SAMPLE SIZE RE-CALCULATION BASED ON THE OBSERVED TREATMENT DIFFERENCE AT AN INTERIM LOOK

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Determination of sample size depends on knowledge of the expected treatment effect. If the actual variance is much larger than expected, the planned sample size will be severely underestimated and consequently it may not be sufficient to give reasonable power to show the treatment efficacy. Recently, flexible designs with updating of sample size in clinical trials have been proposed; the weighted Z-statistic approach and the 50% conditional power approach. In this talk, we propose a new method for sample size re-calculation, which is based on the idea of increasing sample size only when the unblinded interim result is promising. Our method is a modification of the 50% conditional power approach and does not inflate the type I error rate due to the restriction on the maximum sample size. Simulation studies showed that proposed method increased power about 10% compared with the original 50% conditional power approach. Compared with the weighted Z-statistic approach, proposed method had several promising operating characteristics; a substantial gain in power with the increase of sample size, a low probability of reaching the maximum sample size under the same expected sample size and power, a substantial decrease in the conditional type II error rate, and a conservative property of not increasing sample size erroneously under no treatment effect.