Bayesian design and analysis of external pilot trials for complex interventions

Context: External pilot trials of complex interventions are used to help determine if and how a confirmatory trial should be undertaken, providing estimates of parameters such as recruitment, retention and adherence rates. The decision to progress to the confirmatory trial is typically made by comparing these estimates to pre-specified thresholds known as progression criteria, although the statistical properties of such decision rules are not commonly used to inform how they should be defined. Such assessment is complicated by several methodological challenges, including the simultaneous evaluation of multiple endpoints, complex multi-level models, small sample sizes, and uncertainty in nuisance parameters.

Objective: To develop and illustrate a Bayesian approach for designing and analysing external pilot trials of complex interventions.

Methods: We describe a Bayesian approach to analysing pilot data, making progression decisions, and evaluating the resulting statistical properties of proposed pilot trials at the design stage to inform the choice of sample size. Decisions are based on minimising the expected value of a loss function. By defining loss over the whole parameter space we allow for preferences and trade-offs between multiple parameters to be articulated and used in the decision making process. The assessment of preferences is kept feasible by using a piecewise constant parameterisation of the loss function, the parameters of which are chosen to lead to desirable operating characteristics. We describe a flexible, yet computationally intensive, nested Monte Carlo algorithm for estimating operating characteristics.

Results: The method is used to revisit the design of an external pilot trial of a complex intervention designed to increase the physical activity of care home residents, estimating multiple parameters to inform the progression decision. We show that reasonable operating characteristics of the pilot trial can be obtained without increasing the sample size beyond the original choice.

Conclusion: A Bayesian approach to design and analysis can provide a way for preferences and trade-offs between the multiple parameters assessed in pilot trials to be articulated and used to make better progression decisions, although the computation time required at the design stage may be restrictive in practice.