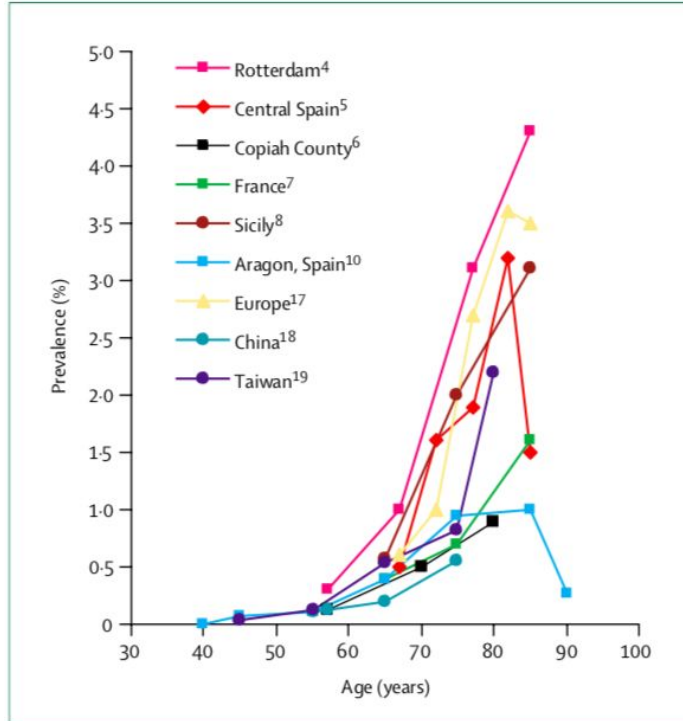# Early Diagnosis of Parkinson's Disease

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15.11.2022

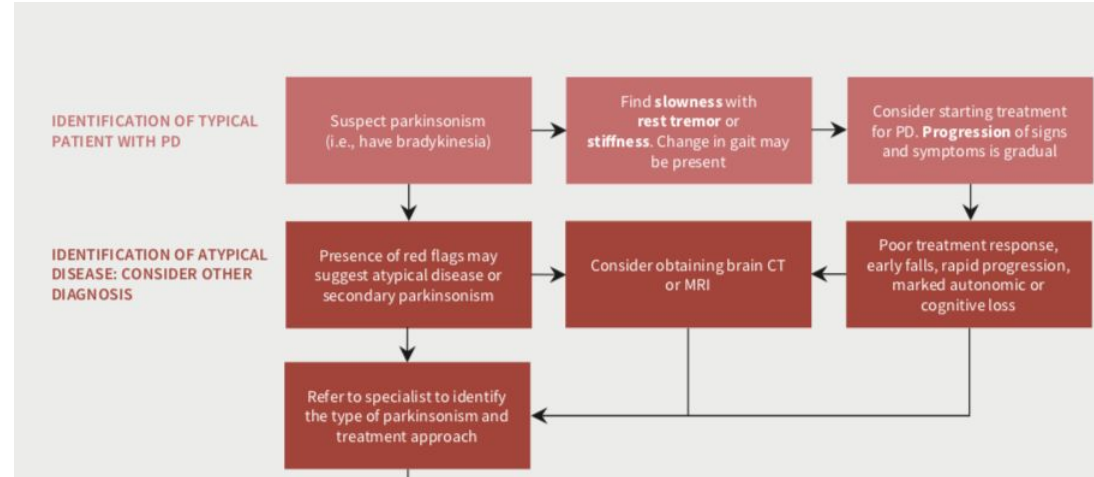# Parkinson Disease

ICD-10 Version:2019: G20

Incidence & Prevalence

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[1] de Lau LM, Breteler MM. Epidemiology of Parkinson's disease. Lancet Neurol. 2006 Jun;5(6):525-35. doi: 10.1016/S1474-4422(06)70471-9. PMID: 16713924.

Diagnostics

Parkinson disease should be suspected in people presenting with tremor, stiffness, slowness, balance problems or gait disorders

Parkinson disease can be diagnosed using the **Movement Disorder Society Clinical Diagnostic Criteria**

IDENTIFICATION OF TYPICAL PATIENT WITH PD — Suspect parkinsonism (i.e., have bradykinesia) → Find **slowness** with **rest tremor** or **stiffness**. Change in gait may be present → Consider starting treatment for PD. **Progression** of signs and symptoms is gradual

IDENTIFICATION OF ATYPICAL DISEASE: CONSIDER OTHER DIAGNOSIS — Presence of red flags may suggest atypical disease or secondary parkinsonism → Consider obtaining brain CT or MRI ← Poor treatment response, early falls, rapid progression, marked autonomic or cognitive loss

Refer to specialist to identify the type of parkinsonism and treatment approach

[2] Grimes D, Fitzpatrick M, Gordon J, Miyasaki J, Fon EA, Schlossmacher M, Suchowersky O, Rajput A, Lafontaine AL, Mestre T, Appel-Cresswell S, Kalia SK, Schoffer K, Zurowski M, Postuma RB, Udow S, Fox S, Barbeau P, Hutton B. Canadian guideline for Parkinson disease. CMAJ. 2019 Sep 9;191(36):E989-E1004. doi: 10.1503/cmaj.181504. PMID: 31501181; PMCID: PMC6733687.

PROBLEM STATEMENT

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Context	**Problem**	**Alternatives**
PD is difficult to diagnose on early stages due to - global inequality in the availability of neurological resources - incorrect perceptions that the decline associated with PD is part of "normal" ageing	PD is diagnosed on late stages when treatment is less efficient PD resulted in 5.8 million disability-adjusted life years, an increase of 81% since 2000, and caused 329,000 deaths, an increase of over 100% since 2000	Telemedicine sharing of videotaped neurological examinations, is a flexible option and is effective for consulting experts elsewhere and for improving local diagnostic skills
Customers People 40-65yo Conscious about their future (or their relatives) Don't have access/time for regular medical check ups	**Emotional impact** Customers will fill validated for their possible struggles and less anxious about their future **Quantifiable impact** Telemedicine studies showed saved costs (up to $370), travel time (up to 3 hours), travel kilometers per patient (up to 160km)	**Alternative shortcomings** Telemedicine requires internet access, video-calls can be unfamiliar environment for patient, examination cost

3

[1] Shalash A, Spindler M, Cubo E. Global Perspective on Telemedicine for Parkinson's Disease. J Parkinsons Dis. 2021;11(s1):S11-S18. doi: 10.3233/JPD-202411. PMID: 33579872; PMCID: PMC8385495.

Mechanism Of Action (MOA)

78% of early untreated PD subjects indicate some form of vocal impairment. [1]

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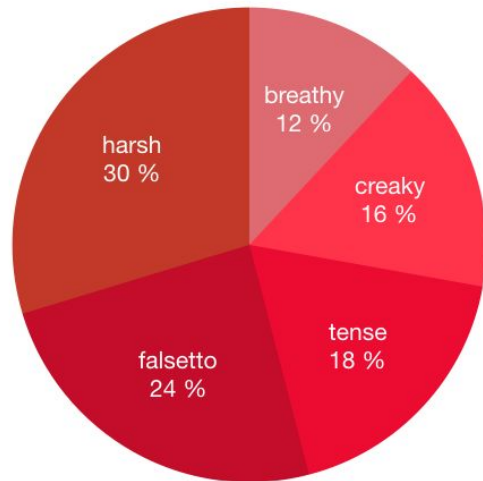
Composition voice quality in Parkinson's speech [2]

Relative characteristics of symptomatic biomarkers [3]

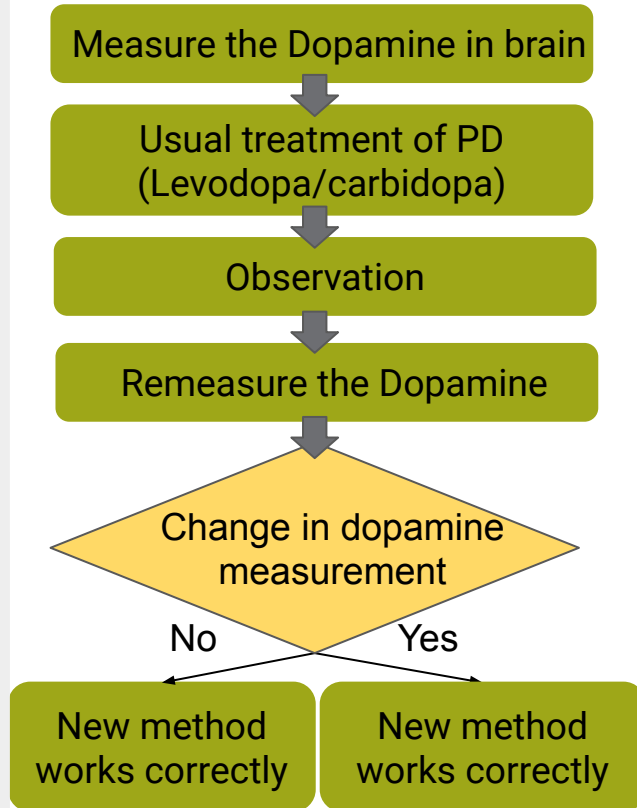|	Sensitivity	Specificity
Rapid eye movement sleep behavior disorder	Low (~50% of PD patients occur RBD in 2 years)	High (76% risk of PD at 10 years)
Olfactory dysfunction	High (>80% of early PD)	Low
Voice	High (65-98.35% according to ~30 papers)	High (67-91.06% according to ~30 papers)

Voice impairment has high both sensitivity and specificity, it's the optimal choice between other early symptomatic biomarkers [1].

[1] J. Rusz, R. Cmejla, H. Ruzickova, E. Ruzicka, Quantitative acoustic measurements for characterization of speech and voice disorders in early untreated Parkinson's disease, J. Acoust. Soc. Am. 129 (1) (2011) 350–367.
[2] Cernak, Milos, et al. "Characterisation of voice quality of Parkinson's disease using differential phonological posterior features." Computer Speech & Language 46 (2017): 196-208.
[3] Ngo QC, Motin MA, Pah ND, Drotár P, Kempster P, Kumar D. Computerized analysis of speech and voice for Parkinson's disease: A systematic review. Comput Methods Programs Biomed. 2022 Nov;226:107133. doi: 10.1016/j.cmpb.2022.107133. Epub 2022 Sep 16. PMID: 36183641..

Proof Of Concept (POC)

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```
┌─────────────────────────────────┐
│  Measure the Dopamine in brain  │
└─────────────────────────────────┘
              ↓
┌─────────────────────────────────┐
│     Usual treatment of PD       │
│     (Levodopa/carbidopa)        │
└─────────────────────────────────┘
              ↓
┌─────────────────────────────────┐
│          Observation            │
└─────────────────────────────────┘
              ↓
┌─────────────────────────────────┐
│     Remeasure the Dopamine      │
└─────────────────────────────────┘
              ↓
        ◇ Change in dopamine
          measurement ◇
         No ╱        ╲ Yes
┌──────────────────┐ ┌──────────────────┐
│   New method     │ │   New method     │
│ works correctly  │ │ works correctly  │
└──────────────────┘ └──────────────────┘
```

More than **90% of PD patients have voice impairments**.

Eliminate the **unwanted features** in voice using **chi-square method**.

We train NN and **test** it on patients diagnosed with PD **in different stages** (late, mid, early).

Using machine learning methods, we compare the voice quality of PD patients and a healthy persons of the same age and gender.

The chosen difference get more easily detected the latest the stage is.

People with **Late stage** of PD → People with **mid stage** of PD → People with **early stage** of PD
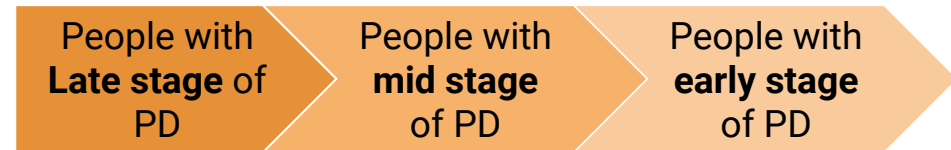
[1] Ali, Liaqat, et al. "Early diagnosis of Parkinson's disease from multiple voice recordings by simultaneous sample and feature selection." *Expert Systems with Applications* 137 (2019): 22-28.
[2] https://www.who.int/news-room/fact-sheets/detail/parkinson-disease#:~:text=Parkinson%20disease%20(PD)%20is%20a,and%20pain%20and%20sensory%20disturbances

Quality Control (QC)

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Old way
Go to a doctor wasting money and time with accuracy 74%
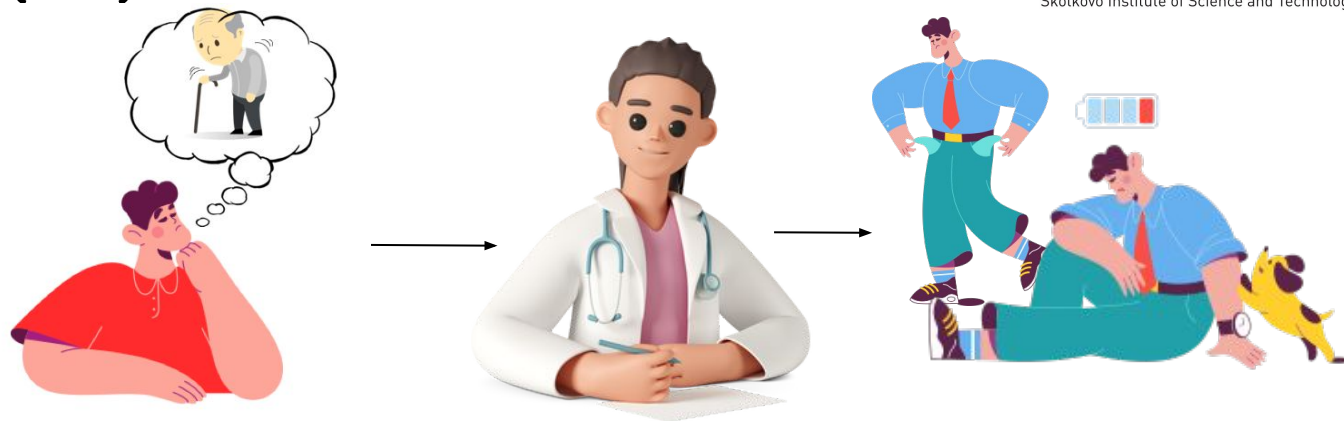
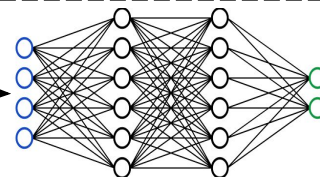**New way**
Use smartphone to diagnose PD with accuracy 93.84%

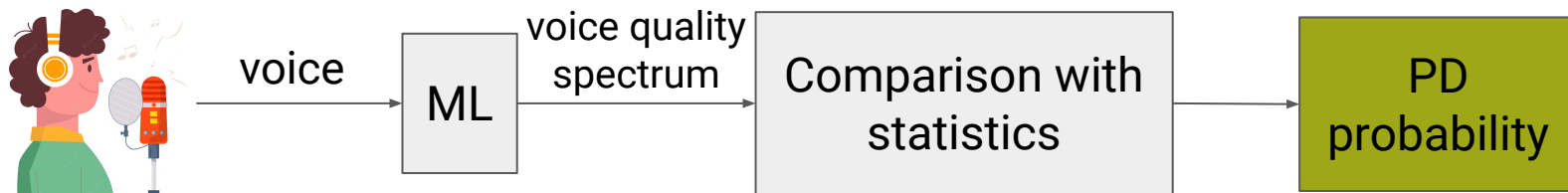Features Extraction → Voice features → Elimination of irrelevant features → Filtered features → NN with Accuracy 93.84% → Possibility of PD

[1] Tolosa, Eduardo, Gregor Wenning, and Werner Poewe. "The diagnosis of Parkinson's disease." *The Lancet Neurology* 5.1 (2006): 75-86.
[2] Senturk, Zehra Karapinar. "Early diagnosis of Parkinson's disease using machine learning algorithms." *Medical hypotheses* 138 (2020): 109603.
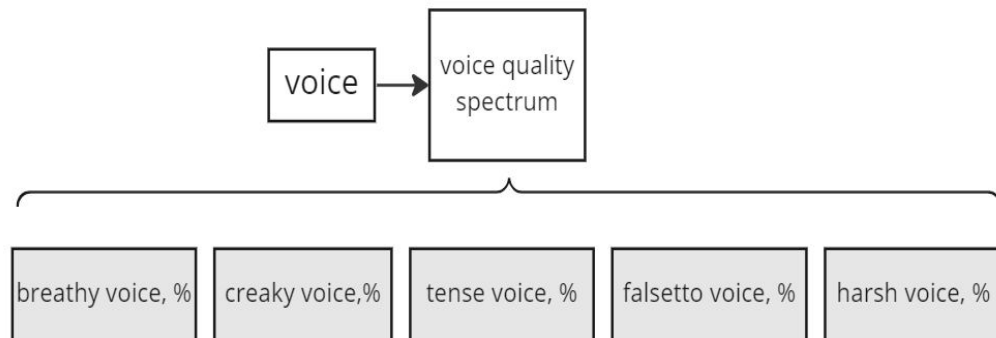
Experiment Design

Experiment:

The algorithm of detecting PD in voice works on both genders accuracy above 94% with a slight difference.

volunteers:

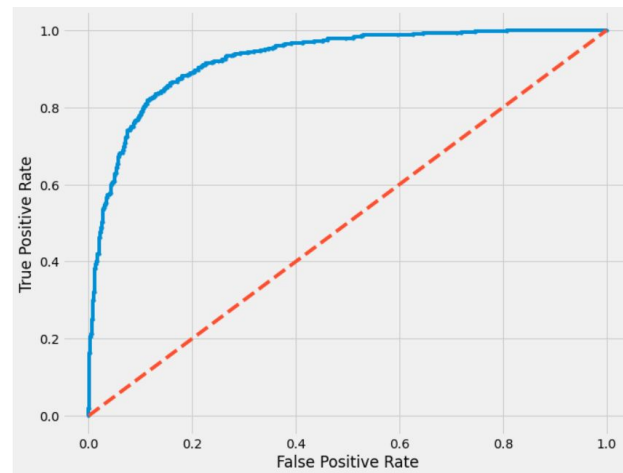|	PD	Healthy
Total	113	200
Male/Fem	54% - 46%	66% -34%
Before/After 60 yo	32% - 68%	57% - 43%
Early - mid - late PD stage	16% - 24% - 60%	...

Data set:

[1] Ngo, Quoc Cuong, et al. "Computerized analysis of speech and voice for Parkinson's disease: A systematic review." *Computer Methods and Programs in Biomedicine* (2022): 107133.
[2] Solana-Lavalle, Gabriel, and Roberto Rosas-Romero. "Analysis of voice as an assisting tool for detection of Parkinson's disease and its subsequent clinical interpretation." *Biomedical Signal Processing and Control* 66 (2021): 102415.

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Experiment Results

Male

Actual state — Health / Sick

	Health	Sick
Health	128	4
Sick	1	60

Predicted state

Female

	Health	Sick
Health	163	5
Sick	1	51

Predicted state

ROC-AUC curve

- Comparably same performance for male/female
- High roc-auc score = 0.96
- Low 1^{st}/ 2^{nd} type errors = 0.03 / 0.02
- The later the better prediction
- Probability get right diagnosis statistically higher than for average docktor, p-value = 0.006
- We estimate our product will save > 2000 lives and 2 billions $ every year

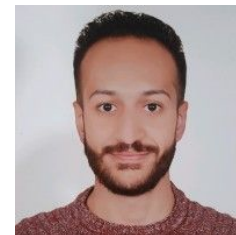| Stage	1^{st}-type error	2^{nd}-type error
Early	0.04	0.02
Mid	0.02	0.01
Late	0.01	0.01

Team Role

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Belukhina Svetlana

Life Science MOA+POC

Oussama Alyounes

SES, QC and patent

Kovalev Vyacheslav

Manuf + QC

Telepov Alexander

DS, Preclin+Reg+Clin