UCSF School of Medicine
Department of Epidemiology and Biostatistics

CLINICAL RESEARCH WORKSHOP

FACULTY NOTES FOR SMALL GROUP SECTIONS

Tuesdays, July 30 to September 10, 2013

Session #4: Study Measurements and Alternative Design

Objectives:
After this session, students should:

1. **Have a clear, detailed understanding of *exactly* how at least one predictor and one outcome variable for their study will be (or was) measured or be aware that they do not have such an understanding and have a plan to acquire it.**
2. **Have experience providing tips to colleagues**
3. **Be able to list and explain the advantages and disadvantages of basic observational study designs, including case-control, cross-sectional and cohort studies**
4. **Be able to propose a logical (if not feasible) alternative design for their research question**

Section (10:10-12:00)
If you are not familiar with **case-crossover studies**, make sure you review Chapter 8, page 108, since that is the focus of one of the recommended exercises. Similarly, the section on **incidence-density case control studies** (pp 104-108) is new for DCR-4, so you might want to review that to be ready to answer any related questions.

- (25 min) Discuss issues from sample size plans that were handed in last time, as well as exercises and other loose ends. Projecting the best sample size plan handed in last time may be helpful. Alternatively, ask students to put any redone sample size plans on the board.

- Although the reading for this week is about observational study designs, including studies of diagnostic tests, Part A of this week's assignment is about reducing measurement error, which is covered in Chapter 4 assigned 2 weeks ago. The second "dream study" part of the assignment is more related to this week's reading.

(Optional) If several students in your section are planning a medical record review (retrospective cohort study or cross-sectional study in which predictors and outcomes are abstracted from clinical records), consider covering the principles of doing a good chart review as outlined by Gilbert et al. posted on the course website as optional reading, with thanks to Michael Kohn. (Gilbert EH, et al. (1996). "Chart reviews in emergency medicine research: Where are the methods?" Ann Emerg Med 27(3): 305-308.) This is a good example of how to standardize measurements and reduce error (especially bias) in one particular type of study.

Training	Train chart abstractors to perform their jobs. Describe the qualifications and training of the chart abstractors. Ideally, train abstractors before the study starts, using a set of "practice" medical records.
Case selection	Use explicit protocols and describe the criteria for case selection or exclusion.
Definition of variables	Define important variables precisely.
Abstraction forms	Use standardized abstraction forms to guide data collection. Ensure uniform handling of data that is conflicting, ambiguous, missing, or unknown.
Meetings	Hold periodic meetings with chart abstractors and study coordinators to resolve disputes and review coding rules.
Monitoring	Monitor the performance of the chart abstractors.
Blinding	Blind chart reviewers to the etiologic relation being studied or the hypotheses being tested. If groups of patients are to be compared, the abstractor should be blinded to the patient's group assignment.
Testing of interrater agreement	A second reviewer should reabstract a sample of charts, blinded to the information obtained by the first correlation reviewer. Report a κ-statistic, intraclass coefficient, or other measure of agreement to assess interrater reliability of the data.

Improving data quality for studies involving chart reviews. From Gilbert et al, (1996).

- (20 min) Divide your section into new sets of pairs and/or trios. In each group, ask that each student spend 10 minutes having the plan for making measurements critiqued.

  -- For studies that involve measurements, tell the students to base their measurement plan critique on whether the strategies in tables 4.2 and 4.4 have been fully exploited (you might also walk through these tables). Ask them also to think whether the list of study measurements is complete and appropriate.

  –- For questionnaire studies, strategies in tables 4.2 and 4.4 do not apply. Instead, have them critique the clarity of the item. This will be covered in greater detail in Chapter 15 (week 6).

- (20 min) Discuss 2-3 of the plans with the whole group using the same format as last time. You can choose which one to discuss by inviting students who haven't had much attention to volunteer, or those with problematic measurement issues.

  (30 min) Discuss the alternative studies that people created for Part C or D of this week's assignment (option of doing this as part of the pairing up device earlier in the session). These are often better or more feasible than the students' original study ideas. Discuss advantages of having both a primary data collection study and a secondary data analysis study (or ancillary study), including that the primary study provides

much needed first-hand experience and credibility as a researcher, while the secondary data analysis can yield a publication with much less effort and is a good thing to return to when the primary study hits a delay.

For the secondary datasets, stress the importance of working with their mentor to think about the possibilities, both at UCSF and worldwide. You could also bring in a list of datasets you are aware of, or describe your personal experience with this efficient approach to clinical investigation.

- (5 minutes) Review and field questions about homework for next time, identify loose ends

- Remind students to email assignments by midnight Wednesday, to be emailed back promptly with comments.

- Alert students that for Session #6 they will need a data collection form from their mentor or another person in their field and for session #7 a sample grant proposal. Advise them to read the HW assignment for those weeks now so they can schedule a meeting.

Faculty lunch

Session #5: Causal Inference and Randomized Trials

Objectives:
After this session, students should:

1. **Be able to define confounding (an increase or decrease in a measure of association due to an extraneous factor that is associated with the predictor, a cause of the outcome and not on the causal pathway) and list 2 design and 2 analysis strategies to control it**
2. **Be able to define interaction or effect modification (when the effect of the predictor on an outcome varies according to the value of a third variable)**
3. **Be able to provide concrete examples from their own or their colleagues' studies of some of the nitty-gritty issues around controlling for confounding, randomization, blinding, and design of studies of diagnostic tests**

Section 10:10-12:00 (Again, feel free to design your own variations)

- As usual, ask the students to sit next to someone new and design your own variations on these instructions

- (10 min) Discuss issues from the measurements plans or the new study outlines that were handed in last time, and any leftover exercises. Consider bringing 10 copies of a plan that merits discussion.

- (20 min) Review the definition of a confounding provided in the text (associated with the putative predictor and causally related to the outcome). You might want to draw a causal diagram for an old favorite like carrying matches as a risk factor for lung cancer, with smoking as the confounder, or use the RQ from one of the students and draw a simple diagram with 1 confounder.

  Another key concept is the distinction between confounding and effect modification. Note that the latter depends on the model (e.g., additive or multiplicative). Review that this week if you haven't already (e.g., in week 2)

  Finally, see if the material on "conditioning on a shared effect" in Chapter 9 made sense to people. That material is new in DCR-4, and I'm wondering how understandable I made it. Question 9.2 should help; make sure you try it.

- (15 min) Divide section into pairs and/or trios; you might want to put the people with diagnostic tests or observational designs together, and those with experiments together--or not.

  --For those with observational studies, does the study plan make sense as a way to answer the research question? Have they correctly identified one or more possible confounders?

  --For those with experiments, have they made good judgments about all the design options? How will they handle the nitty-gritty of randomization and blinding?

  –For those studying diagnostic tests, how will the subjects be sampled, how will index test and gold standard be done, and have they addressed the question of

how the test might improve outcome – i.e., whether it provides new information in addition to what is already available?

--for everyone, discuss the description of the design. Some designs are hard to name; if pairs or trios are having trouble, get the class involved in deciding what name best fits during the next part of the section.

- (50 min) Discuss some examples of observational and experimental study plans in the full group. (Perhaps 1 each: observational, experimental, diagnostic test?) You can continue this next week.)

- (if time permits) Any questions about the readings? Walk through the summaries of Chapters 9-11 and/or the new and improved exercises, highlighting major points from the lecture and leading discussion of questions that come up.

- (5 minutes) Field questions about homework for next time; identify loose ends.

- Remind students to email assignments by midnight Wednesday, to be emailed back promptly with comments.

Faculty lunch

Session # 6: Data Collection and Management

Objectives:
After this session, students should:

1. **Have experienced first-hand the value of having another person try their data collection instrument to identify areas of potential ambiguity**
2. **Understand what is involved in creating a data dictionary**
3. **Have a concrete plan for collecting data, or have clarified the plan that was used for the data they will be analyzing**

Section 10:10-12:00

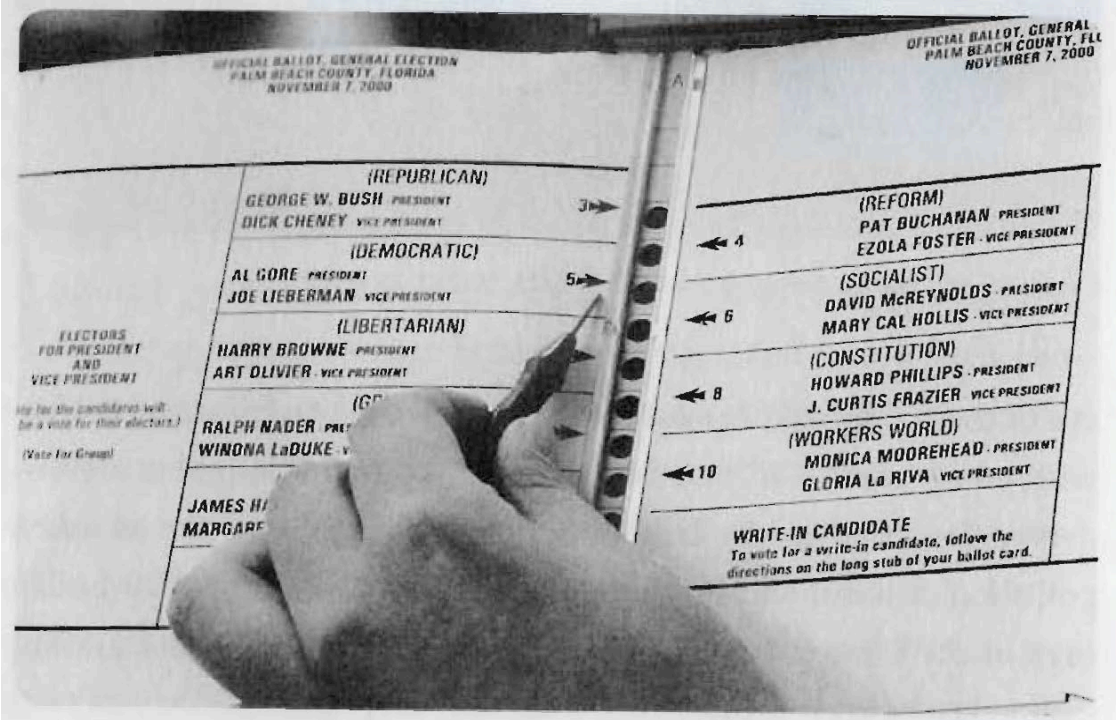
Again, feel free to design your own variations. This is week 6 of 7 and by now we hope you are more confident and that the students are comfortable helping you figure out how to lead the section in a way that maximizes value of the time.

- (10 min) Discuss issues from the homework handed in last time. As usual, consider projecting ones that illustrate good or (gently) bad things.

- (25 -30 min) Pair up (new pairings or trios) and have the students critique each other's original or critiqued data collection forms and data management plans prepared for today. (They can select the parts of the assignment on which they most want feedback from a colleague.) Have them consider the search for a prior instrument, and its validation and adaptation or the development of a new instrument. Are data collection forms visually appealing and clear? Do people have realistic data management plans?

- (60 min) Offer to continue last week's discussion and go over both the big-picture and nitty-gritty for some of the students whose study plans were not discussed last week. Feel free to use your knowledge of who needs extra help from your reading of the homework. This can be in addition to or instead of discussion of their data collection instruments and data management plans.

  Regarding the questionnaire/data form, be sure to pay attention to those students who have looked up and critiqued an instrument from the literature. Commend any who have contacted a distant investigator. You can try filling out one or more data collection forms using imaginary data. Often the student hasn't even tried this, and it may turn up some obvious problems. Do you think anyone in Florida tried out the "butterfly ballot" before asking people to vote with it in the 2000 presidential election (see below)? (You may want to project this for your students.)



Like the sample size assignment, this assignment forces the student to be concrete about what variables she is studying and how she is going to collect the data. Nothing focuses the mind like creating the data collection form (whether it's a paper form or an on-screen form) and identifying who will complete the form and how they will do it.

- (5 min; time permitting) Walk through exercises and/or summaries of the readings.
- (5 minutes) Review and field questions about homework for next time, identify loose ends.
- Remind students to email assignments by midnight Wednesday, to be emailed back promptly with comments. Some may not have a "soft" copy of their data collection instrument, so you can either collect these in class or ask them to scan it and e-mail to you before Wednesday at midnight.

<u>Faculty lunch</u>

Session #7: Pretesting and Implementation

Objectives:
After this session, students should:

1. **Understand all the practical and conceptual issues underlying the trade-offs they made when converting their research question to the study plan they are forming into their 5-page protocols**
2. **Have a plan for pretesting their study, if they are collecting new data**
3. **Have reviewed a research grant and have a better appreciation for what is involved in putting one together**

Section 10:10-12:00

This final section is a chance to clean up any loose ends or gaps in understanding from previous sections, as well as discussing pre-test plans. As always, feel free to use it in a way that is most useful to the students; by now we hope you and they have bonded and they can help you and each other optimize the use of time.

Remind students about the due date for the protocol. Students in the Advanced Training in Clinical Research (ATCR) and Masters in Clinical Research (MCR) programs will review their protocols in the program seminars, but they still need to turn a protocol in by the due date. Students not in the ATCR or MCR programs have the option to schedule a protocol review session; it is not required. Also remind them to fill out a course evaluation form.

- (10 min) Discuss issues from reviewing the questionnaires, data collection forms and data management plans that were handed in last time. As usual, consider handing out illustrative examples.

- (10 min) Ask students what they learned from reviewing their mentor's grant proposals. Discuss differences and similarities between proposals for different funding agencies. Make sure people also know about intramural sources of modest but very handy tangible resources. Students may also have questions about K awards.

- (5 min) Invite issues/questions about research resources at UCSF. Discuss the CTSI Consulting Service.

- (10 min) Some comments on ethics (Chapter 14) are in order. Many will probably be taking the on-line CTSI Responsible Conduct of Research course, but a few may not be and would benefit from some discussion of these things in the project they plan. More generally, it will be good for them to hear you say that ethics is a vitally important consideration in clinical research.

- (Remaining time minus 5-10 minutes) If students like pairing up (by this time you probably know what your students like or feel comfortable asking them), invite them help each other with their pretest plans or lingering questions. During this time you can circulate and get ideas of which protocols/issues it would be most useful to discuss as a large group. If students would rather stay in the big group, ask for

volunteers or pick some students whose protocols have interesting issues for the group to discuss.

- (5+ minutes) Say "good-bye, stay in touch" (with each other as well as with you). Remind them to fill in the course evaluation. Option of inviting them to share ideas about how to improve the course or the textbook.

Final faculty lunch (please come prepared to offer advice (both your own thoughts and those of your students) on next year's DCR Course)