

**University of Florida
College of Medicine
Department of Biostatistics**

GMS 6827 - Advanced Clinical Trial Methods

Time: Tuesday, Period 7 (1:55 - 2:45)
Thursday, Period 7-8 (1:55 - 2:45; 3:00 - 3:50)
Spring, 2013
Location: UST 104
Credits: 3
Instructor: Samuel S. Wu, Ph.D.
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Office Hours: TBA

Course description:

This course covers the statistical principles and methods used in the design and analysis of clinical trials. Topics include group sequential designs, adaptive clinical trials, and Statistical Monitoring of Clinical Trials.

Objectives:

Upon completion of the course, students will be able to:

- 1) Understand classical estimation and testing procedures for group sequential designs.
- 2) Perform statistical design and analyses of adaptive clinical trials.
- 3) Understand the complexity in monitoring a trial for recruitment process, quality of data, adherence to patient care or prevention standards, and early evidence of benefit or harm.

Course materials:

The course will be based primarily on journal papers. However for general background, the following books are recommended:

1. Jennison C and Turnbull BW. *Group Sequential Methods with Applications to Clinical Trials*. Boca Raton: Chapman and Hall/CRC Press, 2000. (JT00)
2. Chang M. *Adaptive Design Theory and Implementation using SAS and R*. New York: Chapman & Hall/CRC, 2008. (C08)
3. Proschan MA, Gordan Lan KK, Wittes JT. *Statistical Monitoring of Clinical Trials: A Unified Approach*. New York: Springer, 2006. (PGW06)
4. DeMets DL, Furburg CD, and Friedman L. *Data Monitoring in Clinical Trials: A Case Studies Approach*. New York: Springer, 2005. (DFF05)
5. Ellenberg SS, Fleming TR, and DeMets DL. *Data Monitoring Committees in Clinical Trials: A Practical Perspective*. West Sussex, England: John Wiley & Sons, 2003. (EFD03)

Prerequisites:

STA 6326 & 6327; PHC 6020

Completion of all masters degree classes in Statistics or Biostatistics. Students missing some of these prerequisites should consult the instructor.

Grading:

Student evaluation in this course will be based upon homework assignments and the course project. **All students are required to perform all work independently.** This implies that the student neither received assistance from nor provided assistance to ANYONE on these assignments. The students may be asked to give their pledge in writing that this was indeed the case. Violation of this pledge will result in an Honor Code violation and will be reported as such.

Homework Assignments: One question per week (2 points each); Two answers per week (2 points each).

Course project: Each student will be asked to conduct, summarize, and present a course project. The project will require the student to choose one of the topics introduced in the course and explore the topic in more detail. This can be done in several ways. For example, although by no means an exhaustive list, a student may present a more advanced feature of the topic than was covered in the course or the student may summarize several current papers dealing with the topic. The student will present the project to the class at the end of the semester. At the time of the presentation, the student should also turn in a written summary (no more than 10 pages) of the project.

The allocation of weights for this set of deliverables is given as follows:

Homework (Best 10 out of 12 Assignments @ 20% each)	60%
Course Project (Written)	20%
Course Project (Presentation)	20%

The final grade will be assigned according to the following scale: A (93 or higher), A- (90-92), B+ (87-89), B (83-86), B- (80-82), C+ (77-79), C (73-76), C- (70-72), D (60-69), and F (<59).

Class Attendance

Class attendance is mandatory. Excused absences follow the criteria of the UFL 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. More than three unexcused absences will result in a failure. Regardless of attendance, students are responsible for meeting the scheduled due dates for class assignments.

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." Cheating or plagiarism in any form is unacceptable and inexcusable behavior.

Tentative schedule:

Week	Date	Topics Covered
1		LEAPS (Body-Weight-Supported Treadmill Rehabilitation after Stroke; Locomotor Experience Applied Post-Stroke Trial)
2		Statistical Considerations in the LEAPS Trial
3		CAR (Covariate Adaptive Randomization, based on my talk and Rho talk)
4		DLD (Two Stage Drop-the-Loser Design)
5		DED (Improvements in Design of FIFA World Cup by Double Elimination Schemes) - Rating Teams and Scheduling Games
6		ACT (Adaptive Clinical Trial review paper by Schafer et al)
7		Adaptive Model-Based Designs in Clinical Drug Development (Draglin papers)
8		Ethnicity (UW lectures/course; Statistical Science papers)
9		Analysis of missing data
10		Parameter Estimation Following An Adaptive Treatment Selection Trial (Luo paper)
11		Some Statistical Issues in Adaptive Clinical Trials (BATTLE Trial example)
12		AED (Adaptive Enrichment Design, Mehta, Wang and Sam papers)
13		A Case Study with emphasis on interaction with FDA
14-15		Student presentations of recent papers dealing with current topics of interest in clinical trials.

Other Topics of Interest:

Week	Date	Topics Covered
		Classical sequential hypothesis tests (JT00, Ch 2)
		Estimation and repeated confidence intervals (JT00, Ch9; PGW08, Ch 7)
		Adaptive treatment assignment (JT00, Ch 17; C08, Ch 14; the ECMO study)
		Introduction to adaptive designs (C08, Ch 3)
		Testing procedures in adaptive designs (C08, Ch 4, 5, 7)
		Sample-size re-estimation (C08, Ch 9)
		Multiple-endpoint multiple-arm adaptive design (C08, Ch 10, 11)
		Data monitoring in clinical trials (DFF05; EFD03)