Abstract:

Often the effect of at least one of the prognostic factors included in a Cox regression model (CR) changes over time, which violates the proportional hazards assumption of this model. As a consequence, the average relative risk (over time) for such a prognostic factor is under- or overestimated. While there are several methods to appropriately cope with non-proportional hazards, in particular by including parameters for time-dependent effects, weighted estimation in Cox regression (WCR) is a parsimonious alternative without additional parameters. Furthermore, WCR extends the univariate tests by Breslow and by Prentice to multiple covariates and interactions as does CR for Mantel's test. Also WCR is more robust to outlying observations than CR. The methodology has been presented by Schemper (1992) and by Sasieni (1993) but has fallen into oblivion despite its usefulness for samples with a limited number of events and/or in the presence of many covariates. The weighted approach reduces the complexity of an analysis, in particular if time-dependencies of continuous covariates or of interactions are observed.

Therefore, in this presentation we give an update on WCR based on recent work by our group. We define the concept of an average hazard ratio (Kalbfleisch and Prentice, 1981) and show that it can be seen as the odds of \( P(X<Y) \), where \( X \) and \( Y \) denote survival times in two groups. It is thus a simple function of the most elementary nonparametric effect size measure for the two-group case. An average hazard ratio as well as the basic effect size measure can be obtained within WCR.

The possible advantages of WCR over CR are demonstrated by means of a Monte Carlo study of efficiency and bias, and by comparative analyses of a big multicenter lung cancer study. Our empirical investigations permit us to recommend WCR, which is implemented in a SAS macro and in an R package available at: [www.muw.ac.at/msi/biometrie/programs](http://www.muw.ac.at/msi/biometrie/programs).