Event History Regression Models with Risk-Free Fraction And Crossing Hazards

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1. Introduction

Cox's (1972) proportional hazards regression model has been the most popular statistical method in studying risk factors of clinical trials and epidemiological studies. In this talk, we discuss two generalizations of Cox's model: a logistic-Cox mixture regression model and a heteroscedastic hazards regression model.

Progress in randomized controlled trials has enhanced the long-term survivorship or the cured fraction of patients. In general, subjects, without related genes nor deleterious environmental exposures, might not be susceptible to the disease. Nevertheless, conventional statistical methods in event history analysis presume that a study subject is susceptible to the event of interest. They are not virtually applicable to risk-factor studies of subjects in a sample with a risk-free fraction. Dealing with right censored data, Kuk and Chen (1992) proposed a logistic-Cox mixture model by identifying risk fractions with the logistic regression and by analyzing the times to event with Cox's proportional hazards regression. Frequently in medical follow-up studies, we cannot observe subjects' exact ages or indications of event onset, but right censored times in combination of exact observations, left and interval censored times. We present a logistic-Cox mixture regression model to handle this complicated censoring mechanism.

On the other hand, in contrast to the assumption of proportional hazards, the phenomenon of crossing hazards often emerges from clinical trials and epidemiological studies. Hsieh (2001) proposed a heteroscedastic hazards regression model to analyze studies of this kind. We present two testing procedures for model validation: one for goodness-of-fit and the other for heteroscedasticity.

2. StatisticalInference

The marginal likelihood, as in Kuk and Chen (1992), can be derived for the logistic-Cox mixture regression model with general interval censorship. To circumvent its problem of computational complexity, we here proposed a joint estimating procedure for piecewise-constant hazards and regression parameters based on the full likelihood using an alternating estimation scheme.

In a Cox-type regression model accommodating heteroscedasticity via a power factor of the baseline cumulative hazard, Hsieh (2001) proposed an over-identified estimating equation approach with the method of sieves. We consider model validation procedures. An omnibus goodness-of-fit statistic is derived for overall model checking. A Wald-type statistic and a score-type statistic are presented for testing the aptness of proportional hazards. They are asymptotically distributed as chi-square random variables.

3. Results

Data analyses in a study of early menarche onset and in a cancer clinical trial are presented in illustration of these two event history models. Further investigation integrating both risk-free fractions and crossing hazards into a regression model is in progress.

REFERENCE

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