A Bayesian Adaptive Design for Clinical Trials in Rare Diseases

Peter Jacko
Lancaster University, UK

Abstract

Development of treatments for rare diseases is challenging due to the limited number of patients available for participation. Learning about treatment effectiveness with a view to treat patients in the larger outside population, as in the traditional fixed randomised design, may not be a plausible goal. An alternative goal is to treat the patients within the trial as effectively as possible. Using the framework of finite-horizon Markov decision processes and dynamic programming (DP), a novel randomised response-adaptive design is proposed which maximises the total number of patient successes in the trial and penalises if a minimum number of patients are not recruited to each treatment arm. Several performance measures of the proposed design are evaluated and compared to alternative designs through extensive simulation studies using a recently published trial as motivation. For simplicity, a two-armed trial with binary endpoints and immediate responses is considered. Simulation results for the proposed design show that (i) the percentage of patients allocated to the superior arm is much higher than in the traditional fixed randomised design; (ii) relative to the optimal DP design, the power is largely improved upon and (iii) it exhibits only a very small bias and mean squared error of the treatment effect estimator. Furthermore, this design is fully randomised which is an advantage from a practical point of view because it protects the trial against various sources of bias. As such, the proposed design addresses some of the key issues that have been suggested as preventing so-called bandit models from being implemented in clinical practice.

The presentation is joint work with Faye Williamson (STOR-i DTC, Lancaster University, UK), Thomas Jaki (Department of Mathematics and Statistics, Lancaster University, UK) and Sofía S. Villar (MRC Biostatistics Unit, University of Cambridge, UK)