Basel Biometrics Society Training
Basel, 12th and 13th February 2024

Causal thinking in clinical trials

Date: February 12th (13:00-18:00) and 13th 2024 (9:00-16:30)

Location: Novartis Campus, Auditorium Building 210, Basel

Fees: Industry: CHF 250
Academia: CHF 125
Students: 10 seats available free of charge

Instructors: Kelly Van Lancker, Oliver Dukes and Stijn Vansteelandt (Ghent University, Belgium)

Registration: **link** (Register early as places are limited.)

Course Description

Causal thinking and inference have gained increasing attention in global drug development in light of the recently published ICH E9(R1) guideline on estimands and sensitivity analysis (2019) and the FDA draft guideline on covariate adjustment (2021). Even so, causal inference remains somewhat of a mystery to many.

The goal of this face-to-face course is to provide insight into the use of causal thinking and methods to better inform decision making. We introduce causal inference methods based on different drug development settings, including estimands, covariate adjustment, and the use of external control data.

This introductory course is aimed at researchers in the pharmaceutical industry and academia working with clinical trial data; it does not demand prior familiarity with causal inference. We foresee a mix of lectures and hands-on exercises. The participants will strengthen their understanding of the concepts and methods explained during the lectures by analyzing real clinical trial data sets during the practical sessions using R.

Logistics

The event will include coffee breaks. Participants are responsible for arranging their own lunch, with plenty of opportunities on the Novartis Campus.

After completing registration using the link above, a note with the payment details will appear on the screen. Please use these details to **pay the fees in advance** (latest by January 29th) to confirm registration. Cancellations requested no later than February 2nd may be eligible for up to 90% refund, but only if the seat can be filled by an interested attendee from a waiting list, else fees are **non-refundable**.

Places are limited to 60, and registration will close when reaching the limit. There will be an option to register on a waiting list to fill spots for which registration is not confirmed or in case of last-minute cancellations. If you need assistance with the registration (e.g. your company restricts access to Google Forms) please email bibiana.blatna@novartis.com.

Interested students: Please email giusi.moffa@unibas.ch to express your interest. A final decision will be made by February 5th.

The organizing committee of this event are Giusi Moffa (University of Basel), Achim Guettner (Novartis), Fred Sorenson (Cencora), Bibiana Blatna (Novartis) and Frank Bretz (Novartis).

Slides and recordings of the talks may be made available after the event on the BBS webpage, both depending on speakers' approval.

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Program (tentative)

DAY 1

13.00 - 13.05	**Welcome**	Kelly
13.05 - 13.30	**Introduction round** What do you hope to learn during this course?	Stijn - Oliver - Kelly
13.30 – 15.00	**Pre-specifying the estimand based on counterfactual outcomes (including hands-on)** Important to enable the discussion of causal inference problems is the counterfactual/potential outcomes model. In this session we introduce this framework and explain how it can be helpful to define (causal) estimands. We will cover the different estimands defined in the addendum on estimands as well as estimands.	**Stijn** - Oliver - Kelly
15.00 - 15.30	**Coffee break**	
15.30 - 16.20	**Causal inference methods for treatment-policy estimand: covariate adjustment** Covariate adjustment methods have been claimed to yield more powerful intention-to-treat analyses of randomized trials, at no 'cost'. The aim of this session is to provide insight into covariate adjustment: how it succeeds to gain power, and when and how it can be used. In this session we will also cover targeted maximum likelihood estimation.	Kelly
16.20 – 16.35	**Coffee break**	
16.35 - 17.35	**Hands-on (computer): covariate adjustment** We demonstrate the impact of covariate adjustment using completed trial data sets in multiple disease areas. We will provide step-by-step, clear documentation on how to apply the software in each setting. Participants will have the time to apply the software tools on a real clinical trial dataset in small groups.	**Kelly** - Stijn - Oliver
17.35 – 18.00	**Causal inference methods for treatment-policy estimand: transportability and historical controls** A criticism of estimates of marginal treatment effects is that they can not be interpreted as a marginal treatment effect for the population of interest. In this regard, we will discuss methods, along with their advantages and disadvantages, to combine data from a trial with external information about the target population, in order to estimate the effect in the latter.	Kelly

DAY 2

9.00 – 10.30	**Introduction to DAGs (including Hands-on)** Another important framework, besides counterfactual outcomes, to enable the discussion of causal inference problems is Directed Acyclic Graphs (DAGs). In this session we explain how to use DAGs to represent the causal relationship that we believe exist between the variables of interest. We also discuss how one can recognize problems of selection or confounding bias. In the hands-on part the participants will discover why standard adjustment for time-varying covariates does not provide a valid adjustment for time-dependent confounding, what instrumental variables are and how to utilize them for detecting causal effects.	**Oliver** - Stijn - Kelly
10.30 - 11.00	**Coffee break**	
11.00 - 12.15	**Causal inference for the hypothetical estimand: time-varying confounding** Starting from different hypothetical estimands (e.g., due to treatment switching), we review different methods to adjust for time-varying confounding.	Stijn
12.15 – 13.45	**Lunch break (not included)**	
13.45 - 15.00	**Hands-on (computer): time-varying confounding** Focus on a real trial with treatment switching.	**Kelly** - Stijn - Oliver
15.00 – 15.50	**Causal inference for the hypothetical estimand: Instrumental variables** In this session we demonstrate how to use instrumental variables to correct for non-compliance.	Oliver
15.50 - 16.30	**Group discussion on causal estimands and methods**	Stijn-Oliver-Kelly