Parkinson's disease

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Date: December 9th, 2021

Model assumptions

Table 1: Summary of model parameters and values used for management of Parkinsons's disease in FairChoices – DCP Analytics Tool

Population:	All prevalent cases of parkinson, both genders, all ages (Dw=0.15 in average untreated)
Intervention	– Diagnostics of Parkinson's disease – Drug treatment – Physical therapy, basic – Physical therapy, extensive
Comparator	No intervention
Outcome	Disability weight (health related quality of life)
Effect	– Diagnostics of Parkinson's disease: 0% effect – Drug treatment: 70% reduction of disability or improvement of HRQoL – Physical therapy, basic: 5% reduction of disability or improvement of HRQoL – Physical therapy, extensive: 10% reduction of disability or improvement of HRQoL
Unit cost**	Diagnostics: 2.1 US$ LIC; 5.9 US$ LMIC Drugs: 82.7 US$ LIC; 88.2 US$ LMIC Physical therapy, basic: 1.9 US$ LIC; 5.8 US$ LMIC Physical therapy, extensive: 5.6 US$ LIC; 17.4 US$ LMIC

HRQoL= Health Related Quality of Life

** Annual cost per treated patient, 2021 currency, see cost assumptions and calculations below

Description of condition and intervention

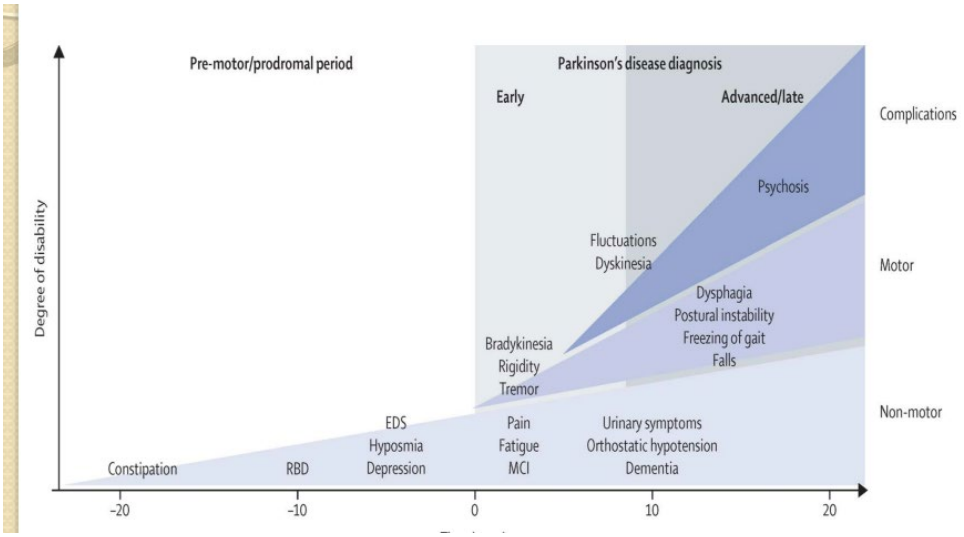
The management of Parkinson's disease, including drug treatment, surgery and physiotherapy.

Intervention Parkinson 1	Parkinson's drug treatment (levodopa/carbidopa)
Intervention Parkinson 2	Parkinson's disease surgery (pallidotomy, thalamotomy, DBS)
Intervention Parkinson 3	Physical therapy for Parkinson's patients

About Parkinson's disease

Parkinson's disease is a neurodegenerative disease that presents in motor symptoms such as tremor, rigitidy of the muscles, bradykinesia (slowness or absence of spontaneous movements) or gait- and balance problems. Because of the many motor symptoms affected, Parkinson's disease is categorized as a movement disorder. Although the pathways of developing Parkinson's disease are not yet clear, and many origins are plausible, the result is a degenerative process in the basal ganglia of the brain, called the substantia nigra, responsible for dopamine production. Therefore, Parkinson's disease is resulting in reduced dopamine levels, that affect and impair movement (neuro in Africa). The onset of Parkinson's disease occurs most often around 60 years of age, and deterioration is slow, on average around 10/15 years.

Development of Parkinson's disease: Kalia et al., 2015 (the lancet)



Diagnosis

Parkinson's disease is frequently underdiagnosed. Diagnosis of Parkinson's disease is often based on the clinical presentation of symptoms, as MRI or lumbar punctions or other type of biomarkers are not always an option in low-and low-middle income countries. Clinical tests such as the Movement Disorder Society – Unified Parkinson's Disease Rating Scale can be used to assess symptoms. The MDS-UPDRS is a test that consists of 4 parts: 1. Mentation, Behavior, and Mood 2. Activities of daily life 3. motor symptoms 4. Modified Hoehn and Yahr Scale, and 5) Schwab and England ADL scale. The maximum score of 199 indicating the worst score on all segments, the minimum score is 0. For physiotherapy, part 3: motor symptoms is the most important subscale, with a maximum of 132 points.

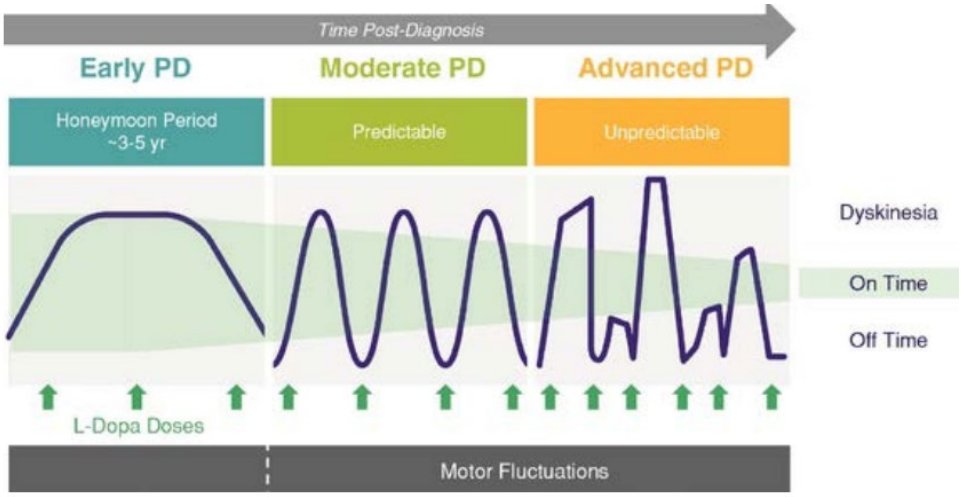
In cases where tremor presents as the main symptom, Parkinson's disease is relatively easily recognizable. However, there is a treatment gap for Parkinson's disease, as it is not always recognized in the community

due to a lack of awareness. Parkinson's disease is highly associated with witchcraft or stigma, and often treatment is sought with natural healers, maintaining the treatment gap. Further issues are the lack of resources, funding and adequately trained health personnel.

Treatment of Parkinson's disease

Parkinson's disease can be managed with drugs that aim improve movement, for example by substituting the body's dopamine deficiency with Levodopa. Parkinson's disease can be treated by dopamine agonists, as well as levodopa. The golden standard in drug therapy is combining levodopa with carbidopa. Levodopa is converted to dopamine in the brain, whereas carbidopa prevents the breakdown of levodopa in the body, resulting in a higher concentration of levodopa in the brain. Within the early phase of the disease, between 0-5 years after diagnosis, around 70% of patients start up with a dopamine agonist or levodopa, and after 5-8 years all Parkinson's patients require drug treatment.

However, no effective treatment is available that can halt the progression of Parkinson's disease. Despite the initial positive effectivity of drug treatment on Parkinson's disease (the so-called honeymoon phase), due to the progressive nature of the disease, effectivity of the drugs is reducing over time. This is also defined as the OFF-state, the state in which medication wears-off. Over time, Parkinson's patients spend more time in an OFF-state. Furthermore, drug treatment needs to be revised often due to the side effects. Side effects of the medication include nausea, excessive movements (dyskinesia), and hallucinations.



It is possible to perform surgery on patients that suffer from Parkinson's disease to treat the symptoms associated with the disease, particularly the motor symptoms associated with the disease. This is often done as a last possible option, when the effects of drug therapy are reduced. Three types of surgery are available out of which deep brain stimulation (DBS) is the most used, where electrodes are inserted in the brain (subthalamic nucleus, globus pallidus or the thalamus) in order to send out electrical pulses that help the connections in the brain (Bratsos et al., 2018.

More accessible is physiotherapy. A meta-analysis provides evidence that different types of physiotherapy and physical activity can reduce motor symptoms, balance and improve gait and quality of life in Parkinson's disease patients. Physiotherapy consequently can lead to a reduction on the MDS-UPDRS part 3: motor symptoms. (Radder et al., 2020). However, due to the progressive nature of Parkinson's disease, the efficacy of physiotherapy goes down when the Hoehn and Yahr score goes up. Despite learning the tools that patients can apply themselves, over time the effects of physiotherapy decline.

Socio-economic burden of Parkinson's disease in LLMICs

As the number of Parkinson's patients is rising, so are the socio-economic costs and burden (see table 1) accompanied with the disease. Parkinson's patients retire early due to their symptoms, resulting in a loss in productivity both for the individuals and society. Furthermore, as the disease can result in high disability and premature death, caregivers play an important role, causing loss of production in this group as well. In the USA alone, the indirect costs of Parkinson's disease add up to $26,5 billion in 2017, a number that will only go up as the prevalence goes up (Levin Group, 2019).

Table 1: Baseline characteristics of Parkinson's disease (source: GBD results tool 2019)

Mortality (number of estimated annual deaths) Globally Low SDI socio-demographic index (SDI) Low-middle socio-demographic index (SDI) Easter sub-Saharan Africa	 363 000 211 000 23 000 4 000 4 600
DALYs lost annually Globally Eastern sub-Saharan Africa	 3.2 million 6,292,616
Prevalence (global) Prevalence (Eastern sub-Saharan Africa)	8,511,022 77,829
Incidence (global) Incidence (Eastern sub-Saharan Africa)	1,081,723 10,664

***SDI** is a summary measure that identifies where countries or other geographic areas sit on the spectrum of development. Expressed on a scale of 0 to 1, SDI is a composite average of the rankings of the incomes per capita, average educational attainment, and fertility rates of all areas in the GBD study. [source IHME, GBD]*

International guidelines for Parkinson's disease

Organization	Guidelines for Parkinson's disease	Applicability in LIC & Lower MIC settings
Royal College of Physicians: National Collaborating Centre for Chronic Conditions (UK)	Parkinson's Disease: National Clinical Guideline for Diagnosis and Management in Primary and Secondary Care. London: Royal College of Physicians (UK); 2006. PMID: 21089238.	Limited
International Parkinson and Movement Disorder Society	Update on Treatments for Nonmotor Symptoms of Parkinson's Disease—An Evidence-Based Medicine Review (2019)	Limited
International Parkinson and Movement Disorder Society	Evidence-Based Medicine Review: Update on Treatments for the Motor Symptoms of Parkinson's Disease (2018)	Limited

Intervention attributes

Type of interventions

Chronic management care

Delivery platform

Hospital level.

Equity

In addition to considerations like cost-effectiveness and health systems factors, dimensions of equity can be relevant for priority setting. The opportunity for a long and healthy life varies according to the severity of a health condition that individuals might have, so there are inequities in individuals' opportunities for long and healthy lives based on the health conditions they face. Metrics used to estimate the severity of illness at an individual level can be used to help prioritize those with less opportunity for lifetime health. FairChoices: DCP Analytics Tool uses Health adjusted age of death (HAAD), which is a metric that estimates the number of years lived from birth to death, discounting years lived with disability. A high HAAD thus represents a disease less severe in terms of lifetime health loss, while a low HAAD represents a disease that is severe on average, causing early death or a long period of severe disability. It is also possible to estimate the distribution of HAAD across individuals with a health condition. FairChoices shows for each intervention an average HAAD value of the conditions that are affected by respective interventions that have health effects. Additionally, a plot shows HAAD values for around 290 conditions (Johansson KA et al 2020).

Time dependence

Moderate level of urgency and treatment outcomes will not be highly affected by some days of delay.

Population in need of interventions

All individuals diagnosed with Parkinson's disease.

Disease stage addressed

Disease stage is assumed to be post-diagnosis in order estimate adequate disease management. *Disability weights (Salomon et al, 2015):* Mild 0.010; Moderate 0.267; Severe 0.575.

Intervention effectiveness and safety

See description of condition and intervention for more information regarding the interventions included in this evidence brief.

Model assumptions

Table 2: Summary of model parameters and values used in FairChoices – DCP Analytical Tool

Category	Model parameter	Notes
Treated population	All	
Gender	Both	
Age		

	All ages	
Affected Population	Prevalent cases	
Baseline disability	Mild: 0.010 Moderate 0.267 Severe 0.575	
Mortality Reduction (RRR)	Not applicable	
Disability Reduction (RRR) Drug therapy(Levodopa, Carbidopa, Selegiline, Ropinirole, Rotigotine)	50-80%	Based on 10 years, Zhuo et al., 2017
Levodopa/carbidopa (Sinemet)	Mild (0-5 years): 80% effective Moderate (5-9 years): 30% effective Severe (9+ years): 8% effective	Based on expert opinion. Years after diagnosis.
Prevalence according to state	Mild: 100/(100+95+80) = 0.36 Moderate: 95/(100+95+80) = 0.35 Severe: 80/(100+95+80) = 0.29	Assume 5% die in the first 5 years (~baseline mortality in mild period). Assume 15% die in the next 4 years (moderate period) Assume 80% die later (severe period)
Disability Reduction (reduction of total UPDRS scores) Surgery (DBS) Disability reduction (reduction of UPDRS part 3. Motor symptoms) Surgery (DBS) in ON-phase Disability reduction (reduction of UPDRS part 3. Motor symptoms) Surgery (DBS) in OFF-phase	-5.14 (-6.18, -4.10); P < 0.00001) SMD 1.63 (95% CI: 0.28–2.98) SMD 3.43 (95% CI: 0.04–6.89, p < 0.01)	Compared to best medical therapy, reduction on UPDRS total score. Bratsos et al., 2018 Mao et al., 2019 Mao et al., 2019
Disability Reduction (measure?) Physiotherapy	(MDS)-UPDRS (n = 26; SMD 0.48, 95% CI 0.35 to 0.60, P < .001)	Radder et al., 2020
Prevalence Reduction (RRR)	Not applicable	
Incidence Reduction	Not applicable	
Fertility Reduction	Not applicable	

A study assessing the minimal clinical important differences (CID) on the UPDRS scores indicate the following scores (Horváth et al, 2015):
Improvement: −3.25 points minimal, but clinically significant decrease in UPDRS scores
Worsening: - 4.63 points minimal, but clinically significant increase in UPDRS scores.

Non health benefits:

- Treatment of motor symptoms can lead to less stigmatization as the disease symptoms are not that obvious
- Increased productivity in work or school work, impacting the whole family and society
- Diagnosis can lead to more awareness of the disease and result in more social participation
- Treatment of Parkinson's disease can remain a patient's independence in ADL, depending less on their family as well as the health care system.

Need for future research

Long term-controlled design studies with sufficient power and follow-up period needed to estimate the effects of management on mortality and morbidity, disability, incidence/prevalence of Parkinson's disease in LLMICs.

Intervention Cost

The cost of the self-managed treatment of Parkinson's disease primarily focuses on the drug costs, however costing of the full intervention is disaggregated into human resource costs, and drugs/supply costs. Costing for drugs is based on Levodopa/Carbidopa, 4x daily. The dosage of Levodopa/Carbidopa varies widely throughout the disease progress and from individual to individual. The first phase, a lower dosage is used (on average around 200mg) and can be maximized until 1000 mg in a later phase. Costing for the surgery intervention is not plotted, as currently there are no neurosurgeons that can perform this surgery. The costs for a deep brain stimulation in India are estimated between $10.000 to 20.000. The costs for physical therapy are based on the HR costs for physical therapists in a LIC/LMIC setting.

Human resource unit cost

The time that should be spent per health professional per patient suffering from Parkinson's disease can be found in Table 3. The salaries of the health care workers can be found in table 4. The costs per minute for LIC are averaged between the salaries of Ethiopian health workers and Malawian health workers. The salaries for Zanzibar are not included as no information source was found.

Table 3: Human resource component for treatment of Parkinson`s disease patients (anually)

Human resources	Number of outpatient visits	Number of minutes per visit	Total minutes
Diagnosis			
Neurologist	1	30	30
Nurse	1	10	10
Drug treatment			
Neurologist	4	10	40
Nurse	4	15	60
Surgery			
Physical therapy (basic)	2	30	60
Physical therapy (extensive)	6	30	180

Table 4: Salaries health care personell LIC / LMIC settings

	Cost per minute Ethiopia	Cost per minute Malawi	Cost per minute Tanzania	Cost per minute Zanzibar	Cost per minute LIC (average)	Cost per minute LMIC (Tanzania)
Neurologist	0,060	0,064	0,178	unreliable	0,062	0,178
Pharmacists	0,024	0,028	0,070	unreliable	0,026	0,070
Medical doctor	0,047	0,044	0,131	unreliable	0,045	0,131
Nurse	0,019	0,020	0,054	unreliable	0,020	0,054
Community health worker	0,014	0,005	0,020	unreliable	0,010	0,020
Physical therapist	0,029	0,033	0,097	unreliable	0,031	0,097
Clinical health officer	0,014	0,016	0,038	unreliable	0,015	0,038

Drug and supply unit cost

Table 5: Drug/supply component for levodopa

Drug/Supply	Number of units	Times per day	Days per case	Units per case	Drug/supply unit cost (in US$)	Costs per case (in US$)
Levodopa/carbidopa (100mg/25mg)	1	4	365	1460	0,0546	79,72

Table 6: Total unit costs

	Total HR Costs LIC(in US$)	Total HR Costs LMIC (in US$)	Total drug costs	Other costs	Total costs LIC	Total costs LMIC
Diagnosis	2,06	5,87	n/a	n/a	2,06	5,87
Drug treatment	2,98	8,49	79,72	n/a	82,7	88,2
Physical therapy basic	1,85	5,8	n/a	n/a	1,85	5,8
Physical therapy extensive	5,56	17,39	n/a	n/a	5,56	17,39

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