

University of Florida
Colleges of Medicine and Public Health & Health Professions
Department of Biostatistics
PHC 6022: Design & Conduct of Clinical Trials (3 credit hours)
Fall 2019
On-Campus
Course Website: <http://elearning.ufl.edu/>

Instructor Names: **Arlene Naranjo**, Ph.D. and **Qinglin Pei**, Ph.D.
6011 NW 1st Place, Gainesville, FL 32607

Room Number: Communicore C1-4

Time: Mondays, 1:55–3:50pm (Periods 7-8)
Wednesdays, 1:55–2:45pm (Period 7)

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Office Hours: By appointment

Prerequisites

STA 2023 (Introduction to Statistics I) or equivalent, and permission of the instructors. Students are expected to have basic statistical knowledge.

PURPOSE AND OUTCOME

Course Overview

Students will learn about ethics, principles and conduct of clinical trials for medical research. The protection of study participants and the need for equipoise will be covered, including regulatory restrictions and the latest patient privacy regulations for the dissemination and use of data associated with the participants in clinical trials. Various study designs will be discussed, including single-arm, crossover, factorial, sequential multi-stage, and dose-finding designs, plus the means to allocate study participants to appropriate treatment groups using randomization (blocked or stratified) and prognostic factors. Writing the study protocol, data collection, analyses methods and reporting of results of a trial will be discussed. The importance of equipoise, informed consent, and the use of intent-to-treat analysis will be emphasized. Data collection and management for the conduct of clinical trials will be addressed. The course will also include discussions on the application of the appropriate analytic methods for each specific type of study endpoint, approaches to performing interim safety monitoring, and adaptive trial designs. Translational research plays an increasing role in clinical trials, and the identification and rationale for the use of prognostic factors will be covered. Other topics to be touched upon include health-related quality of life measures, longitudinal data analysis, and meta-analysis. The roles of the Institutional Review Board (IRB), Data Safety Monitoring Committee (DSMC) and federal regulatory agencies in the approval and review of ongoing

clinical trials will be discussed. Homework assignments will be extremely applied and will make use of real clinical trials designs and data.

Course Objectives and/or Goals

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

- (1) Explain key concepts in the design of clinical trials.
- (2) Describe the study designs commonly used.
- (3) Identify key issues in data management for clinical trials.
- (4) Describe the roles of Regulatory Affairs in clinical trials.
- (5) Identify the appropriate data analytic technique to match the study endpoint.
- (6) Describe safety monitoring issues in clinical trials and related data analysis methods.
- (7) Describe the basics of longitudinal data analysis and meta-analysis.
- (8) Understand alternative trial designs.

Instructional Methods

Class sessions will be a combination of presentation of major topics and class discussion of the presentations and additional readings. 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 assigned readings prior to each class session. Students are expected to take an active role in initiating and leading discussions and debates.

DESCRIPTION OF COURSE CONTENT

Topical Outline/Course Schedule

Week	Topic(s)
1	<ul style="list-style-type: none"> ▪ Introduction, Motivation, and Ethics of Clinical Trials
2	<ul style="list-style-type: none"> ▪ Introduction, Motivation, and Ethics of Clinical Trials ▪ Privacy ▪ Phases, Contexts, Examples
3	<ul style="list-style-type: none"> ▪ Phases, Contexts, Examples
4	<ul style="list-style-type: none"> ▪ Study Population & Cohort ▪ IRB
5	<ul style="list-style-type: none"> ▪ Study Protocol ▪ Research Question and Outcomes
6	<ul style="list-style-type: none"> ▪ Study/Trial Design
7	<ul style="list-style-type: none"> ▪ Study/Trial Design ▪ Treatment Allocation
8	<ul style="list-style-type: none"> ▪ Measurement and Data Capture ▪ Hypothesis Testing

Week	Topic(s)
9	<ul style="list-style-type: none"> ▪ Hypothesis Testing ▪ Analytic Methods for Specified Endpoints, Assumptions & Diagnostics
10	<ul style="list-style-type: none"> ▪ Analytic Methods for Specified Endpoints, Assumptions & Diagnostics ▪ Random Error & Bias
11	<ul style="list-style-type: none"> ▪ Introduction to Power and Sample Size ▪ Design and Analysis Methods for Translational Research
12	<ul style="list-style-type: none"> ▪ Alternate Trial Designs ▪ Issues in Data Analysis
13	<ul style="list-style-type: none"> ▪ Health-Related Quality of Life
14	<ul style="list-style-type: none"> ▪ Safety Monitoring ▪ Regulatory Affairs
15	<ul style="list-style-type: none"> ▪ Longitudinal Data Analysis
16	<ul style="list-style-type: none"> ▪ Adaptive, Enrichment, and Seamless Designs ▪ Reporting of Results
	<ul style="list-style-type: none"> ▪ Student Presentations (M 12/9, 10am-12pm, Communicore C1-4)

Course Materials and Technology

Required Text:

Friedman, Furberg, and DeMets. *Fundamentals of Clinical Trials (4th Edition)*. Springer, 2010. Free text available online at <http://dx.doi.org/10.1007/978-1-4419-1586-3>.

Optional Texts:

- Machin and Fayers. *Randomized Clinical Trials: Design, Practice and Reporting*. Wiley-Blackwell, 2010.
- Piantadosi S. *Clinical Trials: A Methodologic Perspective (2nd Edition)*. New Jersey: John Wiley & Sons, 2005.
- Meinert CL. *Clinical Trials: Design, Conduct, and Analysis*. Oxford University Press, 1986.
- Pocock SJ. *Clinical Trials: A Practical Approach*. John Wiley & Sons, 1996.

Additional course materials are available via E-Learning at <http://elearning.ufl.edu/>.

For technical support for this class, please contact the UF Help Desk at:

- Learning-support@ufl.edu
- (352) 392-HELP - select option 2
- <https://iss.at.ufl.edu/help.shtml>

ACADEMIC REQUIREMENTS AND GRADING

Assignments

There are four requirements:

1. Homework. Based on material covered during Weeks 5, 6-7, 8-9, 9-10, and 10-11 and due via e-mail, E-Learning, or next class session. Assignments must be each student's individual work; plagiarism is prohibited. (5x8%=40%).
2. Quizzes. There will be a quiz covering material from Weeks 2-4, 7, 11-13, and 14-16. (4x5%=20%).
3. Class participation. Class attendance (5%) and reading the required class assignments prior to each class session and active participation in all class discussions (5%) is required. Attendance will be taken every class. Missing three or more unexcused scheduled sessions will result in receiving 0 points for class participation. All students must participate in each class discussion by providing responses to teacher's requests on sharing thoughts or solutions. (2x5%=10%)
4. Written report and presentation at the end of the course. (30%)

Grading

Grades will be based on homework assignments (40%); quizzes (20%); attendance and class participation (10%); written report (15%) and presentation (15%).

The following grading system will be used:

Points Earned	92.5%-100%	89.5%-92.49%	86.5%-89.49%	82.5%-86.49%	79.5%-82.49%	76.5%-79.49%	72.5%-76.49%	69.5%-72.49%	59.5%-69.49%	Below 59.49%
Letter Grade	A	A-	B+	B	B-	C+	C	C-	D	E

Letter grade to grade point conversions fixed by UF:

Letter Grade	A	A-	B+	B	B-	C+	C	C-	D+	D	D-	E	WF	I	NG	S-U
Grade Points	4.0	3.67	3.33	3.0	2.67	2.33	2.0	1.67	1.33	1.0	0.67	0.0	0.0	0.0	0.0	0.0

For greater detail on the meaning of letter grades and university policies related to them, see the Registrar's Grade Policy regulations at:

<http://catalog.ufl.edu/ugrad/current/regulations/info/grades.aspx>.

Exam Policy

No midterm or final exam will be required in this course but there will be 4 quizzes.

Policy Related to Make up Exams or Other Work

Any assignment turned in within 24 hours after the deadline will be penalized 10%. Assignments that are more than 24 hours late will not be accepted and will not receive any credit. Any requests for make-up quizzes or extensions for late or missed work must be accompanied by a documented excuse. Excused absences must be consistent with university policies in the Graduate Catalog (<http://gradcatalog.ufl.edu/content.php?catoid=10&navoid=2020#attendance>) and require appropriate documentation. Additional information can be found here:

<https://catalog.ufl.edu/ugrad/current/regulations/info/attendance.aspx>.

Please note: Any requests for make-ups due to technical issues MUST be accompanied by the ticket number received from E-Learning when the problem was reported to them. The ticket number will document the time and date of the problem. You MUST e-mail the instructors within 24 hours of the technical difficulty if you wish to request a make-up.

Policy Related to Required Class Attendance

Class attendance is mandatory. Excused absences will follow UF policy (e.g., illness, serious family emergency, military obligations, religious holidays; see below), and should be communicated to the instructors prior to the missed class day when possible. Missing three or more unexcused scheduled sessions will result in receiving 0 points for class participation. 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.

For information regarding the UF Attendance Policy see the Registrar website for additional details:

<https://catalog.ufl.edu/ugrad/current/regulations/info/attendance.aspx>.

STUDENT EXPECTATIONS, ROLES, AND OPPORTUNITIES FOR INPUT

Expectations Regarding Course Behavior

Students are expected to show up for class prepared and on time. Cell phones are to be silenced during class unless there is an emergency, in which case please inform the instructor.

Communication Guidelines

Students are expected to participate in class discussions. Assignments must be clearly written in reasonably good English.

Academic Integrity

Students are expected to act in accordance with the University of Florida policy on academic integrity. As a student at the University of Florida, you have committed yourself to uphold the Honor Code, which includes the following pledge:

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

You are expected to exhibit behavior consistent with this commitment to the UF academic community, and on all work submitted for credit at the University of Florida, the following pledge is either required or implied:

“On my honor, I have neither given nor received unauthorized aid in doing this assignment.”

It is your individual responsibility to know and comply with all university policies and procedures regarding academic integrity and the Student Honor Code. Violations of the Honor Code at the University of Florida will not be tolerated. Violations will be reported to the Dean of Students Office for consideration of disciplinary action. For additional information regarding Academic Integrity, please see Student Conduct and Honor Code or the Graduate Student Website for additional details:

<https://www.dso.ufl.edu/sccr/process/student-conduct-honor-code/>

<http://gradschool.ufl.edu/students/introduction.html>

Please remember cheating, lying, misrepresentation, or plagiarism in any form is unacceptable and inexcusable behavior.

Online Faculty Course Evaluation Process

Students are expected to provide feedback on the quality of instruction in this course by completing online evaluations at <https://evaluations.ufl.edu>. Evaluations are typically open during the last two or three weeks of the semester, but students will be given specific times when they are open. Summary results of these assessments are available to students at <https://evaluations.ufl.edu/results/>.

SUPPORT SERVICES

Accommodations for Students with Disabilities

If you require classroom accommodation because of a disability, you must register with the Dean of Students Office <http://www.dso.ufl.edu>. The Dean of Students Office will provide documentation of accommodations to you, which you then give to the instructors of the course to receive accommodations. Please make sure you provide this letter by the end of the second week of the course. 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>. Online 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.
