Recent Progress on Bayesian Decision-Theoretic Clinical Trial Designs

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Abstract

We will briefly review the idea behind the adaptive clinical trial designs developed in the Bayesian decision-theoretic framework which allows for maximising the benefit for both the in-trial and after-trial patients. In the academic literature, this approach was first proposed in 1933 by William R. Thompson, a biostatistician from Yale University, using the following words "...there can be no objection to the use of data, however meagre, as a guide to action required before more can be collected ... Indeed, the fact that such objection can never be eliminated entirely-no matter how great the number of observations-suggested the possible value of seeking other modes of operation than that of taking a large number of observations before analysis or any attempt to direct our course... This would be important in cases where either the rate of accumulation of data is slow or the individuals treated are valuable, or both." The practical application of this approach has been long hindered by its computational complexity, and a variety of approximations (including the non-Bayesian designs based on the stay-with-the-winner property) have been developed and studied by biostatisticians in order to overcome this issue and to deal with practicalities prescribed by the regulators. Problems similar to the above decision-theoretic design of adaptive clinical trials have been studied in other scientific disciplines (including probability, statistics, operational research, economics, marketing, machine learning, computer simulation, computer science, and communications engineering), under the umbrella framework known as the multi-armed bandit problem. Recently, however, a few novel designs, sometimes referred to as the bandit-based designs, have been developed and proposed especially for rare and/or life-threatening diseases, and are being implemented in a growing number of trials, mainly in cancers, where patients are stratified into smaller groups based on a number of biomarkers. We will show that computationally, much larger and more complicated trials can be designed in this framework than what is usually believed.