

Non-Proportional Hazard: how to analyze the Time-to-event Outcomes in Clinical Trials?

María del Carmen Pardo, Department of Statistics and O.R., Complutense University of Madrid; Queen Mary University of London, Visiting Professor

sites.google.com/view/mcapardo

Time to event data is one of the most common data types in clinical trials. Traditionally, a log-rank test is commonly performed to investigate the equivalence of two survival distributions under right censoring. However, in numerous trials such as in immuno-oncology clinical trials this approach fails due to the presence of non-proportional hazards, resulting in difficulties of interpreting the hazard ratio and a loss of power. A review of statistical methods included some news for a between-treatment comparison of survival times in randomized clinical trials is presented. Simulations are performed to examine power of these tests when the data are uncensored to heavily censored under scenarios proportional hazards and several types of non-proportional hazards.

On the other hand, when considering equivalence or non-inferiority trials, the commonly performed log-rank based tests are similarly affected by a violation of non-proportional hazard assumption. In this talk, non-parametric tests for showing non-inferiority of a new treatment compared to reference therapies when data are censored are proposed. The performance of the test procedures is investigated in a simulation study under several scenarios. The methods are illustrated with real data examples.

Key words: clinical trials, time-to-event outcomes, non-proportional hazards, weighted tests, equivalence, non-inferiority trial