

Swarm-Based Search Procedure for Finding Optimal Multi-Stage Designs for Phase II Clinical Trials

Ping-Yang Chen

Department of Statistics, National Taipei University

Abstract

Multi-stage Phase II clinical trials offer advantages over single-stage designs by enabling interim analyses that can accurately inform early termination of the trial if there is evidence that the treatment is likely to be ineffective or effective. However, identifying optimal designs for multi-stage trials poses considerable computational challenges. In addition to having to optimize many integer-valued variables, there are multiple constraints, including order constraints. Traditional exhaustive search methods lack scalability and quickly become computationally infeasible when the number of stages is three or more. To overcome this challenge, we utilize a spherical coordinate system and reformulate the design problem as a continuous optimization task. The new formulation enables us to efficiently use Particle Swarm Optimization (PSO) to extend Simon's celebrated two-stage Phase II designs to three or more stages. Specifically, we show that our proposed search procedure not only reproduces the two-stage designs and certain three-stage designs found in the literature but also able to achieve the results more efficiently than traditional exhaustive search methods. We provide R codes for reproducing the optimal designs in this paper, which can be easily customized to generate tailor-made optimal designs for specific user needs.

Keyword: Adaptive Design, Maximum Sample Size, Minimax Design, Nature-Inspired Metaheuristics, Particle Swarm Optimization