BIOS668 HW#4
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Honor Code: On my honor, I have neither given nor received unauthorized aid on this assignment.

Q1)

① Note that we observe n_1 outcomes in one arm and n_2 outcomes in the other.

We assume that $n_1 = kn_2$.

To determine where to evaluate power, we can use the following test statistics based on the sample means $\bar{X}_1, \bar{X}_2$.

$$\bar{X}_1 \sim N\left(\mu_1, \frac{\sigma^2}{n_1}\right) = N\left(\mu_1, \frac{\sigma^2}{kn_2}\right)$$
$$\bar{X}_2 \sim N\left(\mu_2, \frac{\sigma^2}{n_2}\right)$$

We can then compare these two means:

$$\bar{X}_1 - \bar{X}_2 \sim N\left(\mu_1 - \mu_2, \frac{\sigma^2}{kn_2} + \frac{\sigma^2}{n^2}\right) = N\left(\mu_1 - \mu_2, \frac{(k+1)\sigma^2}{kn_2}\right)$$

If we denote $\sigma_*^2 = \frac{k+1}{k}\sigma^2$ and $\mu = \mu_1 - \mu_2$ we are left with

$$\bar{X}_1 - \bar{X}_2 \sim N\left(\mu, \frac{\sigma_*^2}{n_2}\right)$$

We now have a standard 1-sample superiority test. So, we know that

$$n_2 > \frac{(z_{1-\alpha/2} + z_{1-\beta})^2}{(\delta/\sigma_*)^2} = \frac{\sigma_*^2 (z_{1-\alpha/2} + z_{1-\beta})^2}{\delta^2} = \frac{(z_{1-\alpha/2} + z_{1-\beta})^2 \sigma^2 (k+1)}{\delta^2 k}$$

Then, since $n_1 = kn_2$,

$$n_1 = kn_2 > \frac{k(z_{1-\alpha/2} + z_{1-\beta})^2 \sigma^2 (k+1)}{k\delta^2} = \frac{(z_{1-\alpha/2} + z_{1-\beta})\sigma^2 (k+1)}{\delta^2}$$

① Note that we observe n_1 outcomes in one arm and n_2 outcomes in the other.

We assume that $n_1 = kn_2$.

We can evaluate power at $\mu_1 = \mu_2 - \delta + \varepsilon$

We define our test statistics based on sample means $\bar{X}_1$ and $\bar{X}_2$:

$$\bar{x}_1 \sim N(\mu_1, \frac{\sigma^2}{n_1}) = N(\mu_1, \frac{\sigma^2}{kn_2})$$

$$\bar{x}_2 \sim N(\mu_2, \frac{\sigma^2}{n_2})$$

We can then compare these two means:

$$\bar{X}_1 - \bar{X}_2 \sim N(\mu_1 - \mu_2, \frac{\sigma^2}{kn_2} + \frac{\sigma^2}{n_2}) = N(\mu_1 - \mu_2, \frac{(k+1)\sigma^2}{kn_2})$$

If we denote $\sigma_*^2 = \frac{k+1}{k}\sigma^2$ and $\mu = \mu_1 - \mu_2$ we are left with

$$\bar{x}_1 - \bar{x}_2 \sim N(\mu, \frac{\sigma_*^2}{n_2})$$

We now have a standard 1-sample non-inferiority testing problem. So,

$$n_2 > \frac{(z_{1-\alpha} + z_{1-\beta})^2}{(\varepsilon/\sigma_*)^2} = \frac{\sigma_*^2(z_{1-\alpha} + z_{1-\beta})^2}{\varepsilon^2} = \frac{(z_{1-\alpha} + z_{1-\beta})^2\sigma^2(k+1)}{k\varepsilon^2}$$

Then, since $n_1 = kn_2$,

$$n_1 = kn_2 > \frac{k(z_{1-\alpha} + z_{1-\beta})^2\sigma^2(k+1)}{k\varepsilon^2} = \frac{(z_{1-\alpha} + z_{1-\beta})^2\sigma^2(k+1)}{\varepsilon^2}$$

Q2)

Sample size calculation:

$$n_2 > \frac{2+1}{2} \cdot (49) \cdot \frac{(1.645 + 0.842)^2}{(1.6 - .35)^2} = 290.95$$

$$n_2 > \frac{2+1}{2} \cdot (49) \cdot \frac{(1.645 + 1.282)^2}{1.6^2} = 245.98$$

$$n_2 = 291$$

$$n_1 = 291 \cdot k = 291 \cdot 2 = 582$$

In this study, we plan to test if treatment strategy A is not too different from treatment strategy B for a specific disease. We are measuring this equivalence using time in days to disease resolution since randomization, where ‘not too different’ or equivalence is defined as 1.6 days. Hence, our null hypothesis is that the difference between treatments, in either direction, is ≥ 1.6 days. Our alternative hypothesis is that this difference is < 1.6 days. The study is interested in having 80% power and testing at alpha-level 0.05 for this controlled equivalence test. The true mean difference between treatments is 0.35 days and the standard deviation is 7.0 days. 582 participants are randomized into treatment A and 291 participants are randomized into treatment B in two arms to detect the statistically meaningful difference of 1.6 days under the study conditions. There is no interim analysis and since this is a parallel study design, participants only receive the treatment for the group they were randomized into for the duration of the study. Similar to a one sample design, our rejection region containing the critical values that we use to determine when to reject our null hypothesis is set at |T| ≤ c = $\sqrt{n}\delta - z_{1-\alpha}$, with adjustment for two-sample design.