STA305/1004 Homework 2

Due: In class at 11:10 on Wednesday, February 11, 2015.
Handwritten answers should be neatly written using a pen. If your answers are handwritten or illegible then your answer will not be considered for regrading.

1. Superiority trials are designed to assess whether the new treatment is better than the standard treatment, for which a one-sided hypothesis is formulated as

$$H_0 : \theta \leq 0 \text{ versus } H_1 : \theta > 0.$$

When the main dependent variable in the trial is the response rate then $\theta = p_1 - p_2$, where p_1 is the response rate in the new treatment group and p_2 is the response rate in the standard treatment group. The power of this test is given by

$$1 - \beta = P\left(Z \geq \frac{z_\alpha \sqrt{\bar{p}(1-\bar{p})(1/n_1 + 1/n_2)} - \theta}{\sqrt{p_1(1-p_1)/n_1 + p_2(1-p_2)/n_2}} \right), \ |\theta| > 0,$$

where Z is the standard normal random variable defined as,

$$Z = \frac{\hat{p}_1 - \hat{p}_2 - \theta}{\sqrt{p_1(1-p_1)/n_1 + p_2(1-p_2)/n_1}}.$$

z_α is the $100\,(1-\alpha)$th percentile of the standard normal (i.e., $\Phi\,(z_\alpha) = (1-\alpha)$, where $\Phi(x)$ is the standard normal cumulative distribution function) and $\bar{p}$ is the pooled proportion,

$$\bar{p} = \frac{n_1 p_1 + n_2 p_2}{n_1 + n_2}.$$

See Yin, Chapter 6, page. 176.

   (a) Briefly describe what the power function above calculates when designing a superiority trial. Clearly define each of the variables that must be specified in order to calculate the power function.

(b) Show that

$$\theta = z_\alpha \sqrt{\bar{p}(1-\bar{p})(1/n_1 + 1/n_2)} + z_\beta \sqrt{p_1(1-p_1)/n_1 + p_2(1-p_2)/n_2}$$

(c) Use your answer in the previous part to show that if $n_1 = rn_2$, where $r > 0$ then

$$n_2 = \frac{1 + 1/r}{\theta^2} \left(z_\alpha \sqrt{\bar{p}(1-\bar{p})} + z_\beta \sqrt{\frac{p_1(1-p_1)/r + p_2(1-p_2)}{1 + 1/r}} \right)^2$$

2. A phase III clinical trial to test an experimental drug for prostate cancer is being designed by a group of university researchers. The response rate of the standard chemotherapy for prostate cancer is 22%, and the researchers expect that the experimental drug would increase the response rate of the standard treatment by 50% .

(a) State the null and alternative hypotheses.

(b) The researchers would like to have a an allocation ratio between the experimental and standard arms of 3:1. If the type I error rate is $\alpha = 0.025$ then how many patients should the researchers recruit into the experimental and standard arms so that their study has 85% power? Write an R function to calculate the sample size. Hand in your R code and output.

(c) Use the R function to plot sample size versus the allocation ratio r using the parameters in the previous question (e..g. 85% power, $\alpha = 0.025$). Does the sample size increase or decrease as the allocation ratio r increases? Hand in your R output.

(d) Briefly describe what 85% power with a type I error rate $\alpha = 0.025$ means.

3. The NHEFS survey was designed to investigate the relationships between clinical, nutritional, and behavioural factors assessed in the first National Health and Nutrition Examination Survey NHANES I and subsequent morbidity, mortality, and hospital utilization, as well as changes in risk factors, functional limitation, and institutionalization. For more information see http://www.cdc.gov/nchs/nhanes/nhefs/nhefs.htm. This question will involve using this data to estimate the average causal effect of smoking cessation on weight gain.

(a) Individuals were classified as treated if they reported, being smokers at baseline in 1971-75, and having quit smoking in the 1982 survey. The latter implies that the individuals included in our study did not die and were not otherwise lost to follow-up between baseline and 1982 (otherwise they would not have been able to respond to the survey). That is, we selected individuals into our study conditional on an event (responding to the 1982 survey) that occurred after the start

of smoking cessation. If smoking cessation affects the probability of selection into the study, we might have selection bias (Hernan, Robins, 2014 Chapter 12, page 11).

Would a randomized experiment of smoking cessation have this problem? How could a randomized experiment of smoking cessation be designed? What is the major difference between the latter randomized experiment and this study (NHEFS survey)?

(b) Should a statistician be concerned that using the NHEFS data to compare weight loss in the group of subjects that quit smoking versus those that did not quit smoking is biased? If yes then state why you think the comparison might be biased, otherwise state why the comparison is unbiased.

(c) Use R to estimate the propensity score for each subject in the study. Use the variables: sex, race, age, education.code, smokeintensity, smokers, exercise, active, wt71 as covariates. After calculating the propensity score use the Match function in R to match subjects on the propensity score. Does the balance between the two groups improve after matching? Hand in your R code and output.

(d) Estimate the effect of smoking cessation on weight loss using propensity score matching? Did the propensity reduce the bias in estimating the treatment effect? What assumption can make to conclude that smoking cessation causes weight loss? Do you think this assumption is valid? Briefly explain. Hand in your R code and output.