A comparison between landmarking and joint modeling for producing predictions using longitudinal outcomes

Magdalena Murawska[1,*], Dimitris Rizopoulos[1], Emmanuel Lesaffre[1,2]

[1] Department of Biostatistics, Erasmus University Medical Center, PO Box 2040, 3000 CA Rotterdam, The Netherlands,*e-mail: m.murawska@erasmusmc.nl
[2] I-Biostat, Catholic University of Leuven, Belgium

Abstract: Motivated by current trends towards personalized medicine, there is great interest nowadays to develop prognostic models. Examples are numerous and come from a wide spectrum of diseases, including prognostic models applied in cancer research, risk scores for cardiovascular diseases, such as the Framingham score, and prognostic models for HIV infected patients. The common characteristic for all these diseases is that the rate of progression is not only different from patient to patient but also dynamically changes in time for the same patient. Hence, it is medically relevant to investigate whether repeated measurements of specific biomarkers can ultimately provide a better understanding of disease progression.

In this work we compare two approaches for producing dynamic predictions of survival probabilities using the recorded longitudinal information, namely landmarking (van Houwelingen and Putter, 2011) and joint modeling (Rizopoulos, 2012). Landmarking requires adjusting the risk set at the landmatk point and fitting a Cox model, whereas joint modeling explicitly takes into account all the longitudinal history of a subject to produce predictions. We show that because the subject-specific longitudinal trajectories can be quite complex (e.g. nonlinear, plateaus) different features of these trajectories may be more predictive for the event of interest. To this end we study how the aforementioned approaches perform under different functional relationship between the longitudinal and event time outcomes.

Our proposals are exemplified in the primary biliary cirrhosis (PBC) study conducted by the Mayo Clinic between 1974 and 1984. We aim to find which characteristics of the serum bilirubin profile are most predictive for death. To model longitudinal serum bilirubin level a mixed effects model is postulated with natural cubic splines to account for nonlinear character of the marker evolution. For the survival process a standard relative risk model was considered with different forms of the association structure with the longitudinal part. We use Bayesian methods for the joint models estimation and perform a series of simulations to evaluate both methods of constructing dynamic predictions.

Keywords: Dynamic predictions; Joint models; Landmarking.