

Comparison of Outcomes in Different Parkinson's Disease Subtypes in the AAN Axon Registry[®]

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Objective

To compare outcomes between Parkinson's Disease (PD) subtypes using measures extracted from clinical notes from the American Academy of Neurology (AAN) Axon Registry[®], a neurology-specific patient registry of real-world de-identified electronic health record data.

Background

- Akinetic-rigid (AR) and tremor-dominant (TD) subtypes have been identified in PD, with the latter demonstrating a milder progression.^{1,2}
- Past studies have commonly leveraged scores on the Unified Parkinson's Disease Rating Scale (UPDRS) to classify patients into these subtypes.^{3,4}
- However, the UPDRS is not commonly administered at every neurology visit. Demonstrating that real-world data (RWD) can be leveraged to identify subtypes, and therefore distinctions in disease progression, will enable studies aimed at understanding differences in pharmaceutical targets of the subtypes.

Design/Methods

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 Axon Registry. To curate disease-specific data modules (Qdata[®]), Verana Health leverages VeraQ[®], its clinician-directed and AI-enhanced population health data engine. Through the Qdata Parkinson's Disease module, over 15,000 PD patients were identified.

Classifying Patients into PD Subtypes

Patients' severity of tremor, bradykinesia, and rigidity scores at the earliest encounter within one year of their first PD ICD code were leveraged to classify patients into AR and TD subtypes.

- Severity of tremor, bradykinesia, and rigidity scores were curated from patients' clinical notes using fine-tuned deep-learning models, where at each encounter, patients' severity for each individual sign was classified into a score ranging from 0 (none) to 3 (severe).
- A severity ratio was then calculated using the following formula:
Tremor Score / Mean of Bradykinesia and Rigidity Scores
- Patients were classified as TD for ratios ≥ 1 and AR for ratios < 0.8 (adopting Kang et al., 2005 methodology). All remaining patients were classified as Other.

Comparing Outcomes of PD Subtypes

- Subtypes were compared by **presence and time to first presence** on outcome measures of interest using chi-square and Mann-Whitney U tests, respectively.
- Outcome measures of interest include **postural instability, motor fluctuations, dyskinesia, and deep brain stimulation (DBS)**.
 - DBS was curated from linked claims data. All other measures were curated from clinical notes using deep-learning and/or rule-based approaches.

All variables curated from clinical notes were developed and assessed with notes labeled by a clinical expert. All algorithms achieved weighted model F1-scores ≥ 0.8 when evaluated against held-out test sets (n cases ≥ 150).

Results

Distribution of PD Subtypes

There were 3,641 PD patients who had entries for tremor, bradykinesia, and rigidity on the same encounter, within one year of their first PD ICD code. Of these patients, the largest proportion (48%) was classified into the AR subtype.

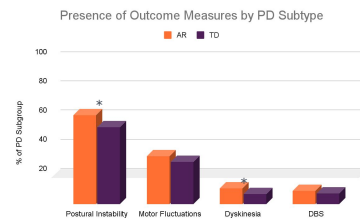
Demographic information is presented below for the AR, TD, and Other groups. The remaining analyses do not include the Other subgroup.

Age and Sex of PD Subtypes

	AR (n = 1764)	TD (n = 693)	Other (n = 1184)
Mean (SD) age at first PD ICD code	71.50 (9.42)	70.73 (9.47)	71.34 (9.28)
Mean (SD) age at severity encounter	71.63 (9.42)	70.86 (9.48)	71.48 (9.29)
N (%) males	1044 (59.18%)	430 (62.05%)	709 (59.88%)

Comparing Outcome Measures of PD Subtypes

- The AR subtype had a higher proportion of patients with postural instability (61% vs. 53%) and dyskinesia (11% vs. 7%), p-values $< .01$.



Results (cont.)

- The AR subtype had a shorter time to first encounter with postural instability, dyskinesia, and motor fluctuations, p-values $< .05$.
- No differences in DBS were found between subtypes.

Median (IQR) Months to First Encounter with Outcome Measure

	AR	TD	p
Postural Instability	0 (0 - 1.06)	0 (0 - 4.71)	< 0.01
Motor Fluctuations	3.87 (0 - 18.06)	6.35 (0 - 19.52)	0.03
Dyskinesia	7.23 (0 - 27.16)	25.06 (3.94 - 39.81)	0.02
DBS	6.26 (0.13 - 27.87)	8.19 (1.06 - 28.35)	0.63

Conclusions

Using RWD, we successfully identified AR and TD subtypes and differences in progression profiles with the TD subtype showing milder progression patterns consistent with the previous literature. Differences in dyskinesia were particularly notable. Not only was there a higher proportion of patients with dyskinesia among the AR subtype, but the median time to first dyskinesia encounter was about 18 months earlier compared to the TD subtype. These findings demonstrate that RWD can be leveraged for subtype studies and outcome differences within PD.

References

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