Chapter 13 Homework

1. Complete the Human Participant Protections Education for Research Teams course which can be found at: http://cme.cancer.gov/clinicaltrials/learning/humanparticipant-protections.asp. This course presents information about the rights and welfare of human participants in research. The tutorial is designed for those conducting research involving human participants. Complete the exercises at the end of each of the six content areas. Print a certificate of completion upon completing the course.

2. You are a researcher working on a vaccine for malaria, which is caused by a parasitic protist. You are interested in performing clinical trials for your vaccine.

a. During Phase I testing, you must recruit about 100 healthy volunteers. What are you trying to determine through this testing?
b. During Phase II testing, what should your malaria vaccine be tested against?
c. Phase III testing involves a double-blind study. What does this mean and why is it important?

3. You are designing a study to test a new implantable artificial kidney for patients with end-stage renal disease. You divide your patients into two groups: one will receive an implanted artificial kidney, the other will receive tri-weekly hemodialysis (standard of care in end stage renal disease). Your primary endpoint is mortality for all causes at one year, a secondary endpoint is patient quality of life at one year, which will be assessed via questionnaire.

a. What is a type I error? What are the possible consequences of making a type I error in this study? What is a type II error?
b. What are the possible consequences of making a type II error in this study?
c. Define the p-value.
d. Define power (if you use Greek letters in your definition, you must define these as well).
e. Why would blinding be difficult in this study?
f. Which of your endpoints is more likely to be affected by a lack of blinding?
g. Assuming you expect 30% mortality at one year for the control group and 20% for the treatment group, what sample size would be required to achieve 80% power? What p-value should you use? Justify this value.

4. You are designing a clinical trial to compare the performance of a new thrombolytic agent to dissolve blood clots associated with acute myocardial infarction. You design a trial to compare the new agent to the standard of care, streptokinase. You choose the 30 day mortality as your primary endpoint. There will be some statistical uncertainty associated with the measured mortality rate in the treatment and control groups. Your goal in selecting the sample size for the trial is that this uncertainty be significantly less than the difference in the mortality rate between control & treatment group. We must set acceptable levels for the risks of type I and II error.

a. Define type I error and type II error.
b. Suppose you expect a mortality rate in the group treated with the new drug stent of 5%, while the expected restenosis rate in the group treated with the current stent is 7%. You calculate a standardized difference of 0.19. If you can tolerate a 20% risk of type II error and a 5% risk of type I error, how many patients are needed in the trial? Use the following figure to indicate how you calculated your answer.
c. If the mortality rate for the new drug was expected to be 1%, would the required sample size increase or decrease?
d. List one secondary outcome you would want to monitor in this trial.

5. Consider the Acute Respiratory Distress Syndrome Network trial of low versus traditional tidal volume ventilation in patients with acute lung injury and acute respiratory distress syndrome published in 1996. Mortality rates in the low and traditional volume groups were 31% and 40%, respectively, corresponding to a reduction of 9% in the low volume group. What sample size would be required to detect this difference with 90% power using a cutoff for statistical significance of 0.05?