Semi-competing risks methods accounting for interval-censoring

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Abstract

Semi-competing risks data arises when a subject is at risk of both a terminating and an intermediate event. In this situation we encounter a bivariate survival analysis problem with dependent censoring if these two events are related. In this work we extend the semi-competing risks data problem to the case where the intermediate event is interval-censored.

Keywords: semi-competing risk, interval-censoring, bivariate survival

Summary

Semi-competing risks arises when subjects may experience an intermediate event -the individual continues under observation after the occurrence of the event-, or a terminating event -the follow-up of the individual is stopped at the occurrence of the event-. In the common situation where the intermediate event is either relapse or progression of disease, death -terminating event- can preclude the observation of the intermediate event, inducing in this way a dependent censoring mechanism on the intermediate event. If we denote by T_1 and T_2 the times to the intermediate and terminating event respectively, we are tackling a bivariate survival problem with dependent censoring.

When the interest relies on the terminating event, conditional models for T_2 given T_1 are enough to take into account the effect of the intermediate event on the terminating event. However, when the main goals rely on the association between T_1 and T_2, or on the estimation of the marginal distribution of the intermediate event, T_1, then semi-competing risks methods are a convenient alternative. Indeed, the existence of dependent censoring prevents the consistent estimation of the marginal T_1 based only on empirical data, and a model for the bivariate distribution needs to be assumed to recover this distribution. We follow the work of Fine, Jiang and Chappell [1], where a Clayton's copula model with a single association parameter is assumed for the joint survival function.

In this work we propose a methodology to deal with a semi-competing risks data problem when, in addition, the intermediate event T_1 is interval-censored. In effect, in many longitudinal studies the occurrence of the intermediate event is evaluated at periodic visits, so T_1 is only known to lie between the times of two specific visits and we are under the presence of interval -censored data. The estimating procedure proposed in [1] used an estimator for the association parameter based on the concordance index for a pair of two *observable* or *comparable* pairs, and a plug-in estimator for the marginal distribution. We extend this procedure in two ways: (i) we introduce an iterative algorithm to jointly estimate the association parameter and the marginal distribution, and (ii) given that the *comparable* sample in the case of interval-censoring produces a biased estimator, we propose alternatives to correct this bias. We assess the performance of the proposed method by presenting simulated and real data.

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3. Bibliography

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