Einladung zum virtuellen Biometrischen Kolloquium

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DELAYED TREATMENT EFFECTS, TREATMENT SWITCHING AND HETEROGENEOUS PATIENT POPULATIONS: HOW TO DESIGN AND ANALYSE RCTS IN ONCOLOGY

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Meeting password: GkS9ZVVdu52 (45799883 from video systems)

HOST: Franz König

ABSTRACT:

In the analysis of survival times, the logrank test and the Cox model have been established as key tools, which do not require specific distributional assumptions. Under the assumption of proportional hazards, they are efficient and their results can be interpreted unambiguously. However, delayed treatment effects, disease progression, treatment switchers or the presence of subgroups with differential treatment effects may challenge the assumption of proportional hazards. In practice, weighted logrank tests emphasizing either early, intermediate or late event times via an appropriate weighting function may be used to accommodate for an expected pattern of non-proportionality.

We model these sources of non-proportional hazards via a mixture of survival functions with piecewise constant hazard. The model is then applied to study the power of unweighted and weighted log-rank tests, as well as maximum tests allowing different time dependent weights. Simulation results suggest a robust performance of maximum tests across different scenarios, with little loss in power compared to the most powerful among the considered weighting schemes and huge power gain compared to unfavourable weights.

The actual sources of non-proportional hazards are not obvious from resulting population-wise survival functions, highlighting the importance of detailed simulations in the planning phase of a trial when assuming non-proportional hazards.

We provide the required tools in a software package, allowing to model data generating processes under complex non-proportional hazard scenarios, to simulate data from these models and to perform the weighted logrank tests.