P8142 Homework 1

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Problem 1

Since the study aim to have 80% power to detect a difference of 10% in a two-sided t-test at $\alpha = .05$ level. And from the pilot study, we know the standard deviation of the change score was 15%. Since we are comparing two proportions, regarding the change score as a continuous random variable range from 0 to 100, the sample size we need should satisfies the following formula.

$$d = (z_{\alpha/2} + z_\beta) \times s.d. \times \sqrt{\frac{1}{n_T} + \frac{1}{n_C}} = (z_{\alpha/2} + z_\beta) \times s.d. \times \sqrt{\frac{2}{n}} \text{ (if } n_T = n_c = n)$$

where $\alpha = 0.05, \beta = 1 - 80\% = 0.2$. n_T is the number of subjects we need in the treatment group and n_C is the number of subjects we need in the control group. Since we are assuming equal sample size for the two intervention arms, we have $n_T = n_c = n$. $d = \mu_T - \mu_C = 10\%$ is the effect size of our test, μ_T and μ_C are the population mean of treatment and control group, respectively. Then we can derive the sample size n we need for each intervention arm:

$$\begin{aligned} d &= (z_{\alpha/2} + z_\beta) \times s.d. \times \sqrt{\frac{2}{n}} \\ \Rightarrow d^2 &= (z_{\alpha/2} + z_\beta)^2 \times s.d.^2 \times \frac{2}{n} \\ \Rightarrow n &= \frac{2(z_{\alpha/2} + z_\beta)^2 \times s.d.^2}{d^2} \end{aligned}$$

By plug-in the design parameters we have, we can get:

$$\begin{aligned} n &= \frac{2(z_{\alpha/2} + z_\beta)^2 \times s.d.^2}{d^2} \\ &= \frac{2(z_{0.5/2} + z_{0.2})^2 \times 15^2}{10^2} \\ &= \frac{2(1.96 + 0.84)^2 \times 15^2}{10^2} \\ &= 35.28 \end{aligned}$$

However, since the retention rate is 85% and there is a cross-over rate of about 5% for both groups. We should adjust for them. Since the retention rate is 85%, we need $n_{\text{adjust for missing}} = n/0.85 = 35.28/0.85$, and the cross-over rate is 5%, which is same in both group, we need an additional adjustment: $n_{\text{adjust for cross-over}} = n_{\text{adjust for missing}}/(1 - 0.05 - 0.05)^2 = 35.28/(0.85 \times 0.90^2) \approx 51.24$

Since the intervention will be delivered in group sessions with an average group size of 11, intra-class correlation coefficient should be used to measure the reliability of measurements for clusters. Assume $ICC = 0.1$[1]:

$$VIF = (1 + (n_c - 1) \times ICC) = (1 + (11 - 1) \times 0.1) = 2$$

therefore, the required sample size adjust for intra-class correlation is:

$$n_0 = 51.24 \times VIF = 102.48$$

Therefore, the total sample size we need is $102.48 + 102.48 \approx 103 + 103 = 206$.

[1]Thompson, D. M., Fernald, D. H., Mold, J. W. (2012). Intraclass correlation coefficients typical of cluster-randomized studies: estimates from the Robert Wood Johnson Prescription for Health projects. Annals of family medicine, 10(3), 235–240. https://doi.org/10.1370/afm.1347

Problem 2

We define effect size as the minimal clinical meaningful worthwhile difference that we would like to have a required statistical power to reject the null hypothesis. In this case, we set it to 10%.

If one says that the effect size is usually smaller than 10%, the calculated sample size n_0 based on a effect size of 10% would be smaller than the sample size needed to conduct the study, since $d' < d$, we would not reach the statistic power and significant level we pre-defined and we have to recalculate the sample size.

Problem 3

Same as what have been talked in problem 2, if one says that the effect size is usually greater than 10%, the calculated sample size n_0 based on a effect size of 10% would be bigger than the sample size needed to conduct the study, since $d' > d$, we could reach the statistic power and significant level we pre-defined, however, it may not be efficiency because extra subjects will be recruited into the trial.

Problem 4

If we are going to use imbalanced randomization with 2:1 randomization ratio (2 intervention and 1 control) to get sufficient number of participants to actually "receive the intervention", we are actually losing statistic power.

Let $n'_T = 2n'_C$ denotes the number of subjects under treatment and control arm respectively under this 2:1 randomization. Let $n_{\text{total}} = 2n$ denotes the total size of subjects the trial recruited. Hence, $n'_T = 4/3n, n'_C = 2/3n$.

From the effect size:

$$
\begin{aligned}
d &= (z_{\alpha/2} + z_\beta) \times s.d. \times \sqrt{\frac{1}{n_T} + \frac{1}{n_C}} \\
\Rightarrow z_\beta &= \frac{d}{s.d. \times \sqrt{\frac{1}{n_T} + \frac{1}{n_C}}} - z_{\alpha/2} \\
&= \frac{d}{s.d. \times \sqrt{\frac{2}{n}}} - z_{\alpha/2}
\end{aligned}
$$

However, after this imbalanced randomization, the $z_{\beta'}$ of the test becomes:

$$
\begin{aligned}
z_{\beta'} &= \frac{d}{s.d. \times \sqrt{\frac{1}{n'_T} + \frac{1}{n'_C}}} - z_{\alpha/2} \\
&= \frac{d}{s.d. \times \sqrt{\frac{9}{4n}}} - z_{\alpha/2} < z_\beta
\end{aligned}
$$

and the power of the test becomes:

$$
\text{Power}' = 1 - \Phi(-z_{\beta'}) < 1 - \Phi(-z_\beta) = \text{Power} = 0.20
$$

Noticing that there is a decrease in power, therefore, such change doesn't fix the problem.

Problem 5

According to problem 4, if we want to fix the problem by keeping the same statistic power, then we need to re-calculate the sample size we need.

Here, the problem is actually an extra cross-over (since there already exists cross-over in each arm with a rate 5%) from intervention arm to control arm, with a rate $p_{T\to C} = \frac{1}{3}$. Because $\frac{1}{3}$ of the intervention group doesn't actually received intervention and their outcome are mostly recorded. Since there is no cross-over from control to intervention group, the corresponding cross-over rate is $p_{C\to T} = 0$.

Hence, by setting the same significant level and statistic power, we can get the new sample size we need for each arm:

$$\begin{aligned} n' &= n_0/(1 - p_{T\to C} - p_{C\to T})^2 \\ &= 102.48/(2/3)^2 \\ &= 230.59 \end{aligned}$$

Therefore, the new sample size we need for each arm in order to retain the statistic power is $230.59 \approx 231$

(If we are not considering the information from pilot study in this case, the sample size we need for each arm is just $n/(1 - p_{T\to C} - p_{C\to T})^2 = 35.28/(2/3)^2 = 79.38 \approx 80$)

Problem 6

In this case, we are actually going to conduct a test for the proportions between two arms, so the sample size calculated in problem 1 might not suited into this problem, we need to re-calculate the sample size based on two sample proportion test setting.

Let P_T, P_C denotes the underling true proportion of participants with successful outcome in intervention and control arm respectively. According to the information, $P_C = 0.25$. Since we want to declare a 35 percentage points difference as statistically significant, then we have $P_T - P_C = 0.35$ and $P_T = 0.60$ under hypothesis.

Under same statistic power and significant level plus equal sample size design structure, we can calculate the required sample size[2]:

$$n' = \frac{\left(z_{\alpha/2}\sqrt{2\bar{P}\bar{Q}} + z_\beta\sqrt{P_TQ_T + P_CQ_C}\right)^2}{(P_T - P_C)^2}$$

where $Q_T = 1 - P_T = 0.40, Q_C = 1 - P_C = 0.75, \bar{P} = \frac{P_T+P_C}{2} = 0.425, \bar{Q} = 1 - \bar{P} = 0.575$, therefore,

$$\begin{aligned} n' &= \frac{\left(z_{\alpha/2}\sqrt{2\bar{P}\bar{Q}} + z_\beta\sqrt{P_TQ_T + P_CQ_C}\right)^2}{(P_T - P_C)^2} \\ &= \frac{\left(1.96\sqrt{2\times 0.575\times 0.425} + 0.84\sqrt{0.60\times 0.40 + 0.25\times 0.75}\right)^2}{(0.35)^2} \\ &= 30.076 \end{aligned}$$

[2]Based on Sample size formula for comparing two proporitons on Canvas

By incorporating the continuity correction, the sample size required is:

$$\begin{aligned} n &= \frac{n'}{4}\left(1+\sqrt{1+\frac{4}{n'\,|P_2-P_1|}}\right)^2 \\ &= 30.772 \end{aligned}$$

Assuming the retention rate and cross-over rate are the same, the final required sample size for each arm is:

$$\begin{aligned} n_0 &= \frac{n}{1-0.15}\frac{1}{(1-0.05-0.05)^2}\times 2 \\ &= 44.695 \end{aligned}$$

Therefore, the total required sample size in this case is $44.695 + 44.695 \approx 45 + 45 = 90$.