e-Methods

Calculation of Risk Scores:

1. **Risk score 1: Liu et al. (2017) Prediction algorithm for global cognitive impairment** (Adapted from Liu et al 2017)

Step one: Calculate I - 'Individual' cognitive risk
Firstly, the age at diagnosis of PD, years of education, current MMSE, current MDS-UPDRS III scores, as well as the values for gender, and depression are multiplied by the coefficients from the Cox model run by Liu et al.:

- I = (0.0813 × age at onset) + (0.3803 × gender [1=male]) – (0.0863 × years of education) + 0.4599 – (0.2819 × MMSE score) + 0.0219 × MDS-UPDRS III) + 0.4287 × depression status [0=no depression])

Step 2: Calculate G - 'Global' cognitive risk
Secondly, the sum G of the "coefficient × mean value" products is calculated for the discovery population:
G = 0.0813 × 60.4 (mean of age at onset) + 0.3803 × 0.619 (proportion of male) – 0.0863 × 13.7 (mean of years of education) – 0.2819 × 28.6 (mean of baseline MMSE score) + 0.0219×26.5 (mean of baseline MDS-UPDRS III) + 0.4287 × 0.207 (proportion of depression) = -3.3828.

Stage 3: Calculate B - Individual risk in relation to global risk
Thirdly, calculate the exponent of the individual risk minus the global risk:

- Take I from G (i.e., I-G)
- Then calculate the natural exponential function to get the inverse. Ie., $B = e^{I-G}$ (e being the exponential function)

Stage 4: Calculate risk of dementia at 10 years
Finally, the estimated 10-year risk of PD global cognitive impairment risk is formally calculated as 1 minus the survival rate at 10 years. The cognitive risk score is then defined as the estimate of the 10-year risk of global cognitive impairment calculated as one minus the survival rate at 10 years of disease duration.

- S(t) = 0.7989, the 10-year survival rate S(10) derived from the optimized Cox model.
- Cognitive risk score = $1-S(t)^B$

2. **Risk score 2: Schrag et al. (2017) Cognitive impairment at 2 years post diagnosis. (**Adapted from Schrag et al 2017)

First, the HADS depression score was converted to Geriatric Depression Score, using a scalar conversion: (HADs score/21)*15
This scalar conversion was also performed to convert the Sniffin' sticks score to the UPSIT: (Sniffin' sticks score/16)*40
Then Risk score was calculated, excluding CSF and DAT data which were not available for our cohort: 100*EXP(Constant[-5.69] + (Age * 0.06) + (UPDRS motor score * 0.017) + (GDS equivalent * .04) + (UPSIT equivalent * -0.06) + (RBDSQ * 0.17)) / (1+EXP (Constant[-5.69]+ (Age * 0.06) + (UPDRS motor score * 0.017) + (GDS equivalent * .04) + (UPSIT equivalent * -0.06) + (RBDSQ * 0.17))). The constants and coefficients are from Bootstrapped results of multivariate logistic regression (Schrag et al., 2017).

3. **Risk score 3: Velseboer et al. (2016) Model for unfavorable prognosis at 5-year assessment.** (From Velseboer et al 2016).

First we extracted axial scores from the MDS-UPDRS assessment: Q3.9 Arising from chair, Q3.10 Gait, Q3.11 Freezing of gait, Q3.12 Postural stability.
Then calculate the probability of unfavourable outcome using coefficients from Velseboer et al. (2016) Appendix e-1 algorithm calculator:
'Log odds' = Intercept (-3.125) + Age * 0.059 + UPDRS axial scores * 0.379 + animal verbal fluency score * -0.068 * 1.267
The probability of unfavourable outcome = ROUND(1/(1+EXP(-(Log odds score))), 2).