

Scoring Discrepancies in MDS-UPDRS Part III in Clinical Trials of Parkinson’s Disease Undergoing Independent Review

Objectives

The Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) part III is the most widely used tool to measure changes in motor function over time in clinical trials of Parkinson's disease (PD) [1] and has demonstrated to have good intra and inter-rater reliability [2,3]. Independent Review (IRev) is a surveillance method commonly used in clinical trials to independently verify primary endpoint data. In this project, we evaluated IRev data collected in PD trials using the MDS-UPDRS part III, with the following objectives:

- Evaluate frequency of MDS-UPDRS part III scoring discrepancies identified by independent reviewers in PD clinical trials.
- Identify items that are most prone to discrepancies during IRev.
- Assess whether the frequency of discrepant scores varies by disease severity measured by the MDS-UPDRS part III total score.

Methods

Aggregated MDS-UPDRS part III data collected by site raters in three multi-national double-blind clinical trials of PD were evaluated to determine frequency of scoring discrepancies identified by external reviewers. Part III assessments were independently reviewed via video recording (N = 20,239) by a team of trained and tightly calibrated clinicians (ICC 0.86). Assessments were divided into quartiles according to severity of motor symptoms based on part III total score, and discrepancy rates were calculated for each severity group. Discrepancy rates were calculated as the sum of discrepancies divided by the number of assessments.

Table 1: Descriptive Summary by Quartile

QUARTILE	N	% ASSESSMENTS WITH DISCREPANCY	MDS-UPDRS III TOTAL SCORE (MEAN)	MDS-UPDRS III TOTAL SCORE (SD)
1	5041	28%	12.32	3.70
2	5040	26%	21.36	2.20
3	5041	25%	29.38	2.51
4	5041	22%	42.02	7.20

Figure 2: Discrepancies Per Assessment by MDS-UPDRS Part III TS Quartile

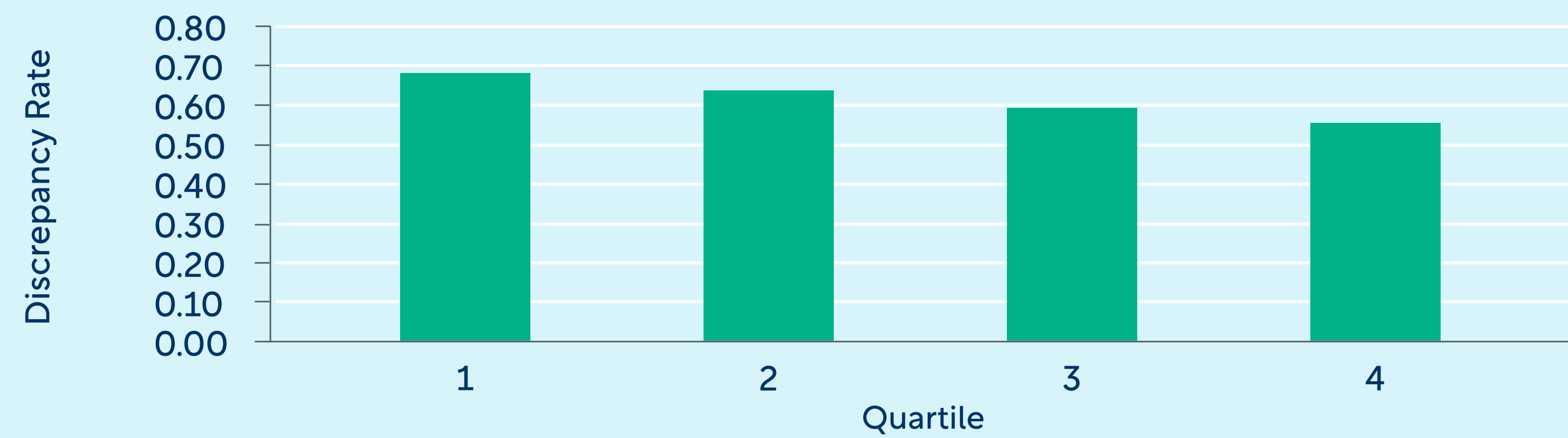
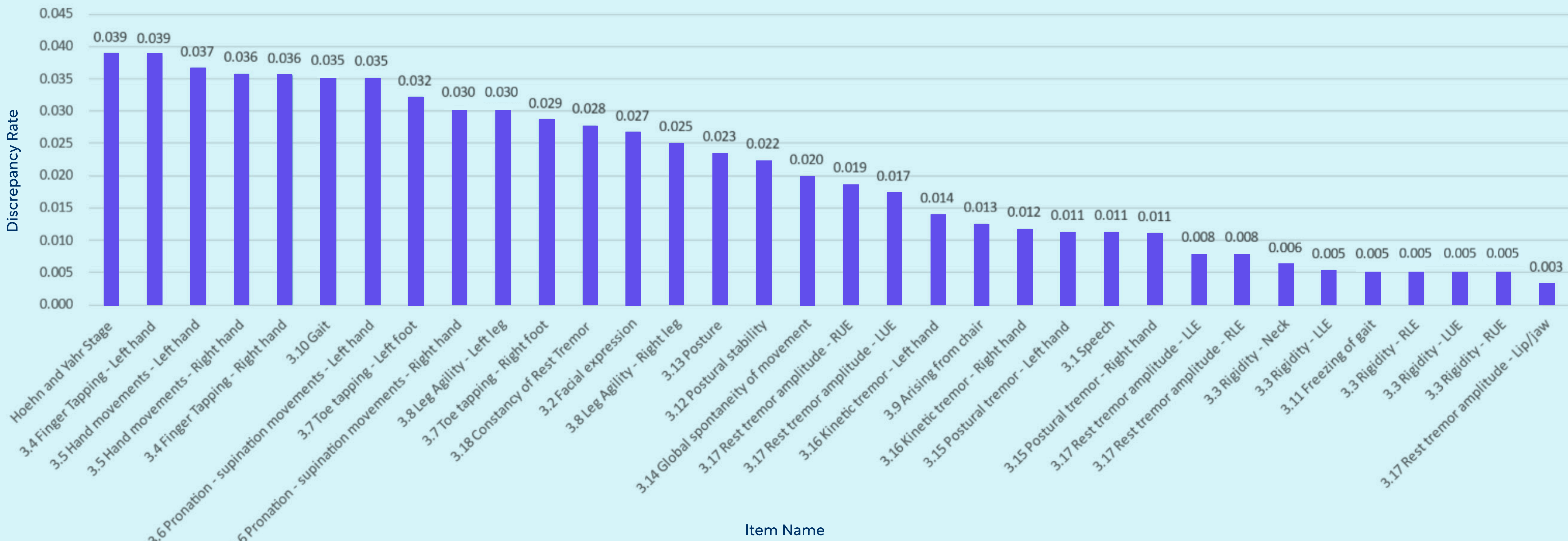


Figure 1: Discrepancy Rate by MDS-UPDRS Part III Item



Results

- Approximately 25% of assessments reviewed had at least one scoring discrepancy following IRev. Table 1 shows descriptive summary for proportion of discrepancies broken down by quartiles, along with mean and scoring discrepancies for the MDS-UPDRS part III total score.
- Discrepancies were highest for Hoehn and Yahr (H&Y), finger tapping and hand movements, and lowest for rest tremor amplitude items, freezing of gait and speech (Figure 1).
- Assessments with lower Part III total score had the highest rate of discrepancies (Figure 2).
- Differences among severity quartiles were statistically significant with discrepancy rates decreasing with motor symptom score increase ($F = 18.57$; $df = 3, 20159$; $p < .001$).

Conclusions

Despite the wide use of the MDS-UPDRS part III total score as primary outcome measure in PD trials and robust training provided by MDS, motor assessments conducted by experienced raters are still prone to subjective interpretation and/or scoring discrepancies, particularly the H&Y. Scoring discrepancies were highest in the group with lowest part III scores, suggesting raters find subjects with milder motor symptoms more difficult to rate.

References

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