DEVELOPMENT AND PERFORMANCE OF NPDE FOR THE EVALUATION OF TIME-TO-EVENT MODEL

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Objectives: Normalised prediction distribution errors (npde) are used to evaluate graphically and statistically continuous responses in non-linear mixed effect models [1]. Here, our aim was to extend npde for time-to-event (TTE) models and to evaluate their performances.

Methods: Let V denote a dataset with TTE observations. The null hypothesis $H_0$ is that observations in V can be described by a model M. Residuals called npde [1] can be computed and adapted for TTE observations with a management of censoring inspired by Nguyen [2]. $H_0$ can be tested by examining the $N(0,1)$ distribution of the npde.

We evaluated the performance of npde for TTE data through a simulation study inspired by the work of Desmée et al. [3]. They characterised the relationship between the biomarker PSA (prostate specific antigen) and survival in 500 prostate cancer patients via joint modelling. We simulated event times from the joint model, based on the predicted PSA trajectories, for different sample sizes. We evaluated the type I error and power of npde to detect different types of model misspecifications for the TTE component in several scenarios.

Results: Type I error was found to be close to the expected 5% for all tested sample sizes, and the percentage of rejection was closer to 5% when censored events were considered. npde were able to detect misspecifications in the baseline hazard as well as in the link between the longitudinal variable and survival. The power to detect model misspecifications was more important as the difference of survival was large. As expected, the power also increased as sample size increased.

Conclusion: npde can be readily extended to TTE data, and we found that they performed well with an adequate type I error.