Modeling Strategies for Developing Treatment Response Indices

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To find biosignatures of treatment response, clinicians are interested in identifying patient features at baseline that predict differential response to different treatment. The treatments could be drug and placebo, or different drugs. These differential predictors may be termed "moderators of treatment effect", because the differences between the efficacies of the treatments depend on the levels of those predictors. It is common in clinical research to model the outcome as a linear function of the predictor and to test for significance of the interaction between treatment and the predictors in order to find moderators of treatment effect. Also, typically, moderators are identified either one by one, using one model for each potential predictor, or from a large model which includes all potential predictors and their 2-way interactions with treatment, but not interactions between the potential predictors. However, neither of these modeling strategies aids in the determination of combinations of patient characteristics that could be used to select patients who have high probability to respond to a given drug. In this talk we present flexible methods that extend the existing approaches for identification of differential predictors of treatment response in two directions: (1) allowing for non-linear association of the potential predictors with the outcome and (2) identifying combinations of predictors that are the "best" moderators of treatment effect, i.e. offer the largest differences between the efficacies of the treatments as a function of the combination.

Key words: moderators of treatment effect; non-linear models; combination of moderators of treatment effect, biosignatures