Reference Textbooks

Fundamentals of Clinical Trials
By Friedman, L.M., Furberg, C.D. and DeMets, D.L.

Clinical Trials: A Practical Approach
By Pocock, S.J.

These texts are useful in describing principles of clinical trials from an applied perspective. The intended audience is clinicians and others interested in learning what clinical trials are. These are not intended as books to develop statistical methodology and consequently are not necessary for this course. The course will be based primarily on lecture notes that will be available on the course website. http://www.stat.ncsu.edu/people/tsiatis/courses/st520/

Co-requisites:
ST501 or ST701 or equivalent.
Recording Notice: Please be advised this course is being recorded for current and potential future educational purposes. By your continued participation in this recorded course, you are providing your permission to be recorded. Providing your consent to be recorded does not entitle you to access to the recorded lectures.

Policy on Academic Integrity: The University policy on academic integrity is spelled out in the NCSU Code of Student Conduct. For a more details see the NCSU Office of Student Conduct website http://www.ncsu.edu/student conduct/. For this course, you may work together on homework assignments. However, copying another students work or programs will not be tolerated; you must turn in your own solutions and programs. The midterm and final will be closed book.

Disability Reg: Reasonable accommodations will be made for students with verifiable disabilities. In order to take advantage of available accommodations, students must register with Disability Services for Students at 1900 Student Health Center, Campus Box 7509, 515-7653. For more information on NC State’s policy on working with students with disabilities, please see the Academic Accommodations for Students with Disabilities Regulation (REG02.20.01)

Grades:

- 25% Homework (approximately every two weeks)
- 30% Closed book midterm (75-90 minutes during a class time TBA)
- 40% Closed book final
- 5% Instructor discretion

Conversion of these scores into letter grades will be made according to the following: A, 93-100; A-, 90-93; B+, 85-90; B, 80-85; B-, 75-80, C, 65-75. Scores below 65 will be handled on a case-by-case basis. Except for 100, the upper score in each range belongs to the next higher grade. The grade of A+ will be given at the discretion of the instructor for truly stellar individual performance. Depending on overall class performance, these ranges may be adjusted (but only downward—criteria will become easier, not harder).
Course Outline

• Introduction to Epidemiology and Clinical Trials, brief history of clinical trials

• The different phases of clinical trials research

• Phase I dosing trials, Clinical pharmacology

• Phase II clinical trials (screening and feasibility)
  – review of confidence intervals
  – Gehan’s two-stage design
  – Simon’s two-stage sequential design
  – Discussion of surrogate markers

• Phase III clinical trials– fundamentals
  – What is the question? primary, secondary
  – study population
    * whom to target
    * likelihood of seeing event
    * identifying compliant population
    * generalizability
    * control group
  – Randomization
    * Role of randomization to control bias
    * competing designs (historical and literature controls)
    * types; simple, blocked, permuted block
    * stratification; pros and cons, how many strata?
    * dynamic balancing
    * response adaptive designs
- Blinding
  * reasons, single blind, double blind
  * use of placebo controlled trials
- Implementation
  * Administrative Issues
  * Institutional review boards (IRB’s)
  * Ethical Issues
  * Protocol Documents/Forms
  * Quality Control-data management

**Statistical Methods**

- Endpoints
  - Continuous
    * t-test for two-sample comparison
    * ANOVA- F-tests for K-sample comparisons
    * Linear regression to adjust for covariates
  - Categorical
    * proportions test for two-sample comparisons
    * Chi-square test for K-sample comparisons
    * arc-sin square root transformation to stabilize variance
  - Time to event
    * staggered entry and censoring
    * Life-table methods and Kaplan-Meier estimator
    * Logrank tests for two and K-sample comparisons
  - For all endpoints
    * power and sample size considerations
    * multiple comparisons
- Equivalency and Non-superiority trials
- Intention to treat analysis
  * compliance
  * drop-outs
  * missing data
  * causal inference
- Monitoring Clinical Trials
  * group-sequential designs
  * Data safety monitoring boards