e-Methods

Calculation of Risk Scores:


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.:

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

Step 2: Calculate G - 'Global' cognitive risk
Secondly, the sum G of the “coefficient × mean value” products is calculated for the discovery population:

\[ G = 0.0813 \times 60.4 \text{ (mean of age at onset)} + 0.3803 \times 0.619 \text{ (proportion of male)} - 0.0863 \times 13.7 \text{ (mean of years of education)} - 0.2819 \times 28.6 \text{ (mean of baseline MMSE score)} + 0.0219 \times 26.5 \text{ (mean of baseline MDS-UPDRS III)} + 0.4287 \times 0.207 \text{ (proportion of depression)} = -3.3828. \]

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

\[ B = e^{I-G} \] (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.

\[ S(t) = 0.7989, \text{ the 10-year survival rate } S(10) \text{ derived from the optimized Cox model.} \]

\[ \text{Cognitive risk score} = 1-S(t)^B \]


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: 

\[ 100 \times \text{EXP}((\text{Constant}[-5.69] + (\text{Age} \times 0.06) + (\text{UPDRS motor score} \times 0.017) + (\text{GDS equivalent} \times 0.04) + (\text{UPSIT equivalent} \times -0.06) + (\text{RBDSQ} \times 0.17)) / (1+\text{EXP}((\text{Constant}[-5.69] + (\text{Age} \times 0.06) + (\text{UPDRS motor score} \times 0.017) + (\text{GDS equivalent} \times 0.04) + (\text{UPSIT equivalent} \times -0.06) + (\text{RBDSQ} \times 0.17)))). \]

The constants and coefficients are from Bootstrapped results of multivariate logistic regression (Schrag et al., 2017).

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).