

Sample size calculation for comparing two groups

Summary:

Consider a problem of compare two groups (two therapies, two treatments etc.) on an outcome. The next question could be how many study subjects (or patients) per group do we need for meaningful comparison. We may not want too few people so that we have some confidence about our results. Other wise we could always base our conclusion by conducting the expiring on one person from each group. On the other hand we do not want too many few people either because of resources (time and cost) and other factors (e.g. exposing too many people if therapy that is not promising).

Background information for computing sample size to compare two groups:

H_0 : Mean of group 1= m_1 ,

H_1 : Mean of group 2= m_2 ,

Common standard deviation (SD) = σ

$$\text{Effect Size} = \frac{m_1 - m_2}{\sigma} = \text{Difference per SD (DSD)}$$

(Ignore which mean is greater just use the positive difference).

Alternative forms of effect size

$m_1 = m_2 + \sigma \times k$ or $m_2 = m_1 + \sigma \times k$, then the *effect size*= k (equivalently, the difference between the two means is k standard deviations).

So if you have some idea about the difference between two means and the standard deviation (from previous similar studies, guesstimates etc.), then you can compute the effect size and get the sample size needed per group from the tables in the next page.

Example: If the effect size is 0.35, then you will need 130 subjects per group with 80% power and 174 subjects per group with 90% power (see the table below)

(See below for complete worked out examples)

Examples:

Example1: Suppose we want to investigate the analgesic efficacy of a new drug. Lane et al (NEJM, 2010; 363:1521-31) have found that Tanezumab administered at 50 $\mu\text{g}/\text{kg}$ (N = 72) decreased pain score by 29.0 ± 2.4 (Table 2 of Lane et al.) from baseline through week 16. During the same period the placebo group decreased by 16.2 ± 2.4 (N=73). If we expect similar effect of this new drug then we can use this information to compute effect size and look up the tables to get sample size. However, there is no information on standard deviation. The numbers given are mean \pm standard error. We can use the following formula to estimate the standard deviation (σ)

$$\sigma = \text{standard error} \times \sqrt{N}.$$

Hence, using the information from the placebo group, $\sigma = 2.4\sqrt{73} = 20.51$. Therefore,

$$DSD = \frac{m_1 - m_2}{\sigma} = \frac{29.0 - 16.2}{20.51} = 0.62$$

From the sample size Table, to detect an effect size of 0.62 we will need at least 43 study subjects per group with 80% power at 5% level of significance.

Note: Standard deviation (SD) could have been estimated, from treatment group, or from both groups. But for demonstration purpose, placebo group was chosen to estimate standard deviation.

Example 2: Suppose it is desired that the new drug should reduce the pain by at twice that of placebo, then

$$\text{Effect Size} = \frac{m_1 - m_2}{\sigma} = \frac{32.4 - 16.2}{20.51} = 0.79$$

From the sample size Table, to detect an effect size of 0.79 we will need at least 27 study subjects per group with 80% power at 5% level of significance.

Note: Smaller effects size corresponds to larger sample size. So sample size may increase with (i) smaller difference between means the with same SD or (ii) larger SD with the same difference between means.