Sample Size Calculation for Continuous Outcome

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1 Introduction

Our hypothesis $H_0 : \delta = 0$ vs $H_1 : \delta \neq 0$ which may be re-written as $H_0 : \mu_0 = \mu_1$ vs $H_1 : \mu_0 - \mu_1 \neq 0$ or $H_1 : \mu_0 \neq \mu_1$ when there are two groups with μ_0 is the mean in the placebo or control group and μ_1 is the mean in the treatment group.

2 Sample Size Formula

We want to detect a difference of $\delta = \mu_1 - \mu_2$ between the groups.

The null hypothesis is $H_0 : \mu_1 = \mu_2$, and the alternative hypothesis is $H_1 : \mu_1 \neq \mu_2$.

Assuming a two-sided test at significance level α, the critical value for a standard normal distribution is $z_{\alpha/2}$. We need to consider two 'alternative' cases $\mu_1 > \mu_0$ and $\mu_1 < \mu_0$. These two are ideally symmetric cases.

Assuming $\mu_1 > \mu_0$:

The sample size justification is rooted in comparing the regions where H_0 will be rejected. This region is also called the critical region. From the data point of view, if the observed difference is larger than some fixed 'value', null will be rejected.

Now our decision rule should be if observed mean $\bar{x} > C$, then H_0 will be rejected. In Figure 1, type I is controlled if the null is rejected for the observed difference being greater than $\mu_0 + \frac{1}{\sqrt{n}}\sigma Z_{1-\alpha/2}$.

Type II error for this decision rule is controlled at $1-\beta$ if the null is rejected for the observed difference being greater than $\mu_1 + \frac{1}{\sqrt{n}}\sigma Z_\beta$.

Hence, for consistency, we need $\mu_0 + \frac{1}{\sqrt{n}}\sigma Z_{1-\alpha/2} = C = \mu_1 + \frac{1}{\sqrt{n}}\sigma Z_\beta$. (As we do not know which hypothesis is true, the decision rule should not be hypothesis-dependent.) Upon simplification, we get $n = \left(\frac{z_{1-\alpha/2}+z_\beta}{(\mu_1-\mu_0)}\right)^2 \sigma^2$

Since $\delta = \mu_1 - \mu_0$, we have

$$n = \left(\frac{z_{1-\alpha/2} + z_\beta}{\delta}\right)^2 \sigma^2$$

Where:

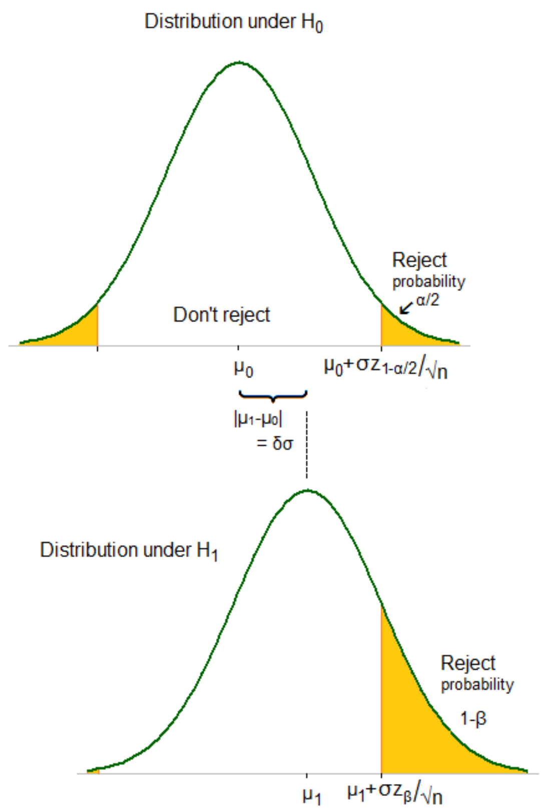

Figure 1: Caption

- n = sample size per group
- $z_{\alpha/2}$ = critical value for $\alpha/2$ from standard normal distribution
- z_β = critical value for β from standard normal distribution
- δ = 'minimum' clinically meaningful difference
- σ = standard deviation

Since the sample size calculation strategy relies on comparing the two critical regions, we are required to specify the minimum detectable difference (δ) beforehand along with the significance level and power.