Monday 22 July 2024

15:30-17:00 Invited Session 3 (Main Room)

Innovative Complex Adaptive Designs for Confirmatory Clinical Trials with Multiple Primary Research Questions (Chairs: Babak Choodari-Oskooei and Ian White)

Using Bayesian methods to include non-concurrent controls in the analysis of platform trials: benefits and limitations

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An appealing feature of platform trials is the fact that the trial can include one shared control arm for several treatment arms that enter over time. If a treatment arm is included after the start of the platform trial, this implies that not only concurrent but also non-concurrent controls recruited before the start of this arm are available for comparison. One approach to deal with this situation is to consider the controls as historical/external data that inform the comparison to the concurrent controls (see, e.g. Bofill Roig et al 2023). Many approaches for borrowing from external data have been proposed. Even though these methods are mainly based on Bayesian approaches by incorporating external information into the prior for the current analysis, frequentist operating characteristics of the analysis strategy are of interest. In particular, type I error and power at a prespecified point alternative are in the focus. For a fair comparison of test procedures without and with borrowing, the tests are calibrated to achieve the same type I error rate (Kopp-Schneider et al. 2024). We will consider approaches that dynamically borrow information according to the similarity of current and external data, e.g. the power prior approach that incorporates external data in the prior used for analysis of the current data. This prior is proportional to the likelihood of the external data raised to the power of a weight parameter. An Empirical Bayes approach for the estimation of the weight parameter from the similarity of external and current data has been proposed by Gravestock et al. (2017). We will also consider the robust mixture prior approach (Schmidli et al, 2014), a popular method that uses a weighted mixture of an informative and a more dispersed prior to address potential prior-data conflict and robustify the analysis. In the frequentist framework, power gains are not possible when borrowing external control data to the current trial, a finding that had been proven in general before (Kopp-Schneider et al. 2020). In fact, we have observed that the power in a comparison including non-concurrent controls may even lead to power losses compared to the test calibrated to borrowing.

References:

Bofill Roig M et al (2023). *Trials*, *24*(1), 408.

Gravestock I, Held L et al (2017). *Pharmaceutical Statistics* 16:349-360.

Kopp-Schneider A et al (2020). *Biom J* 62(2): 361-374.

Kopp-Schneider A et al (2024). *Pharm Stat* 23(1):4-19.

Schmidli H et al (2014) *Biometrics* 70(4), 1023-1032.