Using Generalized Linear Mixed Models for Jointly Modeling Multivariate Longitudinal Data and Discrete Time-To-Event Data: Application to Primary Biliary Cirrhosis Data

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Abstract

In medical studies, patients are often followed up over time and their disease related biomarkers are measured repeatedly. Together with these multiple longitudinal biomarkers, the survival status (time to death) of such patients are observed. When the analysis is focused on evaluating the effect of multiple longitudinal biomarkers on the time to an event (death), such analysis is often carried out by using joint models of multiple longitudinal data and time-to-event data. The multiple longitudinal biomarkers are correlated within a patient since the measurement of one patient exhibits more similarity than measurement from different patients. This research utilizes the joint modeling capability of Generalized Linear Mixed Models (GLMMs) with multiple longitudinal biomarkers along with the date of measurement are considered as the predictors of the GLMM and the response of the model is taken to be the time to death. The need of joint modeling of GLMMs arose due to the fact that time-to-event data are concerned with both actual deaths and censored observations. Therefore, the response variable is expressed dichotomously giving both the time to the event (death) and the status of the event (censored or not). The time to death (number of days) was taken to be a Poisson response variable while the status (censored or not) was taken as a Binary random variable in the joint GLMM. The proposed methodology was applied to a set of Primary Biliary Cirrhosis (PBC) data. The results of the joint model expressing time to death of PBC patients revealed that presence of edema, serum bilirubin level, prothrombin time, age of the patient, and the interaction of Bilirubin and Albumin levels are significantly associated with the survival of the PBC patients. The goodness of the fitted joint model was satisfied by the Generalized Pearson Chi-square goodness of fit test statistics.

Keywords: Clustered Data, Generalized Linear Mixed Models (GLMM), Joint Modeling, Longitudinal data