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# FORECAST PARKINSON DISEASE PROGRESSION TO BETTER SELECT PATIENTS INTO TRIALS

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**Objectives** Subject recruitment is a burden that hampers clinical trials, especially in neurodegenerative diseases inducing long-term and subtle worsening of abilities. Better selecting them allows to reduce their required number - or conversely to improve the proven effect size.

**Methods** We extracted one-year separated visits in PPMI to model the placebo arm. For each patient, we derive a treated counterpart by applying an individual treatment effect calibrated so to get an effect size that correspond to a 4 point MDS-UPDRS II + III improvement and from which we derive a required sample size. Then, thanks to individual outcome predictions [Schiratti et al, 201] from which we derive a individual ratio of MDS-UPDRS II + III change, we select a subset of patients that minimizes the sample size for the previous effect size. The optimal ratio value is estimated on 80% of the PPMI patients and tested on the last 20%. We then test this ratio on DIGPD. The operations are bootstrapped 100 times on 50% of the data.

**Results** By selecting patients whose one-year MDS-UPDRS II+III ratio of predicted change is of 0.078 and for 0.4 of effect size, the number of patients needed to show a 0.4 effect size is reduced by  $45\pm(11.4)SD\%$  (resp.  $55\pm(7.6)SD\%$ ) on the test set (resp. DIGPD evaluation).

**Conclusions** The use of our prediction model can concretely improve clinical trials on Parkinson's disease by helping to better select patients and thus reduce the cohort size for a fixed treatment effect size.

## References

[Schiratti et al, 201] Schiratti J-B, Allasonniere S, Colliot O, Durrleman S. *A Bayesian mixed-effects model to learn trajectories of changes from repeated manifold-valued observations*. In *Journal of Machine Learning Research (JMLR)* 18(1):4840-4872. 2017.

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