

Determination of Power and Sample Size in the Design of Clinical Trials with Failure-Time Endpoints and Interim Analyses

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Abstract:

An important but difficult task in the design of a clinical trial to compare time to failure between two treatment groups is determination of the number of patients required to achieve a specified power of the test. Since patients typically enter the trial serially and are followed until they fail or withdraw from the study or until the study is terminated, the power of the test depends on the accrual pattern, the noncompliance rate and the withdrawal rate in addition to the actual survival distributions of the two groups. Incorporating interim analyses and the possibility of early stopping into the trial increases its complexity, and although normal approximations have been developed for computing the significance level of the test when the logrank or other rank statistics are used, there are no reliable analytic approximations for evaluating the power of the test. This article presents methods, based on Monte Carlo simulations and recent advances in group sequential testing with time-to-event responses, to choose appropriate test statistics, to compute power and sample size at specified alternatives, to check the adequacy of commonly used normal approximations of the Type I error and to assess the performance of different interim analysis strategies. It also presents a computer program implementing these methods.