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Joint Longitudinal and Survival Models to Predict Survival Outcomes

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Abstract

Survival analysis is the common name of statistical methods where the time until an event is analysed. These methods are used extensively in medical research to analyse, for example, time until death or the development of a disease over time. Longitudinal data consists of repeated measurements taken over a period of time, for example blood pressure. Combining the Cox regression model used to analyse survival data with the linear mixed effect model for longitudinal data results in the joint longitudinal and survival model. In this thesis, the joint model is applied to a subset from the AMORIS (Apolipoprotein related mortality risk) cohort. The AMORIS cohort contains observations from subjects, collected between 1985 and 1996 in Stockholm, who provided blood and urine samples which were analysed. The subset used in this thesis includes all men aged 40-50 at observation who provided measurements of the four longitudinal biomarkers: Apolipoprotein A, Apolipoprotein B, total cholesterol and triglycerides. This resulted in a dataset containing 33 930 observations from 23 768 subjects. The joint model was applied to these data for each longitudinal biomarker separately, where the time until event in the survival submodel was if the subjects had died at the end of study. The Cox model and linear mixed effect model were fitted separately and then applied to the joint model following the adaptive Gauss-Hermite quadrature rule. The application of the joint model on these data allowed to predict conditional survival probabilities for the subjects who were still alive at the end of the study, following a Monte Carlo simulation scheme. In addition to the survival probabilities, subject specific dynamic survival probabilities were predicted, that is, how the survival probability change over time as more longitudinal observations are obtained. Martingale residuals for the survival part and marginal and subject specific residuals for the longitudinal part in the joint model were also computed and illustrated. The result of the joint model fit to the data indicated that a one unit increase of each of the four longitudinal biomarkers increase the risk of death.

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