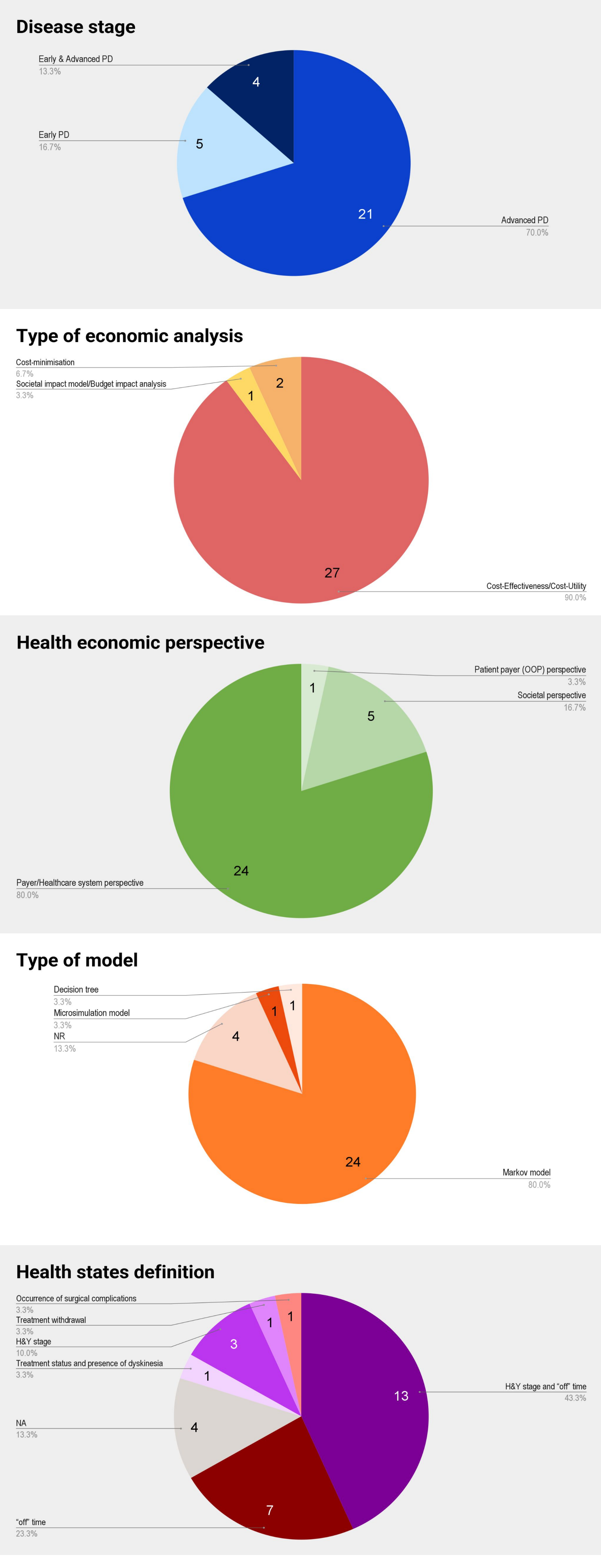
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## Acknowledgements

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## Results

The evidence base for this review comprised 30 economic evaluations. These evaluations were comprehensively reviewed for key insights, with 10 recent evaluations having been published between 2022 and 2025.<sup>2,5-15</sup>



Of the 30 studies, <sup>2, 5-15</sup> only four full economic evaluations (cost-effectiveness analysis and cost-utility analysis) and one partial economic evaluation (budget impact analysis) claimed a **societal perspective**. Even within these models, the perspective was consistently narrow, primarily including patient direct medical/non-medical costs and indirect costs (productivity losses) but omitting patient out-of-pocket costs and all caregiver costs and utilities/disutilities (see Table 2).

Table 2: Societal perspective elements in economic evaluations

Study (Year), Analysis type, Country	Patient				Caregivers		
	Direct costs (medical and non-medical)	Out of pocket costs (OOP)*	Indirect costs**	Utilities	Direct costs (OOP)*	Indirect costs**	Utilities
Groenendaal (2010), USA, Cost-Effectiveness/Cost-Utility	✓	✗	✓	✓	✗	✗	✗
Fann (2020), Taiwan, Cost-Effectiveness/Cost-Utility	✓	✗	✓	✓	✗	✗	✗
Verschuur (2022), The Netherlands, Cost-Effectiveness/Cost-Utility	✓	✓	✓	✓	✗	✗	✗
Chaudhuri (2024), UK, Societal impact model / Budget impact analysis	✓	✓	✓	NR***	✓	✗	✗
Nyholm (2025), Sweden, Cost-Utility	✓	✗	✓	✓	✓	✗	✗

✓ Included ✗ Not included

\*Out of pocket costs: travel, accommodation, etc. \*\* Indirect costs: for patient consider productivity loss due to illness (paid and unpaid work), while indirect costs of caregivers derived from informal care time/productivity loss. \*\*\*Not Reported: The societal impact model does not include utilities.

### Non-Motor Symptoms: A Critical Gap in Existing EEs of PD

- Existing models severely **under-represent NMS** (e.g., cognitive, mood, sleep, urinary dysfunction, constipation, pain, and fatigue), despite these being core drivers of QoL burden and overall cost. <sup>4,16</sup>
- Models primarily rely on H&Y stages, which fail to capture NMS explicitly. Furthermore, even incorporating ‘OFF’ time captures only incomplete, indirect NMS effects via increased cost.
- Many models rely on broad disutilities, leaving sleep, fatigue, mood, and cognition only partially captured. <sup>7,13,14</sup>

### Limitations Still Presented in Recent EEs of PD

- Over-reliance on **traditional models** (e.g., Markov structures) which struggle to capture complex PD dynamics.
- Failure to account for **all relevant costs**, especially non-hospital costs such as caregiver time/support and long-term care/nursing home costs.
- Persistent issues with **data quality**, including a lack of robust long-term clinical trial data, the use of historical/inconsistent data sources, and the absence of head-to-head evidence for comparators.
- Failure to account for **patient heterogeneity** or the true extent of **loss of productivity**.
- Use of **simplifying assumptions**, which affects the **generalisability of inputs** and leads to reliance on hypothetical effects or results requiring further validation.

## Discussion & Conclusion

Based on recent findings, we propose a new conceptual framework that addresses **five critical aspects** to deliver robust and reliable economic evaluations in PD:

**Acknowledge Full Disease Progression**

- Model the full disease continuum, from diagnosis to late stage.
- Recognize patient heterogeneity.
- Incorporate realistic discontinuation and switching patterns.

**Holistic Outcomes**  
(QoL impacts, patient-centered outcomes, incorporate both motor and NMS)

- Include objective measures (e.g., MDS-UPDRS).
- Account for the impact of NMS on utilities and costs for a comprehensive value assessment, especially for DMTs.

**Societal Perspective**

- Account for patient and caregiver costs and utilities, including out-of-pocket (OOP) expenses, productivity impacts (paid/unpaid work), and health spillover effects.

**Treatment Effect Separation**

- Model symptom control separately from progression to accurately assess DMTs.
- Test plausible effect-waning scenarios over short, medium, and long-term horizons.

**Enhance Credibility by Developing a Comprehensive and Simple Model**

- Design a simple, validated model that permits sensitivity analysis.
- Incorporate institutional care costs (e.g., nursing, home help, respite, equipment) and include all active comparators based on local guidelines.
- Conduct expert validation to ensure both clinical and economic credibility.

## Future Challenges

The complexity of PD presents inherent modeling challenges:

- The need for face validity requires simplification of the highly heterogeneous PD progression.
- Robust data collection for model parameterization, especially across all NMS, remains a major source of uncertainty.
- While a societal perspective was recommended, additional elements like equity, health system capacity, environmental impacts of health technology, and gross domestic product (GDP) impacts were not fully integrated.

**Next Steps:** The proposed framework requires expert validation to ensure both its clinical and economic credibility.