

Multivariate survival analysis for case–control family data

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SUMMARY

Multivariate survival data arise from case–control family studies in which the ages at disease onset for family members may be correlated. In this paper, we consider a multivariate survival model with the marginal hazard function following the proportional hazards model. We use a frailty-based approach in the spirit of Glidden and Self (1999) to account for the correlation of ages at onset among family members. Specifically, we first estimate the baseline hazard function nonparametrically by the innovation theorem, and then obtain maximum pseudolikelihood estimators for the regression and correlation parameters plugging in the baseline hazard function estimator. We establish a connection with a previously proposed generalized estimating equation-based approach. Simulation studies and an analysis of case–control family data of breast cancer illustrate the methodology’s practical utility.

Keywords: Case–control family study; Cox proportional hazards model; Familial aggregation; Frailty model; Innovation theorem.

1. INTRODUCTION

There is an increasing interest in the application of multivariate survival analysis techniques to population-based case–control studies for estimating the marginal hazard function and the dependencies of correlated ages at disease onset (Li *et al.*, 1998; Shih and Chatterjee, 2002; Hsu *et al.*, 2004). An interesting example is a breast cancer study conducted at the Fred Hutchinson Cancer Research Center (Malone *et al.*, 1996). In this study, the breast cancer incidence cases were ascertained from the Surveillance, Epidemiology, and End Results registry, which is a set of geographically defined, population-based cancer registries in the United States. The controls were obtained through random digit dialing and were matched

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