Abstracts

The challenge of time-to-event analysis: Specialties in a competing risk setting

Judith Vilsmeier, Institute of Statistics, Ulm University, Germany

Time to first event analysis often considers a combined endpoint like time from a hematopoietic stem cell transplantation to relapse or death whatever comes first, or time until hospital admission or death. Although, a relapse or death after transplantation in the first example means a failure of the transplantation, it is often important to distinguish the type of events because a relapse allows further treatment. The talk will explain the extension to competing risks where the type of event is considered. This setting provides more information about the behavior of the disease and possible covariables. A focus will be on the difference of hazard and probability estimation and its interpretation. Nonparametric and semi-parametric models and their assumptions will be explained. A data example from leukemia patients shows that results on hazard level are needed to explain results for the probability that seem implausible at first glance. Furthermore, we suggest to estimate a time dependent effect piecewise constant to facilitate the interpretation. This talk is suitable for those who haven't had much experience with competing risks.

The challenge of time-to-event analysis: New insights when extending the model

Sandra Schmeller, Institute of Statistics, Ulm University, Germany

Clinical trials often compare a treatment to a control group with respect to multiple possible combined time-to-event endpoints like time to hospitalization and time to death. Thereby, the first endpoint may occur more than once (recurrent), whereas the second endpoint is absorbing, that is, after observing the second endpoint an individual can no longer experience any other events. However, usually only the time until the first occurrence of an event for a patient is analyzed. Inclusion of all observed events in the analysis can increase the power and provides a more complete picture of the disease but needs more sophisticated methodology. The talk will give a stepwise guidance on how to extend the time-to-first event model to complex multistate methodology, where multiple events are incorporated. We thereby consider nonparametric methodology and semi-parametric methods and show how they are related. Special attention is given on the prerequisites of the models, e.g., the Markov property, and their (causal) interpretation. A data example from the Interdisciplinary Network for Heart Failure where the efficacy of a nurse-coordinated disease management program is compared to usual care for patients that were first hospitalized for systolic heart failure will demonstrate theoretical results and show that more insights are gained when considering multiple events. This talk is an extension of the previous talk on competing risks.

Estimating a treatment effect for survival when assignment to the target population is partially hidden using restricted mean survival times

Marilena Müller, Biostatistics, German Cancer Research Center, Heidelberg, Germany

We consider a two-arm randomized clinical trial with time-to-event endpoint. Patients in the control arm solely receive standard of care (SOC) treatment whereas patients in the experimental arm are offered personalized treatment. However, a big portion of patients in the experimental arm will not receive personalized treatment due to various causes; the main causes are that no personalized treatment is available and that patients do not consent to treatment. These patients also receive SOC.

The estimand of interest is the treatment effect in the population that "potentially receive personalized treatment", i.e. that would receive personalized treatment if randomized to the experimental arm. Direct estimation of this effect is not feasible, since information on which patients in the SOC arm would have received personalized treatment if randomized to the experimental arm is missing.

In the first step of this approach we have to estimate the survival function of the subpopulation of the treatment arm nonparametrically. For the SOC arm the usage of the Kaplan-Meier-estimator is possible. These estimated survival curves are then compared using the restricted mean survival time and hypothesis testing is performed via bootstrap resampling.

This work presents a novel rigorous model for the analysis of treatments effects in the presence of mixtures or asymmetric trials.

Survival analysis of cancer screening: biases and lead time estimation

Ema Požek, Institute for Biostatistics and Medical Informatics, Faculty of Medicine, University of Ljubljana, Slovenia

Cancer screening programmes aim to detect disease at an early stage, when treatment options may be broader and chances of recovery may be greater. However, evaluating the benefits of screening programmes is not straightforward, as naïve comparisons of survival of those invited and those not invited to the programme are biased. Apparent improvements in survival among screen-detected cases may simply reflect earlier diagnosis (lead time bias), preferential detection of slower-growing disease (length time bias), or detection of cases that would never have been detected in the absence of screening (overdetection). These mechanisms can inflate observed survival without necessarily reducing cancer-specific mortality. In this talk, I will first give a concise overview of the main biases that affect observational evaluation of screening. I will then focus on recent work by Vratanar and Pohar Perme (2023), who formalized the relevant target estimand for programme evaluation and showed that the total bias in survival can be decomposed into lead time, length time, and overdetection components. Because lead time plays a central role in this framework, its estimation is an important methodological issue. I will briefly review commonly used approaches to lead time estimation, with emphasis on their assumptions, strengths, and limitations.