

Maximizing Efficiency in Platform Trials with Shared Controls: Optimal allocation strategies

Marta Bofill Roig^{1,}, Ekkehard Glimm², Tobias Mielke³, Martin Posch¹*

¹Section for Medical Statistics, Center for Medical Data Science, Medical University of Vienna

²Advanced Methodology and Data Science, Novartis Pharma AG, Basel

³Statistics and Decision Sciences, Janssen-Cilag GmbH

*marta.bofillroig@meduniwien.ac.at

Platform trials are randomized clinical trials that allow simultaneous comparison of multiple interventions, usually against a common control. Arms to test experimental interventions may enter and leave the platform over time. Therefore, the number of experimental intervention arms in the trial can change over time. Determining optimal allocation rates to allocate patients to the treatment and control arms in platform trials is challenging because the change in treatment arms implies that also the optimal allocation rates will change when treatments enter or leave the platform. In addition, the optimal allocation depends on the analysis strategy used.

In this talk, we describe optimal treatment allocation rates for platform trials with shared controls, assuming that a stratified estimation and testing procedure based on a regression model is used to adjust for time trends. We consider analysis methods using concurrent controls only as well as methods based on also non-concurrent controls. Assuming that the objective function to be minimized is the maximum of the variances of the effect estimators, we show that the optimal solution depends on the entry time of the arms in the trial and, in general, does not correspond to the square root of k allocation rule used in the classical multi-arm trials. We illustrate the optimal allocation and evaluate the power and type 1 error rate compared to trials using one-to-one and square root of k allocations by means of a case study.

Keywords: Clinical trials, Optimisation, Shared controls.