

Stochastic modeling and simulation in the design of multicenter clinical trials

Frank Mannino, Richard Heiberger, Valerii Fedorov

The design of multi center trials requires careful balancing and synchronization of closely related components such as selection of sample size, test statistics, treatment randomization method, customer and sponsor risks, number of centers, duration of trial, logistics of drug supply and manufacturing under uncertainty or randomness of input information. The effective way to understand how these aspects interact and affect each other is through the use of stochastic models and Monte Carlo simulations, as many of these models are difficult or practically impossible to handle analytically, especially when used in combination. By simulating our trials we can get a better sense of the properties including variability of statistical power for various patients outcomes under competing models, treatment imbalances, length of the trial, amount of drug needed, and overall costs. An R package and RExcel interface have been developed to handle these simulations in real time setting to quantify and support decision making in development of new drugs.