A SEMI-MARKOV MODEL WITH INTERVAL CENSORING AND NON-PROPORTIONAL HAZARDS

 $\underline{Y \text{ Foucher}}^{\dagger 1}$, M Giral², JP Daures¹

¹University of Montpellier 1, France; ²Hospital fo Nantes, France

[†]E-mail: *yohann.foucher@iurc.montp.inserm.fr*

In studies of chronic diseases, multistate approach is becoming increasingly common in order to analyze complex evolution of patients. For example, the evolution of kidney transplant recipients can be decomposed into several clinical states, with more than one final stage.

Motivated by this application, we propose a general and parametric semi-Markov model. The distribution functions are fitted to the staying times, and it is shown the relevance of generalized Weibull distribution. The corresponding Likelihood function allows interval censored data and the determination of initial states according to covariates.

The main originality of the method is the introduction of covariates through the probability density functions of the staying times, without assuming the proportionality of hazards. Time interaction and accelerated failure time approach are introduced. Indeed, the majority of authors used the PH assumption on the staying time distributions. We also proposed a simple graphical method to test the proportionality in the context of parametric semi-Markov multistate processes.

In order to analyze the relevance of our methodology, we apply two models to cohort of recipients: the first assuming proportional hazards, contrary to the second. The new proposal clearly leads to more precise results and to a more parsimonious model.