Interaction of treatment with a continuous variable: Comparison of approaches and an IPD meta-analysis to summarize results across several studies

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Interactions between treatments and covariates in RCTs are a key topic. Standard methods for modeling treatment-covariate interactions with continuous covariates are categorization or linear functions. To use full information of the data spline based methods are one alternative and we have proposed to estimate a continuous treatment effect function with the multivariable fractional polynomial interaction (MFPI) procedure (R&S 2004). Four variants of MFPI, allowing varying flexibility in functional form, were suggested. MFPI is applicable to most of the popular regression models, including Cox and logistic regression.

We conducted a large simulation study to investigate significance level and power of the MFPI approaches, versions based on categorization and on cubic regression splines. We believe that the results provide sufficient evidence to recommend MFPI as a suitable approach to investigate interactions of treatment with a continuous variable (R&S 2013).

Meta-analyses are an important building block of evidence based medicine. Methods are well developed to investigate the effect of a binary variable (e.g. treatment in an RCT, sex as risk factor in epidemiology). In the context of continuous prognostic factors averaging of functions across several trials has been proposed to use the full information for a continuous variable of interest (S&R 2011). Individual participants’ data (IPD) are required.

We combine the two techniques to produce a method of IPD meta-analysis in which continuous treatment-effect functions are averaged across studies. We use the new approach to investigate four potential treatment effect modifiers in a meta-analysis of IPD from three randomised trials in acute lung injury, where the main outcome of interest was 60-day in-hospital mortality (Briel et al 2010). In contrast to cutpoint-based analyses, the results give more detailed insight into whether treatment effects are influenced by any of the four factors considered.
References:


