

Title:

Efficient Group Sequential Tests for Superiority and Non-Inferiority Hypotheses in Clinical Trials

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Abstract:

In designing an active controlled clinical trial, one sometimes has to choose between a superiority objective (to demonstrate that a new treatment is more effective than an active control therapy) and a non-inferiority objective (to demonstrate that it is no worse than the active control within some pre-specified non-inferiority margin). It is often difficult to decide which study objective should be undertaken at the planning stage when one does not have actual data on the comparative advantage of the new treatment. By making use of recent advances in the theory of efficient group sequential tests, we show how this difficulty can be resolved by a flexible group sequential design that can adaptively choose between the superiority and non-inferiority objectives during interim analyses. While maintaining the type I error probability at a pre-specified level, the proposed test is shown to have power advantage and/or sample size saving over fixed sample size tests for either only superiority or non-inferiority, and over other group sequential designs in the literature.