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The Model and the Inference for the Clustered Recurrent Event

Kang Fang Yuan*

School of Applied Science, Beijing Information Science and Technology University, Beijing 100192, China

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***Corresponding author:** Kang Fang Yuan, School of Applied Science, Beijing Information Science and Technology University, Beijing 100192, China, Email: fykang_003@163.com

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Abbreviations: IPCW: Inverse Probability of Censoring Weighting; CGD: Clinic Study on Chronic Granulomatous Disease

Short Communication

In medical studies, subjects may experience one event of interest repeatedly over a period of time, which is termed recurrent event. The examples include multiple infection episodes and tumor recurrences. In many other settings, the subjects may be clustered according to some property, because they are correlated owning to some common factors. For example, medical environment and genetic inheritance have influence on the recurrence of disease. Thus, during the modeling for the recurrent event, some subjects may have dependence because of same medical facility or same family, and therefore are in the same cluster.

The recurrent event has been discussed extensively. Generally, there are two modeling methods: one is modeling for intensity function for the process [1]. The other is modeling for rate function (mean function), such as Lin et al. [2], Dai et al. [3]. The recurrent event is often precluded by a terminal event such as death. Recently, there have been several models for recurrent event with a terminal event. In many applications, however, the gap time is a natural outcome of interest [4]. Some methods have been developed for the analysis of recurrent gap time data [5-7]. For the clustered recurrent event, most of the research focuses on the marginal rate function model. Schaubel & Cai [8] studied the marginal cox-type rate model. He et al. [9] established an additive marginal rate model. Liu et al. [10] considered a clustered recurrent event in the presence of a terminal event. However, many important models such as additive rate model, additive-multiplicative rate model and accelerated model have not been studied. Besides, there is seldom research about the clustered gap times for recurrent event.

For the clustered recurrent event in the presence of a terminal event, we developed an additive marginal rate model. Applying the estimating equation and inverse probability of censoring weighting (IPCW) technique [11], we obtained the estimator and verified the asymptotic normality. We conducted some simulating which worked well. A bladder cancer data including 117 patients was analysed (Table 1) [12,13]. For the clustered recurrent gap time, we also developed an additive hazard model. We obtained the estimator utilizing estimating equation. We simulated a clustered gap time, and then compared the clustered model and the non-clustered model. The results showed that the clustered model worked better than non-clustered model. Finally, an application to a clinic study on chronic granulomatous disease (CGD) was illustrated (Table 2).

Table 1: Estimation of the Clustered Additive Rate Model.

Covariate	Initial Number	Treatment
Estimate	0.0078	-0.0181
SE	0.003	0.0104
P-value	0.0042	0.0413

Table 2: Estimation for CGD data under clustered model.

Covariate	Treat	Age
Estimate	-0.0098	-0.0022
SE	0.0022	0.0028
P-value	0	0.4293
95% confidence interval	(-0.0142,-0.0078)	(-0.0054,0.0033)

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