

University of Florida
College of Public Health and Health Professions and College of Medicine
GMS 6827: Advanced Clinical Trial Methods

Classroom: Communicore CG-056 (Monday)
Communicore CG-057 (Wednesday)

Fall 2022 (Aug 24 – Dec 07)

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Class Schedule: Monday 12:50 – 2:45 pm @ COMM CG-056
Wednesday 12:50 – 1:40 pm @ COMM CG-057

Instructor Office Hour: 9:30-10:30 am, Wednesday, or by appointment

Course Webpage: We will use the e-learning CANVAS system of the address <http://elearning.ufl.edu/>. Once you logged into the system, click on “Courses” in the menu on the left side. Then, you should be able to find the course GMS 6827. I will post lecture slides, homework assignments, handouts and other materials on the course web site.

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.
2. Chang M. *Adaptive Design Theory and Implementation using SAS and R*. New York: Chapman & Hall/CRC, 2014.
3. Proschan MA, Gordan Lan KK, Wittes JT. *Statistical Monitoring of Clinical Trials: A Unified Approach*. New York: Springer, 2006.
4. DeMets DL, Furburg CD, and Friedman L. *Data Monitoring in Clinical Trials: A Case Studies Approach*. New York: Springer, 2005.
5. Ellenberg SS, Fleming TR, and DeMets DL. *Data Monitoring Committees in Clinical Trials: A Practical Perspective*. West Sussex, England: John Wiley & Sons, 2003.
6. Yin G. *Clinical trial design: Bayesian and frequentist adaptive methods*. John Wiley & Sons; 2012.

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.

Prerequisites:

STA 6326 & 6327; PHC 6020

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

Tentative Course Schedule

Week	Date	Topics Covered
1-2	08/24,08/29	Introduction and LEAPS (Body-Weight–Supported Treadmill Rehabilitation after Stroke; Locomotor Experience Applied Post-Stroke Trial)
2	08/31	Statistical Considerations in the LEAPS Trial
3	09/05	Holiday, no class
3	09/07	Statistical Considerations in the LEAPS Trial
4	09/12	Adaptive designs from Adaptive Designs Working Group - Part 1, Adaptive one-arm two-stage designs for cancer trials
4	09/14	Conference, no class
5	09/19,09/21	Adaptive designs from Adaptive Designs Working Group - Part 2
6	09/26,09/28	Inference for Pick-the-Winner Designs, and Adaptive Two-Stage Designs
7	10/03,10/05	Aducanumab trial to treat Alzheimer's disease, statistical challenges.
8	10/10,10/12	Sequential Parallel Comparison Design (SPCD)
9	10/17,10/19	Covariate Adaptive Randomization and Response Adaptive Randomization
10	10/24,10/26	Adaptive Enrichment Designs
11	10/31,11/02	Adaptive Dose Finding Designs
12	11/07,11/09	Bayesian Adaptive Designs
13	11/14,11/16	Analysis of Missing Data in Clinical Trials
14	11/21	Some Statistical Challenges in Adaptive Clinical Trials
15-16	11/28,11/30 12/05,12/07	Student presentations of recent papers dealing with current topics of interest in clinical trials.

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 (50 points).

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 2 pages) of the project.

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

Homework (Best 5 out of 6 Assignments @ 20% each)	50%
Course Project (Written)	20%
Course Project (Presentation)	20%
Participation (Presentation)	10%

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).

Depending on the overall class performance, these ranges may be adjusted.

ATTENDANCE POLICY

Students are strongly recommended to attend the classes. It is understandable if you would like to skip one or two classes to attend the conferences or meetings of your interest. But be sure to let me know in advance. If you have difficulty in catching up with the missed materials, feel free to contact me during my office hours. Online students should watch all posted videos and ask questions online or by emails. Feel free to make appointments with the instructor to have an online Q&A session.

MAKE-UP POLICY

Make-up Policy: No late assignments or tests will be allowed, except for urgent need.

STUDENTS WITH DISABILITIES

Students requesting a disability accommodation must first register with the Dean of Students

Office, which will provide documentation to the student. The student should then provide this documentation to the instructor.

ACADEMIC INTEGRITY

Do not share any homework or exam solutions from previous years. Students are expected to act in accordance with the University of Florida policy on academic integrity (see Graduate Student Handbook for details). Cheating or plagiarism in any form is unacceptable and inexcusable behavior.

We, the members of the University of Florida community, pledge to hold ourselves and our peers to the highest standards of honesty and integrity.

Online Faculty Course Evaluation Process

Students are expected to provide professional and respectful feedback on the quality of instruction in this course by completing course evaluations online via GatorEvals. Guidance on how to give feedback in a professional and respectful manner is available at <https://gatorevals.aa.ufl.edu/students/>. Students will be notified when the evaluation period opens, and can complete evaluations through the email they receive from GatorEvals, in their Canvas course menu under GatorEvals, or via <https://ufl.bluera.com/ufl/>. Summaries of course evaluation results are available to students at <https://gatorevals.aa.ufl.edu/public-results/>.

Classroom policy

As students pursuing a path in the health professions or public health, it is crucial to demonstrate professional behaviors that reflect integrity and commitment to the health of patients, fellow health professionals, and to populations we serve. To accomplish this, a strong responsibility for the well-being of others must be evident in our decisions, along with accountability for our actions. Professionalism in the health disciplines requires adherence to high standards of conduct that begin long before graduation. This is particularly true during times of health emergencies such as the COVID pandemic, given our professional habits can have a direct impact upon the health of persons entrusted to us.

If you are not vaccinated, get vaccinated. Vaccines are readily available at no cost and have been demonstrated to be safe and effective against the COVID-19 virus. Visit this link for details on where to get your shot, including options that do not require an appointment: <https://coronavirus.uflhealth.org/vaccinations/vaccine-availability/>. Students who receive the first dose of the vaccine somewhere off-campus and/or outside of Gainesville can still receive their second dose on campus.

In response to COVID-19, the following professional practices are in place to maintain your learning environment, to enhance the safety of our in-classroom interactions, and to protect the health and safety of ourselves, our patients, our neighbors, and our loved ones.

- Masks are welcomed in all Health Science Center classrooms.
- If you are sick, stay home and self-quarantine. Please visit the UF Health Screen, Test & Protect website about next steps, retake the questionnaire and schedule your test for no sooner than 24 hours after your symptoms began. Please call your primary care provider if you are ill and need

immediate care or the UF Student Health Care Center at 352-392-1161 (or email covid@shcc.ufl.edu) to be evaluated for testing and to receive further instructions about returning to campus. UF Health Screen, Test & Protect offers guidance when you are sick, have been exposed to someone who has tested positive or have tested positive yourself. Visit the UF Health Screen, Test & Protect website for more information.

- Continue to follow healthy habits, including best practices like frequent hand washing.
- Avoid crowded places (including gatherings/parties with more than 10 people)

Sanitizing supplies are available in the classroom if you wish to wipe down your desks prior to sitting down and at the end of the class. Hand sanitizing stations will be located in every classroom.

Course materials will be provided to you with an excused absence, and you will be given a reasonable amount of time to make up work. If you are withheld from campus by the Department of Health through Screen, Test & Protect you are not permitted to use any on campus facilities. Students attempting to attend campus activities when withheld from campus will be referred to the Dean of Students Office.

Continue to regularly visit coronavirus.UFHealth.org and coronavirus.ufl.edu for up-to-date information about COVID-19 and vaccination.

COVID-19 SYMPTOMS

See <https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html> for information about COVID-19 symptoms, which may include fever, cough, shortness of breath or difficulty breathing, fatigue, chills, muscle or body aches, headache, sore throat, congestion or runny nose, nausea or vomiting, diarrhea, and loss of taste or smell.

Policy Related to Guests Attending Class:

Only registered students are permitted to attend class. However, we recognize that students who are caretakers may face occasional unexpected challenges creating attendance barriers. Therefore, by exception, a department chair or his or her designee (e.g., instructors) may grant a student permission to bring a guest(s) for a total of two class sessions per semester. This is two sessions total across all courses. No further extensions will be granted. Please note that guests are **not** permitted to attend either cadaver or wet labs. Students are responsible for course material regardless of attendance. For additional information, please review the Classroom Guests of Students policy in its entirety. Link to full policy: <http://facstaff.php.ufl.edu/services/resourceguide/getstarted.htm>

SUPPORT SERVICES

Accommodations for Students with Disabilities

If you require classroom accommodation because of a disability, it is strongly recommended you register with the Dean of Students Office <http://www.dso.ufl.edu> within the first week of class or

as soon as you believe you might be eligible for accommodations. The Dean of Students Office will provide documentation of accommodations to you, which you must then give to me as the instructor of the course to receive accommodations. Please do this as soon as possible after you receive the letter. Students with disabilities should follow this procedure as early as possible in the semester. The College is committed to providing reasonable accommodations to assist students in their coursework.

Counseling and Student Health

Students sometimes experience stress from academic expectations and/or personal and interpersonal issues that may interfere with their academic performance. If you find yourself facing issues that have the potential to or are already negatively affecting your coursework, you are encouraged to talk with an instructor and/or seek help through University resources available to you.

- The Counseling and Wellness Center 352-392-1575 offers a variety of support services such as psychological assessment and intervention and assistance for math and test anxiety. Visit their web site for more information: <http://www.counseling.ufl.edu>. On line and in person assistance is available.
- You Matter We Care website: <http://www.umatter.ufl.edu/>. If you are feeling overwhelmed or stressed, you can reach out for help through the You Matter We Care website, which is staffed by Dean of Students and Counseling Center personnel.
- The Student Health Care Center at Shands is a satellite clinic of the main Student Health Care Center located on Fletcher Drive on campus. Student Health at Shands offers a variety of clinical services. The clinic is located on the second floor of the Dental Tower in the Health Science Center. For more information, contact the clinic at 392-0627 or check out the web site at: <https://shcc.ufl.edu/>
- Crisis intervention is always available 24/7 from:
Alachua County Crisis Center:
(352) 264-6789
<http://www.alachuacounty.us/DEPTS/CSS/CRISISCENTER/Pages/CrisisCenter.aspx>

Do not wait until you reach a crisis to come in and talk with us. We have helped many students through stressful situations impacting their academic performance. You are not alone so do not be afraid to ask for assistance.

Inclusive Learning Environment

Public health and health professions are based on the belief in human dignity and on respect for the individual. As we share our personal beliefs inside or outside of the classroom, it is always with the understanding that we value and respect diversity of background, experience, and opinion, where every individual feels valued. We believe in, and promote, openness and tolerance of differences in ethnicity and culture, and we respect differing personal, spiritual, religious and political values. We further believe that celebrating such diversity enriches the

quality of the educational experiences we provide our students and enhances our own personal and professional relationships. We embrace The University of Florida's Non-Discrimination Policy, which reads, "The University shall actively promote equal opportunity policies and practices conforming to laws against discrimination. The University is committed to non-discrimination with respect to race, creed, color, religion, age, disability, sex, sexual orientation, gender identity and expression, marital status, national origin, political opinions or affiliations, genetic information and veteran status as protected under the Vietnam Era Veterans' Readjustment Assistance Act." If you have questions or concerns about your rights and responsibilities for inclusive learning environment, please see your instructor or refer to the Office of Multicultural & Diversity Affairs website: www.multicultural.ufl.edu