Bachelor (or Master) thesis: Bayesian shrinkage estimation for subgroups in clinical trials

**Background:** Subgroup analyses are commonly and increasingly performed in confirmatory clinical trials, where the treatment effect is estimated in subgroups of the overall trial population defined by certain patient characteristics, eg age, gender, region, severity of disease, or co-medications.

The appropriateness of subgroup-specific treatment effects has been debated for a long time, eg Yusuf et al (1991) have argued that the treatment effect estimate in the overall population is usually a better guide to the effect in a subgroup than the subgroup-specific estimate. There is probably some truth to this, at least for exploratory subgroups without biological plausibility of a differential treatment effect.

Shrinkage estimation methods combine the overall effect estimate with the estimate within in a given subgroup. They thus offer a compromise between the assumption that there is no difference across the subgroups and assumption that the subgroup effects are completely unrelated. Their potential usefulness in bringing extreme chance findings into perspective is also mentioned in the recent draft European Medicines Agency (EMA) guideline on subgroup analyses in clinical trials (2014). Shrinkage estimation is usually performed within a Bayesian framework, examples include Simon (2002) and Jones et al. (2011); and generally some form of prior distribution for the interaction effect is assumed. Empirical Bayes methods are also an option.

The bachelor thesis should include implementation in and application of Bayesian shrinkage estimation methods to data from recent clinical trials done by Bayer. Software packages to be used are WinBUGS and SAS. A potential master thesis might be also investigate Bayesian search methods for subgroups with a superior treatment effect, see for example Berger et al. (2014).

**Useful prior knowledge:**

- Bayesian statistics and WinBUGS
- Experience with SAS

**Organization:**

The thesis is supervised by Prof. Dr. Katja Ickstadt and Dr. Arno Fritsch (Bayer). Part time presence at the Bayer research center in Wuppertal would be an advantage.

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References:


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