Counter-factual responder analysis in parallel group RCTs using covariates

Objectives:

If treatment A is quite expensive and/or causing relevant side effects compared to B it may be of interest to give treatment A only to those patients which will respond to A but not to B. Treatment B may be given to the other three counterfactual responder types. In general only a cross-over study allows identifying the response type of a patient. Biomarker associated with the response type may help to predict the suitable treatment for a patient.

Methods:

A trivariate normally distributed model is introduced which implements the counterfactual view also for RCTs. This model uses ideas of FM. Lord and G. Gadbury. ML theory is presented which allows to estimate the parameters and to calculate the probabilities that response under treatment A is better as under treatment B given a biomarker messurement. Some ideas using proper scoring rules are provided how to test if the data under study fit the model sufficiently well.

Results:

I present conditions under which a counterfactual responder analysis based on a covariate can be performed in parallel group studies. Specific scenarios are discussed in details.

Conclusions:

The possibility to determine the counterfactual response type of a patient allows introducing a more refined treatment allocation in many clinically relevant settings. The presented ideas represent strategies for sensitivity analyses which check the potential of a biomarker for improved treatment allocation.Furthermore, the ideas can be generalized towards binary and survival outcomes.