Efficient Sample Size Adaptation Strategy With Adjustment Of Randomization Ratio

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Abstract: In clinical trials, sample size re-estimation is a useful strategy to mitigate the risk of uncertainty in design assumptions to ensure sufficient power for the final analysis. In current literature, sample size re-estimation and corresponding type I error control are discussed in the context of maintaining the original randomization ratio across treatment groups, which we refer to as "proportional increase." In practice, not all studies are designed based on an optimal randomization ratio due to practical reasons. In such cases, when sample size is to be increased, it is more efficient to allocate the additional subjects such that the randomization ratio is brought closer to an optimal ratio. In this research, we propose an adaptive randomization ratio change when sample size increase is warranted. We refer to this strategy as "nonproportional increase," as the number of subjects increased in each treatment group is no longer proportional to the original randomization ratio. The proposed method boosts power not only through the increase of the sample size, but also via efficient allocation of the additional subjects. The control of type I error rate is shown analytically. Simulations are performed to illustrate the theoretical results.