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Context-dependent response-adaptive randomization for continuous endpoints and applications

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Luca Rondano
Please provide a brief biography for the Presenting author(s)
I am a PhD student in Biostatistics at the Politecnico of Turin. The main topics of my research are group sequential designs, probability of success of a clinical trial, bioequivalence and response-adaptive randomization, but I am interersted in any other methodology. Aside from statistics, I like to play sports and games.

Pavel Mozgunov
Please provide a brief biography for the Presenting author(s)
I am an MRC Investigator (Programme Leader Track) working on the development and implementation of (response-) adaptive designs in clinical trials. Currently, I work on the following topics: Adaptive Designs, Dose-Finding Trials, Platform Trials, Bayesian Response-Adaptive Designs, and Quantitative Benefit-Risk analysis.

I provide statistical support in a number of trials, including AGILE-ACCORD (https://www.agiletrial.net/), an early phase trial studying novel therapies for COVID-19 treatments.

If you believe that the trial(s) you are planning can benefit from an adaptive design, feel free to reach me for the discussion – I will be happy to help.

I also consult a number of pharmaceutical companies on the development of novel adaptive designs and support their implementations in ongoing privately funded clinical trials.

Gianmarco Caruso
Please provide a brief biography for the Presenting author(s)
I am a post-doctoral researcher at MRC Biostatistics Unit (University of Cambridge, UK) working on efficient design of clinical trials. My research focuses on the development of novel statistical methodology for Phase I-II clinical trials, with particular emphasis on multi-arm response-adaptive designs, group sequential trials and Bayesian methods to incorporate historical information into study designs.

Single topic, multi-speaker session, Workshop or Single presentation submission

A single presentation/poster

Single presentation or poster submission

Equal randomization is popular since it is easy to implement and associated with high statistical power, but in multi-armed trials we may end up treating many patients in a suboptimal arm. This is especially important in rare disease trials or in situations where being in the “correct” arm may save lives (e.g. oncology trials). Moreover, allocating a fixed number of patients to inferior arms may result in a waste of resources.

A possible solution is to modify the allocation probabilities during the trial, favouring the most promising arms and “softly” dropping those arms with characteristics not aligned with clinical targets. This approach is known as response-adaptive randomization (RAR).

We describe the application of a RAR design for continuous endpoints in a multi-arm phase II clinical trial. In our methodology, the allocation rule is based on a context-dependent measure that we prove to have mathematical properties aligned with the objective of giving more weight to those arms with desirable characteristics, in terms of the observed mean treatment effect and treatment variance. This allows to allocate patients more efficiently than with equal randomization, achieving comparable levels of power and higher patient benefit. Robust performance of the methodology is verified through simulations under different scenarios.

Finally, results of simulations in a Phase II trial context are compared to equal randomization and other common RAR design. The advantages and disadvantages of the proposed methodology are then discussed, both in terms of the statistical gain and of the logistics of planning the trial.