

Designing Outcomes and Clinical Research Workshop – TL1
Syllabus Summer 2016

Textbook (All reading assignments are in this textbook, unless otherwise specified):
Designing Clinical Research. 3rd edition. Hulley, Cummings, Browner, Grady, and Newman.

Professor: Jay Piccirillo, MD, FACS, Office: 9912 McMillan Building 362-8641

Class Location (unless otherwise specified):
Clinical Research Training Center (CRTC), 2nd Floor, Wohl Clinic

No computers are to be used in the classroom. Each session, please bring two copies of your completed session assignment- one to hand-in and one for your reference.

Friday Summer Seminar Series

Attendance is required at summer seminar series.

2015 Predoctoral Summer Seminar Series			
Date	Speaker	Topic	Location
June 3	Dr. Jay Piccirillo	Manuscripts	Erlanger
June 10	Dr. Doug Luke	Data Visualization	Erlanger
June 17	Dr. Lilliana Solnica-Krezel	Research Talk	Erlanger
June 24	Dr. Jane Garbutt	How to be a Good Mentee	Erlanger
July 1	Dr. Tom De Fer Interviews Dr. Eric Leuthardt	Faculty Interview	Erlanger
July 8	Dr. Susan Mackinnon	Research Talk	Erlanger
July 15	Dr. Randall Bateman	Research Talk	Erlanger
July 22	Dr. Nico Dosenbach	Research Talk	Erlanger
July 29	TBD	TBD	Erlanger

Session #1 June 7

11:00 – 1:00pm

Topic: Getting Started: The Anatomy and Physiology of Clinical Research Conceiving the Research Question

- I. Before class please read: Introduction and Chapters 1 and 2

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II. You should have already met with your mentor and have a general idea of your research project

III. Compose the first part of your protocol

Research question. Type a one sentence version of your research question. This question will describe the study you plan to do this summer. (Tip: Use the textbook for instructions on how to construct a research question).

Significance. Compose several sentences to describe the significance of the research you will be doing this summer.

Does your study meet the “*FINER*” criteria (Designing Clinical Research page 19)?

IV. Share Your Research Question with your partner. Prior to class, e-mail your Research Question to your partner. In class, you will be asked to present your partner’s Research Question.

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Session #2 June 8

10:00 – 12:00pm

Topics: Choosing the Study Subjects
 Planning the Measurements

I. Reading Assignment: Chapters 3 and 4

II. Describe the Study Population:

- A. A description of the target and accessible populations. Specify and justify the selection criteria.
- B. A description of how the study subjects will be sampled from the accessible population.
- C. A description of how you plan to recruit potential subjects identified by your sampling process.
- D. A description of your strategies for retaining your study subjects.
- E. Propose and comment on strategies for making your sample more representative of the target population.

III. Describe the independent and dependent measurements (variables) (see Designing Clinical Research Appendix 1.1).

IV. Share your work with your partner -- e-mail your sections to your partner. When you receive your partner's sections, read them carefully and with a red pen make comments, questions, and corrections. Bring this to class and be prepared to discuss.

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Session #3 June 14

11:00 – 1:00pm

Topics: Getting Ready to Estimate Sample Size
Estimating Sample Size and Power

- I. Reading Assignment: Chapters 5 & 6
- II. Compose parts of your protocol (items B or C are to be sent to your partner before class to allow time for them to review and comment on in class).
 - A. If you thought about ways to improve the parts of your protocol that you prepared for Session 2, word-process the improvements and save the protocol outline for later sessions (Do not hand it in.) Then go on to the issue of sample size by doing either (B) or (C), below (option B is preferred for most studies and is more instructive, so do this if you can).
 - B. If your research question is primarily analytic (i.e., involves making a comparison between groups):
 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 one of the variables can be considered continuous:
 - i. Select your statistical test (for a continuous variable this would be the *t*-test)
 - ii. Develop null and alternative hypotheses
 - iii. Specify:
 - a) Effect size (and standardized effect size, if continuous outcome variable)
 - b) Alpha (one-tail or two-tails)
 - c) Beta (power)
 - iv. Turn to Appendix 6A and estimate sample size (Presto!)

Alternatively, search the Internet for helpful Sample Size calculating sites. There are literally hundreds of such sites (see 4

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below for starters). If you find a particularly good site, please share the URL with your colleagues and bring to class.

3. Comment on and justify the following things:
 - i. 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.
 - ii. 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. Use the Web to verify your sample size calculation in a jiffy: <http://statpages.org/> (click on “Power, sample size and experimental design”). You will definitely want to bookmark this site, a treasure trove of interactive statistical tools.

C. If your research question is primarily descriptive, you won't have a hypothesis but you still need to decide on a sample size. Follow the descriptive models set forth in Examples 6.4 and 6.5 in the book, justifying any assumptions and judgments. Then follow the instructions in Section B3a (above), to enhance your knowledge of the literature, and follow instructions in Section B4 (above) to see what the Web can do for you.

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Session #4 June 20

10:00 – 12:00pm

Topics: Designing a Cohort Study
Designing Cross-Sectional and Case-Control Studies
Enhancing Causal Inference in Observational Studies

I. Reading Assignment: Chapters 7, 8, and 9

II. Compose parts of your protocol (items A and B are to be sent to your partner before class to allow time for them to review and comment on in class. Be prepared to discuss Items A and B of your partner's protocol in class):

A. This assignment goes back to material in Chapter 4. Word-process a one page (or less) description of the "Variables" section of your research protocol. This should include:

1. Lists of the main variables in your study:
 - Predictor variables
 - Outcome variables
2. Additional information on one important variable (don't pick a questionnaire item; instead, choose a variable like blood pressure or pulmonary function that requires making a clinical measurement):
 - A description of the variable.
 - The rationale for measuring the variable.
 - A detailed description of how the variable will be measured (Use Appendix 4.1 in the book as a model).
3. Propose and discuss strategies to reduce random and systematic error in your measurements.

B. If you have discovered new ways to improve the other parts of your protocol, word-process in the improvements. As you assemble the parts you have created, it should begin to look like the completed protocol that is one of the objectives of the course. Again, save this for later sessions. (Do not hand it in.)

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Session #5 June 27

9:00 – 11:00am

Topics: Designing a Randomized Blinded Trial
Alternative Trial Designs and Implementation Issues
Designing Studies of Medical Tests

- I. Reading Assignment: Chapters 10, 11, and 12
- II. Stop and dream for a while. Then, as an exercise, design *another* study and write up a short description of it. One option is to design a different study that answers your same research question in another way, for example substituting a clinical trial for an observational design, or an ancillary study or secondary data analysis. If you prefer, design a study for an entirely different research question. Try to create a study outline that might be something you would like to do. Be prepared to discuss in class. You do not need to share this with your partner.
- III. Do either #1 or #2 of the following tasks designed to enhance causal inference:
 1. If you are working on an observational study, make a list of the variables that may be confounders in your study.
 - a. Develop at least two specific plans for coping with these confounders
 - b. Discuss which is best, and comment on the process of drawing causal inference from your study.
 2. If you are working on an experiment:
 - a. 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?
 - Placebo-controlled?
 - b. 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 will maximize the success of the efforts at blinding.

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IV. By now the components for your research protocol are approaching a reasonably complete set. You have your outline of the study you propose to do, and you have additional detail on the following parts:

1. Research question(s)
2. Significance
3. Study subjects
4. Variables
5. Hypothesis and sample size estimate
6. Strategy for coping with confounders in your observational study, or for randomization and blinding in your experiment

Take the time to assemble them and see how things look. Make any improvements that come to mind, but remember that for the purposes of this workshop, the whole shebang will need to be only a few pages long. So parsimony is a virtue. Here is an additional section that you can produce, now that you know all about designs:

- Design. This can usually be described in a few short sentences, amplifying on terms such as cross-sectional and randomized blinded trial by giving more information on timing of visits, measurements, treatments, etc. A schematic diagram with a horizontal time sequence is sometimes useful.

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Session #6 – Final Presentations

Summer TL1 Trainees –

Tuesday, July 26th from 8:00 – 12:00pm

Wednesday, July 27th from 8:00 – 12:00pm

Holden Auditorium

Session #7 – Research Symposium and Poster Session

Summer TL1 Trainees –

October 20, 2016 from Noon – 5pm

Farrell Learning and Teaching Center (FLTC)

Details will be distributed via email in August 2016

Intensive Trainees –

October 2017

Farrell Learning and Teaching Center (FLTC)

Details will be distributed via email in August 2017

Standard TL1 Trainees –

October 2017 (and all subsequent sessions held during TL1 appointment)

Farrell Learning and Teaching Center (FLTC)

Details will be distributed via email in August 2017

Other Notes

- Continue the task of modifying and assembling all the pieces of your protocol that you have been working on for these seven hefty weeks, so that you end up with a reasonably complete draft of your protocol (see suggested format on the next page).
- Ask your mentor if you may look through one of their NIH grant applications, to get a sense of what is involved.

5-page Research Protocol Due July 17

PROTOCOL DEVELOPMENT

1. **No more than 5-pages. There is an absolute limit of 5 pages of text, single space and size 12 font(!), plus up to an additional 5 pages of references and appendices.** The reason for these constraints is not so much to reduce the size of your creative task (although your welfare is always a priority with me) as it is to make the task of critiquing each other's protocols a manageable one. The 5-page limit makes for a considerably more concise protocol than an NIH submission, but is not so different from what is expected for a research training position or small intramural grant. The need to be concise will focus your approach to planning your study. If necessary you can summarize the ways you would flesh some parts of the text out in a longer version.
2. **Final protocol is due on Sunday, July 17. I cannot make exceptions to the due date.**

Please e-mail the protocol as a Microsoft Word attachment to Jessica Chafe at jchafe@dom.wustl.edu. After sending the protocol to Jessica, then share the protocol with your mentor.

The next page provides you with a suggested outline indicating a good way to allocate the five pages (to help avoid such things as spending too much space on the Significance and then neglecting key nitty-gritty aspects of the Methods).

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**5 Page Protocol
Suggested Outline**

Title

Abstract

Statement of Research Problem (500 words or less)

Specific aims/Hypothesis(es) to be tested

Significance (limit this to 1/2 page)

Methods (approximately 1000 words)

- Overview of design
 - time frame and nature of control
- Study subjects
 - selection criteria, target and accessible populations
 - plans for sampling and for recruiting subjects
- Measurements
 - predictor variables (intervention, if an experiment and potential confounders)
 - outcome variables
- Pretest plans
- Statistical issues
 - hypotheses and sample size estimates
- Quality control and data management

Ethical considerations

References (not included in the 5-page limit)

Appendices (do not include)