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CROSSOVER DESIGNS FOR DRUG DEVELOPMENT

Abstract:

In clinical trials, an issue of paramount importance is that of determining the best treatment for an ailment, from among a class of competing treatments. Crossover designs have been widely used in clinical trials for drug development and recent years have seen a surge in research on these designs. In crossover trials, different drugs are applied to each patient over a sequence of time periods, observations being taken at each period. However, since the same patient is exposed to a sequence of drugs over time, the observation taken at any particular time period is influenced by the effect of the drug applied at that period, called the direct effect of a drug, together with an effect of the drug applied in the immediately preceding period, called the carryover effect of the drug. The presence of these two types of drug effects makes the design and analysis of these experiments difficult. Moreover, an observation is also influenced by an effect of the time period and effect of the patient. So, the key issues here include (a) adequate modelling of the observations, (b) estimation of direct and carryover effects, (b) derivation of efficient or optimal design for inference and (c) construction of this efficient design for experimental use.

There are results available for efficient estimation for direct and carryover effects separately. However, a designed experiment finally recommends a single treatment for use over longer time periods, and when this treatment is used, an effect of utmost importance is the total of the direct effect and carryover effect of the same treatment, or the total drug effect. However, no results are available in the literature for this total effect. In this paper we focus on this issue and we develop a rigorous framework for studying the total effects under a non-circular model. Next, we derive the best design for use in this context. Some numerical results are also presented.

Keywords:

Clinical Trials, Total drug effect, Efficient estimation

JEL Classification: C90, I19, C00