

Seminar in Probability Theory & Statistics



Universität
Basel

Department of Mathematics and Computer Science



Use of multistate models to improve decision-making in clinical trials

KASPAR RUFIBACH

EXPERT STATISTICAL SCIENTIST

METHODS, COLLABORATION, AND OUTREACH GROUP (MCO)

DEPARTMENT OF BIostatISTICS, F. HOFFMANN-LA ROCHE, BASEL, SWITZERLAND



In this talk, I will illustrate how critical decisions in drug development are typically based on a tiny fraction of the collected data only. As an example, in early development oncology clinical trials, the decision whether to move a molecule to Phase 3 is typically based on response proportions and duration of response in those that respond, while in Phase 3 the primary endpoint will be long-term endpoints such as progression-free (PFS) or overall survival (OS). Effects on response-based short-term endpoints seldom translate in effects on these relevant endpoints. We propose to make decisions not based on intermediate endpoints, but on a prediction of the OS hazard ratio (HR) between data of the new molecule collected in the early phase trial and historical data of the control treatment. This HR prediction is using a

multistate model based on the various disease states a patient may go through until death. This yields a gating strategy with improved operating characteristics compared to traditional decision rules in the context of early phase clinical trials. If time permits I will further discuss how the joint distribution of PFS and OS as a function of transition probabilities in a multistate model can be derived. No assumptions on copulae or latent event times are needed and the model is allowed to be non-Markov. From the joint distribution, statistics of interest can then readily be computed. As an example, we provide closed formulas and statistical inference for Pearson's correlation coefficient between PFS and OS. Our proposal complements existing approaches by providing methods of statistical inference while at the same time working within a much more parsimonious modelling framework. The main conclusion of this talk is that multistate models are a useful and underutilized tool in the analysis of clinical trial data.

ONLINE ATTENDANCE ONLY, WEDNESDAY, OCTOBER 21ST, 11:00-12:00

A zoom link for the event will be provided per email to all interested participants shortly before the event.