The future of Bayesian clinical trial design

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Abstract

The notion of one treatment serving a large homogeneous patient population is becoming increasingly hard to sustain. Many recent studies are designed to understand and address heterogeneity of patient populations, exploiting features of adaptive treatment allocations, population enrichment and sequential stopping. In an increasing number of studies the discovery of relevant subpopulations for such adaptive treatment is part of the trial design.
We review some novel clinical trial designs that implement such schemes, using examples with increasing levels of adaptation. First, we start the discussion with adaptation based on a patient's first cycle response in a two-cycle treatment. Next we continue with dynamic treatment regimens that include adaptation on the outcome from the initial front-line therapy. The discussion includes an adjustment for lack of randomization in the assignment of later stage salvage therapies. Third, we review a basket trial design for a study of targeted therapies for cancer. In this study adaptation includes the selection of disease, treatment and a patient subpopulation. Common to these examples is the notion of quantifying the value of alternative treatment allocations and outcomes. In all examples we do this using a utility function that formalizes, for example, the tradeoff of toxicity and efficacy outcomes. A last example shows another application of such utility-based designs. This time without the context of adaptation.

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