DESIGNING CLINICAL RESEARCH (1 month)
ASSIGNMENT # FOUR
Due: August 15th at DCR Small Group Section
Written Assignment Due Electronically: August 17th, 2017 at NOON

In Assignment Four you will discuss causal inference and determine the sample size/power for your proposed study. Please be prepared to discuss this assignment during the small group sessions and to submit this assignment electronically to your small group leader by NOON on Thursday to receive comments that will useful for you to incorporate into your final protocol.

To Do:

Task 1) Read DCR-4 Chapters 9, 10 and 11 for Monday's class on causal inference. Chapters 5, 6 and 11 will be important for Wednesday's class on sample size calculations (you may want to get a head start on these). Chapter 19 will continue to guide you on developing your research protocol.

Task 2) Compose parts of your protocol (see I starting Monday, II for Wednesday, III for general notes on the final class protocol)

I. Enhancing Causal Inference (Monday's lecture and small group): Complete either A or B (depending on your study design), plus C for discussion in class on Monday, and email to your instructor by Thursday for feedback:

A. If you are working on an observational study, make a list of up to ten variables that may be confounders in your study. Then, in less than one page:
   i. Develop at least two specific plans for coping with these confounders
   ii. Discuss which is best, and comment on the process of drawing causal inference from your study.

B. If you are working on an experiment, in less than a page:
   i. Make a decision about whether or not to include each of the following strategies, specify how it will be done, and justify your decision.
      - randomized?
      - blinded?
      - run-in design?
      - factorial design?
      - stratified blocked randomization?

   If you are planning to do a randomized blinded trial, describe the nitty-gritty of how you will carry out a tamper proof randomization, and how you maximize the success of the efforts at blinding.

C. **An alternative study design:** Propose an alternative to your proposed study design that might more effectively address causality. This is a thought experiment and need not be a design that is feasible for you to pursue at this point. For example, if you are proposing an observational study, could you imagine an experiment that might address the causal relationship between predictor and outcome?

II. Sample Size (Wednesday's lecture and small group): Complete **either** (A) **or** (B). Do not exceed **one page**.

A. If your research question is primarily **analytic**:

1. Specify your research hypothesis or hypotheses.

2. Develop a sample size estimate using one of the examples in chapter 6 as a model. This involves first deciding which statistical test you will use at the end of the study, then setting out the assumptions, and finally using one of the chapter 6 appendices to estimate the sample size. For example, if you can consider one of your variables continuous and the other dichotomous:
   (a) select your statistical test (in this case, the t test)
   (b) Develop null and alternative hypotheses
   (c) specify:
   - effect size (and standardized effect size)
   - alpha (and number of tails)
   - beta

   (c) turn to Appendix 6A and estimate sample size (Presto!)

3. Comment on and justify the following things:
   (a) How you came up with your effect size and standard deviation. One of the best sources is prior publications of related work, so take this opportunity to become even more familiar with the relevant literature.

   (b) Decisions about number of tails, size of alpha, amount of power, multiple hypotheses, etc. Imagine that you are writing this section for a grant application, and that you must convince a skeptical reviewer of the appropriateness of your plan.

4. If you used the chapter tables, verify your calculation using the UCSF CTSI tool developed by our own Michael Kohn accessible via http://www.sample-size.net

5. Extra credit: look inside the black box and try getting the same answer with a hand calculation (or by creating your own Excel spreadsheet!) using one of the formulas in Appendix 6.

B. If your research question is primarily **descriptive**, you won't have a hypothesis but you still need to decide on a sample size.

1. Follow the descriptive models set forth in Examples 6.4 and 6.5 in the book.

2. Comment on and justify your choice of expected SD or proportion, desired precision (width of confidence interval), and confidence level.

3. Verify your calculation using Michael Kohn's handy sample size spreadsheet from http://www.sample-size.net

4. Extra credit: look inside the black box and try getting the same answer with a hand calculation (or by creating your own Excel spreadsheet!) using one of the formulas in Appendix 6.

III. Protocol. Continue to modify and assemble all the pieces of your protocol that you have been working on for these three hefty weeks so far, so that you end up with a reasonably complete draft of your 5-page protocol by next Wednesday 8/23. Here are some other sections that you could add if appropriate and desired, and if comments from your small group leader would be helpful:

- Statistical issues. Amplify on your sample size calculation by thinking through plans for analysis and interpretation
- Timetable, organizational chart
- Budget, equipment, physical facilities, procedures (be brief)

Objectives for small group section:
After this session, students should:

1. **Be able to propose a logical (if not feasible) alternative design for your research question**
2. **Provide a contrasting point of view to the traditional view that studies with < 80% power are not worthwhile**
3. **Be very comfortable with the 1-sentence study plan summary**
4. **Have justified the decisions/assumptions they used to estimate their sample size**
5. **Know how to use a sample size calculator and the tables in the book to estimate sample size, given the decisions and assumptions they justified**

REFERENCE

1. Bacchetti P. Current sample size conventions: flaws, harms, and alternatives. BMC Med 2010;8:17.