Latent process location-scale mixed-effects model for intensively sampled ordinal patient reported outcomes

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Patient reported outcomes (PROs) are collected on a daily basis in clinical trials to measure patients' quality of life, e.g. symptoms. Often these data are reported in a small range ordinal scale and analyzed without considering their longitudinal aspect.The emergence of electronic data collection methods for home-based measurements has enabled routine capture of various symptom scores such as breathlessness in respiratory diseases, highlighting the need to develop statistical methods for the analysis of these intensive ordinal longitudinal data. Indeed, both the level, long-term fluctuations and short-term variability of these outcomes are expected to be linked to the disease progression and to be affected by treatment. To model the dynamics of ordinal PROs, we propose a location-scale probit mixed-effects model which includes two types of variability: individual trajectories alowing for flexibiility, e.g. using splines and the short-term variability with an error where the variance is expressed as a linear structure of covariates such as treatment arm and a patient-specific random intercept. The model is estimated in the Maximum Likelihood framework with an interface in R. The burdensome high-dimensional intractable integrals in the optimization are approximated using the Quasi-Monte Carlo method. We apply the methodology to a randomized Phase III COPD clinical trial to evaluate the effect of treatment on dynamics of the respiratory symptoms and their variability.