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PRINCIPLES OF CONDITIONALITY AND LAYERING OF ERROR RATES WITH APPLICATION TO PLATFORM TRIALS

Tuesday, 8th of September 2026 at 11:00am

Seminarraum Center for Medical Data Science
Spitalgasse 23, Room 88.03.513
Medical University of Vienna, 1090 Vienna
Host: Martin Posch

Abstract:

This paper examines error-rate control in platform trials, where shared controls create dependencies across treatment evaluations. We show that the layering of error rates arises naturally because decisions are made both at the trial level and across the broader regulatory landscape. Within an individual study, incorrect conclusions about any endpoint may lead to erroneous claims, necessitating strict control. Therefore, FWER of at least one incorrect inference among trial endpoints-should not exceed the prespecified level. At a higher layer, regulators also seek to control the error rate associated with drug approval decisions, corresponding to the incorrect approval rate (IAR).

We show that controlling FWER within a study at 5% inherently controls Incorrect Approval Rate (IAR) across studies at 5-per-100, regardless of study correlations. We also address concerns about IAR stability in Platform trials, where shared controls introduce dependencies. By applying the Conditionality Principle and utilizing an innovative Shiny app, we explore how correlations impact IAR variability, providing deeper insights for informed decision-making. We show that the treatment/control randomization ratio plays a key role in balancing statistical stability, regulatory guarantees, and stakeholder interests, and introduce a tool to guide optimal design choices. It is worth noting that the Conditionality Principle does not diminish frequentist guarantees; rather, it aligns inference with the experiment that actually occurred. Although our discussion of the Conditionality Principle and layered error rates has focused on platform trials, these ideas have broader applicability in other settings.