Additive Hazard Model with Additive Frailty for Semi-Competing Risks Data

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We proposed an illness-death model with Lin and Ying's additive hazard and additive frailty for the regression analysis on semi-competing risks problem in a general morbidity/mortality process. Comparing with the Cox-type hazard, the additive hazard function is more natural and properly partitions the effect of the covariate on one transition into the other transition, internal consistency in the illness-death model. In the proposed model, we adapted the additive frailty to describe the association between the covariates and failure time in terms of the risk difference rather than the risk ratio. For the inference, we considered a full maximum likelihood on the complete data and incorporated an EM algorithm to deal with frailty and Gauss-Laguerre quadrature method for calculating the expectations of the functions of frailty. The proposed model was applied to the data from a national intergroup trial in the 1980's to study the effectiveness of two adjuvant therapy regimens for the improvement of surgical cure rates in stage III colon cancer. We compared the group treated with levamisole plus fluorouracil with the untreated group using the semi-competing risks model with cancer recurrence and death.

Key Words: EM algorithm, gamma distribution, Gauss-Laguerre quadrature, illness-death model, internal consistency, piecewise constant baseline hazard