COMPARISON OF ALGORTIHMS TO GENERATE EVENT TIMES CONDITIONAL ON TIME-DEPENDENT COVARIATES

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Both etiological considerations and increased computational resources contribute to the increasing popularity of longitudinal studies with repeated measurements of prognostic factors. To accommodate such designs, techniques such as the Cox proportional hazards model have been extended to incorporate time-dependent (TD) variables. Yet, the properties of models with TD covariates have not been extensively investigated using simulations, possibly because of the lack of validated algorithms to generate survival times conditional on TD covariates. We evaluate and compare three algorithms to simulate cohorts with event times conditional on TD covariates. The first algorithm is the permutational algorithm (Mackenzie and Abrahamowicz, *Stat Comput*, 2002) that matches the marginal distributions for the failure and censoring times with vectors of time-dependent covariates based on the Cox model partial likelihood. The second algorithm (Miloslavsky et al, *J R Statist Soc B*, 2004) relies on logistic distributions. The third algorithm generates survival times based on a survival function evaluated after each time increase, which depends on updated values of TD covariates. The 3 algorithms will be compared with respect to: accuracy, flexibility in accommodating complex time-dependent variables and non-linear effects, flexibility in specifying marginal and/or conditional distributions of covariates, censoring and failure times, implementation ease, and running-time.