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Gender Disparity of Dyskinesia in Patients with Parkinson's Disease: Deep Learning Text Classification Applied to the AAN Axon Registry®

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The Axon Registry® is an initiative of the American Academy of Neurology ("AAN"). There are limitations of the Axon Registry data.[3]

The views expressed in this abstract represent those of the authors and do not necessarily represent the official views of the AAN.

[3] Baca, C. M., Ranish, S., Vidovszky, A., Lundgren, K., Maglioccо, B., Schierman, B., Palmer, L., & Jones, L. K., Jr (2019). Axon Registry® data validation: Accuracy

Gender differences in iPD presentation

- The incidence of idiopathic Parkinson's Disease (iPD) is twice as high in men, but women have a higher mortality rate and faster progression.[1]
- Progression of iPD is associated with decreased effectiveness of dopaminergic therapies and complications of these therapies such as dyskinesia.
- In particular, previous studies have found that women have increased risk of dyskinesia and develop dyskinesia in a shorter time frame compared to men. [2, 3]
- Yet, most research studies in iPD have been skewed towards educated white men.
- Of studies focused on examining gender differences in the development of dyskinesia, many are cohort-studies that leverage scores on the Unified Parkinson's Disease Rating Scale (UPDRS), but the UPDRS is not commonly administered at every neurology visit. [3, 4]

[1] Cerri, S., Mus, L., & Blandini, F. (2019). Parkinson's Disease in Women and Men: What's the Difference?. Journal of Parkinson's Disease, 9(3), 501–515.
[2] Hassin-Baer, S., Molchadski, I., Cohen, O. S., Nitzan, Z., Efrati, L., Tunkel, O., Kozlova, E., & Korczyn, A. D. (2011). Gender effect on time to levodopa-induced dyskinesias. Journal of Neurology, 258(11), 2048–2053
[3] Eusebi, P., Romoli, M., Paoletti, F. P., Tambasco, N., Calabresi, P., & Parnetti, L. (2018). Risk factors of levodopa-induced dyskinesia in Parkinson's disease: results from the PPMI cohort. NPJ Parkinson's Disease, 4, 3.
[4] Bjornestad, A., Forsaa, E. B., Pedersen, K. F., Tysnes, O. B., Larsen, J. P., & Alves, G. (2016). Risk and course of motor complications in a population-based incident Parkinson's disease cohort. Parkinsonism & Related Disorders, 22, 48–53.

Objectives

- To compare the prevalence of clinically significant dyskinesia (CS-dyskinesia, i.e., dyskinesia prompting treatment modification) across genders of patients with iPD using a real-world data (RWD) set – namely, the American Academy of Neurology Axon Registry®, a neurology-specific patient registry of real-world de-identified electronic health record data.

- To demonstrate the feasibility in leveraging deep-learning methodologies to capture CS-dyskinesia from unstructured clinical notes.

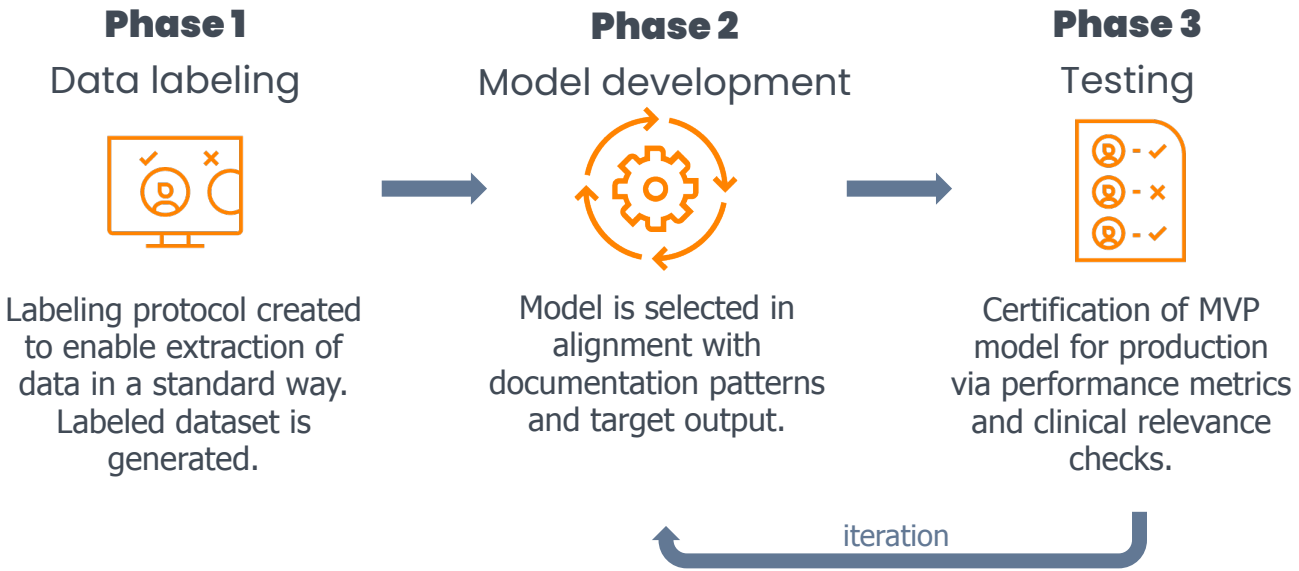
Methods

Study Population

- At the time of the study (February 2023), there were 41 million patient visits from more than 2.6 million patients across more than 1,000 registered providers and 150 practices in the AAN Axon Registry.
- Of these patients, more than 15,000 iPD patients were identified using structured ICD codes and PD related keywords in clinical notes between the study period of January 2015 and February 2023.
    - The algorithm was validated to be 84% accurate via the review of clinical notes from 350 randomly sampled PD patients identified by the algorithm. Patient notes were reviewed by a clinical expert.

Methods

Clinically significant dyskinesia and severity of cardinal symptoms (tremor, bradykinesia, rigidity) severity were curated from clinical notes using deep-learning approaches.



Methods

Phase 1
Data labeling

Cardinal signs guidelines: On a given note date, capture patient's most severe assessment for the given cardinal sign.

Dyskinesia guidelines: On a given note date, capture if the patient is having clinically significant dyskinesias that requires a change of therapy.

Phase 2
Model development

Cardinal signs: Individual **clinical-longformer models** were fine-tuned to classify, for a given clinical note, a patient's severity (none, mild, moderate, severe, or present, but severity unspecified) for each cardinal sign.

Dyskinesia: A **clinical-longformer model** was fine-tuned to classify, for a given clinical note, whether the patient experienced no dyskinesia, or whether they experienced clinically significant dyskinesia.

Phase 3
Testing

Table 1. F1-scores for held out test sets (n = 300–360) for individual cardinal sign algorithms

	Tremor	Rigidity	Bradykinesia
None	0.90	0.93	0.93
Mild	0.90	0.94	0.89
Moderate	0.93	0.94	0.94
Severe	0.94	0.93	0.98
Present, but severity unspecified	0.85	0.81	0.85

Table 2. F1-scores for held out test set (n = 154) for the dyskinesia algorithm

	F1-score
Clinically Significant Dyskinesia	0.83
No Dyskinesia	0.94

Methods

Statistical Analysis

- Three logistic regression models were used to assess the association between documentation of CS-dyskinesia during the study period and gender:
  - Unadjusted
  - Adjusted for race, ethnicity, and age at first documentation of dyskinesia or most recent non-dyskinesia encounter for non-dyskinesia patients.
  - Adjusted for demographics, plus the most severe symptom *across* the patient's journey for each cardinal sign (i.e., tremor, rigidity, and bradykinesia).
- For all three models, patients were grouped into two groups: those who *ever* had CS-dyskinesia and those with no documented CS-dyskinesia.

Results

- There were 1,195 (7.96%) iPD patients with at least one documented CS-dyskinesia encounter.

Figure 1. Percentage of patients with moderate to severe symptomatology by cardinal sign and dyskinesia status

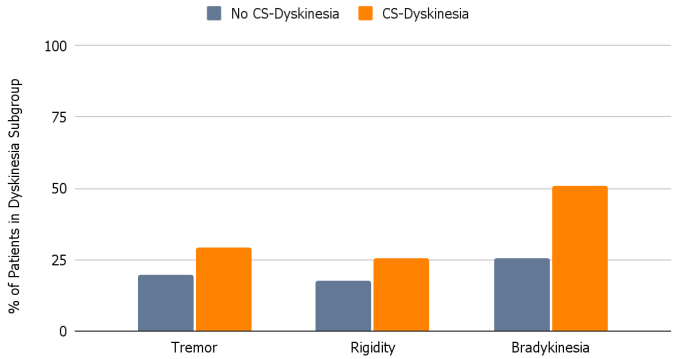


Table 3. Demographics of iPD patients

	No CS-Dyskinesia (n = 13820)	CS-Dyskinesia (n = 1195)
Age[1]	74.31 (8.98)	69.58 (9.81)
% Males	8511 (61.58%)	600 (50.21%)
Race		
White	6416 (46.43%)	636 (53.22%)
Black or African American	303 (2.19%)	6 (0.50%)
Asian	157 (1.14%)	14 (1.17%)
Other	93 (0.67%)	12 (1.00%)
2 or More Races	11 (0.08%)	0 (0.00%)
Unknown	6840 (49.49%)	527 (44.10%)
Ethnicity		
Hispanic or Latino	628 (4.54%)	57 (4.77%)
Not Hispanic or Latino	5261 (38.07%)	602 (50.38%)
Unknown	7931 (57.39%)	536 (44.85%)

[1] Age was calculated from time of first documentation of CS-dyskinesia, or most recent non-dyskinesia encounter for non-dyskinesia patients.

Results

- Females had significantly greater odds of dyskinesia across all three models.

Table 4. Odds ratio of unadjusted and adjusted dyskinesia status by gender logistic regression models

Model	OR	95% CI	p-value
Unadjusted	1.59	1.41 - 1.79	< 0.001
Adjusted for age, race, and ethnicity	1.69	1.50 - 1.91	< 0.001
Adjusted for demographics and severity of cardinal signs	1.82	1.61 - 2.06	< 0.001

Discussion

- In the Axon Registry, females with iPD have 1.59 to 1.82 greater odds of having dyskinesia than males during their patient journey, providing additional support to previous findings of sex differences in the presentation of iPD.
- Novel to past studies that have used UPDRS scores to capture dyskinesia, we were able to demonstrate clinical notes can be leveraged in studies aimed at better understanding dyskinesia in iPD.
    - In particular, performance metrics and a clinically consistent pattern (i.e., expected gender differences) produced by the model output provide support that a deep-learning approach can be employed to extract CS-dyskinesia from clinical notes.
- Findings from this study show a gender disparity in disease progression, as captured in clinical assessments and real world documentation, that could prompt new management approaches.