Abstract

“Exposure-lag-response associations: Smoothly time-varying and cumulative effects with leads and lags”

Andreas Bender, LMU, Munich

Complexity of time-to-event data analysis increases in the presence of time-dependent covariates or possibly smooth, smoothly time-varying effects. Especially in case of time-dependent covariates (also referred to as "exposures"), e.g. exposure of miners to different doses of radiation or the amount of calories received by critically ill patients during their stay in the intensive care unit (ICU), can complicate the analysis in four regards:

- The magnitude of exposure (its intensity) varies over time
- The effect of the exposure can, additionally, vary over time
- The effect might only be "in effect" in a certain time window (nutrition on day one might only affect hazard on days four through fifteen)
- The effect can be cumulative (one day of malnutrition might not necessarily be damaging, but protracted malnutrition on five of six days might accumulate to have a hazardous effect)

We present a new approach to modeling these so called exposure-lag-response associations using piece-wise exponential models. This allows us to exploit the advanced toolbox available for generalized additive models, including various (bivariate) smoothing techniques, random effects and fast, as well as robust software implementations thereof.
We show results of a study on the effect of caloric intake (recorded during the first 12 days of ICU stay) on survival of almost ten thousand patients in critical care.