Main Results

# Descriptive Statistics

## Patient characteristics

Table 1: Baseline demographics and disease characteristics. Values are presented as mean (SD) unless stated otherwise. Montreal cognitive assessment scale (MoCA); Modified Schwab and England activities of daily living (MSE-ADL); Questionnaire for Impulsive-Compulsive Disorders in Parkinson’s Disease (QUIP); Levodopa Equivalent Daily Dose (LEDD).

|  |  |
| --- | --- |
| Variable | Value |
| n | 302 |
| Age (Years) | 61.3 (9.7) |
| Gender (% Men) | 66.9 |
| Education (Years) | 15.6 (2.9) |
| Disease Duration (Years) | 0.5 (0.5) |
| MDS-UPDRS I | 5.6 (4.1) |
| MDS-UPDRS II | 6.2 (4.2) |
| MDS-UPDRS III | 21.1 (8.8) |
| MoCA | 27.1 (2.3) |
| MSE-ADL | 92.8 (6.0) |
| SCOPA-AUT | 9.7 (5.9), NA:1 |
| QUIP (% any) | 19.0 |
| LEDD @ 2 years | 370.0 (292.7) |
| LEDD @ 3 years | 469.9 (330.4), NA:19 |
| LEDD @ 4 years | 546.0 (349.3), NA:42 |
| Treatment 0.5 years | 37 |
| Treatment 1 year | 54 |
| Treatment 1.5 years | 180 |
| Treatment 2 years | 31 |

## Disease Progression

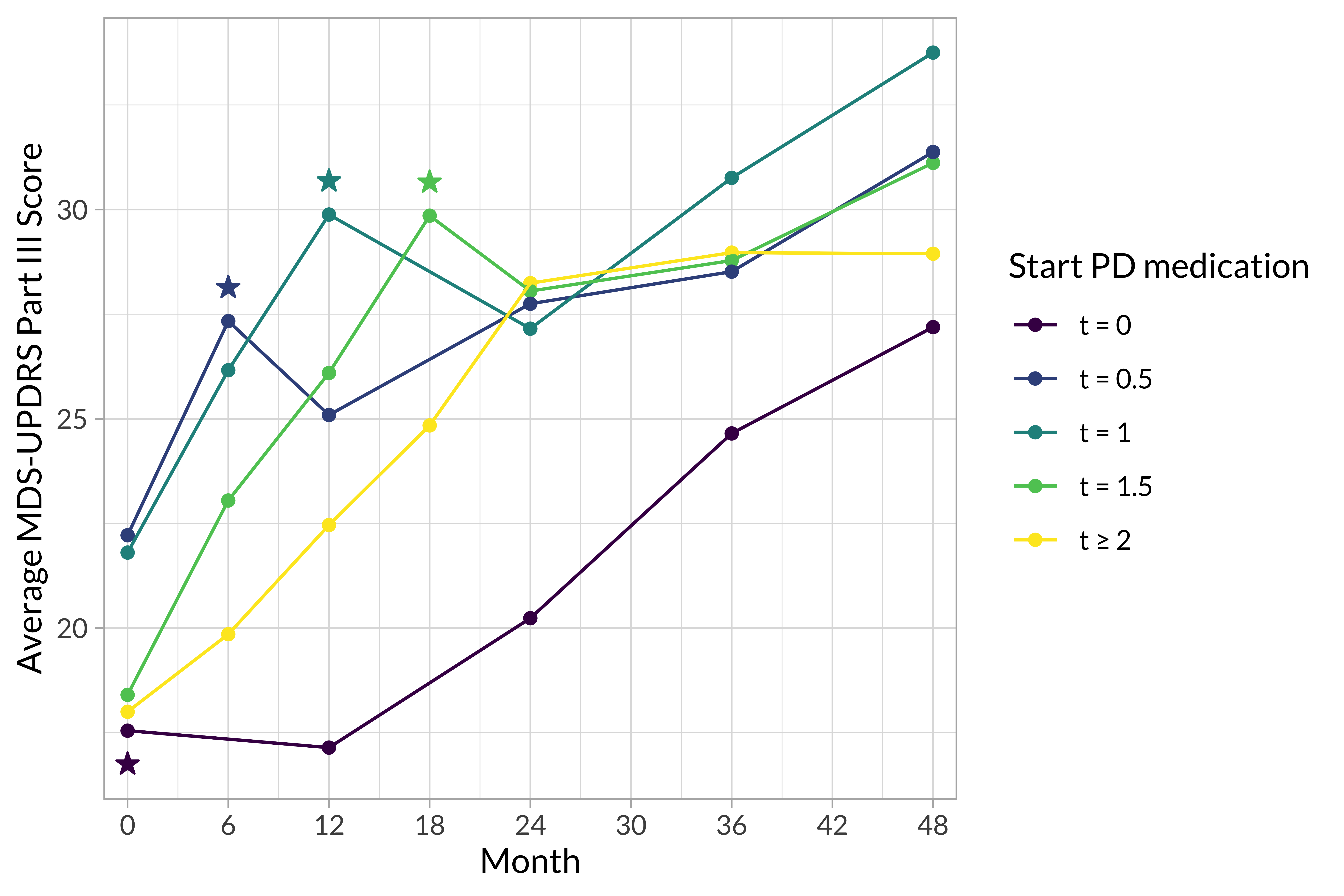


Figure 1: Average MDS-UPDRS III in OFF-state scores in the first four years, categorized by number of treatment years in the first two years of follow-up. Scores are obtained during biannual measurements until treatment initiation and annual measurements after treatment initiation.

# Confounding adjustment

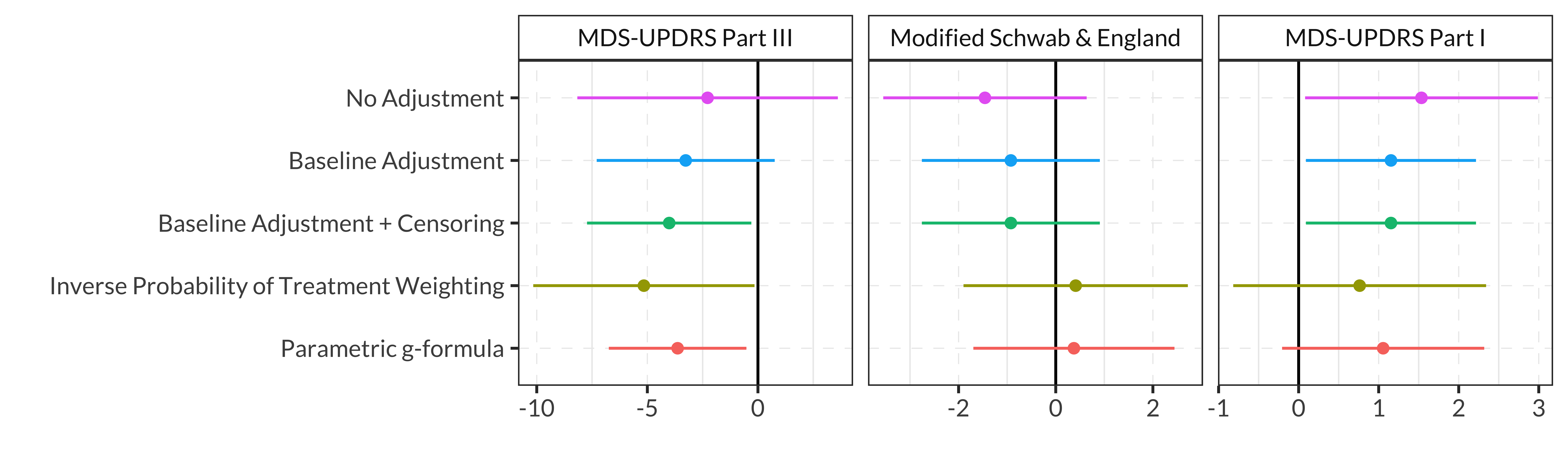


Figure 2: Effect of an additional year of PD medication therapy on outcomes after two years in the subpopulation of patients that had started therapy at the time of measurement, estimated using different methods. For MDS-UPDRS, higher scores correspond to worse outcome, for Modified Schwab & England, lower scores correspond to worse outcomes. Adjusting for more of the (time-varying) confounding removes more of the spurious negative effects due to worse-off patients being more likely to start therapy early.

# Main Outcomes

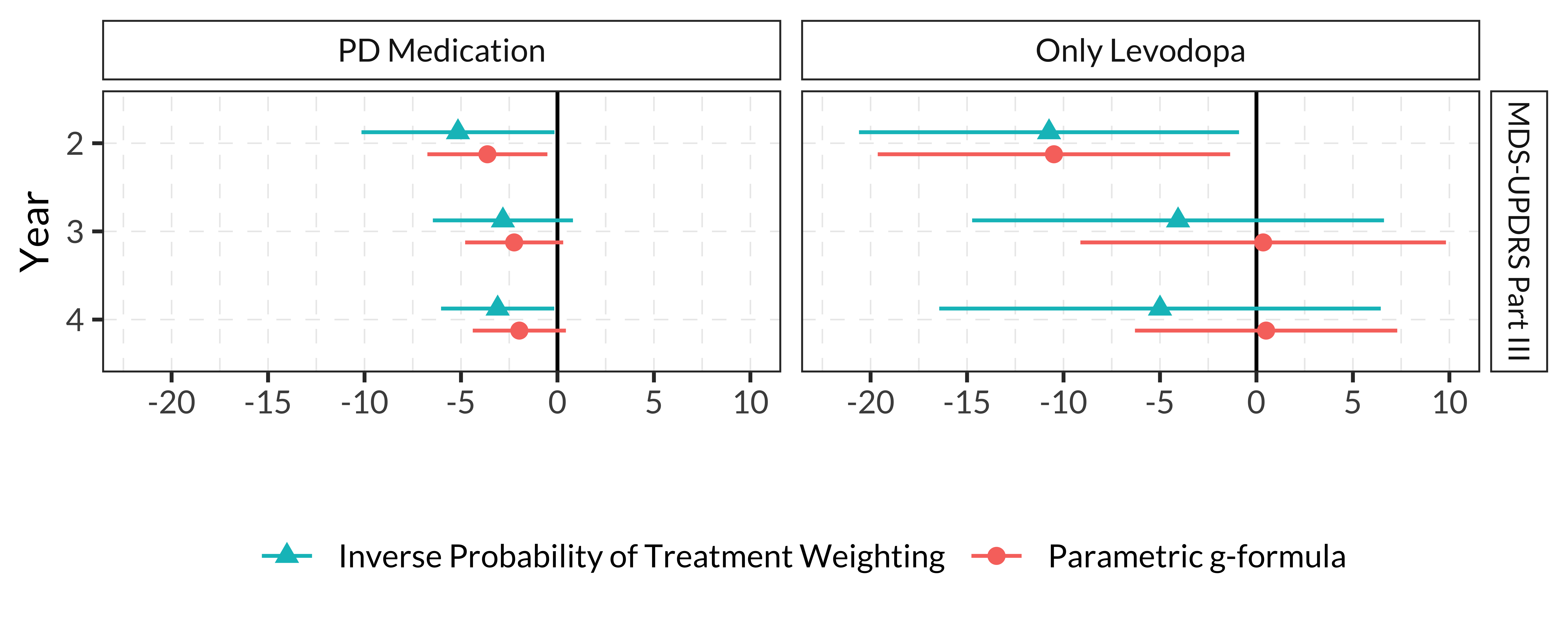


Figure 3: Effect of one year of PD medication treatment during the first two years of follow-up. Effect on MDS-UPDRS Part III subscore measured at year 2, 3 and 4, for inverse probability of treatment weighting and the parametric g-formula. Only patients who have started medication therapy at the time of the outcome measurement are included in the analysis.

In the table below: obs refers to the number of non-missing measurements used for the esitmation for the IPTW models, and to the number of simulated outcomes for the g-formula (4 treatment options times 100 simulations per patient for the year 2 outcomes and 5 treatment options times 100 simulations per patient for the other outcomes).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Model | Year | estimate | CI | obs |
| Inverse Probability Weighting | 2 | -5.16 | (-10.06 - -0.25) | 155 |
| g-formula | 2 | -3.63 | (-6.68 - -0.58) | 120800 |
| Inverse Probability Weighting | 3 | -2.83 | (-6.39 - 0.73) | 178 |
| g-formula | 3 | -2.24 | (-4.73 - 0.25) | 155500 |
| Inverse Probability Weighting | 4 | -3.10 | (-5.97 - -0.22) | 194 |
| g-formula | 4 | -1.98 | (-4.34 - 0.39) | 147500 |

# Auxiliary outcomes

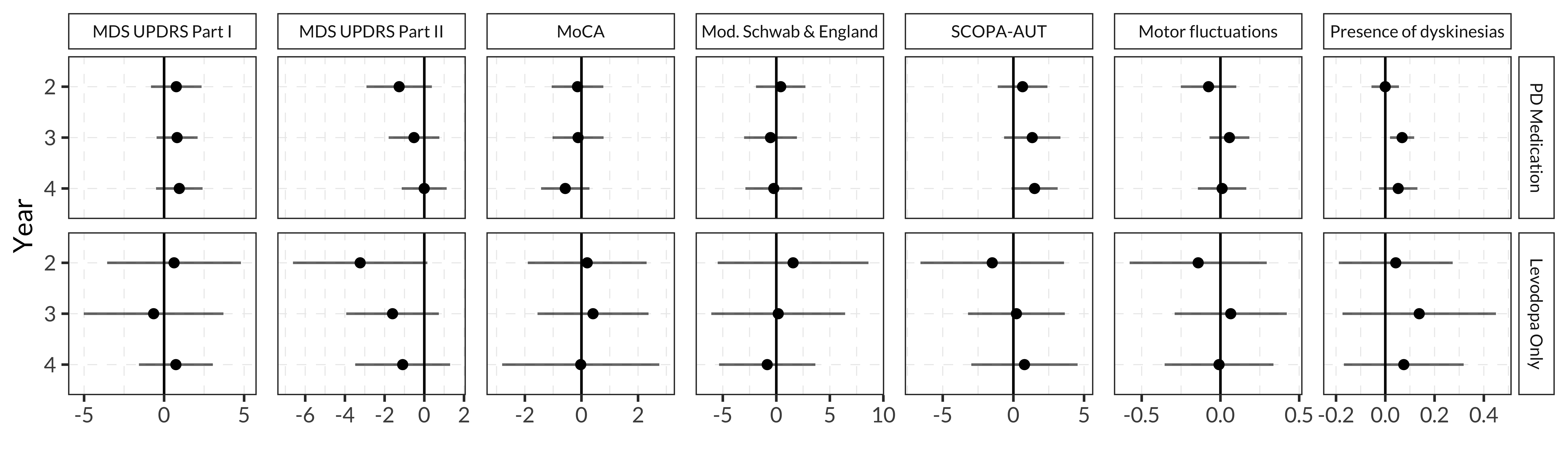


Figure 4: Effect of one year of PD medication treatment during the first two years of follow-up. Effect on auxiliary outcomes at year 2, 3 and 4 for inverse probability of treatment weighting. Only patients who have started medication therapy at the time of the outcome measurement are included in the analysis.