

Semi-competing risks approach for intermediate events

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The term semi-competing risks data was first introduced by Fine, Jiang and Chappel [1] when referring to the situation of a bivariate time distribution (T_1, T_2) where T_2 dependently censors T_1 . Semi-competing risks patterns arise in those situations where some of the individuals in the sample are at risk of experiencing both an intermediate event and a terminal event. Since the occurrence of the terminating event precludes the observation of the intermediate event, the time T_1 to the intermediate event is censored by T_2 , the time to the terminating event. Often the interest relies on the terminating event and, in these situations, conditional models for T_2 given T_1 take into account the effect of the intermediate event. However, when the main goals rely on the association between T_1 and T_2 -and thus on the joint distribution (T_1, T_2) -, and on the estimation of the marginal distribution of the intermediate event, T_1 , then semi-competing risks methods are a convenient alternative.

Two medical studies motivate our work and the analysis by means of semi-competing risks methods. In the first study, a cohort of newly diagnosed bladder cancer cases may experience recurrences of the tumour, that is, superficial local reappearances of the tumour. These patients are as well at risk of progression or death from the disease, hence the occurrence of either one acts as a terminal event for recurrence. In this setup, it is relevant to understand the marginal process which generates a recurrent event, since efforts to reduce them are of paramount clinical importance. The second data set refers to a cohort of frail elderly patients followed after an acute medical illness requiring hospitalization. The patients, admitted in a geriatric care unit, are expected to recover their normal functional and nutritional levels, which have decreased critically during their previous hospitalization. The association between mortality -acting here as a terminating event- and recovery of normal levels -here the intermediate event-, as well as the recovery process by itself, are in this study clinically relevant.

In this work, we analyze the two data sets by means of semi-competing risks models and we extend them in two directions. First, we explore how different choices of general copula models may reflect distinct dependence structures in distinct areas of the plane. Secondly, for some individuals in our data sets, the time to the intermediate event or the time to the terminal event are interval-censored. We propose some extensions to handle semi-competing risks data in the presence of interval-censored data, considering the scenarios where only the intermediate event is interval-censored, only the final event is interval-censored, of both events are interval-censored.

References

[1] Fine JP, Jiang H, Chappell R (2001) On semi-competing risks data. *Biometrika* 88:907-919