COURSE DESCRIPTION
The sequence of courses, Design and Conduct of Clinical Trials I and II, is designed to introduce the complex issues surrounding the analysis and interpretation of clinical trials. In Design and Conduct of Clinical Trials II, students will learn how to select the appropriate analytic method depending on the type of endpoint needed to address a study objective. Various approaches to performing interim safety monitoring will be discussed, including multi-stage sequential designs and the use of monitoring boundaries. More modern trial issues and designs such as late effects, analysis of longitudinal data, meta-analysis, and adaptive designs will also be explored. Translational research plays an increasing role in clinical trials, and the identification and rationale for the use of prognostic factors will be covered. Homework assignments will be extremely applied, and will make use of real clinical trials designs and data.

COURSE OBJECTIVES
By the end of this course, the student should be able to:

1. Identify the appropriate data analytic technique to match the study endpoint.
2. Describe safety monitoring issues in clinical trials and related data analysis methods.
3. Describe the basics of longitudinal data analysis and meta-analysis.
4. Understand newer trial designs such as adaptive and translational.

METHODS OF INSTRUCTION
Attendance and active participation in all class discussions is required, and will be evaluated as part of the student’s grade for the course. Students must read the required readings prior to each class session. This course is a graduate seminar where students are expected to take an active role in initiating and leading discussions and debates.
TESTS
No midterm or final exam will be required in this course but there will be 3 quizzes.

ASSIGNMENTS
There are four requirements:

1. **Class assignments.** Based on material covered during Weeks 2-3, 6, 10, and 11-12 and due via e-mail, E-Learning, or next class session. (4x10%=40%).

2. **Class participation.** All students must participate in each class discussion. (10%)

3. **Quizzes.** There will be a quiz at the beginning of Weeks 2, 6, and 10. (3x5%=15%)

4. **Written report and presentation at the end of the course.** (35%)

EVALUATION AND GRADING
Grades will be based on class assignments (40%); attendance and class participation (10%); quizzes (15%); written report (15%) and presentation (20%). All deadlines must be met. Any assignment turned in after the deadline will be penalized, including non-acceptance of the assignment, at the discretion of the instructors.

The following grading system will be used: A (92.5% or higher), A- (89.5%-92.49%), B+ (86.5%-89.49%), B (82.5%-86.49%), B- (79.5%-82.49%), C+ (76.5%-79.49%), C (72.5%-76.49%), C- (69.5%-72.49%), D (65.5%-69.49%), and F (<59.49%).

CLASS ATTENDANCE
Class attendance is mandatory. Excused absences follow the criteria of the UF Graduate Catalogue (e.g., illness, serious family emergency, military obligations, religious holidays), and should be communicated to the instructor prior to the missed class day when possible. Missing three or more unexcused scheduled sessions will result in a failure. Regardless of attendance, students are responsible for all material presented in class and meeting the scheduled due dates for class assignments. Finally, students should read the assigned readings prior to the class meetings, and be prepared to be called upon to discuss the material for each session.

E-LEARNING SUPPORT SERVICES
Course information, readings, and grades are available on the Sakai system at [http://lss.at.ufl.edu/](http://lss.at.ufl.edu/). Click on the “e-Learning in Sakai” button and enter your GatorLink username and password into the boxes.

STUDENTS WITH DISABILITIES
Students requiring accommodations must first register with the Dean of Students' Office. The Dean of Students' Office will provide documentation to the student who must then provide this documentation to the faculty member when requesting accommodation. The College is committed to providing reasonable accommodations to assist students in their coursework.

ACADEMIC INTEGRITY
Each student is bound by the academic honesty guidelines of the University and the student conduct code printed in the Student Guide and on the University website. The Honor Code states: “We, the members of the University of Florida community, pledge to hold ourselves and our peers to the highest
standards of honesty and integrity." While topical discussion is encouraged, all writing and presentation assignments are to be solely the work of the individual student. Cheating or plagiarism in any form is unacceptable and inexcusable behavior.

**POLICY ON STYLE FOR CITATION AND PLAGIARISM**

The two key purposes of citation are to (1) give appropriate credit to the authors of information, research findings, and/or ideas (and avoid plagiarism) and (2) facilitate access by your readers to the sources you use in your research.

**Quotations:** When directly quoting an outside source, the borrowed text, regardless of the amount, must be surrounded by quotation marks or block quoted. Quoted text over two lines in length should be single-spaced and indented beyond the normal margins. Every quote must include a source—the author, title, volume, page numbers, etc.—whether an internal reference, footnote, or endnote is used in conjunction with a bibliography page.

**Paraphrasing or Citing an Idea:** When summarizing an outside source in your own words or citing another person’s ideas, quotation marks are not necessary, but the source must be included. This includes, but is not confined to, personal communications from other students, faculty members, experts in the field, summarized ideas from published or unpublished resource, and primary methods derived from published or unpublished sources. Use the general concept of “when in doubt – cite.”

Plagiarism is a serious violation of the academic honesty policy of the College. If a student plagiarizes others’ material or ideas, he or she may receive an “E” in the course. The faculty member may also recommend further sanctions to the Dean, per College disciplinary action policy. Generally speaking, the three keys of acceptable citation practice are: 1) thoroughness, 2) accuracy, and 3) consistency. In other words, be sure to fully cite all sources used (thoroughness), be accurate in the citation information provided, and be consistent in the citation style you adopt. All references should include the following elements: 1) last names along with first and middle initials; 2) full title of reference; 3) name of journal or book; 4) publication city, publisher, volume, and date; and 5) page numbers referenced. When citing information from the Internet, include the WWW address at the end, with the “access date” (i.e., when you obtained the information), just as you would list the document number and date for all public documents. When citing ideas or words from an individual that are not published, you can write “personal communication” along with the person’s name and date of communication.

**Required Text:**

**Optional Texts:**


TENTATIVE SCHEDULE OF TOPICS

Week 1 (1/7): Review

Week 2 (1/14): Analytic Methods for Specified Endpoints, Assumptions and Diagnostics. Quiz #1
   a. P-values and confidence intervals
   b. Matching the method to the endpoint, diagnostics
      i. Binary (Ex: logistic regression)
      ii. Categorical (Ex: Fisher’s exact test)
      iii. Ordinal (Ex: Kruskal-Wallis test)

Week 3 (1/21): Analytic Methods for Specified Endpoints, Assumptions and Diagnostics (Cont’d)
   a. Matching the method to the endpoint, diagnostics
      i. Continuous (Ex: ANOVA)
      ii. Linear models (Ex. ANCOVA)
      iii. Time to event (Ex: Kaplan-Meier curves, logrank test, Cox PH model)

Week 4 (1/28): Longitudinal Data Analysis

Week 5 (2/4): Issues in Data Analysis
   a. Missing data
   b. Intent-to-treat analysis
      i. Evaluability and exclusions
   c. Subgroup analyses

Week 6 (2/11): Prognostic Factors. Quiz #2
   a. Identification
      i. Multivariable models
      ii. Parsimonious model selection
      iii. Interactions
   b. Application for risk/treatment group assignment
   c. Adjusted analyses of comparative trials
   d. Power and sample size in PFAs

Week 7 (2/18): Safety Monitoring
   a. Toxicity
   b. Data Safety Monitoring Committee
      i. Advocacy for study participants
      ii. Accrual
      iii. Toxicity
      iv. Efficacy
      v. Release of outcome data
      vi. Limitations to the role of the committee
   c. Statistical methods
      i. Early stopping rules
      ii. Multi-stage sequential designs
      iii. Conditional power
      iv. Monitoring boundaries
Week 8 (2/25): Design and Analysis Methods for Translational Research

Week 9 (3/4): Spring Break, No Class

Week 10 (3/11): Equivalence Studies and Alternative Trial Designs. Quiz #3
   a. Equivalence and non-inferiority trials
   b. Alternatives to RCTs
      i. Single-arm trials
      ii. Historical controls
      iii. Other trial design choices

Week 11 (3/18): Adaptive, Enrichment, and Seamless Designs
   a. Adaptive designs for exploratory development
   b. Seamless phase II/phase III clinical trials
   c. Adaptive designs for phase III clinical trials
      i. Group sequential methods
      ii. Sample size re-estimation/internal pilots
      iii. Combination methods (IPIA)
   d. Barriers to using adaptive designs in clinical trials

Week 12 (3/25): Adaptive, Enrichment, and Seamless Designs (Cont'd)

Week 13 (4/1): Health-Related Quality of Life
   a. Design considerations
   b. Types of assessments
   c. Selecting a QOL instrument
   d. Data collection and analysis

Week 14 (4/8): Reporting of Results
   a. Timing of report
   b. Analyses
   c. Interpretation of results
   d. Secondary analyses

Week 15 (4/15): Meta-Analysis

Week 16 (4/22): Presentations