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 (% Male) | 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) |
| 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 | 176 |
| Treatment 2 years | 35 |

## Disease Progression

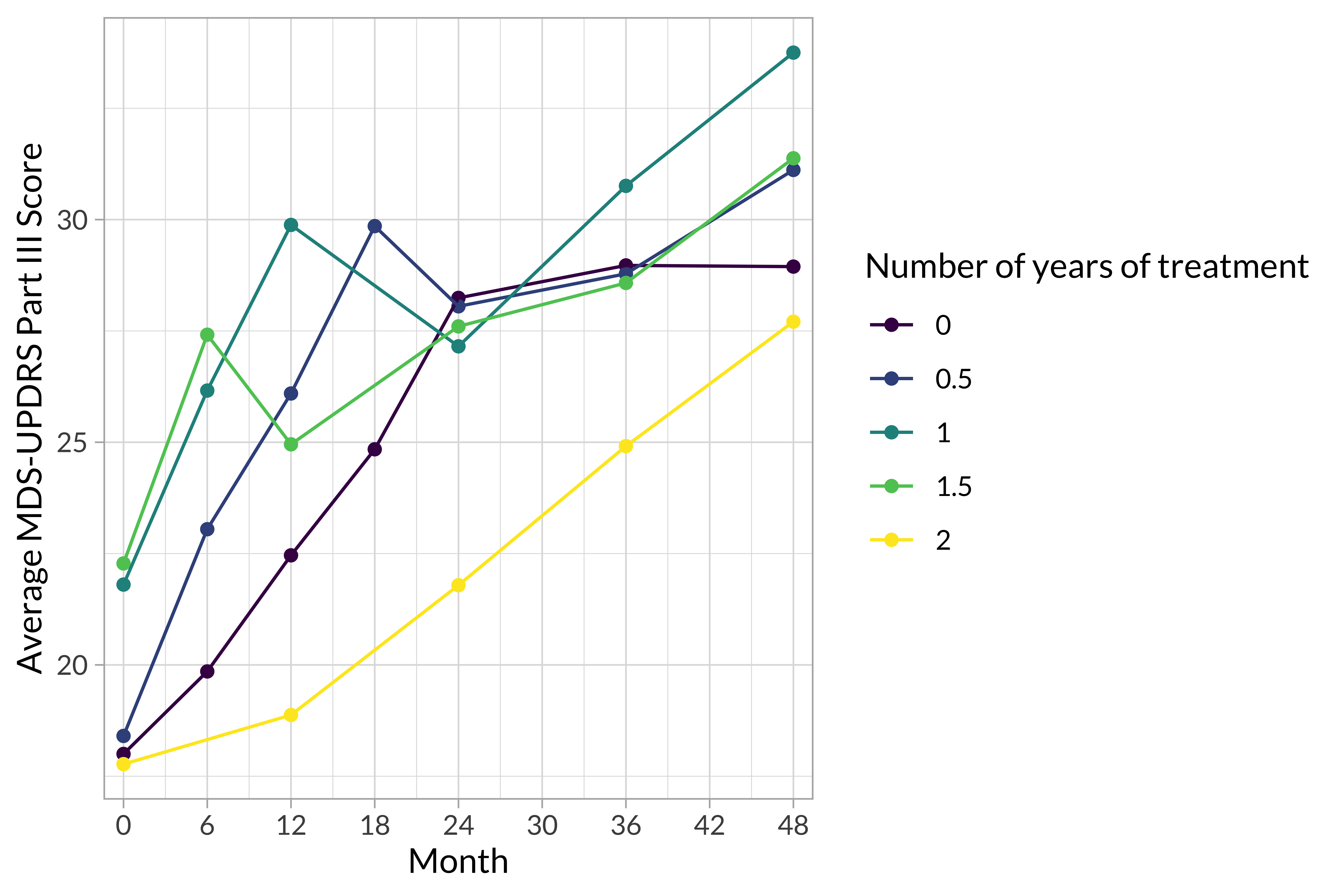


Figure 1: Descriptive MDS-UPDRS III Progression. Average MDS-UPDRS III progression in the first 4 years, categorized by number of years of treatment in the first 2 years of the disease. Only “Off” measurements are shown. These included semi-annual measurements until treatment initiation and annual measurements after treatment initiation (because only the annual measurements were specifically defined as “Off” state in PPMI).

# Confouding adjustment

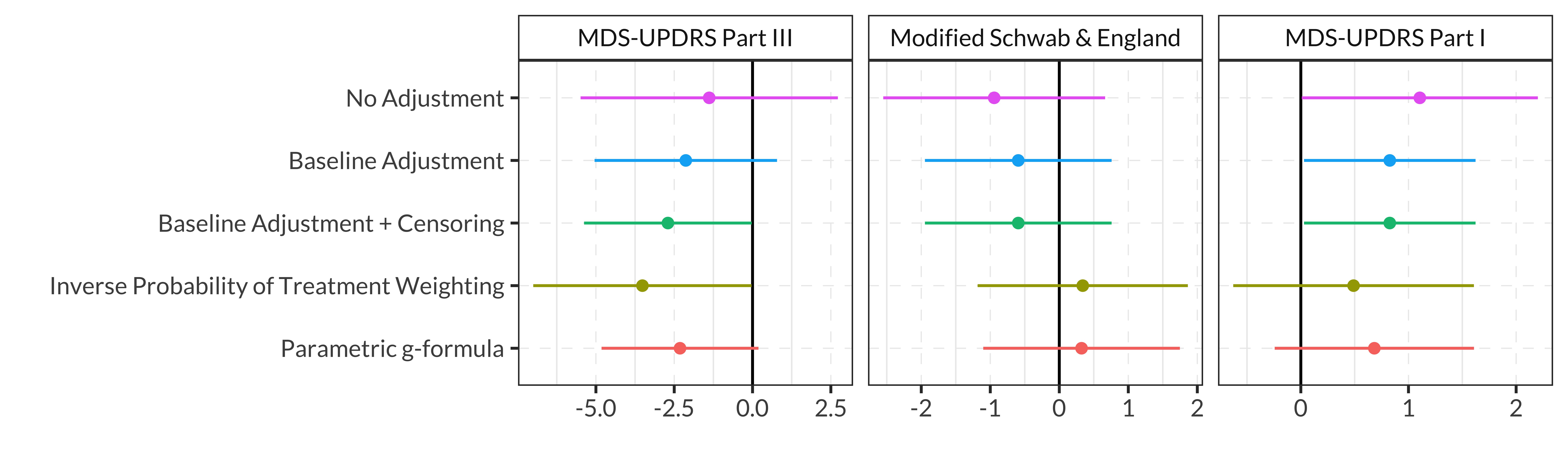


Figure 2: Effect of an additional year of PD medication therapy on outcomes after two years and considering all observations, estimated using different methods. For MDS-UPDRS, higher scores correspond to worse outcome, for Modified Schwab & England, lower scores correspond to worse outcomes. Adjusting 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

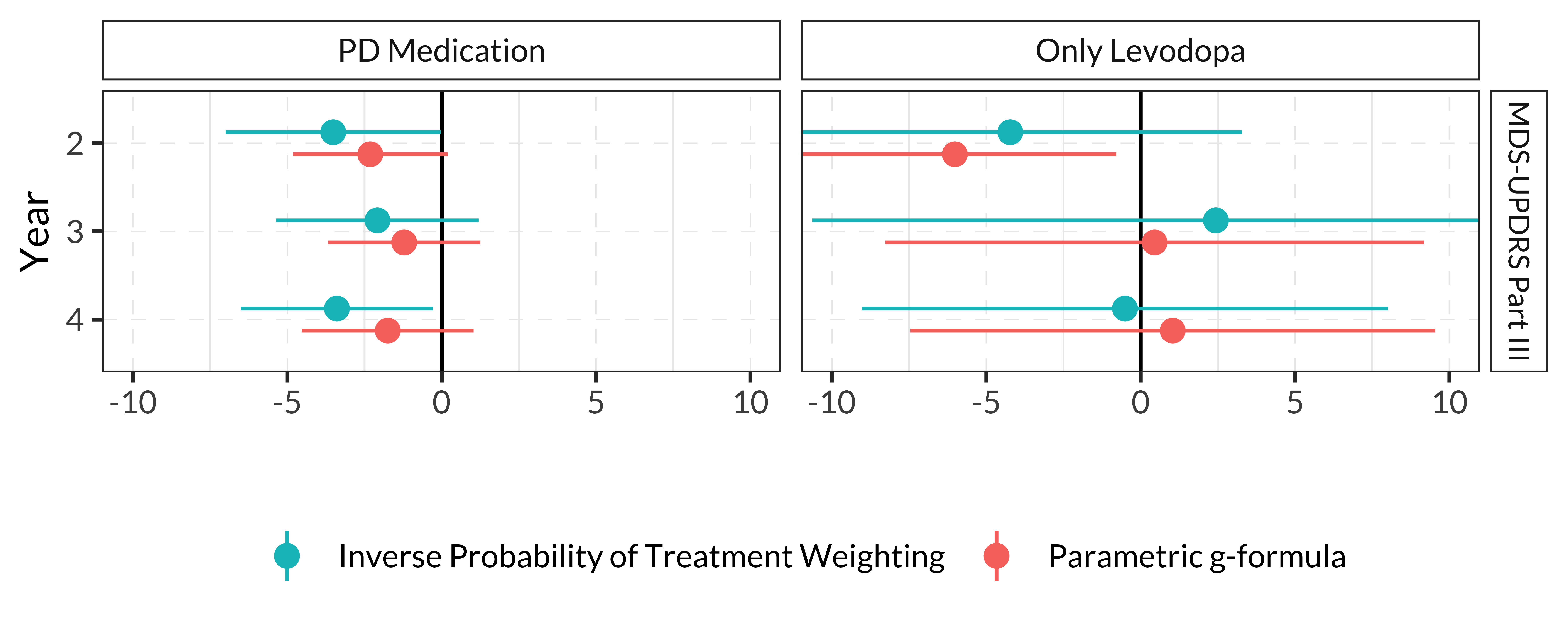


Figure 3: Effect of one year of PD medication treatment during the first two years of follow-up. Effect on MDS-UPDRS Part III subscore measured at year 2, 3 and 4, for inverse probability of treatment weighting and the parametric g-formula. Only patients who started medication therapy within two years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

|  |  |  |  |
| --- | --- | --- | --- |
| Model | Year | estimate | CI |
| Inverse Probability Weighting | 2 | -3.52 | (-6.93 - -0.1) |
| Inverse Probability Weighting | 3 | -2.08 | (-5.3 - 1.13) |
| Inverse Probability Weighting | 4 | -3.40 | (-6.45 - -0.34) |
| g-formula | 2 | -2.32 | (-4.77 - 0.14) |
| g-formula | 3 | -1.22 | (-3.63 - 1.2) |
| g-formula | 4 | -1.75 | (-4.47 - 0.98) |

# Auxiliary outcomes

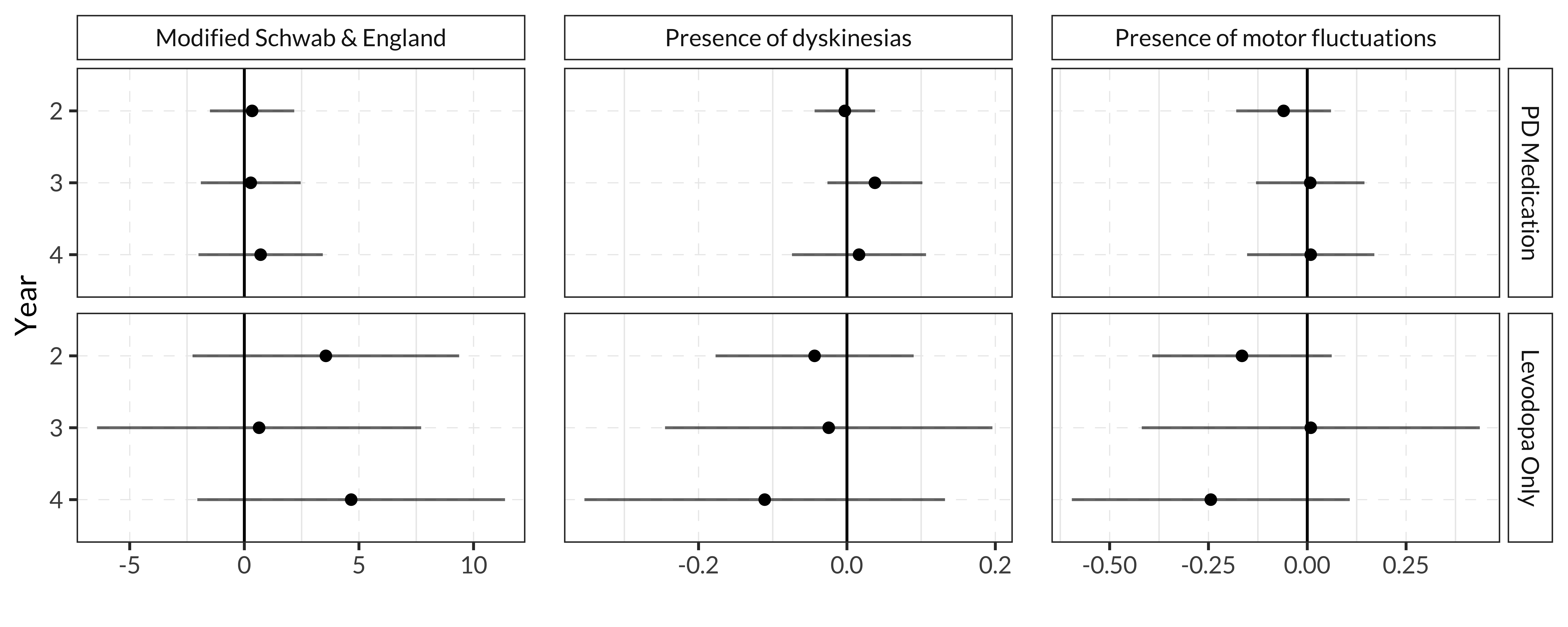


Figure 4: Effect of one year of PD medication treatment during the first two years of follow-up. Effect on auxiliary outcomes at year 2, 3 and 4 for inverse probability of treatment weighting. Only patients who started medication therapy within two years are included in the analysis.