

Target Group

This is the eighth in a series of annual Summer schools which target people interested in planning and analyzing, e.g. clinical studies. Basic knowledge in statistical methodology and working skills in using R are assumed and required.

Time and Date

Wednesday 26 June until Saturday 29 June 2024

- Please arrive on Wednesday by 14:30
- Course finishes Saturday by 12:30

Location

Bundesinstitut für Erwachsenenbildung (bifeb)
Bürglstein 1-7
5360 Strobl, Austria

Registration / Waiting List

Please submit your **request for registration by 1 March 2024** via email to:

Andrea Baumgartner, Andrea.Baumgartner@plus.ac.at

Please also indicate if you had tried to register for one of the previous Summer Schools in Strobl but could not be admitted because it was booked out.

Registration Fees

Membership in one of the sponsoring societies is mandatory. Please note that some of the societies offer free student membership.

Academic / Government: 410 Euro
Business / Industry: 570 Euro
Student: 280 Euro

Accommodation

Accommodation and food are included in the registration fees.

How to Get There

Please see the description (in German) at <http://www.bifeb.at/das-bifeb/kontakt>

Contact & Information

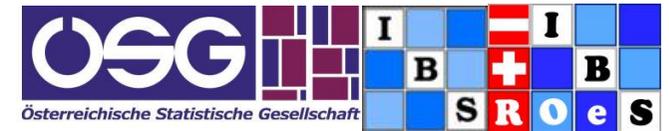
For questions, please ask

Andrea Baumgartner or Arne Bathke
Universität Salzburg,
Dep. of Artificial Intelligence and Human Interfaces
Hellbrunner Str. 34
5020 Salzburg, Austria
Tel. +43 (0)662 8044 5302
Andrea.Baumgartner@plus.ac.at



Cancellation

Your registration will become binding on **30 April 2024**. If you have to cancel, we will try to admit someone from the waiting list. However, if this is not possible and your cancellation is on 1 May 2024 or later, your registration fees cannot be returned.



Deutsche und Österreich-Schweizer Region der Internationalen Biometrischen Gesellschaft (IBS-DR, -ROeS)
Österreichische Statistische Gesellschaft (ÖSG)
Research Center Trustworthy Data Science and Security
Intelligent Data Analytics Lab, Universität Salzburg



Summer School 2024

Time-to-Event Analysis

26 – 29 June, 2024
Strobl am Wolfgangsee, Austria

Instructors

Paul Blanche (København)
Sarah Friedrich (Augsburg)
Kaspar Rufibach (Basel)
Helga Wagner (Linz)

The 2024 Summer School in Strobl is about the analysis of time-to-event data (censored data). Topics will range from practice-oriented to methodological.

The presenters are well-known authorities on time-to-event analysis and its application, and there will be plenty of room for informal discussions with the experts.

An optional social program includes an excursion to the Schafberg mountain with spectacular views across the Salzkammergut lake region, and a barbecue evening (weather permitting).

On the conference site, there are options for various outdoor activities (jogging, football, swimming,...), and participants regularly bring their portable music instruments along for impromptu performance sessions.

Sarah Friedrich: Introduction

Time-to-event data are omnipresent in fields such as medicine, biology, demography, sociology, economics, reliability theory, and data science. In biomedical research, the analysis of time-to-death (hence the name survival analysis) or time to some composite endpoint such as progression-free survival is among the most prominent advanced statistical techniques. A major difference to other data situations is that event times are usually not fully observed - you have to wait for an event to occur. If the event does not occur by the end of the observation period, it is called right-censored. This is one reason why the analysis of time-to-event data is based on hazards. The statistical methodology for hazards differs from standard methods of applied statistics.

In this introduction, we will recall the basic approaches of nonparametric estimation (Nelson-Aalen, Kaplan-Meier) and regression models (Cox PH-model, Aalen's additive model), discuss the subtleties of censoring and truncation and extend the approaches to more complex situations like competing risks and multi-state models. We will also discuss alternatives to the omnipresent hazard ratio as effect measure and briefly touch upon the topic of estimands and causal inference.

Paul Blanche: Logistic Regression with Right Censored (Survival) Data: What, Why, How?

After a brief reminder about logistic regression, we will present the opportunities it provides with typical survival data. We will then contrast this approach to more popular approaches such as Cox regression. Examples from medical research will be presented.

We will discuss why logistic regression can be relevant to analyze both observational data (subject to confounding) and data from randomized clinical trials. We will also touch upon its relevance to the competing risks setting, which is the rule rather than the exception in epidemiological follow-up studies. We will explain why, in all these contexts, using logistic regression can facilitate the necessary discussions between clinicians and statisticians at the time of writing a statistical analysis plan.

Finally, we will explain how to fit logistic regression models with right censored data via inverse probability of censoring weighting. We will present both the main ideas behind the estimating equations and their asymptotic properties and straightforward software implementations (e.g., *metS* R package).

By the end of the session, the participants should be able to critically discuss the pros and cons of logistic regression for survival data and to perform the analysis in R.

Kaspar Rufibach: Clinical Trials With Time-to-Event Endpoint

We will start by discussing how one designs a clinical trial with a time-to-event endpoint, one analysis for efficacy, and using the logrank test as primary hypothesis test. This basic set up will then be extended in various directions: First, by allowing for more than one look at efficacy (i.e. introducing interim analyses), second by illustrating simulation-based trial design for hypothesis tests based on other effect measures than the hazard ratio (to which the logrank test is connected). Drug development and health authority considerations for the latter situation are discussed.

We will also illustrate the difference between the effect we power at and the minimal detectable difference, i.e. the critical value of the hypothesis test on the effect scale, an often overlooked subtlety in trial design. I will conclude the session with sharing some recent research work using multistate models to either improve early-phase development decision-making or Phase 3 trial design via an illness-death model that connects PFS and OS. The latter scenario is relevant insofar as it entails that the proportional hazards assumption can virtually never hold for OS, a result that implies that many large clinical trials do not have the properties that are claimed in their protocols.

Relevant R packages that will be used for illustration are *rpact* and *simIDM*, both also available on CRAN.

Helga Wagner: Beyond the Proportional Hazards Model

The most popular model for the analysis of survival data, the Cox proportional hazards (PH) model relies on the assumption that effects of covariates change the baseline hazard by a constant factor and hence the hazard ratio of two subjects with different covariate values is constant over time. However, this assumption is often violated in real data.

We will discuss methods to check the proportional hazards assumption and strategies to model survival data with non-proportional hazards, particularly stratification and time-varying covariate effects in the PH model, as well as alternative models. We will then focus on hazard regression models with time-varying coefficients, where both baseline hazard and covariate effects are assumed to be piece-wise constant or modelled as smooth functions.

Lab Exercises

Some sessions may involve hands-on examples using R. Please bring your own laptop, with R / Rstudio installed. We will inform you ahead of time regarding the installation of certain packages.