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Region Österreich – Schweiz

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CAUSAL INFERENCE AND THE HYPOTHETICAL ESTIMAND IN RANDOMISED CONTROLLED TRIALS

Wednesday 26th of November 2025 at 9:15am

Seminarraum Center for Medical Data Science
Spitalgasse 23, Room 88.03.512
Medical University of Vienna, 1090 Wien
Host: Robin Ristl

Abstract:

The presence of post-baseline intercurrent events in randomised controlled trials complicates the estimation of treatment effects, especially when interest lies in the direct or biological effect of a treatment rather than the effect of prescribing it. In line with the ICH E9(R1) guideline, which emphasises the need for clear strategies to handle intercurrent events, we explore methods from causal inference to address these challenges within the hypothetical estimand framework.

When estimating treatment efficacy under a hypothetical strategy, the common practice is to use a Mixed Model for Repeated Measures (MMRM) restricted to data collected before the intercurrent event. In this work, we investigate whether it is possible to make use of the "contaminated" data instead of discarding it, by applying a semiparametric causal approach Longitudinal Targeted Maximum Likelihood Estimation (LTMLE). Through simulations and empirical analysis, we assess how these methodologies perform under varying amounts of intercurrent events.