Syllabus for Biostatistics 558
Clinical Trials and Experimental Design

Instructors:
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Course Goals:
This course is designed for individuals interested in the scientific, policy, and management aspects of clinical trials. Topics include types of clinical research, study design, treatment allocation, randomization and stratification, quality control, sample size requirements, patient consent, and interpretation of results. This course will additionally briefly cover strengths and limitations of alternative study designs such as quasi-experiments and observational studies. Common sources of bias in these alternative study designs will be described along with design approaches to minimize bias. Also key to this course is the application of this knowledge. Several sessions in this course will focus on core issues in clinical research including protocol versus proposal development, local resources available to support clinical trials, issues regarding data management and safety monitoring, and budgeting for clinical trials.

Organization:
The schedule below is a rough goal for the timing of topics in this course. It is very much subject to adjustment according to the needs of the class.

Textbooks:

Piantadosi: *Clinical Trials: A Methodologic Perspective*, 2nd Edition, 2005. John Wiley & Sons.

Cook & Campbell: *Quasi-Experimentation -- Design & Analysis Issues for Field Settings*. 1979. Houghton Mifflin Company.

Other References:

Friedman, Furberg & DeMets: *Fundamentals of Clinical Trials*, 3rd Edition, 1996. Mosby-Year Book, Inc.

Pocock: *Clinical Trials, A Practical Approach*. 1983. John Wiley & Sons.

Meinert: *Clinical Trials: Design, Conduct and Analysis*. 1986. Oxford University Press.

Hulley & Cummings: *Designing Clinical Research: An Epidemiologic Approach*, 2nd Edition. 2001. Williams & Wilkins.

Rosenbaum, Paul: *Observational Studies*, 2nd Edition, 2002. Springer.

Redmond & Colton (Editors): *Biostatistics in Clinical Trials*. 2001. John Wiley & Sons.

Crowley (Editor): *Handbook of Statistics in Clinical Oncology*. 2001. Marcel Dekker, Inc.

Finkelstein & Schoenfeld (Editors): *AIDS Clinical Trials*. 1995. Wiley-Liss, Inc.

Chow (Editor): *Encyclopedia of Biopharmaceutical Statistics*. 2000. Marcel Dekker, Inc.

Grading:
Your grade will be based on 2 homework assignments (50%), a midterm (25%) and a final exam (25%).

The following is a list of homework assignments along with their due date. These homework assignments will be graded (10 points max) and categorized as exceptional (10 points), satisfactory (8 points), and unsatisfactory (6 points).

- HW#1: Grant Specific Aims, Hypotheses and Significance (Due January)
- HW#2: IRB Proposal (Due May)

Additionally all students are required to complete the following PEERRS Modules by November 10th (http://www.research.umich.edu/training/peerrs.html#modules)

- Foundation of Responsible Research
- Conduct of Research Administration
- Conflict of Interest
- Human Research

Projected Course Timeline

Date	Time	Instructor	Topic
October 15, Sat 8:30am-10:20am 10:30am-12:20pm	4 hours	Spino	Introduction Definition/Phases of Clinical Trials Ethics Standard Clinical Trials Designs: parallel group, cross-over; control arms, single arms, active control, placebo; observational trials: prospective, retrospective; case-control, matching, cohort Hypotheses / Aims: superiority, non-inferiority, equivalence primary, secondary Subject Populations
November 10, Thu 1:30pm-3:20pm November 11, Fri 1:30pm-3:20pm	4 hours	Spino	Endpoints / Measurements Treatments / Interventions Randomization, Stratification, Blinding Sample Size ***PEERRS Modules Due***
December 10, Sat 8:30am-10:20am 10:30am-12:20pm 1:30pm-3:20pm	6 hours	Ellingrod	Generating Research Ideas and Writing Specific Aims: Discuss how academicians identify research ideas Describe challenges of converting and idea into an excellent grant Outlines strategies for writing specific aims Developing the significance and Impact statements for your proposal Protocol Design Issues: Describe scientific as well as practical to consider issues when developing an adequate and well controlled clinical trial Discuss specific trial types commonly used in the drug development process Understand the concepts of internal and external validity and how protocol design may impact the validity of the study
January 12-15	4 hours	Ellingrod / Spino	Drug Development Process Drug Approval Process Homework #1 DUE
February 9-12	4 hours	Spino	Interim Analyses, Sequential Monitoring Data Safety Reporting MedWatch, DSMB, interim analyses In-class MIDTERM EXAM (2 hours)

Date	Time	Instructor	Topic
March 15-18	4 hours	Ellingrod	Data Management and GCPs: Outline the essential elements of GCPs Development strategies to enhance data management CRFs, verification, blinded data review, clinical monitoring, investigator responsibilities Additional Topics as Needed
April 12-15	4 hours	Spino	Reporting Trial Results peer-reviewed publications; pharma / regulatory: NDAs, SBLs, etc.
May 10-13	6 hours	Spino	Observational Study vs. RCT – Strength of Evidence Homework #2 DUE – IRB Proposal
June 7-10	4 hours	Spino	More Details on Select Topics in CTs
July 19-22	4 hours	Ellingrod/Spino	Local Resources for Clinical Trial Support In-class FINAL EXAM (2 hours)