

SEMIPARAMETRIC TIME-VARYING  
COEFFICIENT REGRESSION MODEL FOR  
LONGITUDINAL DATA WITH CENSORED TIME  
ORIGIN

Qiong Shou

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**Abstract**

In preventive HIV vaccine efficacy trials, thousands of HIV-negative volunteers are randomized to receive vaccine or placebo, and are monitored for HIV infection. The primary objective is to assess vaccine efficacy to prevent HIV infection. An important aspect of vaccine efficacy trials is to assess whether vaccine decreases secondary transmission of HIV and ameliorates HIV disease progression in vaccine recipients who become infected. This thesis investigates the vaccine effect on the post HIV longitudinal biomarkers (e.g., viral loads and CD4 counts) over time since the actual HIV acquisition. The method applies to the situation when the time of the actual HIV acquisition may be missing or censored. The problem is investigated under the semiparametric additive time-varying coefficient model where the influences of some covariates vary nonparametrically with time while the effects of the other covariates remain constant. The weighted profile least squares estimators are developed for the unknown parameters as well as for the nonparametric coefficient functions. The method uses the expectation maximization approach to deal with the censored time origin. The asymptotic properties of both the parametric and nonparametric estimators are derived and the consistent estimates of the asymptotic variances are given. The numerical simulations are conducted to examine finite sample properties of the proposed estimators. The method is also applied to a real data from the STEP study with MITT cases.