

Analysis of semi-competing risks data via bivariate longitudinal models

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Abstract: An example of semi-competing risk data analysis is the evaluation of risk factors for Alzheimer's disease and death, before and after the onset of Alzheimer's. Most existing methods treat the dependence between Alzheimer's and death as nuisance and restrict it to follow simple mathematical models. However, these methods may suffer from model misspecification of the dependence structure. Furthermore, information about the dependence, including its form, trajectory over time and how it depends on covariates can provide new clinical knowledge. Therefore, we propose a novel framework for analyzing semi-competing risks data by the means of bivariate longitudinal modeling. Our methods differentiate between local and global dependence. Local dependence captures the co-occurrence of Alzheimer's and deaths within a short period of time, while global dependence is the long-term effect of Alzheimer's on the risk of death. We incorporate flexible splines into our models to account for changes over time and develop a penalized maximum likelihood estimators and associated inference for the parameters of interest. Our methods are illustrated using the Adult Changes in Thought study.