

Quantitative comparisons of Progressive Supranuclear Palsy rating scales versions using Item Response Theory modeling

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Background

Progressive Supranuclear Palsy (PSP) is a neurodegenerative late-onset disease that can be challenging in terms of assessment. The Progressive Supranuclear Palsy Rating Scale (PSPRS) is the main scale used for measuring the severity of PSP.

Aims:

To quantitatively evaluate and compare the PSPRS, and its reduced subscale versions, communicated by the FDA, before rescoring (PSPRS-10), and after rescoring (rPSPRS-10) using Item Response Theory (IRT) models. To develop a progression model of the disease and assess relative merits of study designs and analysis options for disease-modifying treatment.

Conclusions

- The PSPRS has suboptimal properties with low and heterogeneous correlation between item severities (Fig. 1).
- The 10 FDA selected items have high information content (Fig. 1) and capture a similar disease severity concept, as evidenced by unidimensionality under the IRT model (Fig 3).
- The rescoring suggested by FDA results in a slight loss of information (Table 1).
- Item level analysis of PSPRS-10 require half the sample size for treatment effect identification compared to total score analysis (Table 1).

Methods

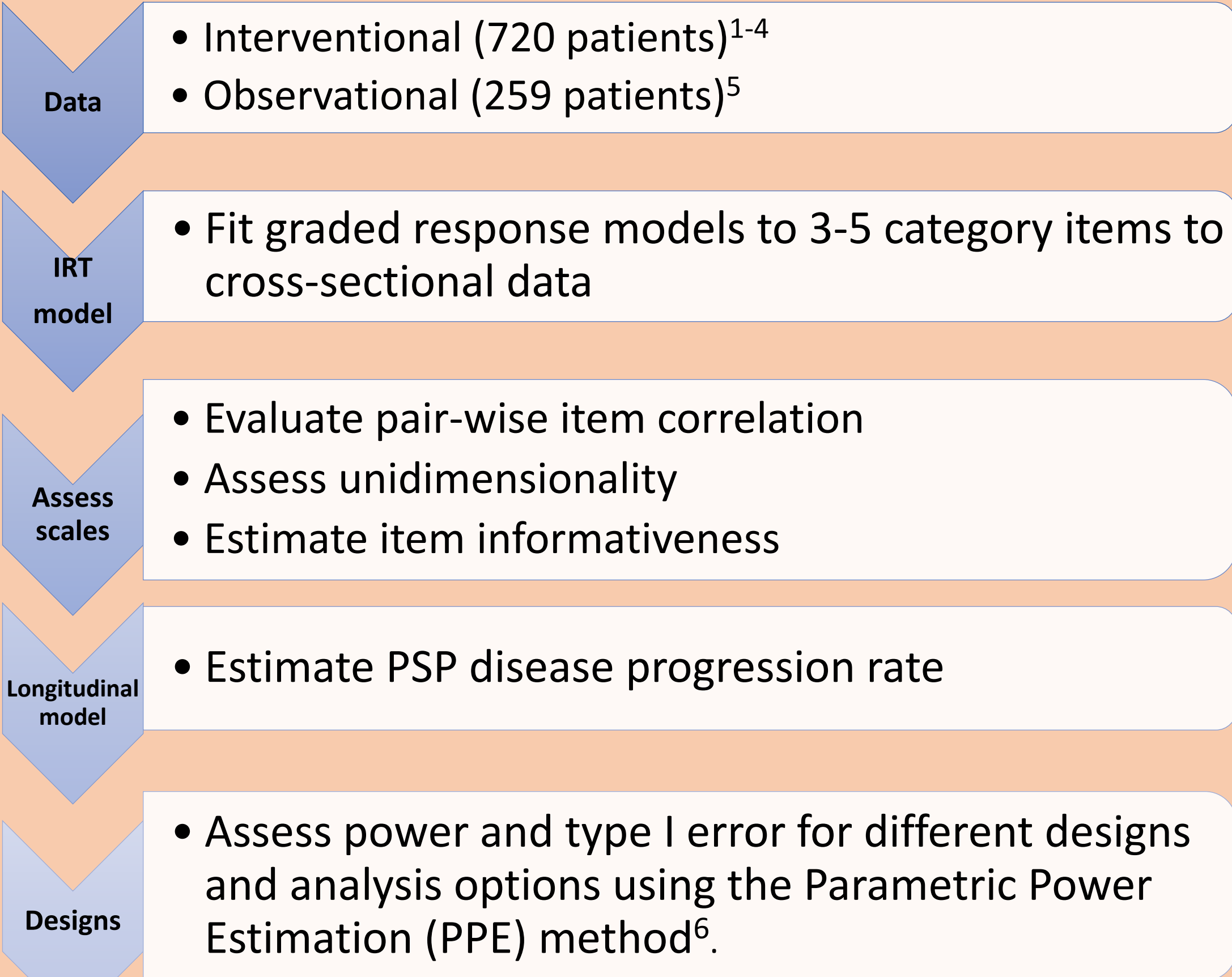


Diagram 1: Flow-chart of investigations

Results

Figure 1: PSPRS Item Characteristic Curves. The numbers are the fisher information

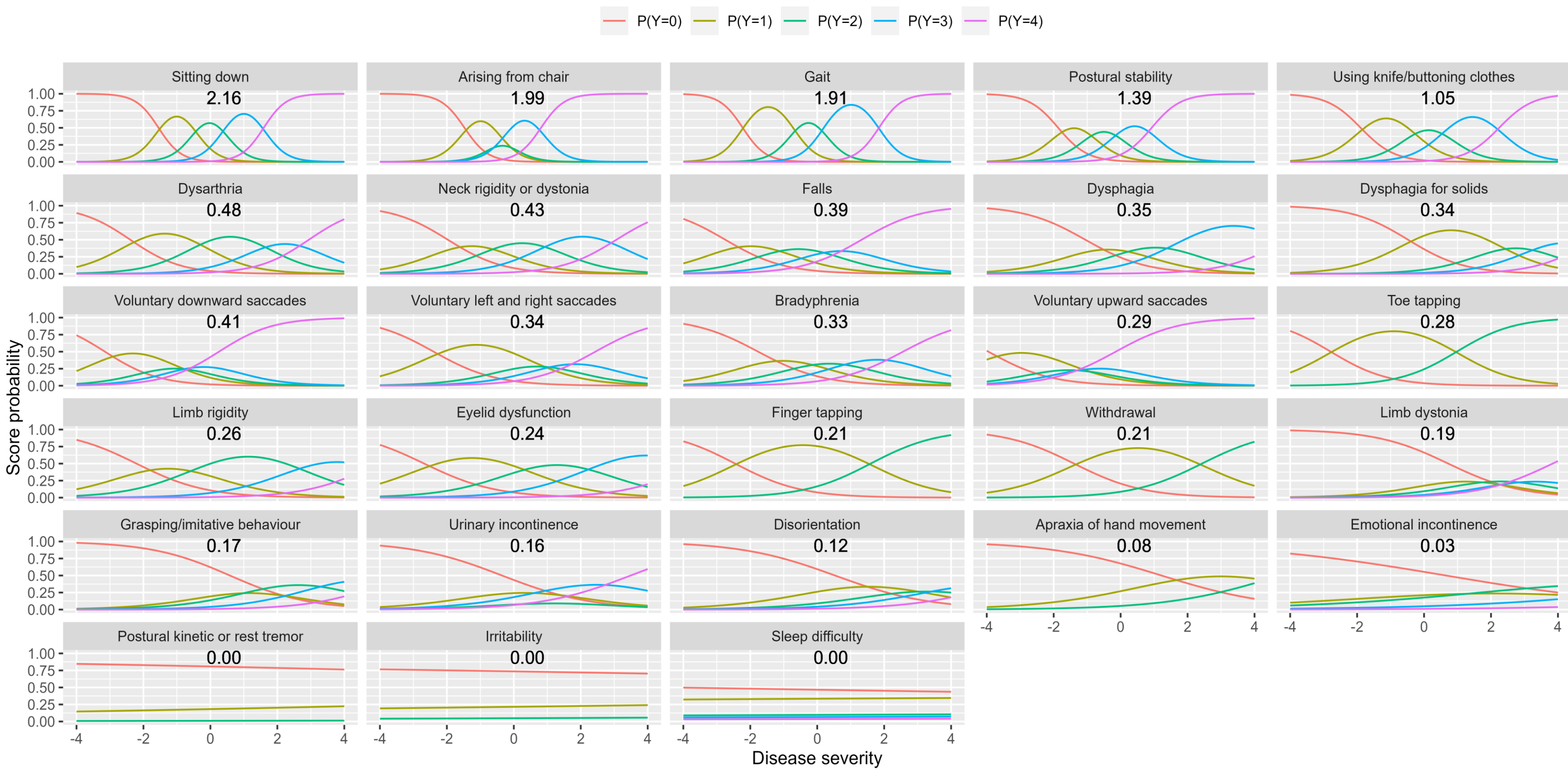


Table 1: Number of subjects per arm needed for 80% power at 5% significance level-for a 1:1 treatment : placebo parallel arm trial of 1 year duration and observations every 3 months

Model	Scale	20% effect	50% effect
Item response theory	PSPRS-10	139	19
	rPSPRS-10	154	22
Item response theory-end of treatment	PSPRS-10	154	22
	rPSPRS-10	178	25
Linear total score	PSPRS-10	303	39
	rPSPRS-10	338	43
Linear total score-end of treatment	PSPRS-10	316	43
	rPSPRS-10	341	46

Type I error was controlled for all analysis models used

Figure 2: Visual predictive check, all data

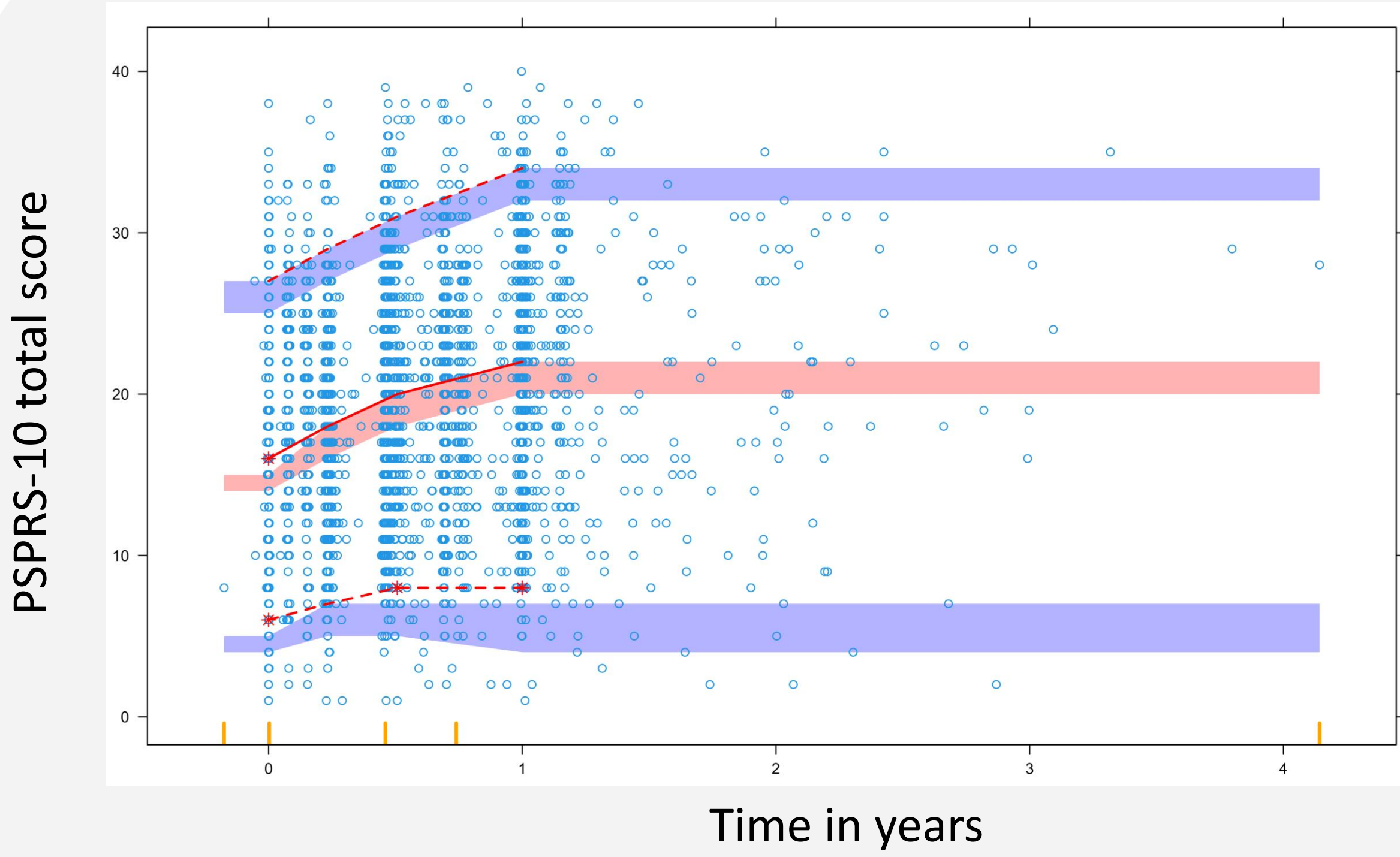


Figure 3: PSPRS-10 pair wise item Pearson correlation coefficients. The lower triangle is the observed correlation, while the upper triangle is the pair-wise correlation of items simulated from the IRT model



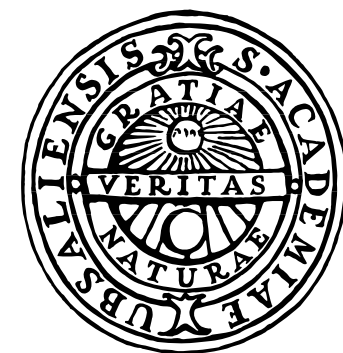
Acknowledgement:

This work was supported by the European Joint Programme on Rare Diseases (EJPRD) (Grant Agreement n°825575) WP20 Innovation Statistics project “EVIDENCE-RND” (to M.K. F.M. R.S. and M.S.), the EJPRD PROSPAX consortium, further supported by the Clinician Scientist program “PRECISE.net” (to A.T, M.S. and R.S.).

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