Title:

"Prediction Models for Competing Risks with time-dependent covariates"

Abstract

Time-dependent covariates are frequently encountered in regression analysis for event history data.
In the competing risks setting, if random (internal) time-dependent covariates are to be included in the model, then it is still possible to estimate cause-specific hazards, but prediction on the cumulative incidence functions and survival probabilities based on these hazards is no longer feasible.
We faced these serious limits when we studied bone marrow transplant data. After bone marrow transplant, patients may develop Graft versus Host Disease (GvHD) during their follow-up time. A challenging issue with these data is to assess the effect of the random time-dependent covariate, GvHD, on the cumulative risks of relapse and death over time.
We aims at providing some strategies for dealing with these prediction problems, when the internal covariates are categorical. In a multi-state framework, a first approach uses internal covariates to define additional intermediate (transient) states in the competing risks model. Another approach is to apply landmark analysis as described by van Houwelingen (Scand. J. Stat., 2007) in order to estimate cumulative incidences at different sub-intervals of the entire study period. The final strategy is to extend the competing risks model by considering all the possible combinations between internal covariate levels and cause-specific events as final states.
In practise, it is unclear which model performs best in predicting the outcome, especially because of different model assumptions. In the landmark approach, information on GvHD disease is recorded at each landmark point only. Therefore, we consider prediction models based on the previous strategies and, in order to assess their prediction accuracy, we compare prediction errors for cumulative risks by means of the expected Brier score. For this measure, a modified estimator based on pseudovalues is proposed.