

University of Florida
College of Public Health and Health Professions and College of Medicine
PHC 6020: Clinical Trials Methods
Spring 2022

Instructor: Zhigang Li, PhD
Associate Professor, Department of Biostatistics
College of Public Health and Health Professions & College of Medicine
University of Florida, P.O. Box 117450
Gainesville, FL 32611
Tel: 352-294-5915 (office); 352-294-1930 (fax);
Email: zhigang.li@ufl.edu
Office: Room 5234, Clinical and Translational Research Building (CTRB)

TA: TBD

Class Schedule: Tuesdays 12:50 – 2:45pm @ HPNP G105
Thursdays 1:55 – 2:45pm @ HPNP G105
NO CLASS ON Spring Break

Instructor Office Hour: 3:00-4:00pm, Thursdays (except the third Thu of each month), or by appointment

TA Office Hour: TBD

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 PHC 6020. I will post lecture slides, homework assignments, handouts and other materials on the course web site.

COURSE DESCRIPTION AND GOALS

This course will introduce some basic statistical concepts and methods used in clinical trials and will focus on the statistical principles and methods used in clinical trials, including designs and analysis methods in phase I to III clinical trials. Although the class will have emphasis on phase III trials, we will also discuss the feature and statistical issues in phase I and II clinical trials. For phase III trials, we will discuss ways of treatment allocation that will ensure valid inference on treatment comparison. Other topics include sample size calculation, survival analysis and early stopping of a clinical trial and noncompliance.

Tentative Course Schedule

| Week | Topic(s) |
|------|--|
| 1 | Overall introduction of clinical trials and epidemiology |
| 2 | Introduction to Phase I trial designs |
| 3 | Introduction to Phase II trial designs |

| Week | Topic(s) |
|------|--|
| 4 | Introduction to Phase III trial designs |
| 5 | Randomization in clinical trials: Fixed allocation randomization |
| 6 | Adaptive randomization and protocol |
| 7 | Two-arm designs |
| 8 | Non-inferiority designs and multi-arm designs |
| 9 | Group sequential designs |
| 10 | Spring break |
| 11 | Group sequential designs |
| 12 | Group sequential designs, and Survival analysis |
| 13 | Survival analysis in clinical trials |
| 14 | Survival analysis in clinical trials, causality, non-compliance |
| 15 | Survival analysis in clinical trials, causality, non-compliance |
| 16 | Final project |

COURSE MATERIALS

Reference Textbook: The course will be based primarily on lecture notes that will be handed out periodically in class and available on the course website. Students have the access to the edited videos of lectures, besides the lecture notes. The recommended books that you may wish to read are:

Steven Piantadosi (2017) *Clinical Trials: A Methodologic Perspective*, Wiley-Interscience, 3rd edition

Friedman, L.M., Furberg, C.D. DeMets, D.L., Reboussin, D.M., and Granger, C.B. (2015) *Fundamentals of Clinical Trials*, Springer, 5th edition

PREREQUISITES

Officially, the prerequisites of this course include STA 6207/STA 6208 or equivalent (i.e., regression analysis and design of experiments I) and some basic knowledge on probability and statistical inference at the level of STA 6326/STA 6327. You can consult with the instructor to see whether the course is appropriate for you in the case you did not take these courses in advance.

COURSE REQUIREMENTS

Homework: We will have 4-5 homework assignments during the semester. Some homework may contain both analytical problems and data analysis problems. Students are encouraged to discuss with each other on homework problems, but everyone should fully understand the solutions, write up the solutions independently, and turn in your own homework. To implement the data analyses, we recommend using R/SAS; examples of the use of these software packages are included in the lecture notes and will be discussed in class.

You should turn in your homework through canvas. You can scan handwritten solutions and then submit it. You should submit a single file. Solutions should be in the same order as the questions, all work should be shown. The solutions are due within one week of the homework assignment

and no late homework will be accepted unless prearranged with the instructor. **There will be no exceptions to this policy.**

Midterm and Final Exams: We will have one midterm exam and one final exam during this semester. The midterm exam will be **in-class** and closed book exam and will only cover the first five chapters. The take-home final exam will be comprehensive, but its majority part will involve materials from chapter 6 to the last chapter. The midterm exam is tentatively scheduled on February 21 (Tuesday) 12:50 – 2:45pm. For online students, please schedule the midterm exam through ProctorU. The take-home final exam will be distributed after the last class on April 25 (Tuesday) and due in three days (tentatively April 25-28).

Final project: There will be a final project which involve be a short presentation in the last class April 25 (Tuesday) 12:50 – 2:45pm. In the presentation, you are expected to summarize what you learned from this course and give an example for one of the topics you have learned. The example does not have to be a real study example. For instance, it could be a simulation study where you demonstrate how a method works. You can also do a project with real data if you have access to some real data sets. You are encouraged to do the project in small groups. For online students, please submit a short video of your presentation.

GRADING

All homeworks, exams and the final project will be graded on a scale of 0-100. A numerical final score on this scale will be determined according to the following breakdown:

| | |
|---------------|-----|
| Homeworks | 50% |
| Midterm Exam | 15% |
| Final project | 5% |
| Final Exam | 30% |

The numerical final score will be converted to the letter grades according to the following scale:

| | | |
|-------------|--------------|--------------|
| 93-100 = A | 90-92.9 = A- | 85-89.9 = B+ |
| 80-84.9 = B | 75-79.5 = B- | 70-74.9 = C+ |
| 65-69.5 = C | | |

Scores below 65 will be handled on a case-by-case basis.

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 or TA 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.

ACADEMIC INTEGRITY

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/>.

On Campus Face-to-Face

We will have face-to-face instructional sessions to accomplish the student learning objectives of this course. In response to COVID-19, the following policies and requirements are in place to maintain your learning environment and to enhance the safety of our in-classroom interactions.

- You are required to wear approved face coverings at all times during class and within buildings. Following and enforcing these policies and requirements are all of our responsibility.
- 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.
- Follow your instructor's guidance on how to enter and exit the classroom. Practice physical distancing to the extent possible when entering and exiting the classroom.
- If you are experiencing COVID-19 symptoms (<https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>), please use the UF Health screening system (<https://coronavirus.ufhealth.org/screen-test-protect/covid-19-exposure-and-symptoms-who-do-i-call-if/>) and follow the instructions on whether you are able to attend class.
 - 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 (<https://catalog.ufl.edu/UGRD/academic-regulations/attendance-policies/>).

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.phhp.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