

The L-dopa response in Parkinson's disease

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Overview

- The L-dopa response
- Factors potentially affecting the response
- The PPMI study
- Results
- Conclusion

The L-dopa response

- Levodopa (L-dopa) gold standard treatment for PD
- Measured with standardized clinical rating scales (MDS UPDRS) ¹
- Embedded in MDS diagnostic criteria ²

¹Goetz C et al, Mov Disord 2008, 24, 2129-70

²Postuma RB et al, Mov Disord 2015, 30, 1591-99

The L-dopa response

Motor examination

- MDS UPDRS 3
- L-dopa challenge test
- UPDRS 3 scale >30% cut-off ²
- MDS UPDRS 3 scale \geq 24.5% cut-off ³

²Postuma RB et al, Mov Disord 2015, 30, 1591-99

³Merello M et al, Parkinsonism Relat Disord, 2011, 17, 705-707

The L-dopa response

Motor complications

- MDS UPDRS 4 scale
- Dyskinesia
- Motor fluctuations
- Dystonia

The L-dopa response

L-dopa in the the MDS criteria ²

Supportive criteria

(Check box if criteria met)

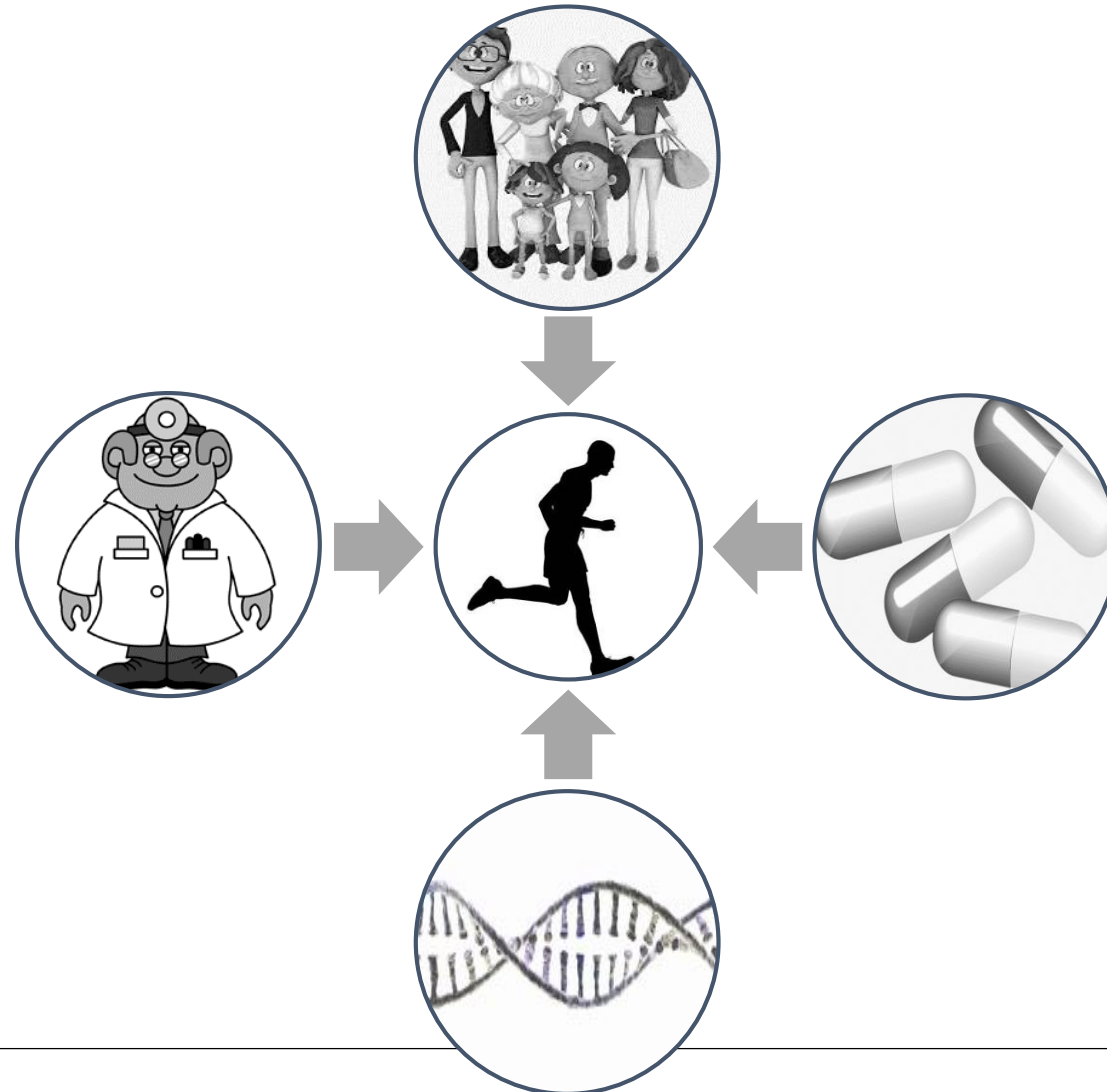
- 1. Clear and dramatic beneficial response to dopaminergic therapy. During initial treatment, patient returned to normal or near-normal level of function. In the absence of clear documentation of initial response a dramatic response can be classified as:
 - a) Marked improvement with dose increases or marked worsening with dose decreases. Mild changes do not qualify. Document this either objectively (>30% in UPDRS III with change in treatment), or subjectively (clearly-documented history of marked changes from a reliable patient or caregiver).
- 2. Presence of levodopa-induced dyskinesia

Absolute exclusion criteria: The presence of any of these features rules out PD:

- 6. Absence of observable response to high-dose levodopa despite at least moderate severity of disease

²Postuma RB et al, Mov Disord 2015, 30, 1591-99

What could affect the response?



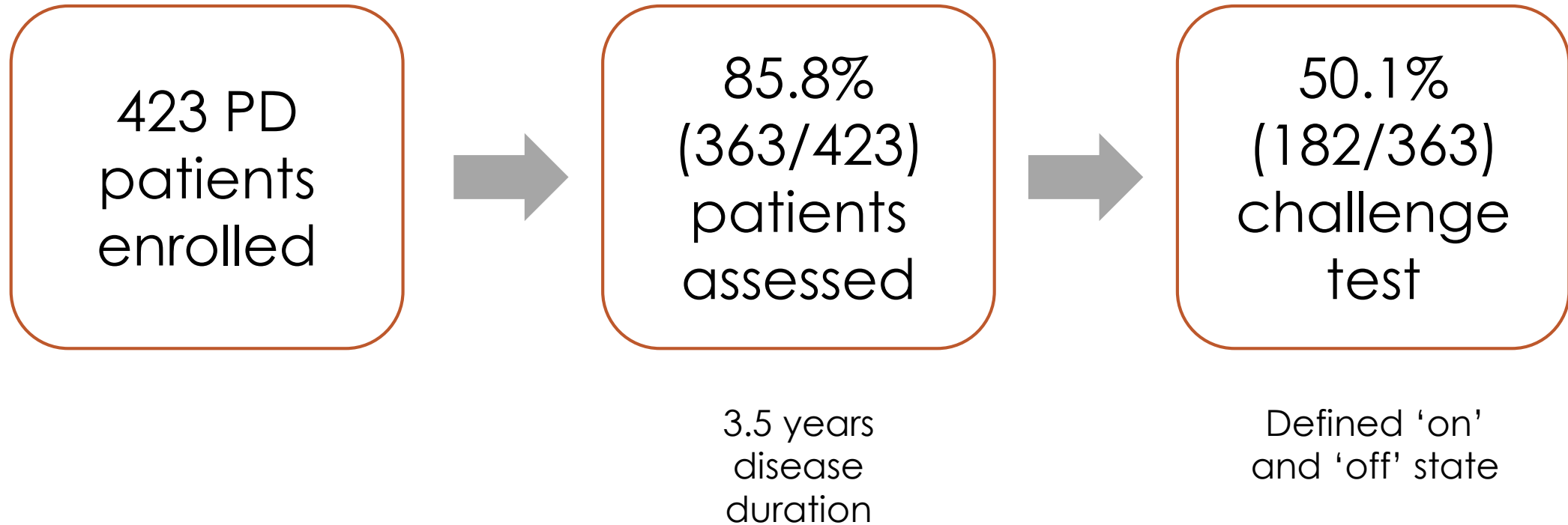
The PPMI study

- Launched in 2011
- 423 PD patients
- Drug-naïve for antiparkinsonian medication

Study inclusion criteria

- PD diagnosis for < 2 years at screening
- H&Y stage I or II at baseline
- 30 years or older at diagnosis
- Dopamine transporter deficit (positive SPECT)
- Not expected to require PD medication within next 6 months

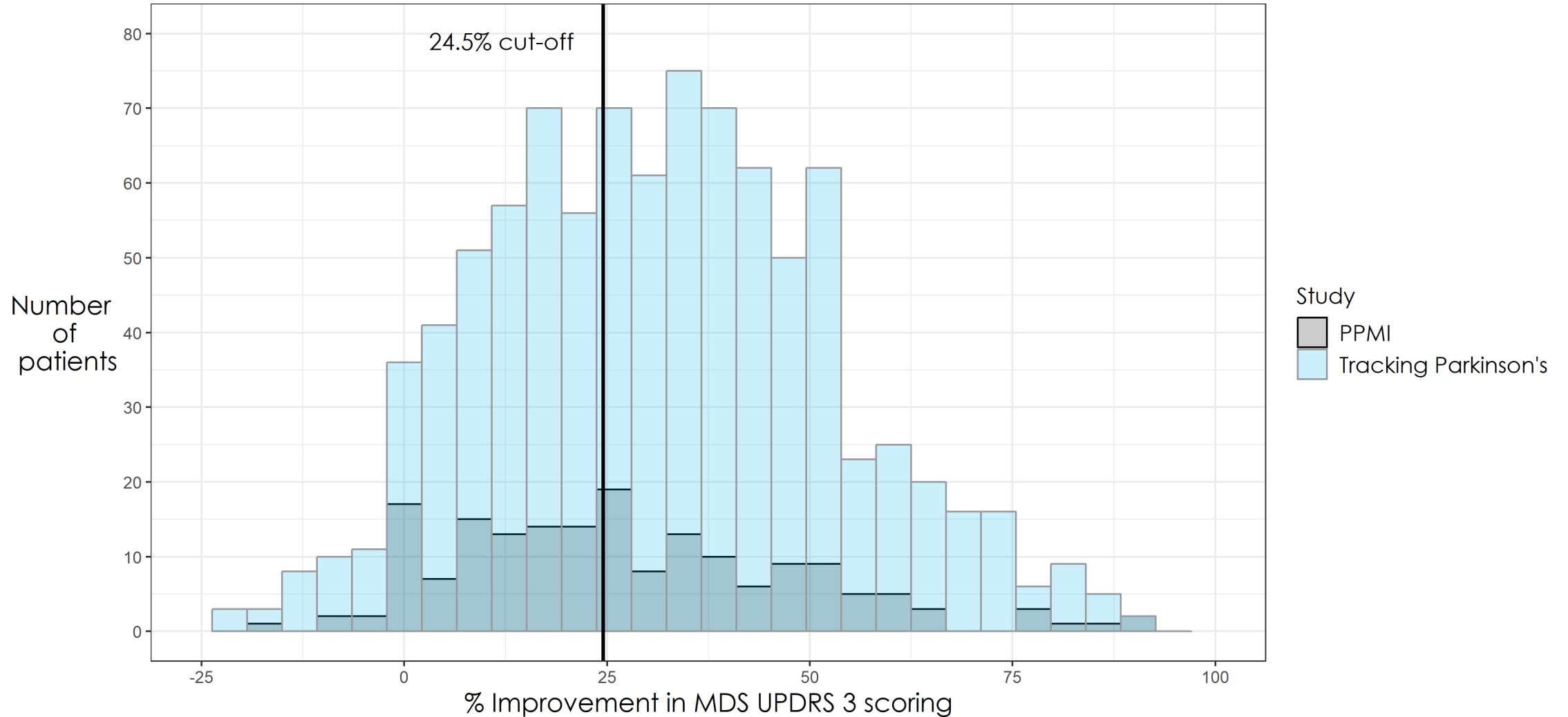
The PPMI study



The Tracking Parkinson's study



Motor improvement



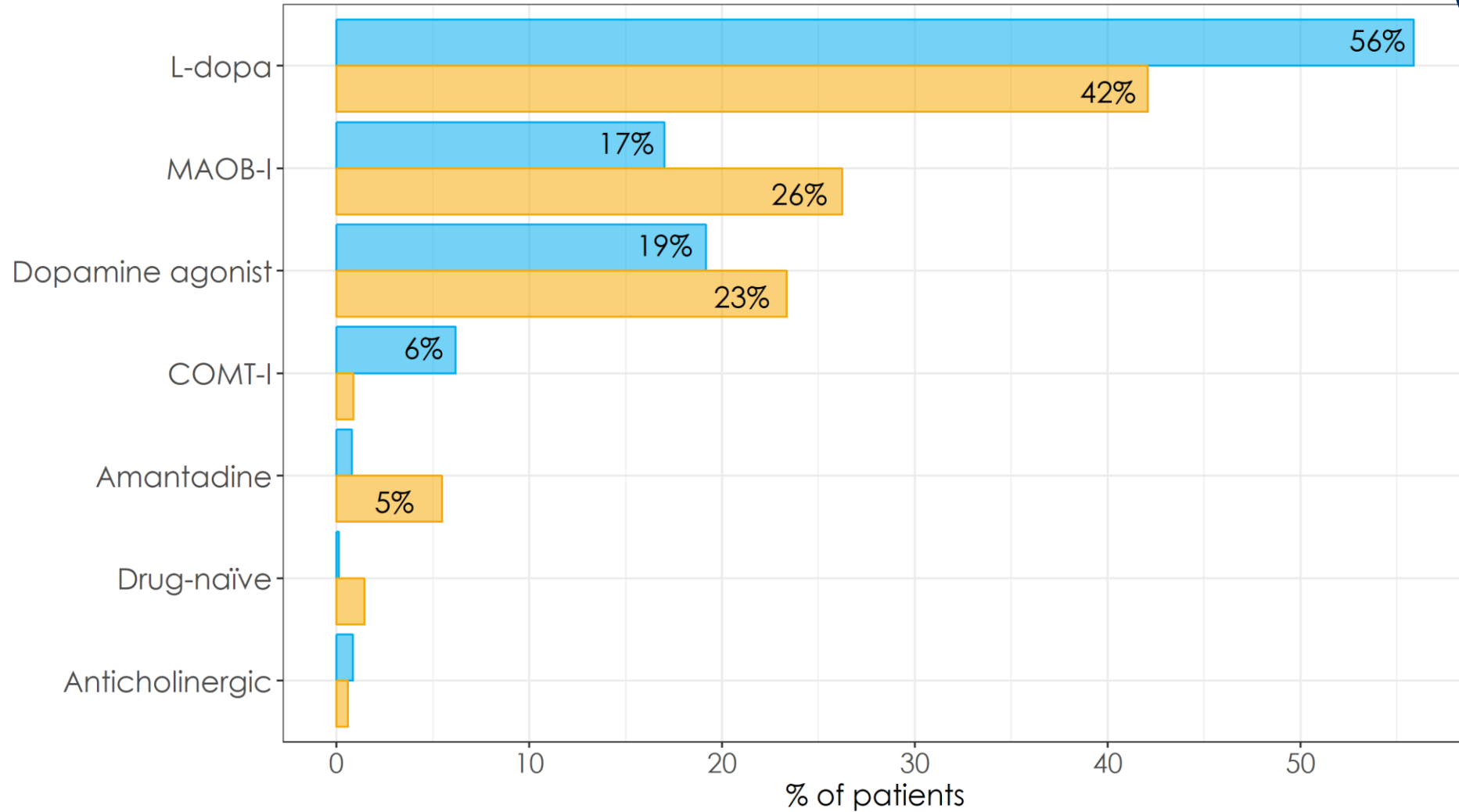
Demographics



Variable	Tracking Parkinson's	PPMI
Number of patients, n	928*	181
Change in diagnosis**, n	7/935 (0.7%)	0
Age at diagnosis, years	66.1 (9.1)	62.1 (9.7)
Age at study entry, years	67.5 (9.0)	62.2 (9.7)
Disease duration at challenge, years	3.4 (0.9)	3.6 (0.6)

* = n of patients with L-dopa challenge test at visit 5 and UPDRS 4 assessment at visit 4, ** = 4x MSA, 1x likely vascular, 1x LBD, 1x post polio syndrome 12

Treatment



Treatment

Variable	Tracking Parkinson's	PPMI
% response L-dopa challenge	30.8 (15.6, 45.5)	24.7 (11.1, 40.7)
Treatment duration, years	3.3 (0.9)	2.1 (0.6)
L-dopa dose in challenge, mg	110.9 (45.0)	132.6 (62.9)
LEDD at challenge	520.1 (235.7)	546.7 (369.2)

MDS UPDRS 4

Variable	Tracking Parkinson's	PPMI
MDS UPDRS 4	1.1 (2.1)	1.1 (2.0)
Dyskinesia, n (%)	33 (3.6)	14 (7.7)
Motor fluctuations, n (%)	38 (4.1)	47 (25.8)
Dystonia, n (%)	65 (7.0)	17 (9.3)

Conclusions

- Variation in L-dopa responsiveness shown in both studies
- Link between L-dopa responsiveness and motor complications confirmed in PPMI, analysis underway in Tracking
- Next steps:
 - What causes this variation?
 - Does this tie in to disease subtypes?

Thank you for your
attention