UCSF School of Medicine
Department of Epidemiology and Biostatistics

CLINICAL RESEARCH WORKSHOP
FACULTY NOTES FOR SMALL GROUP SECTIONS 1-3

Updated 5/31/22 by Tom Newman
Accompanies Designing Clinical Research, 5th Edition

The following notes were originally created by Steve Hulley, revised over many years with help from Michael Kohn and other faculty, and further revised (with help from other faculty and from students) beginning in 2009 by Tom Newman, with help from Michael Kohn, and Joel Simon. They were designed with a course in mind that meets 3 hours weekly for 7 weeks (beginning near the end of July), with the first 50 minutes or so a lecture, and then students split into 2-hour faculty-led small group sections, in which students review each other's developing research protocols. An important component of the course is weekly homework, which is read by the small group leader and returned to the students. See the publicly available recent syllabus for the course.

General suggestions for small group leaders:

- **Write an outline of the day's section plan on the board** before the session starts, with an estimate of what time you hope to start each activity. This can help the students keep you and themselves on track. Plus, you get the satisfaction of crossing things off the list as you cover them.

- Pairing up students (1) to get everyone talking, and (2) to increase the amount of individual review (by peers) can be an especially useful learning device. Having to explain research plans to a peer can be very helpful in clarifying ambiguities.

- When a question comes up in class, try to turn it over to the students—get them to answer it (whether or not you know the answer) then get others to comment on the answer before throwing in your own 2 cents.

- Be a vigorous moderator. Don't allow any student (or yourself!) to embark on monologues.

- Learn their names early in the course. They will appreciate your effort to know them, and forgive any lack of success. You may want to snap photos with your cell phone, if it is OK with them.

- All the rooms have white-boards, and this is where you should often be, summarizing things while the students are talking. And sometimes it's good to get the students up at the board. Pack some extra Dry-Erase markers with you in case your room is depleted.

- The rooms should also have a video connection that you can connect to your laptop to project what is on your screen. While we generally discourage using PowerPoint, projecting web pages (e.g., for the sample size session) can be helpful because of the immediate feedback it provides, and projecting examples (e.g., of questionnaires) from the class (rather than bringing in 10 copies) can save paper.

- Assign students (or yourself) to track down issues that come up that are not satisfactorily answered. A glorious fact of life—never discovered by some teachers—is that students <u>like</u> it when you say "I don't know," then resolve things the following week after you or someone else has looked things up. It's helpful to reserve a portion of the board for these loose ends or other things you do not want to forget to come back to later.

Suggestions for specific activities for each session listed below are **OPTIONAL.** We encourage section leaders to be flexible and responsive to their students. These are adult learners who will have opinions about what works and what doesn't. For example, some section leaders find that their students do not like pairing up, so they stop doing it. Similarly, we have students write out answers to some of the chapter exercises for the first 2 assignments, then let students and section leaders decide together whether to continue that practice.

Homework Assignments

Each session is associated with a student assignment (usually a write-up of one page or less). We ask students to bring a laptop to be ready to share the completed assignment for discussion, and give them until **midnight Wednesday** to incorporate comments and insights from section and email it as a MS Word document to their section leader. You can then make comments using "Track Changes" and return it within 24-48 hours. The midnight Wednesday deadline prevents the students from working too long on one assignment and gives you time to get your comments back to them before the weekend, so the course policy is not to accept late assignments. Enforcement of this policy is left up to section leaders, however, so if you choose to be more flexible we will not object.

Optional Topics to Cover as "Chalk Talks"

Some section leaders may opt to take 5-10 minutes during section for a "chalk talk" on topics from the readings such as the following:

1) Study Designs:
    - Experimental
    - Observational
        - Cross-Sectional
        - Case-Control
        - Cohort
    - Studies of Diagnostic Tests (Cross-sectional vs. case-control sampling)

   When discussing a study, the students should present it with a standard sentence like *"The [clever acronym] study is a [design] study of the association between [predictor] and [outcome] in [study population]."* (They'll get extra practice doing that from exercise 2 of Chapter 1.)

2) Variable Types: Numeric (continuous or discrete) vs Categorical (dichotomous, nominal and ordinal). Measurement Precision, Accuracy and Validity.

3) Measures of Disease Association When Predictor and Outcome Are Dichotomous
    - Risk
    - Absolute Risk Difference
    - Relative Risk, Relative Risk Reduction
    - Odds Ratio and when to use it
        - Good reasons for using OR: Case control study, logistic regression
        - Bad reasons: Farther from 1.0 than RR; looks better; ignorance

4) Sample Size "Ingredients"
    - Effect Size
    - Variability (SD for t-test)
    - Alpha, Beta

5) Definition of a confounder, distinction between confounding and effect modification (don't bother with the difference between effect modification and interaction for this group). How to seek evidence of whether confounding or effect modification is present. Conditioning on a shared effect (see new section in Chapter 10); what is a "collider"?

6) Key considerations in a randomized controlled trial:
    - Randomization, so groups are likely to be equivalent at baseline

Blinding
    of patients and clinicians -- to prevent differential co-interventions
    of patients and outcome assessors – to control the placebo effect and prevent differential outcome assessment.
Minimal losses to follow-up
Intention-to-treat analysis vs. per protocol analysis
Problems with subgroup analysis (ISIS-2 Gemini and Libra example)

7) Some basic data management/questionnaire design/data collection form design issues

Session #1: Research Question and Significance Section

Objectives:
After this session, students should:

1. Know the name and something else about the section leader and each of the other participants
2. Be able state their research question in a single sentence including study design, predictor variable, outcome variable and subjects
3. Be able to explain to another person in a couple of minutes why their research question is worth answering
4. Know how to name their homework document, when to email it to their section leader, and when to expect feedback

BEFORE THE SESSION:

Section 10:10-12:00 (NB. These are only suggestions; feel free to do it your way!)

- Arrange chairs in a circle (a configuration conducive to good interactions) and put a note on the board asking students to sit between two people they don't know.

- 10:10 (5 minutes) Put your email address and cell phone number on the board. The students will email you their first assignment and then you will have their email addresses. Go around the circle to quickly identify who is there and start learning people's names. I like to draw a circle on the board and write at least the first names of

the students to create a name map on the board that people can refer to throughout the session. See photo Jody Steinauer took of her 1st section in 2012.

- 10:15 (10-15 minutes) Ask if there were any questions about exercises 1 & 2 from Chapter 1 of DCR-5; discuss if there is interest. Make sure students know the major study designs summarized in Table 1.2 on page 4.

- Ask about any problems in the Significance sections and with citation management software. Suggest that students get further detailed advice from someone in their home departments, if necessary.

- Any questions about chapters 1 or 2? One option is to walk through the summaries at the end of each chapter to emphasize key points and trigger discussion.

- (5 minutes) Start a table on the board with headings "Investigator," "Design," "Predictor," "Outcome", "Study Subjects" at the top. Introduce yourself, something about you unrelated to work, and put your name under "Investigator" summarize one of your research projects in one sentence, filling in the table headings above. For example, I would write and say:

  "The LIGHT study is a retrospective cohort study of the association between phototherapy for neonatal jaundice and childhood cancer in children born 1995-2011 in Kaiser Permanente Northern California hospitals."

- (20 minutes) Pair up students and refer them to the **Introductions Exercise**, which we will distribute to you. If there is an odd number of students, join a pair yourself or put three in a group. If you have students with a language problem, it might take the pressure off if they are in a trio rather than a pair. You may want to collect the Significance sections the students have brought with them and spend your 20 minutes looking through them. (Set your cell phone alarm to remind them to switch after 10 minutes.)

- (60 minutes or 11:58 minus current time) Check the time you are starting and the time remaining until 11:58, and ask for a student with a smartphone with a timer to volunteer as timekeeper. Invite a student to introduce his or her partner with 3 well-designed sentences:

Figure 2

1. Name, academic affiliation, other biographic details
2. The interesting/unusual fact unrelated to work
3. The proposed study, including design, major predictor and outcome variables, and population

As the student is talking, write the study plan on the board, using the partner and the class to help make sure the single sentence contains the design, predictor variable, outcome variables, and population. (Figure 2, again from Jody in 2012) (Some students will have multiple predictor variables, because their RQ involves identifying the best predictors of some outcome. Have them pick one predictor they are interested in; they'll need this for the sample size calculation.)

Then ask the student whose study it is to provide some brief and nontechnical background information on why this research question is important. If time permits, add a few specifics about the study, making notes on the whiteboard.

Then switch partners and go to other teams. Limit the time spent on each student so you get through most or all of them in 60 minutes. It may seem like a very modest goal, but past experience suggests that just getting the students to describe their study in one sentence is a sufficient accomplishment for this session. If you cannot get through all students in your seminar section, let students who got missed know that you will begin with them next week.

- 11:58 Identify loose ends to be reported back. Make sure that the students know to email their assignments to you by midnight Wednesday. You then will provide brief written comments within 48 hours. Students appreciate these comments, and the quick turn-around allows them to incorporate your feedback into their next assignment.

HOMEWORK NAMING. It will be easier to keep your files for this course organized if the students are consistent in how they name their homework. We suggest (in a document on the website) the format LastnameHW1, LastnameHW2, etc., which matches other TICR courses That way when you drag the file from their email to your Epi 202 directory you won't have to worry about naming it and you can look at that directory and see at a glance who has turned in which HW.

N.B. Please end your section on time—12 noon—even if not everything has been accomplished. You can carry over loose ends to the next session, and students admire a disciplined course and appreciate being able to go on to their other lives on time. Of

course it’s OK to linger a few minutes with interested students after class, but don't be too late for the delicious and informative faculty lunch!

Session #2: Study Subjects

Objectives:
After this session, students should:

1. Know the names and something else about the section leader and each of the other participants
2. Be able to summarize their study plan on a 1-page standard outline
3. Be able to explain the difference between Target Population, Accessible Population, and Sample
4. Write out concrete inclusion and exclusion criteria for their study
5. Understand the rationale and tradeoffs for sampling decisions for their own study and at least 2 other studies in the group
6. Understand sample size ingredients and variable types well enough to use an online sample size calculator

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

- Put today's schedule and a note on the board asking students to sit next to someone new (so that the pairs will be novel). Arrange chairs in a circle.

- While you're waiting for students to assemble, start a conversation about issues that emerged from this morning's lecture and/or the How Do We Know What We Know presentation.

- (5 min) Start by taking turns having people name the students around the room. You go first, then ask for volunteers.

- (10 min) Follow up on loose ends and exercises from last time, especially issues about the literature review and significance sections.

  --Any triumphs with PubMed, Zotero or other citation management software? (If there are questions about software technicalities, chances are that there are experts in your class who can help out.)

  --Stress the value of becoming a thorough scholar in the chosen area, and of a well-developed significance section.

  – Ask about the How Do We Know What We Know presentation. Did people appreciate the DCR approach to the problem? Did they think it was excessively anti-industry?

  – This might be a good time for one of those "Chalk Talks" mentioned at the beginning of these notes. The lecture mentions "Effect Modification," but it goes by

fast. You might want to see if any of the students can define it. An important point (covered in detail later in Example 10.2 and Appendix 10B) is that effect modification depends on the scale used to measure associations. If there is no effect modification on the relative (ratio) scale, there will be on the additive scale (which may be clinically more important)!

- (20 min) Divide the section into novel pairs and/or trios, so that each student has a different partner than in week 1. In each pair/trio, ask that each student spend 10 minutes having protocol parts critiqued—the study outline and the plan for acquiring study subjects.

  --Re the study subjects, tell the students to pay special attention to the issues of internal and external validity, and to consider each of the types of inclusion and exclusion criteria, as outlined in Table 3.1, (which you might briefly walk through before they start, to refresh memories).

  --The distinction between inclusion criteria and corresponding inverse exclusion criteria is somewhat arbitrary. Assure students that they do not have to include the inverse of each inclusion criterion as an exclusion criterion. For example, if they are going to include women aged 50 to 60, they don't have to list age < 50 or age > 60 (or male sex!) as exclusion criteria. Inclusion criteria are usually broad demographic, geographic, temporal, and clinical characteristics. Exclusion criteria are usually more specific clinical characteristics.

  --While the students are talking, you can either participate, or you can do some of your own work. Remind them to switch after 10 minutes.

- (40 min) Ask groups to share their studies as described below. If there were students whose research questions didn't get discussed in the large group in week 1, begin with them and use this assignment to let them introduce themselves and discuss their projects.

  --Have the author present <u>concisely;</u> ask the partner to discuss, invite others to join in.

  --NB, the discussion of a particular component of a project (e.g., the plans for acquiring subjects) should always begin with a one-sentence statement of the study plan (the single sentence that contains the design, predictor and outcome variables, and population). You may want to be at the board, making notes during the presentation and discussion.

--One thing to be alert to at this early stage is the fact that many students will need to make radical changes in their research question and will often not see which way to go. Comfort them—par for the course, everything will be OK in the end. It is worth reinforcing that the primary goal of this course is to *learn the material*. Trying to create a protocol turns out to be a good way to do that and is more educational if it is more realistic and difficult. But many students will not end up with a protocol for a study they actually will do, and that's OK.

- (30 minutes) This schedule calls for finishing the pairing up and discussion of study outlines and study subjects after only 75 minutes of section. This is because most students seem to understand issues of generalizability and feasibility. They usually handle definitions of the target and accessible populations and the sample fairly well. They have been assigned Chapter 4 on planning measurements, precision, and accuracy, but today's assignment does not deal specifically with these issues. They will return to measurements in two weeks. However, they have a sample size calculation due next week, so spend some time now covering material that will help them with their sample size calculation.

    - For the sample size calculation, they will have to identify their predictor and outcome variables and decide whether they will treat them as dichotomous or continuous, so briefly discuss variable types (categorical, ordinal, continuous, etc.) using Table 4.1.
    - For their first sample size calculation, they need to focus on one predictor and one outcome, and at least one of the two should be dichotomous. This may require making an inherently continuous variable dichotomous.
    - Hook your laptop up to the projector and use one of the online sample size calculators at the CTSI sample size website http://www.sample-size.net/ to demonstrate a sample size calculation. Try to pick a student with a dichotomous predictor and dichotomous outcome and another student with a continuous outcome. (Note you can find the sample size calculators from the DCR-5.net website.) You might also want to check out the PS program at https://vbiostatps.app.vumc.org/ps/ It not only estimates your sample size, it produces sample text for a grant application!
    - Not all the students in your section will be able to understand your example(s), but you can start to soften the territory now.

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

- Remind students to email you the study outlines and plans for selecting subjects by midnight Wednesday, to be emailed back as promptly as possible with your brief comments.

Session #3: Sample Size

Objectives:
After this session, students should:

1. **Provide a contrasting point of view to the traditional view that studies with < 80% power are not worthwhile**
2. **Be very comfortable with the 1-sentence study plan summary**
3. **Have justified the decisions/assumptions they used to estimate their sample size**
4. **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**

Section (10:10-12:00)

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

- (10 min) Discuss issues from study outlines and study subject plans that were handed in last time, and any left-over exercises

- (15 min) Discuss this week's lecture, the reading by Peter Bacchetti, and sample size calculations generally. Emphasize that much of the value of setting up the sample size calculation is that if forces investigators to think much more concretely about what they will actually measure in order to answer the research question. Make sure that even those that did not read Peter's article understand the key message – that while many reviewers may expect this, pretending that you are only interested in a large effect size in order to get your power up to 80% does not make a lot of sense scientifically.

- (70 min) We usually don't pair up the students for this session—too difficult. Instead, invite 3 or 4 students to put their work on the board, listing out the predictor and outcome variables, the null and alternative hypotheses, effect size, standard deviation (if necessary), alpha, and beta and their sample size estimate as specified in the assignment. Discuss these one at a time. Consider projecting from your laptop to reproduce the student's sample size calculation.

You can find online sample size calculators by Michael Kohn at http://www.sample-size.net/sample-size-calculators/

- When these first 3-4 calculations have been discussed one at a time, you can have others do the same. Usually about half the students do a fine job on this, and the

other half will have something a bit muddled, or will have a study plan that does not lend itself easily to the simplified models in Chapter 6. Sometimes you can straighten things out right in front of them at the blackboard, but it's OK if you need to go back and think about what advice to give on how to do a more appropriate sample size estimate. You can get counsel from one of the statistical experts at our faculty lunch, then look smart next week. If appropriate, ask them to bring in an improved version next time.

N.B. Many students will have a fixed sample size. In that case it makes sense to estimate the effect size they will be able to detect with reasonable power. The new sample-size.net programs make this easier. Is this effect size reasonable? A common problem, especially when they've done it right, will be the discovery that the study would require more subjects than is feasible. Explore the options in the last few pages of Chapter 6 for increasing power by adjusting the specifications, variables, duration or RQ. If it's back to the drawing board, provide comfort and solace.

- (10 min) Discuss any other issues that have developed, such as in their efforts to use citation management software. Chances are that there are some experts in your class who can help out if you don't know the answers.

- (time permitting) Walk through summaries of Chapters 5 & 6, highlighting main points from lecture and leading discussion of questions that come up.

- (5 min) Field questions about homework for next time, identify students who will bring back new sample size calculations next time.

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

- **Remind students to set up a meeting with their mentor.** Mentors outside the course with subject matter expertise are important for success of the students.