Einladung zum Biometrischen Kolloquium

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BIAS AND PRECISION IN EARLY PHASE ADAPTIVE STUDIES AND ITS CONSEQUENCES FOR THE DECISIONS ABOUT CONDUCTING AND DESIGNING CONFIRMATORY STUDIES

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ABSTRACT:

The literature on adaptive designs largely concerns methods for the primary hypothesis tests in phase III clinical trials and meanwhile includes some limited research on bias and precision of point estimates, especially in early phase trials. However, bias and imprecision remain relevant as they may lead to erroneous decisions for the later phase III clinical trials. With focus on oncology, we studied phase II adaptive designs and methods for efficacy estimation in such designs, and investigated the consequences of bias and imprecision of phase II efficacy estimates on the planning of phase III trials. We discussed and proposed new estimation methods for a class of adaptive phase II designs and approaches for adjusting phase III sample size estimates. In addition, we discussed ideas for new basket designs for oncology phase II trials. More specifically:

- We studied the performance of different estimation methods proposed in the literature for oncology phase II group-sequential and adaptive designs. This was done via simulation studies, and included the commonly used single-arm designs with binary endpoint.
- We proposed new estimation methods for oncology phase II adaptive designs. This was for two-stage adaptive designs with binary endpoint in which the second stage sample size and decision rules are functions of the number of successes in the first stage.
- We analysed the consequences of using effect estimates from phase II adaptive design, which are often biased and imprecise, on planning phase III sample size and we discussed and proposed adjustment approaches in order to obtain adequately powered phase III trials.
- We proposed new design approaches for phase II basket trials in oncology. These designs are mainly modifications of the existing ones to accommodate new scenarios and assumptions. The scenarios include the one in which it is assumed that the treatment effect expectations are different across the baskets.