RESEARCH

Randomized Test-Treatment Studies with an Outlook on Adaptive Designs
Additional File 1

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Appendix

Sample size formula for a binary outcome

If there is a binary outcome Y of primary interest, the sample size calculation involves a comparison of two binomial proportions θ_A and θ_B based on independent samples. Let α denote the type I error probability and β the type II error probability. Accordingly, $z_{1-\alpha}$ and $z_{1-\beta}$ are the critical values of the standard normal distribution with upper tail probability of $(1-\alpha)$ and $(1-\beta)$, respectively. We are using a two-sided test to level α testing the hypotheses $H_0 : \Delta = 0$ vs. $H_1 : \Delta \neq 0$, where $\Delta = \theta_A - \theta_B$. Therefore, the sample size formula for testing the inequality of two binomial proportions θ_A and θ_B with equal allocation of patients to test A or B can be performed along the following lines:

$$n_A = n_B = \frac{[\sqrt{2\bar{\theta}(1-\bar{\theta})}z_{1-\alpha/2} + \sqrt{\theta_A(1-\theta_A)+\theta_B(1-\theta_B)}z_{1-\beta}]^2}{\Delta^2} \tag{1}$$

where $\bar{\theta} = (\theta_A + \theta_B)/2$ [1]. The number of patients randomized to path A and B is denoted by n_A and n_B, respectively.

Sample size formula for a continuous outcome

Assuming a continuous outcome Y, the primary hypothesis of interest is the mean comparison between two test-treatment strategies based on test A and B. Accordingly to the binomial scenario, the difference in mean responses is $\Delta = \theta_A - \theta_B$, where the hypothesis of interest is written as $H_0 : \Delta = 0$ vs. $H_1 : \Delta \neq 0$. If a normal approximation is used and a constant variance for all patients, σ^2, is assumed, the sample size formula for equal allocation of independent samples and testing inequality of two mean responses is given as [1]:

$$n_A = n_B = \frac{2(z_{1-\alpha/2} + z_{1-\beta})^2\sigma^2}{\Delta^2} \tag{2}$$

Here, α denotes the type I error probability and β the type II error probability. Accordingly, $z_{1-\alpha}$ and $z_{1-\beta}$ are the critical values of the standard normal distribution with upper tail probability of $1-\alpha$ and $1-\beta$, respectively. The same applies to the remaining designs.

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