Syllabus

EPID 733- Clinical Trials (Spring 2017)

Class Sessions: Tuesday/Thursday, 9:30-10:45 am. McGavran-Greenberg 1305

Course Instructors:
John A. Baron, MD, MS, MSc (jabaron@med.unc.edu)
Invited faculty

Introduction to the Course

Randomized controlled trials are the strongest research design for identifying the effects of an intervention, whether in a public health or clinical context, and whether aimed at prevention, treatment, or palliation. Therefore, a sound grounding in clinical trial methods helps one understand the evidence base for clinical and public health practice. It can also provide a perspective in which to judge the validity of less robust studies of interventions, such as non-randomized trials and observational studies.

In this course we will examine clinical trials from several perspectives. The core sessions will be about the design, conduct, and analysis of trials and combining trial results (meta-analysis);. We will also discuss the ethics of human experiments and the role of human subjects committees. We will describe how basic methods are adapted to special questions, such as studies intended to establish non-inferiority, trials that randomize groups rather than individuals, very small trials (where randomization is less reliable) and large simple trials (which may be more feasible and generalizable).

This course is intended for health professionals who want advanced training in clinical trial methods to help them conduct clinical trials themselves and to understand their strength and meaning. We assume a basic grounding in research design and statistical methods. (Introductory epidemiology and biostatistics courses are prerequisites.)

Course Objectives:

By the end of the course, students should be able to:

1. Decide whether a proposed trial is ethical and understand how sponsoring institutions participate in the protection of human subjects.

2. Describe the various ways in which clinical trials can be designed and the advantages and disadvantages of each approach

3. Estimate sample size, taking into account the various real-world determinants such as the magnitude of a clinical/policy important effect size, available
resources and patients, and whether randomization is by patient or groups of patients.

4. Describe basic approaches to analysis of clinical trial data, including time-to-event and repeated measures analyses and stopping rules.

5. Know how oversight of clinical trials is accomplished including the roles and responsibilities of Data Safety and Monitoring Boards.

6. Describe guidelines for reporting clinical trials and how trials are published and made accessible to all stakeholders.

7. Be familiar with the basic principles of systematic reviews and meta-analyses of clinical trials.

8. Understand the role of special forms of clinical trials such as non-inferiority trials, small trials, large simple trials, and practical trials.

9. Develop a research protocol for a clinical trial.

Teaching Methods:

Most classroom learning will be in interactive large-group sessions. We will present information and lead discussions with the class as a whole. Often we will use a specific clinical trial to illustrate the concepts being discussed in class that day. You should become familiar with required reading before class to be adequately prepared to participate. Optional reading is listed for those with special interest in a topic. For several sessions, reading of clinical trial reports will be required.

There will be ample opportunity for other kinds of learning, including student presentations and participation of invited faculty.

Draft Monograph:

A work-in-progress monograph is available on Sakai. It covers essential elements of most, but not all, the topics covered in the course. If you detect errors or have suggestions, please contact Dr. Baron.

Textbook:

We recommend Machin D. Fayers PM, Randomized Clinical Trials Design, Practice and Reporting. Wiley-Blackwell, 2010. This is available at the student bookstore. We will not make chapter assignments. Rather, we recommend students to read most of the book, matching chapters to classroom session on their own.
Other useful resources:

Friedman LM, Furberg CD, DeMets DL. Fundamentals of Clinical Trials. 5th ed. Springer, New York 2015. A few copies are available at the bookstore. This is a widely used textbook covering all of the basic issues concerning clinical trials. (The 4th edition would also be acceptable. This may be available at lower cost at Amazon.com.)


Expectations of Students:

1. **Class participation.** You are expected to attend class and to participate in class discussions. Participation does not mean talking a lot but rather being present, thoughtful and well prepared, and making helpful points or raising questions that move the discussion in useful and interesting ways.

2. **Required Readings.** You are expected to have read the required readings before class. Part of class discussion will be based on these readings.

3. **Recommended reading.** We encourage you to read some of the articles on the Recommended Readings, especially in areas of special interest to you or those that you did not adequately understand in class.

4. **Final project.** All students will prepare a research protocol that will be presented to the class, and submitted in writing (see below). This project is expected to synthesize what you have learned in the course and apply it to a research question that especially interests you, perhaps one you may actually study later. Students will be expected to critique each other’s presentations. One student will be assigned to be a lead critic for each protocol and submit a brief written outline of a critique.

Final Report: Protocol

The final report for this course will be an abbreviated research protocol for a randomized controlled trial. The intervention can be anything related to health.

We want you to select a topic and submit it in writing to Dr. Baron (by email) with a brief rationale by **Monday, February 27**. This early date will allow you to have time to refine or change your question if we think it is not particularly promising for the purposes of this course. We encourage you to discuss your plans for the project with us beforehand.

The protocol itself will be in abbreviated form, relative to a full proposal such as one might submit to the National Institutes of Health. The maximum length is 5 pages of
double-spaced text, including references, formatted in no less than 12 point font and 1 inch margins. Most protocols should consider the issues summarized during the Feb 23 session regarding trial protocols. Protocols should be specific to the topic rather than generic statements of clinical trial principles in general, and should reflect the reasons for the choices in design and analyses. We understand that shorter protocols are more difficult than long ones, because you cannot include everything and must decide which issues are more and less important. The protocol should be submitted by email to Dr. Baron as an MS Word document by April 27th. Please title your word document as follows: Your Last name, Abbreviated Project Title (Example: Baron Aspirin for Prevention of Colorectal Cancer)

The last several class sessions are reserved for student presentations. We ask that each of you summarize your protocol, pointing out special challenges and opportunities and how you dealt with them. We estimate that there will be 25 minutes per student (12 for presentation, 5 minutes for formal critique (see below) and 8 minutes for class discussion). The oral presentation should be prepared with Powerpoint images (and paper hand-outs if needed). This should be sent to the assigned discussant (see below) 2 days before the scheduled presentation.

Protocol Critique

Each student will be assigned to critique the strengths and weaknesses of the protocol prepared by one other student. The protocol presenter will provide the discussant with a pdf file of the protocol presentation 2 days before his/her class discussion. The critique should then be prepared in written bullet form, systematically considering the protocol’s weaknesses in no more than 2 pages of double spaced text. This will also be presented to the class with Powerpoint slides in no more than 5 minutes. The written critique should be submitted to Dr. Baron before the protocol presentation.

Grading:

1. Attendance and Classroom Participation. Thirty five percent of the final grade will be based on classroom participation, particularly in exercises that will be discussed in class. As stated above, this is not about sheer volume of comments but how thoughtful, penetrating, and stimulating they are. However, it is fair to say that one cannot display any of these qualities without participating at all. Do not be reticent to comment or question; other students may well share your interest in the issue.

2. Protocol Exercise. Fifty percent of the final grade will be based on the presentation of the protocol and the subsequent written submission. We will grade the protocols on completeness, sound reasons for the approaches taken, appropriateness of design to the research question, understanding of the concepts of randomized trials and the verbal response to the critique.
3. Critique of Final Protocol. Fifteen percent of the final grade will be based on the written critique of another student’s protocol and the presentation of the critique.

4. There is no final examination.