

## Mixed Non-inferiority Margin and Statistical Tests in Active Controlled Trials

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In an active controlled non-inferiority trial, one of the major considerations is the selection of the non-inferiority margin. Hung et al. [*Statist.Medicine*22(2003):213-225] proposed a margin selection based on relative risk. However, based on relative risk, it is difficult to adjust for covariates. On the other hand, Chow and Shao [*Statist.Medicine*25(2006):1101-1113] proposed a method for selecting non-inferiority margins based on treatment difference. In this paper, we propose a method for non-inferiority testing with the use of a mixed null hypothesis which consists of a margin based on treatment difference and a margin based on relative risk. The corresponding statistical tests are derived. An example concerning the efficacy of a test therapy to an active control on a clinical adverse event in the target patient population with cardiovascular disease is presented to illustrate the proposed method. Simulation studies were conducted to assess the type I error rate and the power.

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