

Detekcija outliera u podacima iz krossover dizajna višeg reda Monte Carlo metodama

Higher-Order Crossover Design Outlier Detection using Monte Carlo techniques

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Abstract:

In clinical trials there are two different kinds of study objectives: a superiority hypothesis that the new treatment is more effective than the active control treatment and a non-inferiority (or equivalence) hypothesis that the new (experimental) treatment is clinically no worse than (or equivalent to) the active control within a defined margin or range.

Bioequivalence studies are based on bioequivalence of different formulations of the same treatment, usually taken to mean equivalence with respect to rate and extent of drug absorption. The FDA pre-specified the rule that bioequivalence studies must have at least 80% power of detecting a 10% difference between the parameters of interest. It was also suggested that 90% confidence intervals be used in such circumstances.

The usual approach to testing average bioequivalence for 2 formulations is the "standard" 2x2 crossover design, but higher-order designs are also recommended in some situations. A common problem in bioavailability studies is extremely large or small (i.e., outlying) observations. These observations may influence the conclusion drawn regarding bioequivalence.

In this presentation we'll introduce a new procedure for detecting subject outlier(s) in data from a fully replicated crossover design. The suggested procedure is an adjustment to the Monte Carlo test based on the order statistics of the two-sample Hotelling T^2 , introduced by Liu and Weng (1991). Results from an empirical power study will be presented, indicating that the proposed procedure is, on average, as powerful as, for example, the equivalent procedure for detecting outliers in data from a standard crossover design.